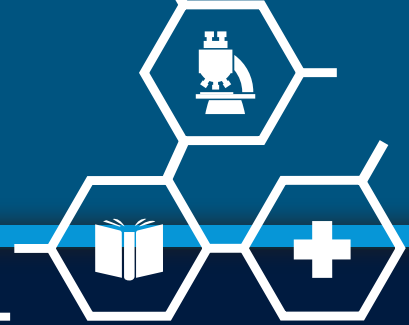




# GW RESEARCH DAYS

APRIL 2&3, 2013

THE GEORGE  
WASHINGTON  
UNIVERSITY  
WASHINGTON, DC



# GW RESEARCH DAYS

## 2013

## ANNUAL RESEARCH DAY

TUESDAY, APRIL 2, 2013

### MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

- 8:30-10:00 a.m.      **Registration and Breakfast** (*Grand Ballroom*)
- 8:30-10:00 a.m.      **Posters Setup** (*Grand Ballroom*)
- 9:00 a.m.-3:00 p.m.      **Research Days Vendor Showcase** (*Continental Ballroom*)  
<http://research.gwu.edu/research-days-vendor-showcase-2013>
- 10:00 a.m.-12:30 p.m.      **Poster Presentations and Judging** (*Grand Ballroom*)
- 1:00-2:30 p.m.      **Poster Removal** (*Grand Ballroom*)

### RESEARCH DAYS 2013 WEBSITE

ONLINE - [HTTP://RESEARCH.GWU.EDU/RESEARCH-DAYS-2013](http://RESEARCH.GWU.EDU/RESEARCH-DAYS-2013)

6:00-6:15 p.m.      **Award Ceremony**

**Dr. Steven Lerman, PhD**  
*Provost and Executive Vice  
President for Academic Affairs*

**Dr. Leo Chalupa, PhD**  
*Vice President for Research*



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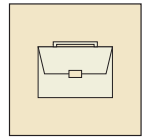
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# BUSINESS

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## SCHOOL OF BUSINESS

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### Social Media: The Professional World

Colleen Tan's professional social media project analyzes the growth and influence of social media in the professional world. Social media is web-based and mobile technologies used for communication and interaction. Its presence has grown in modern society to encompass not only entertainment, but also professionalism as well. Professional social media networks such as LinkedIn and Brazen Careerist have become powerful tools for network and career. In conjunction with major professional social media networks, other social media sites such as Facebook also provide work opportunities and professional endeavors to professionals. With close analyses, we can better utilize social media as a professional tool.

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#### STATUS

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Student

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#### AUTHOR

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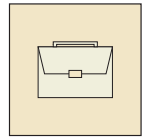
Colleen Tan

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#### FACULTY ADVISOR'S/ DEPARTMENT CHAIR

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Marketing Professor Dr. Marilyn  
Liebrenz-Himes



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## SCHOOL OF BUSINESS

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### Contemporary Practices of Computer Based Trading and their Regulatory Counteracting Strategies

The financial environments around the world have been dramatically changed by the introduction of computer based trading such as high-frequency and algorithmic trading. Some perceive new financial technology as a multiplier for market abuse behaviors occurring in global markets. Making a distinction between market abusive behavior out of good and bad intentions is becoming extremely harder as technology advances beyond the speed of regulatory agency's comprehension. This research mitigates the gap between the contemporary practices of computer based trading and regulator's understanding of those practices, in order to prevent future financial catastrophe that could be eschewed by preemptive regulatory policies.

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#### BACKGROUND:

Market participants need to go beyond the traditional financial strategies to find limited golden opportunities in the financial environment. As a result of the flooding electronic transactions, global markets are overwhelmed by the capacity and liquidity of financial trading. The bubble of financial markets may not be as stable as people assume, and financial regulators are becoming ever more concerned about unforeseen consequences that could potentially decimate the global economy.

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#### OBJECTIVE:

The research attempts to bridge the gap between the contemporary practices of computer based trading and their regulatory counteracting strategies in order to better stabilize the market.

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#### METHOD:

In order to reduce the gap, the research first analyzes multiple examples of trading behavior that have disrupted financial market stability. Then it classifies various behaviors exhibited in electronic trading in financial markets. The classified behaviors are countered by specific regulatory strategies to reduce their negative impact on the financial markets.

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#### RESULT:

The research has reviewed the current solution for financial market crashes caused by computer based trading, and it has proposed a new solution to tackle the crashes. It is in the process of reviewing contemporary literatures related to computer based trading to update its materials.

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#### CONCLUSION:

Controlled financial markets are major participants in the global economy and can contribute to global stability, economic growth, and social prosperity. Classifying electronic trading-related financial market threats and developing efficient strategies to manage these threats provide a series of promising solutions, which could be implemented efficiently.

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Student

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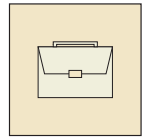
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Prof. Istvan Molnar

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Management at the George  
Washington University*



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## SCHOOL OF BUSINESS

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### Formulation and Enforcement of "Amazon" Taxes

#### BACKGROUND:

Why does Amazon.com collect sales taxes for customers in some states but not others? As of October 2012, 22 state legislatures have passed "Amazon" tax laws. However, Amazon remits sales taxes only in nine of those states. It has agreed to begin collecting taxes in an additional six states beginning as far into the future as January 2016. Furthermore, Amazon has refused to comply with the tax laws of seven states. In those states, its customers continue to buy goods tax free, but at the cost of Amazon terminating its in-state affiliate marketers, thereby depriving the states of their tax revenue.

#### OBJECTIVES:

- Which states took legal action against Amazon, which remained inactive, and why? Does political ideology motivate the implementation of the Amazon tax?
- Of the states taking legal action, which succeeded, which failed, and why?
- Which states have gotten Amazon to remit taxes rather than blacklist them, and why? Does the size of the state's consumer base motivate Amazon's compliance?
- Should a state enact Amazon taxes? Do the Amazon taxes pass the cost-benefit analysis?

#### METHODS:

Regression of Bernoulli Distributions; Simple Economic Modeling; Legal Analysis.

#### RESULTS:

There no correlation between political ideology and willingness to tax Amazon. There is a moderate correlation between Amazon's compliance toward a new state tax law and the economic strength of the state. Additionally, there is no interaction effect between the variables.

#### CONCLUSIONS:

Americans for Tax Reform and other conservative anti-tax groups have been ineffective at lobbying against Amazon taxes. Larger, more economically powerful states will be more successful at convincing Amazon to collect tax rather than terminate its contacts with that state. However, the expected value of tax receipts as compared to the expected loss of tax receipts from terminated in-state affiliates suggests that it is always in state legislators' interest to pass an Amazon law.

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#### STATUS

Student

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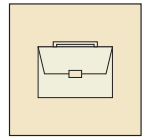
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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Examining the Dynamics of Bank Acquisitions

In this paper, we examine the dynamics of business combinations and the subsequent growth of a financial firm measured in terms of the amount of assets in dollars evaluated over time. Assuming a firm's main objective is to gain profit, a rise in the occurrence of acquisitions can serve as a signal to identify significant changes and shifts within an economy. The objective is to analyze the growth pattern of a firm that actively engages in mergers. By constructing a model to assess the growth of a firm we can develop a mathematical tool to examine the structural anatomy of the combined firm which can be classified and studied to gain further insight on how mergers impact the economy through the newly formed establishment. To this end, we introduce a system in which we use the predator-prey model replicating the Lotka-Volterra equations to analyze the interdependency of the key resources, density of assets ready to be acquired and the amount of financing available for each acquisition. We study this model both analytically and numerically where various equilibrium states will be considered and discussed by altering the initial conditions and each of the key parameters defined in the paper.

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Student

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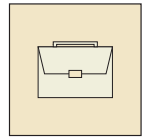
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Svetlana Roudenko

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# BUSINESS

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### A 21st Century Analysis of Business Leadership and Management Strategies in Ancient Rome

The legacy of ancient Rome's economic prosperity too often credits war spoils and real estate purchases as the causes for massive wealth acquisition, yet it pays minimal deference to the *institores* - the business managers - who engineered private sector prosperity on a daily basis. In a society that touted politics as the noblest profession, no such infrastructure existed to provide aspiring managers with any formal business training. In order to shed fresh light on this challenging business climate, this research project examines how *institores* across ancient Rome identified and cultivated superior management skills that resemble those utilized in the 21st century workplace.

The foundational core of this research is a collection of primary sources - historical records, legal documents, and personal accounts - that illuminate managerial experiences across various industries from the late Roman Republic to the early Empire. Additionally, secondary sources from classical historians and former management executives provide the context and criteria to reconcile these ancient management strategies with modern day industry standards. Together, these sources reveal that, without any existing literary corpus or educational institution to prepare them, Rome's wine wholesalers, seafaring merchants, farm owners, and managers in other fields relied almost solely on their experience and self-taught acumen to make critical decisions about production, finances, and even human relations. Both the ancient authors and subsequent scholars lay claim to individuals who recognized and employed modern strategies such as risk mitigation, best practices, and SWOT analysis among other tactics in their enterprises. Continuing research concentrates on identifying and analyzing specific management strategies that functioned more effectively in certain industries than in others.

Ultimately, this research project should serve as a cross-disciplinary study of Classics and Business - a synthesis of the intellectual and the practical - that encourages members of both camps to recognize the striking similarities between 2000-year-old management strategies and those in use today.

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#### STATUS

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# CREATIVE ARTS

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Voices of Youth: Life Changing Moments

#### BACKGROUND:

For the past ten years the GW Department of Theater and Dance has maintained an artistic partnership with the Bokmaoso Life Center of Winterveld, South Africa. This relationship, created and fostered by Professor Leslie Jacobson, has both raised money for the efforts of the Life Center as well as nurtured a cultural exchange between the students of the Department of Theater and Dance and the youth of the Bokamoso Center. As part of the established project, known as *The South Africa Project*, youth from the Bokamoso Center spend one week in residency at The George Washington University attending classes, performing, and living with GW students.

#### OBJECTIVES:

To explore the cultural exchange between the Bokamoso Life Center and the GW Department of Theater and Dance. To shed light on the similarities and differences of youth across continents, socioeconomic divides, and culture in a creative and artistic manner.

#### METHODS:

My research took me to the Bokamoso Life Center in Winterveld, South Africa. There, I participated in arts workshops under the guidance of Professor Leslie Jacobson. I also conducted group interviews with the youth of the Bokamoso Center focusing my questions on personal relationships, community, goals, and important moments in life. Upon return to the United States, I asked the same series of questions to GW students. Based on the responses of both groups, I developed a play titled: *Youth*.

#### RESULTS:

The project resulted in the creation of a new play titled *Youth*. This play, along with that of another student, was presented in a staged reading performed by youth of the Bokamoso Life Center and the GW Department of Theater and Dance in a joint reading in the Marvin Center Betts Theater.

#### STATUS

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Khovanov-type Homology and Homology of Small Categories

We start from describing Khovanov homology in the context of homology of small categories with coefficients in the functor into  $\mathbb{Z}[x]/(x^2)$ -modules. We then speculate on generalization of Przytycki's and Turner's ideas relating Hochschild homology and Khovanov homology using the tool of barycentric subdivision of small categories.

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Jozef Przytycki

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Jozef Przytycki

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# CREATIVE ARTS

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### LGBTQ Homeless Youth Documentary

#### BACKGROUND:

"I'd rather have a dead son, than a gay one." With his mother's last words to him still echoing in his head, Mickey Alvarez left his small, suburban neighborhood hoping to find sanctuary in New York City. Mickey frantically searched for a place he could call home, but with a limited number of beds in the shelters and the growing amount of homeless youth, it seemed nearly impossible. As resources continue to be reduced for this community<sup>1</sup>, so do their chance for survival. The film will follow up to three youth who identify with the LGBTQ community and understand what life is like on the streets.

#### OBJECTIVES:

This Independent research will be centered on creating a short form documentary film [8-15 minutes] about the lifestyle of LGBTQ Homeless Youth in New York City. The film is at the intersection of Political Communication, Journalism and Sexuality Study theories. By interviewing members of this community, the film seeks to find the relationship between the theoretical and the lived experience when sharing personal stories. The documentary is set to screen in May.

#### METHODS:

In order to produce this documentary, interviews with nearly two dozen youth who identify as members of the LGBTQ community will be conducted. A strict observation of lifestyle will be maintained throughout the process.

Results and Conclusions to be established after interviewing and post-production are finalized.

#### STATUS

Student

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#### SOURCES

1. The Advocate: <http://www.advocate.com/society/youth/2012/05/04/homeless-lgbt-youth-lose-7-million-nyc>

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# CREATIVE ARTS

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Getting a Leg Up Through Entrepreneurship and Innovation; Will Art Survive in a Capitalist Economy?

More than ever before, dance artists are struggling to survive and succeed throughout the United States—nowhere more so than in New York City. Existing dance research focuses on dance companies and arts organizations; the subject of independent artists is paid minimal attention. Through analysis of the methodologies used by independent artists in comparison to those utilized by Movement Research (non-profit arts organization), this research offers a deeper understanding of the methods undertaken by independent artists to find greater financial stability within a capitalist economy. To obtain data, fifteen independent artists, with extensive experience working in New York City were interviewed, in addition to staff members of Movement Research. While searching for a specific method of stability, several methods proved successful for thriving artists and organizations. The development of a methodology, regardless of the actual method itself, is imperative to an artists' success. The experiences, practices and advice shared by artists and Movement Research staff offer an invaluable framework for new artists to formulate such methodologies. Research demonstrated that, in comparison to the rest of the economy, and other sectors of the arts industry, independent artists were less negatively affected by economic recession. Findings also suggested generational differences; new artists support themselves much longer than their older colleagues before reaching a point of security. Sharing the experiences and practices of independent artists and of Movement Research contributes to very limited pre-existing research, thus strengthening the field by giving artists the tools to develop their own methodologies for stability. The diverse experiences and viewpoints of the individuals interviewed create hope for generations of artist to come. Their commitment to the continuation of art regardless of the economic situation demonstrates the true entrepreneurial spirit possessed by American dance artists. To be an artist in a capitalist economy is to be an innovator.

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#### STATUS

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# CREATIVE ARTS

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Impact of Art Therapy on the Symptoms, Treatment, and Costs of Pediatric Asthma

In the U.S., approximately 6.8 million children have asthma. In general, minority populations are the most affected. Adolescents and children from low income and single-parent families are particularly at risk. Children with asthma are bed ridden nearly 8 million days annually. The estimated annual cost of asthma in 2007 was \$19.7 billion.

The "Impact of Art Therapy on the Symptoms, Treatment, and Costs of Pediatric Asthma," conducted by The George Washington University in conjunction with the Global Alliance for Arts & Health, and Americans for the Arts, is one of the few studies examining the link between art therapy and pediatric asthma treatment. The mixed methods study, utilizing quantitative randomized controlled trials and qualitative grounded theory approaches, will evaluate the effects of art therapy on pediatric asthma patients. The qualitative portion of the study will examine parent and child perceptions of art therapy and its impact on family dynamics.

The randomized controlled trial utilizes the Pediatric Quality of Life (PedsQL) Asthma Model and the Beck Youth Inventories 2nd Edition. In addition, parents will complete the PedsQL Asthma Model Parent Report for Children before and after the interventions. Participants will be recruited from three U.S. hospitals. They will be randomly assigned to either the control or art therapy group. Both groups will receive standard asthma education course; the art therapy group will receive an additional art therapy intervention. Hospitalization and medication data will continue to be collected for six months. After six months, participants and parents will again complete the assessment inventories. A pilot study involving three participants will be conducted this spring.

The researchers expect to find an increase in Quality of Life, coping skills, and economic benefits for patients receiving art therapy. Furthermore, the research will show art therapy provides psychological benefits for patients and is cost-effective for hospitals.

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Student

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# CREATIVE ARTS

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## ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

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### Lalla Essaydi and the Revision of Stereotypes

Through a range of media extending from photography to calligraphy inscribed in henna, Lalla Essaydi exposes the hidden world of Middle Eastern women to the Western world by using her personal experiences as a Moroccan-born, New York City resident to reveal intimate, private scenes of Muslim women. Her autobiographical, early-twenty-first century work addresses Western stereotypes of Arab women such as those of the Orientalist painting tradition while simultaneously contesting the hegemonic relationship between the West and the Middle East. In her mixed-media portrayals of modern Moroccan women in harems, Essaydi utilizes the same subjects and setting as the Orientalist painting tradition, but transforms them into accurate representations of the Arab female sphere in order to combat Orientalist notions of Arab women as objects of sexual desire. Similarly, by failing to confine her subjects to the private sphere, Essaydi attempts to reverse the Western trend of victimizing Arab women. Essaydi's work also intends to reformulate Western notions of Islam as detrimental to female empowerment by portraying Muslim women as enlightened individuals. Through an analysis of Essaydi's work and relevant sociological texts, I argue, and ultimately conclude, that Essaydi's first-hand portrayals of life in the Middle East not only revise Western stereotypes of the Arab world, but revolutionize relations between her Western viewers and Arab subjects as well.

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#### STATUS

Student

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# EDUCATION

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## ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

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### Understanding International Systems of Teacher Evaluation: Case Studies of Finland, the Netherlands, and England

The climate of education reform shows an increasing emphasis on teacher accountability and quality. This project broadly explores how other countries evaluate their teachers in order to consider the question: *what are the most effective forms of teacher evaluation?* Research was gathered through a consultation of primary and secondary sources discussing the relationship between teacher quality and student achievement as well as the history and current status of teacher evaluation in each country. Finally, a survey was distributed to secondary school teachers in the United States to gain an understanding of how teachers feel about being evaluated.

The results provide a snapshot of the global context. In Finland, there is no formal system of evaluation. Accountability is rooted in teacher trust and a rigorous and competitive teacher training program. In the Netherlands, schools have a high level of autonomy but are subject to formal inspection by the national government. This data is made publically available and provides a platform for school accountability. In England, there is a formal system of evaluation for school and teachers. At the school level, a value-added model is used to calculate the institution's ability to improve student achievement and this data is available to the public. Within schools, teacher evaluation has recently been tied to job security. The survey results show considerable variation between teachers how evaluations should be manifested, but 100% of respondents agreed that teachers should be evaluated at some point in their careers.

This research provides an important introduction to the role of teacher evaluation internationally. By illustrating that teacher accountability and quality are important in countries outside the United States, this work invites further study on the most effective measures of teacher quality internationally.

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#### STATUS

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### The Experience of Thinking Strategically in a Volatile, Uncertain, Complex and Ambiguous (VUCA) Environment

This qualitative phenomenological study addresses the research question: What is the experience of leaders when they think strategically in a volatile, uncertain, complex and ambiguous (VUCA) environment? This study explores the research question in terms of what happens and how it occurs, with specific interest on what triggers strategic thinking, what questions are being asked, and what methods are being used to develop insights that help guide long-term strategies and short term execution decisions. This research uses the strategy and strategic thinking, cognition, and environmental context literature, and is designed to contribute important information to help improve strategy development and execution decision-making in VUCA environments.

Participants in this study satisfy specific experiential and scope criteria. This research is being conducted per the Seidman (2006) phenomenological in-depth interviewing methodology and includes the development of cognitive maps (Huff and Jenkins, 2002) as a triggering mechanism for in-depth interviewing exploration and narrative analysis. The phenomenological data analysis method of Stevick-Colaizzi-Keen as described in Moustakas (1994) has been selected for this study along with the development of individual profiles per Seidman (2006) to assist in the interpretation of interview data.

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#### STATUS

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Student

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### Flows of Social Capital in the Education Meritocracy: First Do No Harm

This study confirmed the prediction of Coleman and Hoffer (1987) that public schools could replicate the functional communities surrounding Catholic Schools that raised the academic outcomes of disadvantaged urban youth by nesting schools within the parents' workplaces. It was found that rather than being created in school communities, social capital had become a commodity in the "education marketplace" that was donated, purchased, and bartered. Working parents indicated that schools with high levels of parental involvement made their personal involvement more manageable. Gatekeepers and school cultures that marginalized parents impaired the flow of social capital into school communities. Longitudinal data surfaced that suggested charitable social capital that marginalized the families of disadvantaged urban children had a negative impact on the career trajectories of 'scholarship kids.' It was also noted that interracial marriages promoted interracial informal familial bonding among co-workers and within school communities. Finally, rather than a single 'something new' between value and functional communities (Reckmeyer, 1990) a whole new spectrum of school communities was evolving within the Workplace Neighborhood School Model.

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#### STATUS

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Student

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Roger Whitaker

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### Wikipedia and Museums: Collaborative Interactivity

This paper is an investigation into the emergent GLAM-wiki movement. The GLAM (Galleries, Libraries, Archives, Museums) initiative encourages cultural institutions to share their knowledge and collections using the Wikipedia platform in order to reach wider audiences. For the first years of its operation, Wikipedia met resistance from advocates of traditional research practices. Why would a museum, historically an authority of “objective” history, link itself with Wikipedia’s free-form, grass-roots campaign for democratic knowledge? Yet, while museums have struggled to make their collections and resources more available to the public via the internet, Wikipedia’s grasp on the top ranks of search engine results has only gotten stronger. Wikipedia is the sixth most visited website in the world. Its usefulness for everyday research has left museums asking, “Why compete?” This paper explores the recent trend in partnerships between Wikipedians and museums. Because this is a new development, little is published on the topic. I look at the movement’s current status by interviewing key players and reviewing its discourse in blogs and conference papers. My research shows museums like the Cooper-Hewitt Museum of Design, the British Museum and the Smithsonian are joining the wiki-revolution, working with “Wikipedians” to share photos and metadata, and to improve Wikipedia articles about museum objects. Museums are also using wiki technologies that involve visitors, asking them to participate in their planning, research and interpretation of objects. Museums’ participation in creating and editing Wikipedia articles, along with their collaboration with the Wikipedia community, establishes an interactive relationship between the museums and their audience by co-creating content with them. This collaboration is mutually beneficial for both Wikipedia and museums, and for visitors to both sites.

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#### STATUS

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Student

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Amelia Wong



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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### The Comparison between India and the USA on Alternatives

Through a comparison of alternatives to public primary schools in India and the USA, this paper explores and explains the differences of alternatives. The percentage of the USA's religious private schools as alternatives to public primary schools is high and the sub-sector is concentrated, while India's religious private schools are comparatively scarce and the sub-sector is segmented. The USA has homeschooling as its characteristic alternative to public primary education; while India's characteristic alternatives are unrecognized low-fee schools. The quality of the USA's characteristic alternatives is high and brings positive effects on children's growth, while the quality of India's is low and the schools have negative effects on children. These three differences are respectively explained by the nation's religious and educational history, proposed "Predestined Model", as well as proposed "National Hierarchy of Educational Needs". This paper argues that alternatives in the USA definitely bring positive effects on primary education, while the effects on education brought by India's alternatives are not clear. This research argues that government should rethink the role of alternatives in education and, through appropriate intervention, make the public schools and alternatives operating well, thus make the whole education system working successfully.

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#### STATUS

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Student

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#### AUTHOR

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### Teachers' speech acts in elementary arts integrated and conventional language arts contexts

#### OBJECTIVE:

The current study frames classroom drama as a contextualized language setting and examines teacher speech acts in lessons with and without classroom drama in two urban, third grade classrooms of students identified with language-based learning disabilities (LD).

#### BACKGROUND:

Recent educational initiatives reflect the concern for literacy achievement of students identified as "at-risk" for school failure due to diverse learning challenges (Novosel, Deshler, Pollitt, Mark, & Mitchell, 2011). One avenue for addressing these populations involves the development of contextualized instructional approaches aimed at increasing students' linguistic productivity and specificity (Anderson, 2012; Westby, 2006; Ukrainetz, 2006). Contextualized learning activities such as those provided by dramatic language arts (DLA) settings transform students' learning by providing an alternative to conventional academic contexts, which tend to exacerbate students' learning challenges (Eisner, 1998). While drama activities enhance student learning (Deasy, 2002; Durham, 2010), limited research exists on the influence of context (i.e. dramatic language arts and conventional language arts (CLA) settings) on teacher language, specifically speech act use.

#### METHODS:

Data sources included video recordings of a total of four language arts lessons: one DLA and one CLA lesson in each classroom. Video recordings of the four lessons were transcribed using Systematic Analysis of Language Transcripts: Research Version (SALT-R; Miller & Iglesias, 2010) and coded for teacher speech act use.

#### RESULTS:

Both teachers showed speech act differences across DLA and CLA language arts contexts, with teachers using significantly more requestive product questions and responsives in the DLA contexts compared to the CLA settings.

#### CONCLUSION:

The DLA context served as a facilitating mechanism for requestive (as opposed to regulative) speech acts for both teachers. Teachers' use of requestive language in the DLA settings provided opportunities for students to produce more elaborative and descriptive language through the use of literate language features (e.g., noun phrases, adverbs, mental/linguistic verbs).

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### Software Engineer Perceptions of Learning Facilitated by Four Asynchronous Web 2.0 Interaction Technologies in a Software Development Environment

Web 2.0 has transformed the way people interact in their personal and, more recently, professional lives. As professionals who create a wide variety of contemporary social media applications, software engineers (or software developers, as they are professionally known) are also early adopters and frequent users of Web 2.0 tools throughout their regular software development work. However, there is insufficient empirical or practical literature available that explores learning that is facilitated by software engineer asynchronous interactions via Web 2.0-supported social media technologies. The purpose of this exploratory quantitative study was to investigate perceived learning by individual software engineers who interact with their colleagues using blogs, microblogs, question-and-answer (Q&A) websites, or tagging applications. The researcher used Bandura's social cognitive theory as a theoretical lens through which potential software engineer learning was investigated in the software development environment.

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# EDUCATION

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### The Social Network Experiences of African American Women – A Phenomenological Study

African American communities are disproportionately affected by social ills like poverty, youth unemployment and homelessness (Roberts, 2004; New Century Foundation, 2005; Robinson, 2000). Research demonstrates how network interpersonal ties of family, friends, fictive kin (strong ties) and acquaintances (weak ties) are a source of, and access to myriad of resources and information, that have the potential for mitigating the social ills occurring in these communities (Stack, 1975; Wellman, 1979; Ibarra, 1993; Oliver, 1988; Granovetter, 1983; Murray, Rankn, & Magill, 1981). Research has also demonstrated an empirical relationship between a network's composition (homogeneous, heterogeneous) and access to resources and information (Ibarra, 1993; McPherson & Smith-Lovin, 1987; Marsden, 1987; Wimmer & Lewis, 2010). African American women have a history of using network ties to support their families and communities (Young, Sundararajan, Stewart, & Stewart, 2009; Robnett, 1996; Barnett, 1993; Stack, 1975), but their experiences are relatively scarce in the network literature. This qualitative, phenomenological study uses a modified version of Seidman's (2006) three-interview series to explore the network experiences of 13 African American women. In contrast to many existing studies that examine how African American women use networks for egocentric needs or to influence behavior, this research explores the experiences of these women using networks to benefit network alters. The researcher used Granovetter's (1973; 1983) tie strength and McPherson, Smith-Lovin and Cook (2001) homophily theories as a theoretical lens to explore the women's network experiences. Preliminary results allude to: alignment with Granovetter's (1973; 1983) tie strength theory, contrast to McPherson, Smith-Lovin, and Cook's (2001) homophily theory as it pertains to access to resources and information, practice of direct contact in the absence of tie connections, strategic use of networks to access resources and information and use of a set of implicit rules to ensure continued access to resources and information. The research is still in the analysis phase so no conclusions have been made.

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### A Study of Birnbaum's Theory of the Relationship Between the Constructs of Leadership and Organization as Depicted in His Higher

#### BACKGROUND:

Birnbaum's (1988) theory of the relationship between the constructs of leadership and organization investigates college and university leadership within the context of the higher education organization. His five higher education models of organizational functioning: bureaucratic, collegial, political, anarchical, and cybernetic (an integration of two or more models) depict the complex characteristics of higher education leadership and organization.

#### METHODS:

This quantitative, nonexperimental study used survey research design and nonparametric statistics to investigate Birnbaum's theory. A research instrument was developed to gather data to test Birnbaum's theory, as no empirical evidence existed to confirm or reject his theory. The sampling frame was full time faculty at Carnegie™ classified master's degree granting institutions. The conceptual framework used was a contextual leadership paradigm, not commonly used to study college and university leadership.

#### RESULTS:

Findings revealed that of the total number ( $n = 482$ ) of respondents, 234 (49%) perceived the cybernetic model of leadership and 313 (65%) perceived the cybernetic model of organization. Of the total number of respondents ( $n = 313$ ), the majority of respondents, 164 (52%), who perceived the cybernetic model of leadership also perceived a cybernetic model of organization. A chi-square test of independence revealed a significant relationship between the cybernetic models of leadership and organization ( $X^2(4, n = 482) = 73.28, p < .007$ ).

#### CONCLUSIONS:

Although Cramer's  $v = .12$  revealed a weak relationship between model scores, the finding of a significant relationship between the cybernetic models of leadership and organization supports Birnbaum's conjecture that no single model can adequately describe the complexity of higher education leadership and organization. Birnbaum's theory is particularly relevant today because it provides higher education leaders with the skills necessary to identify models important for the decision-making process and to determine the tactics necessary to develop a course of action specific to an organization.

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## GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT

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### An Aesthetic Engagement with Promising Futures: A community-based youth development model for learning from urban youth

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#### BACKGROUND:

Empirical evidence lends credence to the role that peer education plays in packaging credible information in a culturally responsive and age appropriate manner for youth audiences.

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#### OBJECTIVE:

This hands-on and highly interactive demonstration will showcase an innovative education model to advance positive youth development outcomes.

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#### METHODS:

The relevant theory in support of its arts-based methods is rooted in cultural studies, which explores the utility of 'edutainment' most commonly experienced as popular culture and hip hop culture. Cultural studies is grounded in post-modernism, which in this case, legitimizes the role of urban youth as storytellers, authors, thought leaders, change agents and producers of truths on their varied lived experiences. The theoretical application of Paulo Friere's (1972) praxis and Augusto Boal's Theatre of the Oppressed (1979) is supported by actively engaging the audience in reflection for the ultimate goal of social transformation.

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#### RESULTS:

Presenter A: This section will include an introduction and overview of the Promising Futures model

Presenter B-C: This section will include a showcase of the arts-based Promising Futures program techniques and engage the audience in the use of theatre, poetry and hip hop

Presenters A-C: This section will include a comprehensive debriefing on the role of peer education (and arts-based techniques) on the positive youth development of the peer educators as well as how to adapt similar pedagogical approaches in classroom settings.

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#### CONCLUSIONS/IMPLICATIONS:

Some educators may be hesitant to engage in contemporary arts-based mediums such as theatre, poetry and hip hop for educational purposes. This session will make clear the agency of youth to lead the learning process with these tools. This work has the potential to challenge ideologies on urban youth, how knowledge is created/shared and raise awareness on the scholarship of aesthetic based teaching (and research) methods.

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#### SOURCES

Boal, A. (1979). *Theatre of the Oppressed*. Pluto Press: London.

Freire, P. (1972). *Pedagogy of the Oppressed*. Harmondsworth: Penguin.



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**GRADUATE SCHOOL OF EDUCATION AND HUMAN DEVELOPMENT**

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## Peer Support Models for Inclusion

Authors investigated the types of peer support models that are offered to general and special education teachers in the inclusion classroom setting. Four peer support models were identified in the research literature that supported students with disabilities in accessing the general education curriculum: (a) peer tutoring, (b) peer mentoring, (c) peer buddy, and (d) service-learning programs. Each of these models has their own benefits and barriers in implementing them in the classroom as well as school-wide. Best practices of incorporating peer support inclusion programs in the school include identifying goals, professional and peer staff development training, and addressing confidentiality. Stakeholders (e.g. teachers, peers, and parents) have provided feedback on the benefits and barriers of peer supported inclusion programs. Authors recommend future research in gathering information from the perspectives of students with disabilities who have participated in the program.

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## COLLEGE OF PROFESSIONAL STUDIES

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### Leveraging Graphics Processing Units to Enhance and Expand the Capabilities of a Virtual Desktop Infrastructure for Enterprises

Virtual desktop infrastructure is popular desktop model rapidly being adopted by many different enterprise customers. Many of those customers that have not yet adopted the desktop delivery model are hesitant due to some of its inherent limitations. Many of the limitations are based on the inability to leverage graphics processing units within the desktop virtual machines utilized by end users. The research performed in this study looks to eliminate the current limitations of virtual desktop infrastructure by integrating both physical and virtual graphics processing units. In order to research this integration a sample fully virtual infrastructure has been setup, to include all server, network, and shared storage infrastructure. The infrastructure includes all three major hypervisors used in today's enterprise networks. Each of the hypervisors has a unique method of integrating graphics processing units into their guest virtual desktops. Integration has been successful into two of the three hypervisors in use. Successful utilization of the graphics processing units has yielded vast increases in virtual desktop rendering in both two-dimensional and three-dimensional applications. Especially in highly intensive applications such as computer aided design software and full motion video rendering software. Research is still being done to test the full capabilities of the virtual desktop to include the ability to render desktop video games and other use cases. A few implementation limitations have been found to include increased bandwidth utilization between the virtual desktop and the end user, which in some cases might introduce complications with implementations over wide area network topologies. Further research is being done to overcome the limitations introduced when integrating the graphics processing units into the guest virtual desktops.

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#### STATUS

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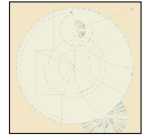
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## COLLEGE OF PROFESSIONAL STUDIES

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### Data Mining Twitter Posts for Correlations Between Geographic Locations and Topics of Interest

Twitter has become an extremely popular part of social media that is used in real time to log events or thoughts by the user. This makes the Twitter posts (known as tweets), a valuable source of data on a wide variety of sociological and cultural topics. Tweets can optionally include the geographic coordinates of where the post was made. To explore the possible utility of linking geographic location with the topic of Twitter posts a Python script was written in to capture Tweets posted within the Washington DC area and log them to a database over a four month period. Hashtags were grouped into categories such as politics, types of interests, types of events, personal categories, etc. The wards of DC were used to define location, and then the topics linked by region for highest frequency. As predicted, some postings showed strong location bias such as events which correlated with the region where events occurred. These data may be useful for determining engagement levels of various locations and activities. Limitations of this method include multiple meanings or usage for similar key words and hashtags which require disambiguation that cannot easily be performed. Advantages and limitations of data mining using this method are analyzed and possible means of improvement are discussed.

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Student

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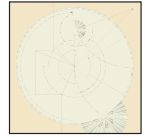
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**SCHOOL OF ENGINEERING AND APPLIED SCIENCE**

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## The Foundation of Nanoscience: Multiple Length/ Time Scale Modeling of Multi-physics for Nano/ Micro Material System

Nanomaterials manifest extremely fascinating and beneficial properties, which can be exploited for a variety of applications, e.g., next-generation computer chips, tougher and harder cutting tools, high energy density batteries, high sensitivity sensors and longer-lasting medical implants. From design, synthesis to application of nanomaterials, theoretical modeling of multiphysics is at the core of the broad field of Nanoscience. For instance, it guides the design of nanomaterials from zero-dimensional nanoparticles, to one-dimensional nanoribbons or nanotubes, to two-dimensional thin films; it may explain and even predict the discovery of many novel phenomena.

Molecular dynamics (MD) has established itself as a widely employed discipline for the study of material behaviors at atomic level. For the modeling of multiphysics, i.e., thermomechanical-electromagnetic coupling phenomena, we recast the governing equations for atoms by reformulating the Nose-Hoover Thermostat and by incorporating with the Maxwell's equations at atomic level. However, we realize that the extension of MD into computational science over a realistic range of length is limited, due to the large number of particles involved as well as the complex nature of their interactions. The limitations are also imposed by the requirement of smallness of the time step, and yet one is interested in events that occur over a much larger time scale. To expand the realm of modeling and simulation, we propose a multiple length/time scale approach along with the employment of massively parallel computing technique<sup>1</sup>. The numerical results can show (i) the wave propagations in acoustic mode and optical mode, (ii) the heat conduction process, (iii) the material responses when it is subjected to external electromagnetic fields, and (iv) the induced polarization, voltage, electrical field and magnetic field, etc.

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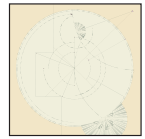
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**REFERENCE**

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1. Jiaoyan Li, Xianqiao Wang and James D. Lee, Multiple Time Scale Algorithm for Multiscale Material Modeling, *Computer Modeling in Engineering and Science*, 85(5), 2012.





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**SCHOOL OF ENGINEERING AND APPLIED SCIENCE**

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## Exploration of Energy Efficient and Environmentally Friendly Magnetic Refrigeration Systems

The magnetocaloric effect (MCE) is the reversible temperature change of a magnetic material upon the application or removal of a magnetic field. In the past 20 years, there has been a surge in research on the magnetocaloric response of materials, due mainly to the possibility of applying this effect for magnetic refrigeration close to room temperature. Our research is devoted to explore and optimize the magnetocaloric properties of known materials, as well to seek for new magnetocaloric features in new materials.

This research is important because magnetic refrigeration is a good candidate for reducing our energy consumption, as it is more energetically efficient than the process based on the compression/expansion of gases.

To characterize a potential magnetocaloric material, there are several relevant magnitudes that should be measured. The most intuitive one is the adiabatic temperature change,  $\Delta T_{ad}$ , which is the temperature change of the material when adiabatically magnetized/demagnetized. A novel test system with fully-controlled magnetic field, temperature, and time capabilities has been designed and implemented. We initiated the research by testing gadolinium which is a generally prominent magnetocaloric material. Next, we introduced a new approach of interpreting the  $\Delta T_{ad}$  measurements to emphasize the reversibility of the magnetocaloric effect, contrasting the common belief in the scientific community. The new approach also gives the most precise measurement of a material's Curie temperature. We are focusing on demonstrating that the magnetic refrigeration is a feasible technology by testing and characterizing potential magnetocaloric materials. Full characterization of gadolinium has been presented leading to new insights about the magnetocaloric effect. Notables include introducing a new interpretational approach to highlight the reversibility of the magnetocaloric effect and delivering a hypothesis of implicitly measuring the latent heat accompanying the phase transformations. These efforts resulted in five publications (4 published and 1 submitted).

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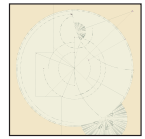
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**SCHOOL OF ENGINEERING AND APPLIED SCIENCE**

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## Distributed Robotic Mapping System

**BACKGROUND:**

The ability to autonomously collect data about an unknown environment is critical. When natural disasters occur accurate information about the area is vital for search and rescue teams. Scientific exploration into dangerous, previously unexplored environments both on earth and in space is valuable to the scientific community. There is a need for a low-cost, accurate, autonomous data collection system for these situations and many others.

**OBJECTIVES:**

The solution for the exploration of dangerous environments is sending low-cost, versatile, autonomous robots. The Distributed Robotic Mapping System is a versatile group of robots which collect information and relay it to a central server which then creates a three dimensional map for people to study.

**METHOD:**

The Distributed Robotic Mapping System focuses on three key problems in data collection: cost, scalability and versatility. Our system is low-cost, at \$300 per robot it is a fraction of the cost of current robot systems. This allows the robots to explore more dangerous environments because the loss of one has minimal cost. It also means a large group can feasibly be deployed even without significant funds. The Distributed Robotic Mapping System is scalable, it is designed to not be dependent on any one robot, therefore the system can involve as many or as few robots as necessary. The Distributed Robotic Mapping System is versatile. Each robot is based on a modular design therefor sensors can be changed easily allowing any type of data collection for which sensors exist.

**RESULT:**

We have designed and built a team of low-cost, versatile deployable robots that can collect data in a dangerous environment and relay it to a central server. Our system is able to deployed in unknown environments and relay accurate data back to a server. This data is then rendered into a comprehensive map.

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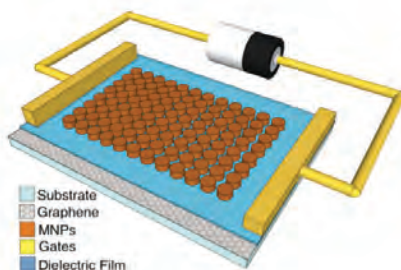
## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Graphene Based Tunable Sensors

For changing testing environments like point-of-care diagnostics, it is advantageous to have sensors with tunable operating ranges. A set of sensors with different operating wavelengths can generate an extensive dataset for greater detection certainty despite any non-ideal environmental conditions. With its controllable optical conductivity and mechanically strong structure graphene can be instrumental for such tunable sensors.

In a typical index-of-refraction sensing setup, the change in the reflected (or transmitted) light intensity due to the change in the flow channel is monitored. Using a resonant structure might increase the contrast of the reflection (or transmission) spectra and make this monitoring easier. For example, if the resonant structure is a metal nano particle array, then localized surface plasmon resonance (SPR) occurs when the interaction of sub-wavelength particles with incident light yield a collective oscillation of valence electrons at their maximum strength and a sharp dip (peak) at the transmission (reflection) spectra is observed near SPR wavelength. The material type, shape, dimensions, and periodicity of nanoparticles, incidence angle, and background affect the resonance wavelength. Apart from the unwanted deformations, most of these parameters cannot be modified after the fabrication. One way of changing the resonance wavelength is changing incidence angle but it requires a meticulous alignment. Another way of designing a tunable sensor would be changing the optical properties of some components of the structure with applied voltage.

Assume a metal nanoparticle (MNP) array is fabricated on top of a graphene coated transparent substrate such as glass. In order to prevent a direct contact between MNPs and graphene, a thin dielectric film might be placed between them. On the two opposite sides of the structure, there are two long metallic contacts in order to make a connection between the graphene layer and a DC source. When the source is off, we have a regular localized SPR based sensor with a resonance wavelength where the transmission (reflection) spectrum has a minimum (maximum). Turning on the DC source changes the optical properties of graphene and the induced dipole moment of the each nanoparticle. By changing the potential distribution along the graphene layer, we physically change the inhomogeneous background and the charge distribution inside the nanoparticles, and hence the surface plasmon resonance of the whole structure. A precisely changed gate voltage should allow us to tune the sensor to any resonance wavelength within a reasonably wide range of wavelengths.



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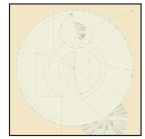
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**SCHOOL OF ENGINEERING AND APPLIED SCIENCE**


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## Self-similarity in $(\partial M/\partial T)_H$ curves for heusler alloys with ferri-to-ferromagnetic and ferro-to-paramagnetic phase transitions

Heusler alloys exhibit first order ferri-to-ferromagnetic and ferro-to-paramagnetic transitions which, through a temperature scaling methodology, presented in this paper, exhibit a self-similar field dependence  $(\partial M/\partial T)_H$  curve. This scaling methodology based on temperature, extends Franco's transformation by (1) adding ferri-to-ferromagnetic transition, (2) performing the scaling methodology on the  $(\partial M/\partial T)_H$  curve instead of  $\Delta S_M(T,H)$  curve, and (3) redefining the arbitrary temperature references used by Franco, by employing constant temperatures which can be determined from  $(\partial^2 M/\partial^2 T)_H$  and  $(\partial M/\partial T)_H$  curves. By taking an analytical characterization approach, the method calculates the composition of ferrimagnetic, ferromagnetic and paramagnetic clusters for Heusler alloys exhibiting first-order phase transition. The self-similarity phenomenon within the material's  $(\partial M/\partial T)_H$  curve aids then in formulating compositions<sup>1</sup>.

By applying the self similarity model, we evaluated the effectiveness of this new analytical characterization approach, the cluster composition functions for  $Ni_{50}Mn_{35}In_{15}$ , which exhibits first-order ferri-to-ferromagnetic and ferro-to-paramagnetic transitions. Self-similarity, which magnetization vs. temperature at each applied field exhibits, is defined in mathematics as an object that is exactly or approximately similar to a part of itself. By rescaling the modified Franco's transformation, all the  $(\partial M/\partial T)_H$  curves collapsed on to the single self-similar curve with a low index of dispersion. Once collapsed, the curve is asymmetric and negatively skewed due to the intrinsic transition differences in the mixed state region. The mixed state region of the self-similar curve is distinctly bell-shaped. The self-similar curves are optimally modelled using the maximum entropy method.

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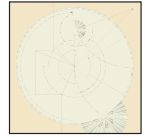
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**SOURCES**


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<http://dx.doi.org/10.1016/j.physb.2011.09.044>



## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Ultra-Compact Electro-Optic Modulator

#### BACKGROUND:

Recent data shows that we are more and more out of sync with Moore's Law which has been keeping track of technology invention for many decades. Current semiconductor and communication technology needs to break away from traditional transistor scaling. The question is: can integrated photonics become the next technology platform for computing and data communication?

#### OBJECTIVE:

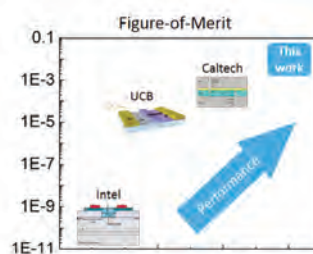
The photonic integrated circuit was proposed to become the next step in this technology evolution. Here we showcase a revolutionary novel design of such a future light 'transistor' featuring unprecedented performance. Our device could become the fundamental cell of every future photonic chip.

#### METHODS:

The electro-optic modulator needs to be extremely small, fast and power efficient. All these performance measures can be achieved when (a) the device is ultra-small, and (b) the light interacts strongly with the active material. However, this is impossible in classical physics, due to the diffraction limit of light. Here, by using surface plasmonic polaritons (light-on-metal) we successfully surpass this physical limit. The key light-modulating mechanism of the device is the switchable optical refractive index by an applied bias voltage; turning this voltage on (off), the absorption of the light inside the modulator will increase (decrease) resulting in light being modulated according to a binary code (e.g. 0-1-0-0-1-1...).

#### RESULT:

The significance of this work can be highlighted by comparing performance targets with competing devices (aka. Benchmarking). Our experimental results show a 10,000x smaller device footprint compared to a design from Intel's Photonics labs, a 5 order of magnitude stronger modulation strength. This results in an ultra-high speed modulation (THz) which is 1,000x faster than current technology. At the same time the energy per-bit can be reduced by 3-4 orders of magnitude resulting in a green computing and communication future at accelerated performance. The figure summarizes these results.



#### CONCLUSION:

We successfully designed and fabricated an ultra-high performance electro-optical modulator (= optical transistor). Our results are the world-record in terms of performance for such a device. Such optical transistor opens entirely new pathways for future high-speed, low power optical circuits, computing and big-data. We have published a journal (Nanophotonics 1, 9-17 (2012)) and a proceedings paper (SPIE Photonics West (2013)). This work has attracted significant interest from industry and collaboration with big players like Intel was formed. A patent is being pursued.

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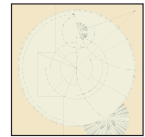
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Automatic registration and mosaicking of conservation images

#### BACKGROUND:

As high-resolution conservation images, acquired using various imaging modalities, become more widely available, it is increasingly important to achieve accurate registration between the images. Accurate registration allows information unavailable in any one image to be compiled from several images and then used to provide a better understanding of how a painting was constructed.

#### OBJECTIVES:

We aimed to implement an automatic registration/mosaicking algorithm to be used by art conservators to: 1) register and mosaic multiple X-ray films, ultraviolet images, and infrared reflectograms to a color reference image at high spatial-resolution (200 to 500 dpi) of paintings (both panel and canvas) and works on paper, 2) register images within visible and infrared multispectral reflectance and luminescence image cubes, and 3) mosaic hyperspectral image cubes (400 to 2500 nm), including those acquired with a scan mirror and thus having optical scan-distortion.

#### METHODS:

The algorithm proceeds as follows: 1) identifies candidate control-points in one image by selecting spatially-distributed maxima of the modulus of the wavelet transform at a given subset of wavelet scales, 2) matches those control points with points in a second image by maximizing the cross-correlation between the images' phase information, and 3) filters the matched pairs of points to obtain the most accurate set of pairs that will be used to compute the spatial transformation coefficients.

#### RESULTS:

To date, the algorithm has been used to register and produce mosaicked infrared reflectograms of over 50 paintings and works on paper, as well as create over 10 large-scale hyperspectral image cubes each consisting of 10 to 40 image cube captures (each 640-by-640 pixels by 256 spectral bands).

#### CONCLUSIONS:

The resulting registered, and/or mosaicked, datasets are used to: 1) identify and emphasize information not visible at the surface of the painting and 2) separate, map, and identify artist materials in situ.

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Experimental Study of Swirling Jets and Axial Forcing on a Round Jet

Swirling flows are often seen in both nature and industrial applications. In nature, tornados and hurricanes have a spiral-like rotation to them, which is indicative of a swirling motion. In aeronautics, swirling flows have a negative effect on delta wings, and can cause the aircraft to loose lift. Swirling flows also have a positive impact in combustion devices, and are used to increase the mixing rate between fuel and oxidant streams, which results in improved combustion efficiency. Controlling and manipulating swirling jet structures is of great interest because it can lead to the overall improvement of the fuel efficiency of automobiles and aircraft, as well as the reduction of harmful pollutant by-products into the environment. Controlling these structures can be conducted experimentally by forcing instabilities and by adding a swirling flow into the jet. Past research in manipulating jets resulted in limited findings because the instabilities were only operated in one direction, or the tests were conducted at low speeds, which is now applicable to combustion processes. A new test facility was designed and built to produce both swirling and non-swirling jets in a vertical water tunnel, where forcing instabilities into the flow are implemented in the axial direction. Images of the flow structures at both high and low speeds are captured by illuminating florescent dye with a laser and recording them on a camera, resulting in Planar-Laser Induced Florescent (PLIF) images. Images of unforced, forced, and swirling jets were captured in both the near field, close to the nozzle, and far field. Natural instabilities of the jet were seen to arise from nozzle, where vortices form, interact and merge, and finally breakdown. When forcing is implemented, a large vortex ring emerges which interacts with the natural instabilities. This causes an increase in mixing close to the nozzle exit, and consequently leads to the enlargement of the spread or width of the jet. These results consistently occur for a range of forcing amplitudes. When swirl is introduced, the flow becomes slightly more complicated and irregular. This causes the natural instabilities to misshapen and rapidly become turbulent. Visually and quantitatively the mixing occurs closer to the nozzle, which indicates that the spread of the jet has increased by adding swirl. The characteristics of the flow structures obtained are sensitive to the initial conditions of the experiment with coherent visualizations of the interaction of vortices due to forcing.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### The Role of Copper (II)-Human Amylin Complex in amylin induced toxicity in pancreatic beta cells

#### BACKGROUND:

Human amylin (hA), a 37 amino acid peptide is co-secreted with insulin by the pancreatic beta cells, and plays a role in type II diabetes mellitus (T2DM). Previous reports reveal that T2DM patients have elevated serum copper levels. Even though the idea of a possible interaction between copper and hA has been proposed, its mechanism is little known. Therefore, the purpose of this study was to investigate the effect of  $\text{Cu}^{2+}$  on amylin aggregation and toxicity in pancreatic rat insulinoma (RIN-m5F) beta cells, and to determine if, and the extent to which,  $\text{Cu}^{2+}$  modulates hA induced ROS (reactive oxygen species such as  $\text{H}_2\text{O}_2$  and  $\text{OH}^\cdot$ ) production.

#### METHODS:

RIN-m5F cells were cultured in RPMI-1640 medium and passaged bi-weekly. hA (20 $\mu\text{M}$ ) or rat amylin (20  $\mu\text{M}$ ) was incubated with RIN-m5F cells in the presence or absence of  $\text{CuCl}_2$  (10  $\mu\text{M}$ ) and/ or reducing agents such as NAC, ascorbate and glutathione. Changes in cell viability were determined by MTT reduction assay and Western-blot analysis of phosphorylation of JNK (c-JUN N-terminal kinase) and caspase-3 cleavage indicating apoptosis. Amylin aggregation and  $\text{H}_2\text{O}_2$  accumulation was determined using ThT-aggregation and Amplex-Red  $\text{H}_2\text{O}_2$  fluorescent assays, respectively.

#### RESULTS:

Both aggregation prone hA and non-amyloidogenic rat amylin produced  $\text{H}_2\text{O}_2$  production *in vitro*. In contrast, human but not rat amylin reduced ROS production evoked by  $\text{Cu}^{2+}$  and glutathione or NAC in solution. The hA- $\text{Cu}^{2+}$  complex also inhibited amylin aggregation in solution which may account for the subsequent inhibition of amylin induced JNK phosphorylation and caspase-3 cleavage, hence down-regulating stress kinase signaling pathways.

#### CONCLUSIONS:

This study highlights the anti-apoptotic property of the copper-amylin complex. We show that  $\text{Cu}^{2+}$  does not promote hA evoked oxidative stress in pancreatic cells and that the production of  $\text{H}_2\text{O}_2$  by amylin is independent of amylin aggregation. The quenching of ROS by the  $\text{Cu}^{2+}$  - amylin complex highlights the anti-oxidative effect and potentially protective role of this complex in diabetic patients.

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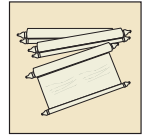
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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Building the U.S Capitol: From Philip Reid to the 41st Congress

The main initiative of this research project is to highlight and celebrate the historical advancements of African-Americans in the United States Capitol by presenting the unexplored narratives that are connected to the statues & artifacts that fill the Capitol.

The project starts with Philip Reid, an enslaved craftsman, who was an integral person in the welding & placement of the Statue of Freedom atop the Capitol Dome in 1863. Following Reid, the project will highlight the Emancipation Proclamation & the impact it had for African-Americans after the Civil War.

Next is the importance of the Amistad court case, which was held in the U.S Capitol Old Supreme Court. The project will focus on the relationship between John Quincy Adams & the battle he faced as he defended the wrongfully captured Africans.

The last focus is in the Senate Gallery. Throughout the floor, there are several portraits that show the victors of the Reconstruction era. The project will choose to focus on Blanche Bruce, the first Black Americana that served a full term in the Senate. He started on February 1874 & became the first Black Americana to preside over the United States Senate in 1879. His forgotten legacy & the connection to his portrait will serve as the culmination to the project. The result is by highlighting and connecting these artifacts together there will be a deeper understanding of African-American influence in the Capitol.

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#### AUTHOR

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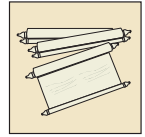
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Jennifer James

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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Mathematical Language Bridging Definition and Practice: A Case Study in Polyhedra

#### BACKGROUND:

Roughly, a polyhedron is a geometrical figure in three-dimensional space that is both regular and bounded by line segments, called edges. This definition leaves much to be desired because polyhedra vary dramatically in their properties. Some extend infinitely into space; some look like stars; others have high degrees of regularity. How does it happen that the ever-more precise mathematicians rely on such a vague term to delimit the scope of a geometrical inquiry after over 2,500 years of study?

We believe that the answer in large measure can be found by paying close attention to the language used to construct frameworks for mathematical inquiry.

#### METHODS:

We studied primary sources, works by eminent geometers from Euclid to the present day, analyzing the language used to prove theorems and give definitions. Using in particular the choice of words, we attempted to track conceptual shifts by following the way in which the author describes polyhedra.

#### RESULTS TO DATE:

We have found that some geometers (Euclid, Descartes) choose words that adhere to their concept of polyhedra in the manner of developing the subject. Others (Coxeter) moved from one conception to another without qualms. There is, in a real sense, a spectrum of choices as to how much the conceptual framework should confine the means of technical development, and we unraveled a variety of such selections.

#### CONCLUSIONS:

We find that this phenomenon, the interplay between conceptual boundaries and a technical exploration of those boundaries, as occurring through language, is an inescapable part of doing and communicating mathematics. In particular, awareness of the target audience can be important in weighing the value of, for example, switching conceptual frameworks to conjure an easier proof. Such a maneuver in a textbook aimed at undergraduates, say, can be prone to cause more confusion than aesthetic appreciation for the different vantage points of the subject.

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#### STATUS

Student

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#### AUTHORS

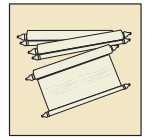
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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## The Best-Kept Secret in America: U Street and the Commodification of Black Literary Intellectuals

Washington, D.C. stands as a unique location due to the close proximity of the government to its constituents, creating a stark division of power and poverty. My senior thesis entitled “The Best-Kept Secret in America: U Street and the Commodification of Black Literary Intellectuals” explores the ideas of gentrification, authenticity, and black literary history in relation to Washington, D.C.’s U Street Corridor. This project investigates two U Street establishments, Eatonville and Bohemian Caverns, determining how black literary history is implemented into each business to create a sense of authenticity and shared memory. Through case studies and historical analysis, this thesis attempts to find how black literary intellectuals and the time period in which they represent are romanticized and commodified in modern spaces. This project contributes to the growing body of research concerning Washington D.C.’s unique racial and economic make-up, and the struggle of current residents to honor the past through shared space by appropriating an illustration of the essence of U Street’s character in a non-romanticized, authentic way.

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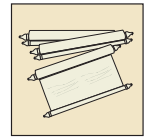
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Elizabeth Anker

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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Sick Jokes: Humor as an Alternative Treatment for Mental Illness in Ken Kesey's *One Flew Over the Cuckoo's Nest*

#### BACKGROUND/OBJECTIVES:

Originally, my objectives were to further explore the Freudian concepts that appear in *One Flew Over the Cuckoo's Nest* and increase my knowledge of mental institutions in the 1950s. After months of research, my objectives took a new turn. Rather than demonstrate how *Cuckoo's Nest* endorses Freudian psychoanalysis, I planned to show how the novel critiques Freudianism through a humor that is subversive and salutary.

#### METHODS:

To achieve my objectives, I read several books, among them Thomas Szasz's *The Myth of Mental Illness*, Erving Goffman's *Asylums*, and seminal works by Freud. I also traveled to the University of Oregon to view the Ken Kesey Papers. The collection contained letters to and from Kesey as well as manuscripts of *Cuckoo's Nest*, *Sometimes a Great Notion*, and several short stories. I am currently writing a draft essay, which I plan to complete by Research Day.

#### RESULTS:

My research has resulted in many insights into the treatment of mental illness and the efficacy of mental institutions. The thinking of academics like Szasz, who openly denounced Freudian psychotherapy, influenced writers like Kesey, who similarly saw the label of mental illness as a means of control over "deviant" members of society. Szasz suggests alternative treatments for mental disorders; Kesey, too, advocates alternative therapies, such as humor. Kesey's own experiences working with patients at Menlo Park Veterans Hospital ultimately inspired him to write the novel, which many readers, some institutionalized themselves, found remarkably true to life.

#### CONCLUSIONS:

My findings have led me to a new conclusion about the novel: By mocking Freudian psychoanalysis, Kesey rejects the pervasive medical treatments of the day and introduces humor as an alternative treatment for mental illness. *Cuckoo's Nest* also invites to think about current therapeutic approaches and consider how we view mental illness today.

#### STATUS

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#### SOURCES

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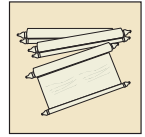
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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### “Actual and Open Rebellion”: Lord William Campbell and the Fight for South Carolina, 1775-1778

Despite wide research on royal governors and their political and military actions during the early revolutionary period, little is known about South Carolina’s own last royal governor, Lord William Campbell, and his impact on developments in Charles Town. Indeed, Campbell has been given scant and often inaccurate attention in existing historical literature. Arriving in June 1775, Campbell was a key alienating figure who increased friction in the province. Despite his best efforts, South Carolinian revolutionaries seemingly won when the governor was forced to flee in September 1775. South Carolina’s fate during this watershed period, however, was still uncertain. Campbell’s efforts over the next three years would help determine the future of this dichotomously divided colony and later state. The object of this study is to analyze what Governor Lord Campbell reported to the British government as he struggled to maintain control over the colony, why he continued to serve the British cause even after he fled Charles Town, and what effects his efforts, perceived and real, had on the political climate in South Carolina. Archival research was conducted at the National Archives, Library of Congress, and Society of the Cincinnati Library in Washington, D.C., the South Carolina Historical Society in Charleston, and the Caird Library and National Archives in London. Research shows that the changing landscape in Charles Town upon Campbell’s arrival quickly spiraled out of his tenuous control and into the hands of a small but radical Provincial Assembly. Campbell’s continued service as a “governor without a colony” and a volunteer in the naval service demonstrated his resolve to aid the loyalist cause and wrestle the colony back under royal authority. As a conspicuous loyalist, Campbell’s presence and actions between 1775 and 1778 helped to crystallize the tensions in revolutionary Charles Town. Further research could reveal how Tory and Whig, loyalist and patriot identities were shaped during this period, and how political and military developments during the early revolutionary years affected these identities in South Carolina. This research consequently informs how the presence of the public, divisive royal governor, Lord William Campbell, influenced not only political and military actions, but how those actions were perceived, processed, and reacted to.

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#### STATUS

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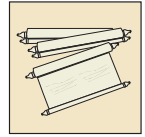
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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Reconstructing the Origins and Destinations of American Immigrants in Europe's Era of Famine and Revolution, 1846-1854

#### OBJECTIVES/BACKGROUND:

Historians studying early American immigration lack hard data. One under-utilized source is the New York ship passenger manifests that list the names, origins and destination of every immigrant. Analysis of these manifests makes it possible to answer basic questions about mid-nineteenth-century immigration that have heretofore gone largely unanswered.

#### METHODS:

We created a sample of 40,000 passengers, 2% of the 2,000,000 who arrived during the peak immigration years from 1846 to 1854. Creating a representative sample was complicated, as we had to sample an appropriate number from each major European port for each year and even each month per year. For ports without many extant manifests, we had to weight our data to bring them in line with that from other ports.

#### RESULTS TO DATE:

Though we tend to associate German immigrants with Midwestern cities such as Cincinnati, St. Louis, and Milwaukee, we found that a 54% intended to settle in New York. An even higher proportion of Irish immigrants, 90%, planned to make New York their new home. We have also determined, for the first time, exactly where in Ireland the immigrants originated. Some results, such as the large number from populous County Cork, were expected. But we found surprisingly large numbers from counties Cavan, Dublin, and Meath, not previously considered large sources of emigration. Protestant Irish, however, preferred Philadelphia to New York.

#### CONCLUSIONS:

Because Germans made up a large proportion of the population in the Midwest, scholars have neglected the fact that most Germans initially settled in New York. They have likewise underestimated how many Irish immigrants lived in New York City before eventually moving elsewhere. Our data also indicates that previous attempts to deduce Irish emigration based primarily on the difference between pre- and post-famine Irish county population does not accurately predict which Irish refugees chose to make the United States their home.

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#### STATUS

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#### AUTHORS

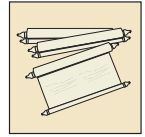
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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Prepping Kennedy for K: Examining the effectiveness of advice on West Berlin given to President Kennedy in preparation for the Vienna Summit, June 3-4, 1961

Coming off the heels of the failed Bay of Pigs invasion and the Soviet's launch of the first man in space, President John Kennedy faced an even more daunting prospect—his first official meeting as president with Soviet Premier Nikita Khrushchev. At this point, neither Kennedy nor Khrushchev knew much about each other, but they both realized the importance of Berlin in the future of the relations between the two states. As part of Kennedy's preparations for the summit, he was briefed extensively on the Berlin situation by a number of advisors. The object of this paper is to determine whether or not the advice Kennedy received on Berlin helped or hindered his conversations with Khrushchev in Vienna. This examination analyzed and compared a series of memorandums, briefing books, and oral histories from multiple advisors who helped Kennedy. These sources are then compared against the Soviet preparations, the summit memorandums of conversation, and actual outcomes of the summit. Results determined that Kennedy entered into the Vienna Summit armed with conflicting recommendations on how to approach Berlin and the premier; it did not help that Khrushchev believed Kennedy was a weak leader who could be steamrolled into accepting Soviet demands. Overall, the summit did not improve relations between the US and the USSR, and in fact heated up tensions between the two leaders over Berlin, eventually leading to the building of the Berlin Wall. The research provides insight into Kennedy's international leadership style, the American understanding of Soviet motivations, and the Soviet mentality towards Kennedy. The paper invites further study of the relationship between Kennedy and his advisors as well as the relationship between Kennedy and Khrushchev, both of which become crucial during the Cuban Missile Crisis.

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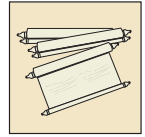
Muriel Atkin



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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### From Public Enemy to History Teacher: Representations of Sitting Bull in American Popular Culture, 1876 - 1976

The nineteenth century Sioux Indian chief Sitting Bull commanded a great deal of public attention during his time in newspapers, public spectacles and pulp fiction. In the decades after his death, he continues to be one of the best known Native American historical figures. Sitting Bull's image has changed considerably since 1876, when he gained fame as the leader of the Indian coalition which defeated the U.S. Seventh Cavalry at the Battle of the Little Big Horn. The media initially demonized him as a bloodthirsty savage and a fervent enemy of the white man. Yet throughout the twentieth century, motion pictures and other media presented Sitting Bull in a far more positive light, culminating in his inclusion in President Barack Obama's 2010 children's book *Of Thee I Sing: A Letter To My Daughters*, which praised Sitting Bull as a "healer" of "broken hearts and broken promises."

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#### STATUS

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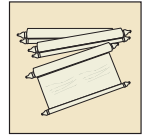
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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Traditionalism in a Contemporary Classic: Jin Yong's *The Legend of the Condor Heroes*

#### BACKGROUND:

This project explores the moral core of Jin Yong's popular martial arts novel, *The Legend of the Condor Heroes*. While the novel was first popular in Taiwan and China, Jin Yong's works are also becoming significant influences in Mainland China because of the relaxation of China's political control on civil life and thought. The novel addresses cultural perceptions of traditional Chinese society, which the Communist regime rejected. As these views are introduced in Mainland China, and could have social and political implications, it is important for the West to understand the moral code within the novel.

#### OBJECTIVE:

The paper introduces an important part of contemporary Chinese literature to English-speaking Chinese academia through literary analysis and examining major themes of the novel. This paper will analyze contemporary perception of traditional Chinese moral codes, and how these moral understanding could be different from the West's traditional moral codes.

#### METHODS:

The George Washington University granted this project the Luther Rice Grant Fellowship. A majority of the paper focused on literary analysis of the novel itself, but also incorporated research material from Taiwan and Hong Kong, which gave the cultural and historical context for the novel and the analyses in the paper.

#### RESULTS:

Since there is little to none research materials on the subject, and the novel has never been translated into English, this project mainly seeks to introduce Jin Yong's representative work and its moral code to Western academia through a research paper.

#### CONCLUSIONS:

The moral code that Jin Yong displays in the novel is an undisputed core to Chinese society. Despite Communist's rejection of traditional worldviews, the public's perceptions of traditional society remain positive, and there is an undeniable admiration for classical teachings and values. These orthodox principles are repackaged in contemporary imitations of classical writing styles and stories, influencing modern views and thinking.

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Shediao Yingxiong Zhuan (*The Legend of the Condor Heroes*)

Menghui Song Chao (*Dreaming of the Song Dynasty*)

Jin Yong Zhuan (*The Biography of Jinyong*)

Jin Yong Shuobu Qingjie: Dong Peixin Huangji (*Plot Moments in Jinyong's Novels: Dong Peixin's New Art Collection*)

Jiefang Jin Yong (*Dissecting Jinyong*)

Jin Yong Xiaoshuo Zhongping (*General Discussions on Jin Yong's Novels*)

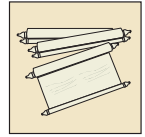
Hanyu Da Cidian (*Comprehensive Chinese Word Dictionary*)

*The Discourse of Race in Modern China*

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# HUMANITIES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Language in Crisis - Chilean Literature during the Pinochet Dictatorship

On September 11, 1973, years before the World Trade Centers collapsed in New York, the democratic government headed by President Salvador Allende was overthrown in a coup d'état lead by Augusto Pinochet. From day one, many Chileans saw the necessity to document the atrocities and horrors of the most brutal dictatorship in Chilean history, and that remaining silent was not an option. Censorship presented a real challenge which was approached in varying ways. Many works were passed along through clandestine networks; however, a great number of authors published through traditional channels, which meant facing state censorship/review.

Two authors, Diamela Eltit with her novel *Lumpérica* and Raul Zurita with his book of poetry *Purgatorio*, exemplify the effects of censorship in their literary reactions to the everyday reality under Pinochet's dictatorial regime. Written in Spanish and published in Chile during the dictatorship, they are technically complicated works that demonstrate how the shadow of censorship forced Chilean authors to break away from literary traditions.

Referred to as experimental and enigmatic, these works on their most basic levels represent "language in crisis". *Lumpérica* and *Purgatorio* are works of art that demonstrate how language has the ability to overcome barriers, but not without costs (broken syntax, loss of clear meaning, etc). My research analyzes these powerful works of literature to understand how they not only use language in novel and interesting ways because of censorship, but to understand how they represent the struggle within Chile to cope and comprehend the dictatorship. These texts serve a purpose in mourning over the loss of democracy and the loss of life, but they also serve in imagining a transition between democracy and dictatorship. Analyzing these texts in an effort to understand those two very different roles will ultimately help us understand the cultural power and importance of literature in denouncing repressive governments.

*El Mercurio*, the most important Chilean daily newspaper played a part in supporting the dictatorship. Authors like Eltit and Zurita chose to do the exact opposite. My research will conclude that these works played a role in the societal act of mourning and serve in calling for a transition from dictatorship to democracy. The resulting original scholarship will examine *Lumpérica* and *Purgatorio* to explore the ideas presented above while using the critical works by Idelber Avelar and Frnacine Masiello. The research will be 30 pages or more and will be written completely in Spanish.

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#### STATUS

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Student

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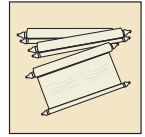
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Sergio Waisman

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# HUMANITIES

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## LAW SCHOOL

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### Decriminalization of Drugs in Portugal and Mexico: Lessons for Public Health

In 2000, Portugal enacted a law decriminalizing the possession of all types of drugs within certain quantities. Instead of being arrested and introduced to the criminal justice system, drug users are referred to a civil commission that determines the appropriate sanction for each offender. In addition, the Portuguese government authorized and funded harm reduction programs for drug users, including syringe exchange and drug substitution. After over ten years of this innovative scheme, rates of drug use and addiction in Portugal have declined in almost every category, including among youth and injecting drug users, while treatment admissions have increased. Furthermore, the rate of HIV among injecting drug users, which had been among the highest in Europe, has significantly decreased.

Portugal's decriminalization system, although not without shortcomings, provides important lessons for other countries trying to reduce the public health impact of drug use and suggests that decriminalization of drug use can be an impactful means of improving public health. This presentation will describe Portuguese decriminalization in detail and the impacts for public health in Portugal. It will then discuss how the lessons learned can be applied in other countries, particularly in Mexico, which has been ravaged by drug-related violence in the past decade. Comparisons will be made between decriminalization in Portugal and Mexico to demonstrate how different methods of decriminalization can produce very different outcomes. The presentation will conclude with recommendations on how to implement the lessons learned from Portugal into drug policy in Mexico to help reduce drug use, addiction, drug use-related violence and health consequences, and over-incarceration.

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Development in Tanzania: Patronage, Policy making and elections in the Multiparty System

In this paper, I examine how patronage influences modern Tanzanian development policy making. Patronage plays an important role in Tanzanian political economy. I assess the influence in two parts. First, I explore how patronage affects elections after the political reforms of the 1990s that introduced multiparty elections. Second, I explore how electoral politics shape development policy in Tanzania. In particular, I focus on how information is exchanged between the society and government to shape the policy, and how resources for development are distributed. Even though Tanzania switched to multiparty electoral system after the 1992 political reform, the former single party Chama Cha Mapinduzi (CCM) still uses patronage to maintain power trading material resources and opportunities for political support in elections, therefore influencing the economic development policy making. By examining information exchange and resource distribution, I will clearly see if in policy making the government favors specific groups that are critical to the elections. This research about Tanzania is a good development politics case study. Tanzania is a typical low income African country with high ethnical diversity, and has gone through series of events of independence, personal rule, and political reforms. A study about Tanzania will examine the common characteristics of most African countries, and help us with development politics studies in Africa. The research is still undergoing, and no final conclusion has been made at this point. However, I expect that certain patterns of information sharing exist, interest groups' messages are important to policy makers, and resources are distributed skewed to interest groups in some degree. I expect that patronage does influence policy making in Tanzania.

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### Building an International Language of Dance: A Comparative Study of Dance in Conflict Around the World

This study is based on previous work in Northern Ireland seeking to understand why, how, and whether a dance project commissioned by the Northern Irish government had been effective in reconciling boundaries among conflicting groups during and following the Northern Irish Troubles. While conducting research, the researcher became involved in a project with US and Afghan youth that used dance as an international community-builder. Involvement in this project raised questions: Could dance, effective in Northern Ireland, work in Afghanistan to reconcile boundaries among conflicting groups? How do historical, cultural and religious contexts affect the answer?

With little existing research to answer these questions, the researcher chose to pursue an exploratory study that would begin to answer them. In combination with the Northern Irish study, the Afghan study lent itself to a comparative analysis of dance in conflict settings around the world and how it may or may not work as a community-builder. These topics comprise the subject of research.

Though research is ongoing, one conclusion may be drawn from data collected thus far: while the researcher began the study believing that dance is a universal panacea for conflict, the researcher has learned otherwise. While in many situations dance holds constructive capacity as a community-builder, it can also be divisive. However, while dance may not be a universal panacea, the researcher's data has demonstrated that dance's capacity as a universal language can still build constructive intra- and international relationships in many instances. One example of the far-reaching voice of dance is the recent "Gangnam Style" song-dance video that has received over 1.3 billion views worldwide. That 1.3 billion people have viewed the same dance and are connected through a common "Gangnam Style" experience in itself speaks to the importance of dance as a universal language with tremendous potential warranting further research.

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## Libya's Transition to Democracy: Bridging Institutional and Governance Gaps

LIBYA IS A COUNTRY IN TRANSITION. By the official start date of the transition process on October 23, 2011, Libya was essentially devoid of the institutional capacities required to operate a functioning state in the traditional Weberian sense. Indeed, the weak central state has led some observers to anticipate the transition to democracy doomed, but this factor has in some sense facilitated a clearer break away from authoritarianism. Freedom from engrained institutional constraints has in many respects allowed Libya the unique opportunity to state-build from a tabula rasa; there are no preconceptions as to how that democratic state should be or the sequencing and methods it should employ to achieve it. Taking into consideration its institutional weakness and the steps that the country's transitional bodies have taken thus far toward establishing a post-Qadhafi state, is Libya on a trajectory towards a successful transition to democracy?

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### Foreign Intervention and Outcome in Civil War: The Afghan Civil War (1978-1992)

#### BACKGROUND:

Foreign intervention is one of the main characteristics of the Afghan Civil War of 1978-1992, but it is scarcely unique. As many as 71% of all civil wars involve external support. Understanding how third-party intervention affects the outcome of ongoing civil wars can help draw useful lessons about civil war management and the current Afghan crisis.

#### OBJECTIVES:

This study explores the relationship between third-party intervention and civil war outcome in the Afghan Civil War. I argue that the ability of a foreign power to achieve its desired outcome to an ongoing civil war is determined by its capacity to affect the internal balance of political legitimacy in favor of its domestic ally.

#### METHODS:

I divide the Afghan conflict into four phases, and explore the impact of my independent variable - foreign intervention - on the dependent variable, the internal balance of political legitimacy. I disaggregate the latter as a combination of (1) intragroup cooperation and unity, (2) military coercion, and (3) control of the population

#### RESULTS:

We observe a correlation between foreign aid and the internal balance of political legitimacy, throughout the four phases. Despite the level of aid it provided to the Afghan government, the USSR was unable to solve internal disputes in the Afghan Communist party; its "scorched earth" strategy had an adverse effect on popular loyalty; and the Soviets were unable to upgrade the Afghan military in the long-run.

#### CONCLUSION:

Foreign interventions have an impact on the outcome of civil war, as revealed by the concept of the internal balance of political legitimacy. Foreign policy-makers should understand the internal dynamics of their domestic ally, and think about how their policies would rally popular support for them and how their use of military force could help build 'political assets'.

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### Rhetoric and Reality: An Analysis of Strategies and Models of Community Driven Development in Liberia

The effectiveness of international development efforts is under constant scrutiny. Many of the criticisms of these efforts center around arguments that development projects take a paternalistic approach that does not address real needs and often diminishes the agency and self-worth of the poor. In response to the many well-documented limitations of these strategies, many organizations are starting to favor community-based projects, maintaining that the greater control and investment people have in the project, the more likely it will be that the benefits will be inclusive and sustainable. The objective of this study is to compare the models that different aid organizations use in these 'community-driven development' efforts to examine whether the rhetoric of ownership and participation is in fact translated into reality in Liberia. Five participatory development projects were identified in Liberia as case studies, and interviews were conducted with three relevant stakeholder groups in each project: the NGO or agency staff, the local leaders of the project within the target communities, and the intended beneficiaries. Results showed that perspectives on the projects greatly differed between each of the three stakeholder groups. While the rhetoric suggests that community driven development strategies will lead to community ownership in its most complex and multidimensional form, in practice, this study showed that 'ownership' often takes on a superficial and contradictory meaning. One of the primary reasons identified to explain this digression in meaning was the persistent inequality that typifies power relations between NGOs and communities. Thus, this research calls into question some of the basic assumptions and strategies of the development community in Liberia today, and shows the need for additional critical discussion and research on the global movement towards a 'community driven development' model and its effects at the community level.

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### The Advances and Challenges of the Decriminalization of Abortion: A Comparative Investigation of Argentina and Uruguay

Unsafe abortion is the leading cause of maternal mortality in Latin America. Annually in Argentina and Uruguay, two of the most developed and wealthy countries in the region, women die from poorly performed abortions at incredible rates. In Argentina, abortion accounts for almost 1/3 of maternal deaths. Statistically, there are between 560,000 and 615,000 induced abortions per year, a figure close to the 700,000 deliveries per year (Bianco 1309). In Uruguay, the current estimate of the illegal abortion rate in Uruguay is 30,000 per year, compared to 64,000 annual births. (Abracinkas 2). An age-old and generally socially condemned practice, abortion has been strictly limited in Argentina and Uruguay due to a history of conservative governments and the strong influence of the Catholic Church. Most importantly, the practice of abortion has become an issue of class, rather than social consensus. Impoverished women, who are more likely to be victims of sexual violence or a lack of sexual education, are inclined to seek abortions from untrained practitioners out of desperation. The resultant complications (uncontrolled hemorrhaging, renal failure, uterine perforation etc.) place extreme burdens on the families of these women, and monetary responsibility on the hospitals that treat them.

Feminist mobilization to demand reproductive rights has grown in influence since the end of the military dictatorships in Uruguay and Argentina: 1985 and 1983, respectively. Particular impact is made by NGOs in Montevideo and Buenos Aires, which engage in lobbying and social organization tactics to promote the decriminalization of abortion. Limited rights have been gained in past years, such as the recent decriminalization of abortion in Uruguay. Nevertheless, such victories are met with equal challenges, such as the lack of abortion funds in national health care plans. This investigation seeks to explain such successes and challenges, by first examining the history of reproductive rights, gender theory, and the role of various governmental and nongovernmental bodies in the decriminalization process. It will also analyze complete legalization with consideration to the effect of poverty, the role of the church, and its potential international impact.

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### The First Year of Humala's Peruvian Impotence: Forced Equilibrism in Latin American International Political Economy

In this case study calling attention to the need to research the new concept of 'forced equilibrism', I contend that Peruvian President Ollanta Humala, as a limited representation of other developing small-country experiences, faces a non-traditional recipe of international economic constraints fluidly intermixing with restrictive demands from the domestic "state/society complex". The resulting conflict delineates the narrow political economic strategies that Humala has chosen from the limited range between the conceptual poles of "pragmatism" or "ideology". While many label him a strategic pragmatist, I contend that Humala should be seen as a 'forced equilibrist' with little independent agency as he navigates an ever more divergent "national role consensus". I base my research on the wealth of analytical knowledge from "critical theory", specifically the British tradition of international political economy (IPE), historical materialism, structuration theory, and constructivist modes like role theory, to describe the Peruvian iteration of the emerging trend in Latin America of 'forced equilibrism'. Methodologically, I focus on three seemingly disjointed "critical points": new mineral taxes to pay for increased social spending, neoliberal compromises alienating leftist support bases regarding free trade agreements and coca eradication, and the authoritarian abandonment of a previously balanced management of widespread protests against several key mining projects. Within each critical point and across the trend that together they illustrate, I take variables from limited traditionalist models to analyze the relationships between them using critical theory, in order to test my hypothesis of 'forced equilibrism', in which other actors essentially impose Humala's policy choices upon him.

I owe a special thanks to E. Cortazar, G. Sojo and O. Medina for their advice, edits, and constructive criticism. As well, I am grateful to Drs. J. Torres and J. Rudolph at the Pontificia Universidad Católica del Perú, as well as Congressman R. Reátegui, for granting me their time during my research and interviews in Peru. Finally, I am indebted to the Center for Economic Policy and Research, whose archives of Latin American news were an invaluable resource.

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### Facebook and the Development of a Political Consciousness in Post-Revolutionary Tunisia

Two years since the Tunisian revolution, political infighting, social divisions, and disappointment at the slow progress of the democratic transition mar Tunisian politics. Young people, the drivers of the 2011 revolution, feel excluded from the official democratic process. However, through their use of social media, more specifically Facebook, youth have developed a stronger political consciousness and have grown as a relatively unified constituency that is prepared to translate their online activity into public political movements. Through interviews with leading Tunisian political personalities and a 100-person survey with Tunisians between the ages of 15 and 25 in the three most politically active cities in the state, this paper explores how Facebook became routinized as a mainstream forum and a significant influence in youths' daily lives, thereby affecting their political consciousness and identity formation. Facebook gained legitimacy as a sociopolitical tool after the revolution, and through exposure to various ideas, discussion forums, and opportunities to organize and attend events and rallies, youth are developing strong political skills and their own foundations for sociopolitical decision making. The paper's exploration has ramifications for how Tunisian politics needs to be re-imagined in a post-revolutionary context.

The era of strictly street politics in the Arab world is over. Social media will become increasingly important for lobbying organizations, the international community, the Tunisian government, political parties, and candidates to achieve a better understanding of a growing and emerging constituency, as well as make predictive assumptions about Tunisia's political trajectory. Facebook in post-Arab Awakening states is not a passing fad and popular tool for revolutionary discourse and organization. Instead, it is a political tool of the future and will have a significant impact on whether or not the revolution's goals will be achieved or if the transition will continue to be marked by political fragmentation and stagnation.

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### Policy & the Real: the Semiotics of Statecraft

Statecraft can be conceptualized as the system by which a political body translates observed stimuli into policy responses. Realist and liberal conceptions of statecraft largely characterize the state as a path-dependent agent of response, which observes both material realities and precedents within the international order to craft accurate policy. However, this conception of reactive statecraft is problematic - within this observation phase, the policymaking process is dependent upon the production and dissemination of knowledge, which informs the decisions and practices of the state. However, the methods by which the state accumulates knowledge open the policymaking process to the possibility of distortion. This article argues that policymaking responds to an internally-constructed worldview, and that the state's intelligence-gathering faculties are the means through which that internal worldview is built. The constructed nature of the state's conception of the external introduces faulty and biased information in to the state's meaning-making process, while simultaneously rendering the external inaccessible to observation. Based in analysis of historical and contemporary predictive intelligence documents, the article applies social theory to observe the ways in which data gathering processes result in the construction of flawed state perceptions, and the subsequent impacts that these biases exert on the development of policy.

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### The Gap between National Law and Local Culture: Girls' Education in India

Many nonprofit organizations work in India to help provide girls with access to education, but not because the government fails to legislate. In 2010 the Right to Education Act was enacted, which declares education to be a human right and provides measures to enforce equal access to, and equal quality of, education for girls. My analysis of the Right to Education Act concludes that India has held to its legal obligation by addressing affordability and quality of education, suitability of location, and the creation of girl-friendly schools, which includes facilitating for health needs. However, India's law has not had the intended effect. A wide gap between access to resources in urban and rural areas remains; moreover, it takes more than a statute to change deeply embedded cultural attitudes toward girls and schooling. The role of the nonprofit is to fill the gaps between urban and rural areas and to connect people with their government, because the nonprofits work on a much more local level. This research is meant to reveal this divergent results as a means of helping future legislators to create effective laws that take local culture into account so that the laws can have their intended effects.

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### The Contributions of “Frauen für den Frieden” to the 1989 Peaceful Revolution in East Germany

Specific political events in the 1980s gave rise to an explosion of political protest and peace groups in the German Democratic Republic. This was impressive, given the autocratic nature of the East German state and illegality of political opposition. The Cold War, fall of the Berlin Wall, and reunification of Germany have been the focus of many historians. Little attention has been devoted to the role of women activists of the 1980s. One group, calling themselves “Frauen für den Frieden”, was founded in 1982 with the initial purpose of protesting plans to introduce mandatory military service for women. Their activities were also designed to expose the lack of transparency in East German government and make the world safer for their children.

This research explores the impact of this women’s movement on societal change in East Germany and the contribution of specific women to the political and social forces behind “Die Wende”, or “the turning point”, and subsequent fall of the Berlin Wall. Through letters and working papers written by “Frauen für den Frieden” as well as reports of the Ministerium für Staatsicherheit (Stasi) and interviews conducted with former group members in the summer of 2012, I analyzed the events and issues that turned these women into activists, focusing on their objectives and the consequences of their activism. I analyzed three parts of “Frauen für den Frieden”’s contributions in the 1980s. I explored the basis for the group’s foundation and examples of their activism, the role of two specific founding members, Irena Kukutz and Bärbel Bohley, and the impact of Stasi infiltration in the group. My conclusion is that women’s participation in social protest forced the East German government to stop viewing the counter-revolutionary protestors of the 1980s as fringe actors and begin understanding they represented a growing dissent within the population.

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### The Bangladesh Liberation War: Cold War Politics in South Asia during the Indo-Pakistan War of 1971

#### OBJECTIVES/BACKGROUND:

The Indo-Pakistan War of 1971 was the third of three wars fought between South Asian neighbors India and Pakistan since their independence from Great Britain in 1947. This conflict, though short in duration, played a much larger role in international affairs, as it served as a microcosm for the Cold War between the United States and Soviet Union. I am researching the impacts of the US-Pakistan and USSR-India relationships relative to the conflict; how did President Nixon's détente with Communist China play into the conflict? Why did India invade East Pakistan, despite opposition from the UN and US? How did the USSR maneuver the situation to protect its interests in South Asia? What was the spark that caused the initial civil war in Pakistan? Was the US aware of the atrocities of Operation Searchlight, a genocide of intelligentsia being committed by West Pakistani troops in East Pakistan?

#### METHODS:

I hope to answer these questions and more with a detailed study of the diplomatic records made available to by the US Department of State and Russian Foreign Ministry. The Foreign Relations of the United States documents include the transcripts of the discussions in the Oval Office between President Richard Nixon and his advisors, including Henry Kissinger; they also contain information on the messages sent by the US consulate in Dhaka. I also plan on researching the foreign relations of China and West Pakistan, and attempt to understand the role of Indian domestic politics in Indira Gandhi's decisions. Lastly, I want to research the decision-making process behind Operation Searchlight in East Pakistan.

#### RESULTS TO DATE/CONCLUSIONS:

My research has allowed me to conclude that the Indian government's decision to move into East Pakistan was both politically and morally motivated. Operation Searchlight's systematic massacre of intelligentsia in the east gave Gandhi an opportunity to weaken Pakistan as well as strengthen India's position in world politics. I still would like to research Nixon's rationale behind his support of West Pakistan.

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### Religiosity and the Ban on the Islamic Veil: The U.S. versus Western Europe

In 2004, the French government passed the so-called “ban on the veil,” prohibiting conscious signs of religious affiliation from public spaces. Almost a decade later, the ban continues to receive great support from the majority of French citizens and a majority of citizens in other Western European countries indicate they would approve of a similar ban in their own countries. Citizens in the United States, however, are strongly against such a proposal. This research will explore if differences in religiosity could contribute to the divergence found between these similarly secular and democratic countries. Raw data from the 2010 Pew Global Attitudes Project Survey was reformatted and analyzed using a cross tabulation test. Results indicated that there is a relationship between religiosity and support for the ban on the veil in the United States and Western Europe. Results showed that individuals who demonstrated a higher level of religiosity were more likely to disprove of the ban on the veil. While many studies have examined subjects like extremism and terrorism, little empirical research has been conducted on this particular relationship. Therefore, these results, while preliminary, should encourage further analysis of this relationship. They also indicate that differences in religiosity should be carefully considered in any cross-national analysis. Furthermore, this research suggests that religiosity could also critically contribute to levels of tolerance and, consequently, the success of immigrant integration.

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### Ghanaian Perspectives on the Effectiveness of U.S. and Chinese Development Aid

The China-Africa relationship has strengthened to the point that China is now Africa's largest trading partner and its foreign direct investment has soared to over USD 12 billion. This growing development partnership has become a critical international issue, as it presents two distinct possibilities: China's "no strings attached" aid policies could weaken already fragile democracies and worsen Africa's security situation, or they could outperform traditional Western aid policies and transform development practices.

This study compares the effectiveness of U.S. and Chinese aid by exploring Ghanaian perspectives. Ghana presents an interesting case study because of its continuously strong relationship with the United States, rapidly growing relationship with China, and status as one of the few stable, middle-income nations in Africa. Qualitative interviews with local NGO and civil society members, government agencies, and international institutions provided a broad assessment of Ghanaian perspectives, and an analysis of these interviews demonstrated the common perceptions supporting the hypothesis that Ghanaians believe Chinese aid is more effective.

The findings of this study conclude that compared to the United States, China is gaining a stronger foothold in economic assistance, one of the development sectors of greatest concern in Ghana. China has emerged as a greater source of investment as its economy continues to grow at a rapid pace, and Ghanaian companies are showing preference toward Chinese investment because there are fewer regulations with which they have to comply and they are able to retain greater autonomy. In addition, Chinese aid is often more visible to local citizens because of its focus on infrastructure, therefore, they perceive that China has done more. These advantages underscore the need for the United States to refocus its aid policies in Ghana if it wants to continue creating a positive economic impact on par with China.

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### Indian Security Policy Shifts in Conflict over Kashmir

The region of Kashmir has been the primary source of conflict between India and Pakistan since partition in 1947 and has been the focus of multiple armed conflicts and continuous political debate. Despite bilateral talks and international intervention, however, little progress has been made towards a long-term solution, and tensions remain high. Some scholars assert that there is no solution to the conflict beyond the current status quo, while others propose different strategies for furthering the peace process. This project attempts to add to the existing literature on the Kashmir conflict by offering an explanation for this lack of progress by pinpointing and analyzing shifts in Indian security policy at pivotal historical moments from 1947 until 2005. International, domestic, and individual explanations for the Indian decisions that have led to continued conflict will be highlighted. This research will show how an understanding of the determinants of Indian security policy towards Kashmir is useful to inform the current decisions of various players in the conflict.

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## Central limit theorem in Bernoulli trials and its relevant application

With the development of society, central limit theorem starts to draw people's attention. This paper mainly discusses the central limit theorem in Bernoulli trials and its application. The study shows, from both theoretical and practical perspectives, that the universality of Bernoulli trial determines the widespread use of central limit theorem in life. Then by studying the origin of the normal distribution, the author investigates the fundamental relation between the normal distribution and the binomial distribution and explains why normal distribution is able to precisely express binomial distribution under certain conditions.

Then, in order to discuss the application of central limit theorem, another important distribution in the theory of probability -- Poisson distribution - is introduced. By making comparison between Poisson approximation and normal distribution approximation in theoretical and practical occasions, the author has found the connection between the two and their respective scopes of application. Finally, by examining some typical examples in daily life, the paper illustrates the widespread use of central limit theorem in reality.

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## The Role of Serotonin in Embryo Gastrulation

**OBJECTIVES AND BACKGROUND:**

During gastrulation in animals, a blastula embryo is reorganized into a three-layered gastrula, and different organs then develop from these germ layers. Despite its importance, the mechanisms that initiate cell movements during gastrulation are unknown. Preliminary studies from Dr. Brown's lab on sea urchin embryos (Kamali et al., 2010; Scully et al., 2010) show that levels of the neurotransmitter, serotonin (5-hydroxytryptamine, 5-HT) peak immediately prior to gastrulation, and serotonin inhibitors block gastrulation. These studies suggest that serotonin may be the molecule that initiates the gastrulation process in these early embryos. In adult nervous tissue, serotonin receptor molecules bind serotonin and mediate its function. In this study I propose to determine the intraembryonic location of serotonin as well as the levels and location of serotonin receptor mRNA molecules (precursor to the receptor) in various stages of sea urchin embryos prior to and following gastrulation. If serotonin mediates gastrulation, these receptors and serotonin itself should be present in the specific embryo cells that are involved in the gastrulation process.

**METHODS:**

Sea urchin eggs are fertilized in vitro, and embryos are cultured to blastula, gastrula and postgastrula embryonic stages. The amount of serotonin receptor mRNA molecules in each stage is determined by quantitative polymerase chain reaction (qPCR). In situ hybridization is used to determine where these mRNA molecules are located within embryos. In this procedure a portion of the receptor gene is cloned and used to produce an antisense receptor RNA molecule that will bind specifically to the receptor RNA. The antisense RNA is then tagged with a fluorescent probe and visualized by confocal microscopy. Serotonin is tagged with a serotonin antibody, and its intraembryonic location is determined by confocal immunofluorescence microscopy.

**RESULTS TO DATE:**

Primers for the PAHTPH and TPH serotonin receptors have been created and sequences for the receptors have been identified in the developmental stages.

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## Characterization of genotype-phenotype mapping of biological networks reconciles robustness-evolvability paradox

Typical biological system is both highly robust and highly evolvable. Yet robustness appears against changes whereas evolvability for changes. The concurrence of these two seemingly incompatible features is a central paradox for contemporary evolutionary biology. Using a Boolean model of yeast cell cycle networks, we quantitatively determine (1) the genotype-phenotype mapping. Here genotype stands for the network structure and phenotype for its dynamics; (2) the precise topology of neutral network, i.e. the interconnecting network of networks of different structures but the same dynamics; and (3) the number of new phenotypes in the vicinity of a neutral network. Our results demonstrate that both biological genotype and phenotype are atypical. We next show via sampling that all neutral networks exhibit a similar topology that is simply connected, fractal and sloppy (stiff in certain dimensions but diffusive otherwise). This percolating nature of neutral network leads to a positive correlation between robustness and evolvability and hence resolves the paradox. A likely explanation for such a correlation is that higher robustness results in a larger neutral network, measured by its designability and radius of gyration, which in turn accesses more new phenotypes.

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### Development Of Gas Electron Multiplier Based Time Projection Chamber To Replace Multiwire Projection Chamber In MAMI Crystal Ball

#### BACKGROUND:

Research was done at the Johannes Gutenberg University, Institute for Nuclear Physics, in Mainz, Germany, at the MAMI electron accelerator.

#### OBJECTIVE:

Equipment development project looking for a faster and more reliable replacement for the multiwire projection chambers (MWPC) in the Crystal Ball. With the Gas Electron Multiplier (GEM) based Time Projection Chamber (TPC) you will be able to perform a whole series of experiments that require higher beam rate and better resolution. One such experiment is the search for the  $f_0$  and  $a_0$  mesons.

#### METHODS:

Development of a new TPC modeled after the Karlsruhe, Germany TPC, and a series of ROOT based simulations to determine ideal orientations and component sizes.

#### RESULTS:

The project is still in the process of being run, and data has yet to be gathered.

#### CONCLUSION:

TPC, GEM sheet, and receptors are built. Simulations still running in order to develop needed circuitry, and run preliminary tests in electron accelerator.

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### Wernicke's and Broca's area homologues in an enculturated bonobo (*Pan paniscus*)

The evolution of neural changes related to the emergence of human language and communication are still poorly understood. In this study we examined cortical language area homologues from the postmortem brain of an enculturated bonobo (*Pan paniscus*) that was raised in captivity and was surrounded his entire life by relatives and other apes that were capable of using a lexigram symbolic communication system. Although he lived in this enriched environment, this 8 year old bonobo did not develop language capacities. Humans and bonobos share 98 percent genetic similarity; therefore, this ape provides a unique opportunity to examine the modulating effect of a language-rich environment on the brain of a species that is among humans' closest living relatives. We defined the cytoarchitectonic boundaries for area Tpt, which is a part of Wernicke's area, and Broadman's area 44 and 45, which comprises Broca's area, in both right and left cerebral hemispheres. Boundaries of interest were identified using serial Nissl stained sections. Design-based stereologic methods were used to determine cortical region volumes, neuron densities, and neuron numbers. Leftward asymmetry in regards to neuron counts was shown in our findings, which is comparable to standard laboratory-reared chimpanzees; however, the degree of asymmetry in this bonobo subject within area Tpt was greater than the range that has been previously observed in a sample of 12 chimpanzee brains. Our findings play an important role in helping to reveal the neuroanatomical changes that occurred after divergence from the last common ancestor of bonobos, chimpanzees, and humans. This project provides strong support for the need to perform further focused studies on more bonobo subjects.

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### Sustainability of Indigenous Iñupiat Ice Cellars (Sig-uaq): A Case Study from Barrow, Alaska

Ice cellars, or Sig-uaq, are excavated into perennially frozen ground, or permafrost, which provides natural refrigeration for whale and other game harvested for subsistence by the indigenous Iñupiat people in Arctic Alaska. This method of food storage has been employed by the Iñupiat for over 1,000 years and continues to be essential to their native life style as it provides secure, accessible year-round frozen storage. However, over the past two decades reports have emerged describing ice cellar failures (including instances of flooding and collapse) thought to be caused by increasing air temperatures due to climatic change.

The village of Barrow, Alaska, was selected for a case study as it is a traditional Iñupiat whaling community with over 60% Native Alaskan residents as of the 2010 census. Five ice cellars were instrumented with HoboPro® miniature temperature data loggers recording internal cellar air temperatures at hourly intervals. After seven years of monitoring, the internal air temperatures appear relatively stable. These results raised the question of how representative the instrumented cellars are of others within the community.

To answer this question, an effort to map all of the ice cellars in Barrow was undertaken with the assistance of the North Slope Borough's Department of Planning and Community Services. In August 2012, a series of interviews, community meetings, and a visual vehicle-based survey were conducted in order to catalogue and map the locations of ice cellars within the village. The resulting map product was shared with the collaborating local government and will be used in public health studies, permitting of construction projects, by snow removal crews, for ice cellar preservation, and in future research on climate-change impacts.

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# NATURAL SCIENCES

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### Analysis of Daasanach growth in relation to ecology and subsistence strategy

Body size is highly variable among modern human populations, influenced by the interactions between genetic information and external nutritional and environmental variables during growth. Across traditional societies a relationship between life history strategy, relative adult body size, and extrinsic variables (e.g. ecology, subsistence strategies) has been documented and serves as a theoretical foundation to explain observed variability. However individual populations are known to deviate from this pattern. Data on height and weight were taken from an ontogenetic sample of Daasanach individuals (n=223) from Ileret, Kenya to test the null hypothesis that the Daasanach conform to the expected growth timings, trajectories, and adult body size parameters for traditional populations of similar ecologies and subsistence strategies. Mean male adult body size was compiled for twenty comparative traditional societies among which stature differed significantly among ecological groups. Our results indicate that Daasanach mean adult male height falls within the parameters for the group of populations with similar ecologies (savanna, desert, dry forest; Z score=1.46), and falls beyond the group of ecologically dissimilar (tropical and neotropical forest, coastal) populations (Z score=4.04). Additionally, Daasanach obtain a lower percentage of adult stature and mass at age 10 compared to other populations, suggesting a delayed growth trajectory. Our results demonstrate that while the Daasanach mean adult male stature is consistent with predictions based on ecology, they raise interesting questions regarding why the Daasanach might deviate from predictions of life history strategy in relation to subadult growth.

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# NATURAL SCIENCES

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### Foot strike patterns vary with running speed in the habitually unshod Daasanach of Ileret, Kenya

Humans and our ancestors have engaged in running for millions of years, but it was not until recently that we did so wearing shoes. It has been argued that habitual barefoot running (today and in our evolutionary past) may necessitate a biomechanical strategy in which runners utilize a forefoot strike (FFS), in order to mitigate the high impact forces and potential risk of repetitive stress injury associated with a rearfoot strike (RFS). However, recent research has shown that FFS running is not typical in a habitually unshod Daasanach population (Ileret, Kenya), and running speed, among other factors, influences variation in strike patterns. Because substrate compliance has been shown to influence strike patterns in shod runners, and the previous study was conducted on a firm pressure pad, in this study we analyzed foot strike angles in a sample of six consenting, habitually unshod Daasanach adults when running on a natural surface trackway. Subjects were asked to run at their preferred endurance running and sprinting speeds while their foot strikes were filmed with a high-speed (240 Hz) camera. In accordance with previous results, the majority of Daasanach subjects used a RFS, and never used a FFS, at endurance speeds. Our results show that foot strike angle is significantly correlated with running speed ( $r = -0.63$ ,  $p < 0.0001$ ) in the Daasanach, with more midfoot strikes and FFS at increased speeds. This study further supports the hypothesis that running foot posture varies across habitually unshod populations and can be influenced by running speed.

Funding for this research was provided by GW Luther Rice Undergraduate Research Fellowship, The Leakey Foundation, the National Science Foundation grants DGE-080163 and BCS-1128170, and The George Washington University Office of the Vice President of Research Undergraduate Research Award.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Dendritic Morphology of Pyramidal Neurons Across the Visual Stream: A Direct Comparison of Chimpanzees and Humans

The morphology of pyramidal neurons in human and chimpanzee cerebral cortex has previously been demonstrated to increase in dendritic complexity and spine density in cortical regions of increasing neural integration, such as prefrontal cortex. The role of brain size scaling on the elaboration of dendritic arbors has been difficult to interpret, however, in part because of the wide diversity of regions previously studied. The present study examines variation in the dendritic morphology of pyramidal neurons between humans and chimpanzees within a functionally-related processing stream of ventral visual regions. Cortical samples from three different visual regions representing increasing integration (V1, V2, and fusiform gyrus) from four chimpanzees and four humans were stained with the rapid Golgi technique. Ten neurons from each region of each individual were traced with NeuroLucida software, for a total of 240 neurons.

The following measures were analyzed: soma area, total dendritic length, mean dendritic segment length, dendritic segment count, dendritic spine number, and dendritic spine density. Univariate analyses indicated that many measures of dendritic complexity increase along the processing hierarchy in both species; however, a repeated measures ANOVA revealed there were no significant species differences in the pattern of regional variation according to any of these measures ( $F=.553 \leq x \leq 4.331$ ,  $P=.083 \leq x \leq .485$ ). These findings suggest that the pyramidal neuron morphology underlying neural integration along the levels of the ventral visual stream of the neocortex is similar in humans and chimpanzees.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### A Genome-Wide Survey of the Expression Patterns of Na<sup>+</sup>/Ca<sup>2+</sup> Exchanger Genes in *Caenorhabditis elegans*

#### BACKGROUND:

Calcium acts as an important messenger in cells, and must be properly regulated. One key mode of regulation is through the use of exchanger proteins. These proteins include the Sodium/Calcium (Na<sup>+</sup>/Ca<sup>2+</sup>, NCX) exchangers, the Sodium/Calcium/Potassium (NCKX) exchanger proteins as well as the Calcium Cation exchanger channels (CCX) which catalyze both Na<sup>+</sup>/Ca<sup>2+</sup> and Li<sup>+</sup>/Ca<sup>2+</sup> exchange. These channels are membrane proteins that serve to balance intracellular calcium levels, which is paramount in achieving homeostasis and health within all cells. It is clear that NCX, NCKX and CCX exchangers are present in the plasma membrane of many human tissue cells, and have been implicated in cardiac disease, ischemic events and Parkinson's disease. Additionally, they play an important role in Ca<sup>2+</sup> regulation during development and regulate cardiac activity throughout the organism's life<sup>1</sup>.

#### OBJECTIVE:

However, despite their relevance, very little is known about the structure and regulation of these exchangers<sup>2</sup>. Attempts to study sodium/calcium exchangers in mammalian systems have proven difficult due to the low viability of mutants, further illustrating the importance of these exchangers within the organism. Here we aim to use *Caenorhabditis elegans* as a model to study sodium/calcium exchanger biology.

#### METHODS:

*Caenorhabditis elegans*, which possesses a simple nervous system and a completely mapped neural wiring diagram<sup>3</sup> provides an optimal platform to investigate the neural circuits affected by the NCX/NCKX/CCX gene family. By using *C. elegans* to study the exchanger genes we have been able to further investigate the molecular diversity and genomic organization of the genes through exploration of online databases, as well as examining tissue expression of exchanger genes.

#### RESULTS AND CONCLUSIONS:

Through the creation of sodium/calcium exchanger gene specific *gfp* reporter constructs<sup>4</sup>, we have successfully identified the regions within this organism that express each sodium/calcium exchanger gene, providing a solid foundation for further research on this gene family.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### A preliminary radiographic analysis of dental development in Virunga mountain gorillas (*Gorilla beringei beringei*) from Volcanoes National Park, Rwanda

Investigations of dental development have figured prominently in attempts to reconstruct fossil hominid life histories. However, comparative data from extant wild great apes of known age remain scarce, particularly from species other than chimpanzees. We report initial results from the first radiographic examination of dental development in wild Virunga mountain gorillas (*Gorilla beringei beringei*), using a well-documented sample of skeletons recovered in Rwanda. Virunga mountain gorillas are the least frugivorous among great apes and, despite their large size, show earlier ages at weaning and first birth. Thus, they provide a unique opportunity to test relationships between dental development, socioecology, and life history among hominoids. We test the hypothesis that mountain gorillas are accelerated in dental development, as they are in other life history traits, compared to chimpanzees. We collected radiographs of mandibular dentitions using a Nomad Pro portable dental x ray, from 16 individuals of known sex and age (0.0-14.9 years). Molar crown and root calcification status was scored following an eight-stage system (Kuykendall, 1996; Demirjian et al. 1973). In only one case did crown calcification stage fall outside of the age range reported for captive chimpanzees (Kuykendall, 1996). Differences were more commonly observed in root formation, where calcification stages were reached at later ages in three mountain gorillas. While these results do not support our hypothesis, future studies will incorporate an expanded sample and more refined staging system. Associated individual records also provide opportunities to test links between dental development, life history and health status in this population.

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## The cosmic snail: spiral structure from the intra-binary shock of the gamma-ray binary B1259-63

B1259-63 is a binary star system in which a pulsar (neutron star) orbits a massive companion star. Both stars emit energetic winds powered by the rotational kinetic energy of the stars. As these winds collide and interact with each other, the pulsar's wind is separated from its companion's wind by an intra-binary shock. This shock causes the pulsar's wind to form a tail that winds around the high mass star.

The wide, highly eccentric orbit of this rare binary allows us to study the interaction between the highly relativistic pulsar wind and much slower and heavier companion wind as a function of separation between the two stars. This provides a way to probe the properties of the winds such as composition and magnetization and learn about the physics of relativistic shock waves.

We have obtained X-ray images and spectra of the binary system with the help of Chandra X-Ray Observatory (CXO) – one of the NASA's flagship space missions. In the current study we focus on modeling the spatial structure of the interacting winds and comparing it to the actual CXO images. Our modeling suggests that the pulsar's tail shape can be satisfactorily described by a ballistic flow model with the flow speed of 2% of the speed of light. Unlike earlier theoretical models whose results lacked comparison with any imaging data we find that the spiral structure of the flow is not destroyed by the Coriolis force and little mixing between the two winds occurs out to a distance of 5,000 AU (much larger than the size of the orbit - 70 AU). The change in the morphology of the extended X-ray emission seen between the two CXO observations suggests the magnetic field of ~2 mG (in the pulsar wind).

Thus, the current analysis of CXO images provides a realistic model for interacting winds in the binary systems of this type. It also advances our further understanding of pulsar winds, Be star winds, and shock physics. The study we have undertaken is unprecedented, it can only be for B1259-63 with CXO, and it is the first time when the colliding shock structure in a binary has been resolved in X-rays.

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### Using Temperature Data to Make Measurements of Snow Depth and Duration

Snow in the Arctic is of crucial importance to the annual energy balance. Its measurements are essential for the study of climate, microtopography, and ground characteristics in the region. Yet, the harsh weather conditions of the Arctic and the remoteness of the region have made taking measurements of snow challenging. For this analysis long-term temperature data was utilized from a series of micro-topographic sites in a north-south transect representative of the different primary climatic gradient of the North Slope of Alaska. Both ambient air temperatures and the variation in soil-surface temperature amplitudes allowed for the determination of winter snow cover duration, and the dates of snow onset and snowmelt. In order to obtain snow depth measurements, a series of Thermochron IButton® temperature loggers were arranged vertically on a series of stakes and installed at the sites in August 2010. The average daily temperatures recorded by the iButtons were used to interpret snow cover duration and snow depth. The low success rate of the iButtons during their first year prevented snow depth measurements from being made, but better results during the second year allowed for further analysis.

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## A Tree-Like Network Leads to “Cost-Free” Adaptation with Limited Robustness

Our recent study of biological adaptation showed that, for the Negative-Feedback-Loop (NFL) aided sensory adaptation processes, energy is constantly dissipated to accurately process information, and there exists an exponential equation that defines the best possible performance-to-cost (tradeoff) relation between the energy dissipation rate, the adaptation speed and the adaptation accuracy (the ESA relation). In this work, we construct a tree-like biochemical network that operates at equilibrium yet still show ability for adaptation. We further demonstrated that such “cost-free” system has limited robustness that can only operate accurately in a narrower signal region comparing the NFL systems, and its performance is sensitive to both the rate parameters as well as the type of perturbations. Interestingly, individual Ryanodine receptors (RyRs) in Cardiac muscle cells were proposed to utilize a similar mechanism for gating regulation of Calcium flux out from the Sarcoplasmic Reticulum (SR), where the Calcium signal to trigger the opening of RyRs (e.g. Calcium-Induced-Calcium-Release) is accurately “pretuned”. These results suggest that living organisms could use such tree-like network as an alternative mechanism to achieve fast and accurate adaptation.

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## SAXS Studies of Tetra-Nucleosome Arrays

Chromatin conformation and dynamics is central to gene functions including packaging, regulation, and repair. At the molecular level, the basic building block of chromatin is a nucleosome core particle (NCP) made of ~147 base pairs (bp) of dsDNA wrapped around an octamer of histone proteins. These NCPs are connected by short 10-90 bps of linker DNA as beads on a string. Key factors determining the packaging of NCP arrays to form chromatin include ionic condition, linker DNA length, and epigenetic modifications, especially of the histone tails. We have investigated how the conformations of model tetra-NCP arrays are modulated by these factors using small angle x-ray scattering (SAXS). Here we present recent studies of the effects of ion (KCl and MgCl<sub>2</sub>), linker length, and histone modification (tail deletions) on NCP arrays. Our SAXS measurement makes it possible to learn about both the global compaction of NCP arrays and local inter-NCP spatial correlations within the same array.

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## Automated building of three-dimensional RNA structures

RNAs have been found to be involved in many biological processes. Difficulties of experimental determination of tertiary structures of RNA limit our understanding of their biological functions. Therefore, some computational methods of building tertiary structures of non-coding RNA have been proposed. However, current algorithms of RNA tertiary structure prediction give satisfactory accuracy only for small size and simple topology and many of them need manual manipulation. Here, we present an automated and fast program, 3dRNA. Since the organization of RNA structure is largely defined by topological constraints encoded at secondary structural level and tertiary contacts, we build the RNA tertiary structure from the smallest secondary elements (SSEs) by using a two-step procedure. We first assemble the SSEs into hairpins or duplexes and then into complete structure since the tertiary structures of hairpins and duplexes usually can be built with a high accuracy. We also use a network representation of the secondary structure to describe the locations and connectivity of the SSEs, which makes it easy to implement the assembling process automatically. In a benchmark test with known crystal structures, 3dRNA can give predictions with reasonable accuracy for RNAs of larger size and complex topology.

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## Role of endosymbiotic bacteria in the insect immune response to pathogenic infections

Endosymbiotic bacteria reside in almost all eukaryotic organisms. In insects, endosymbionts may confer certain fitness advantages to their hosts, such as nutritional effects on the host and protection from parasites or pathogens. *Wolbachia pipientis* and *Spiroplasma poulsonii* are well-known endosymbiotic bacteria, which are able to manipulate the reproductive properties of their hosts. These endosymbionts have recently been shown to interfere with the insect immune response to bacterial and viral pathogens. However, it is currently unknown whether these endosymbionts enhance or reduce the insect immune response to nematode parasites. In addition to carrying beneficial microbes that enhance various physiological functions in the host, insects are also infected by bacterial pathogens and parasites that interfere with immune defense mechanisms. The bacterial species *Photorhabdus luminescens* lives within the nematode parasite *Heterorhabditis bacteriophora*, which is able to invade and kill insects. Because *Heterorhabditis* nematodes are viable in the absence of *Photorhabdus*, each partner of this symbiotic/pathogenic relationship can be separated and studied in isolation and in combination, thus enabling the host immune responses against each player of the interaction to be studied alone or together. We have recently established an assay for infecting *Drosophila melanogaster* and *Drosophila neotestacea* adult flies with the nematodes and their bacteria, separately or together. We have obtained *Drosophila* strains carrying *Wolbachia* endosymbionts only, *Spiroplasma* endosymbionts only, both *Wolbachia* and *Spiroplasma* bacteria as well as strains lacking the endosymbiotic bacteria. We have hypothesized that the presence of endosymbiotic bacteria may improve pathogen surveillance, allowing for rapid recognition and elimination of pathogens that invade the fly. We will provide evidence that *Drosophila* flies containing endosymbionts show increased resistance to infection with the two pathogens. Our long-term goal is to identify the molecular basis of any changes that occur in the immune response of flies harboring endosymbiotic bacteria in the presence and absence of pathogenic infection.

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## Development of Ohmic Contact for p-InP Solar Cell

Photovoltaics have a wide range of applications. They are used to power satellites, employed by some as portable, rechargeable batteries and to generate electricity for cities just to name a few. In order to maximize power extraction from incident photons, the device's resistance should be as low as possible. One area that has an enormous impact on the overall resistance is that of the metal-semiconductor junction. This resistance is referred to as the specific contact resistance ( $\rho_c$ ). Small fluctuations here can greatly affect the overall performance of the system.

We investigate a Au/Zn stack on p-type Indium Phosphide (p-InP) over a range of annealing times and temperatures. We performed all processing and testing in a Class 100 Clean room to ensure minimal contamination. Subsequent measurements were performed using the Transmission Line Measurement (TLM) technique with a four point probe. We measured our lowest value of  $\rho_c$ , the specific contact resistance to be  $1.344 \cdot 10^{-4} \Omega\text{-cm}^2$  when annealed for 165s at 420°C. Analyzing our results, we predict the metallization stack will achieve a minimum  $\rho_c$  on the order of  $10^{-5} \Omega\text{-cm}^2$  when annealed for 160s at 408°C. It should be noted that further research is warranted to determine the effectiveness of this Au/Zn stack as an ohmic contact on p-InP and to explore more thoroughly what caused spreading of metal between the contact pads on some samples post-anneal.

This work was performed in collaboration with the United States Naval Research Laboratory in Washington, DC.

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### A Novel Gene, WBP2NL, Affects Early Neural Development

We performed a microarray screen to identify novel mRNAs that are localized to the embryonic cells that will give rise to the ectoderm. One of these codes for WBP2NL, a protein that contains a WW-domain binding domain, and whose function has not yet been identified. It appears to be involved in some regulation of the size of the epidermis versus neural plate domains in the embryo. Loss-of-function studies with morpholino oligonucleotides injected into dorsal blastomeres, which give rise to the neural plate, resulted in the expansion of the neural plate and reduction of the neural crest and epidermal domains. Gain-of-function studies, by injecting synthetic wild-type mRNA are underway to further characterize its role in development. Using several bioinformatics tools we have identified the gene structure of exons, potential microRNA binding sites, as well as a number of potential neural plate specific transcription factor binding sites in the upstream regulatory region. Greater understanding of the function of this gene during development may provide us with the information needed to modify neural stem cells for our benefit.

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## Cascade-likeness is an intrinsic property of biological processes

A central theme in systems biology is to reveal the intricate relationship between structure, dynamics, and function of biological networks. The biological function is usually realized by the transformation of the relevant molecules through their interacting network. We name this trajectory of transformation as a biological process. In contrast to the structure-centric approach, we take a process-centric view to address such questions as what a biological process looks like and how it differs from an arbitrary process. As an example, we studied a simple Boolean model for the cell cycle process of budding yeast to characterize a large number of putative processes. This computational task was made possible by some highly efficient algorithms we developed. Our results demonstrated that the biological process is very robust and highly designable. Moreover, we uncovered two dynamical rules that dramatically enhance the robustness and designability. Finally, all processes in a system of small size were enumerated and highly designable processes are cascade-like. This implies that cascade-likeness is an intrinsic property of biological processes.

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## A t-Statistics Method of Assessing Cluster Accuracy

Cluster evaluation is a cumbersome task due to the mismatch of the cluster labels obtained by clustering techniques and the exact labels of the known clusters. This paper proposes a new method for re-indexing cluster labels obtained by clustering techniques and efficient matching with the known cluster index. The new method is based on a t-statistics measure computed on the information from the exact cluster and the obtained ones by clustering techniques. A good matching strategy is to consider the smallest t-value between two clusters and then the cluster label is replaced by the exact label. We considered simulated and real data sets to test the algorithm and compare the results with existing cluster evaluation techniques.

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## Using a Learning Tree Decision Algorithm to Classify Celestial Objects

With the advent of new kinds of ground- and spaced-based telescopes there has been a major influx of data concerning the myriad of objects (sources) we can detect and investigate in space. One would spend an enormous amount of time classifying these objects by their physical nature if the classification to be done on the source-by-source basis by humans. In order to alleviate this issue we have taken a radically different, more modern approach of automated classification.

Our ultimate goal is to use an intelligent machine-learning algorithm, known as Learning Tree Decision Algorithm (LTDA), to perform classifications for 50,000 X-ray sources detected by the Chandra X-ray Observatory. We first assembled a training data set with 400 known X-ray sources. For each of these sources, the dataset includes 10 multiwavelength parameters (properties) that will be used for automated classification into 5 types of objects (main sequence stars, Wolf-Rayet stars, active galactic nuclei, X-ray binaries, and neutron stars). Next, we ran internal tests to verify that the LTDA performs as expected. The results are inspected by plotting source properties in 2D slices of 10-dimensional parameter space and observing known types of objects clustering. We then used the X-ray sources from XMM-Newton observations (Lin et al. 2012) to verify the classifications they present using our LTDA procedure. We were able to verify their classifications within their error rates. Here we will describe our training data set and present the results of these verification runs.

As a next step we attempt classifying unidentified sources in the supernova remnant (SNR) G352.7-0.1, observed by NASA's Chandra X-ray Observatory, with the goal to discover a compact object (neutron star or black hole) left after the supernova explosion. We have identified a plausible X-ray counterpart or compact object and will present the results of our classification.

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# NATURAL SCIENCES

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### Longitudinal Weight Calibration for Cross Sectional Surveys

The National Science Foundation's Survey of Doctorate Recipients is conducted every two or three years and collects detailed information on thousands of individuals receiving PhDs in science and engineering in the U.S. and some others with PhDs from abroad in these areas. Survey weights adjust for oversampling of select groups and nonresponse on a cross sectional basis. A significant portion of the sample (e.g., 60% on 3 or more surveys from 1993-2006) appears in multiple survey years and can be linked across time. No longitudinal weight exists that would enable estimation of statistical models or comparison of finite population characteristics using data from multiple survey waves together. This poster presents a method for survey weight calibration for the purposes of enabling longitudinal analysis using multiple survey waves. Theory, simulation results, and application to NSF survey data are presented. Methods presented here have potential applications in several large-scale federal surveys.

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### Impacts of climate change on permafrost and human populations in Siberia

Climate change is impacting humans around the world. This is especially the case in the Arctic where climate is changing at a faster rate compared to the rest of the world. Although populations in the Arctic are often characterized as small subsistence communities, there are also large communities living in urban centers. In Russia more than 70% of the population in Northern Siberia lives in urban areas. Urban areas depend on the strength of the frozen ground, or permafrost, to support their large foundations. As permafrost thaws, due to any number of factors including climate change, this reduces the ability of the soil to support the built environment. This project looked to quantify the ways in which climate impacts these population through the changes in bearing capacity. In this project 6 fully coupled general circulation models (GCMs) from the recent Intergovernmental Panel on Climate Change (IPCC) model inter-comparison project were used in order to look at the differences in bearing capacity. GCMs are the best tool available in modeling future climates, but they also have large uncertainties. No single model is adequate in looking at future climates so an ensemble was used to see how the uncertainties in the climate models translated to uncertainties in the bearing capacity. The results are a series of maps that delineate areas of different degrees of uncertainty in Siberia.

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## Proliferation of Coelomocytes and a Search for their Source in the Purple Sea Urchin

Coelomocytes in the purple sea urchin, *Strongylocentrotus purpuratus*, are immune cells that respond to pathogens by phagocytosis and encapsulation. In agreement with previous studies, we found up to a 6-fold increase in the number of coelomocytes when sea urchins were challenged with heat-killed marine bacteria, *Vibrio diazotrophicus*. However, it was unclear whether the increase in coelomocytes resulted from proliferation of new immune cells, the release of pre-existing cells into coelomic fluid (CF), or both. Therefore, we developed a method to measure proliferation of coelomocytes using ethynyl deoxyuridine (EdU), which is a synthetic thymidine analogue that is incorporated into DNA during DNA synthesis. Sea urchins were injected either with EdU (n=3) or with EdU plus *Vibrio* (n=3), and samples of whole CF containing coelomocytes were withdrawn each day for 15 days. Coelomocytes were fixed, permeabilized and stained for EdU, nuclear DNA and actin. Evaluation of the percent of total nuclei that were EdU-labeled indicated that EdU-labeling was higher in immune-challenged animals, but only accounted for at most 9% of coelomocytes that appeared after challenge, suggesting that 91% of additional coelomocytes that appeared post-challenge in the CF were not newly proliferated. Of the glass-adherent subset of coelomocytes, polygonal phagocytes and small phagocytes were primarily EdU-labeled. When proliferation was induced by withdrawal of 1.5% of CF three days after EdU injections, preliminary results show six times more EdU-labeled coelomocytes, which presumably replaced cells that were removed by CF withdrawal. In parallel, the axial organ (a suggested site of coelomocyte proliferation) showed 30% less EdU-labeled nuclei after CF removal, suggesting that replacement coelomocytes proliferated in and were released from the axial organ. Our results demonstrate that EdU-labeling is an effective method to measure cell proliferation in *S. purpuratus*, which can be employed to characterize the rate of coelomocyte proliferation and to identify their source.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### Molecular Modeling Of Three Representative Examples of Multiple-Exciton-Generating Dye Sensitized Solar Cells

Despite the economic and environmental advantages of dye sensitized solar cells (DSSC), they cannot currently compete with traditional crystalline silicon photovoltaic cells due to a typical conversion efficiency value of less than 10%, well below the predicted Shockley-Queisser limit of 31% for single-exciton formation. But DSSC with organic crystals of molecules that undergo singlet fission can bypass this limit and lower the rate of recombination by generating multiple excitons, or many electron-hole pairs upon the absorption of a single incident photon. The current maximum rate of quantum efficiency for singlet fission is 200%, which has been experimentally measured for 1,3-Diphenylisobenzofuran (DBF) at 77K. These encouraging results have led us to model crystalline DBF, tetracene, and pentacene to explore the energy differences between the spin-neutral (SN) and spin-separated (SS) states, the rate of spin recombination, and begin exploring the mechanism for the multi-exciton formation. The modeled triclinic supercells of DBF, tetracene and pentacene each were  $51.6\text{\AA}\times 55.5\text{\AA}\times 57.6\text{\AA}$ ,  $63.2\text{\AA}\times 60.3\text{\AA}\times 67.7\text{\AA}$  and  $63.2\text{\AA}\times 60.6\text{\AA}\times 48.03\text{\AA}$ , with 16730, 16800, and 17280 atoms in each cell, respectively. A dimer was randomly selected in each cell to serve as the spin-separation reaction center and a  $20\text{\AA}\times 20\text{\AA}\times 20\text{\AA}$  simulation box was centered on this pair.

We used the CP2K molecular modeling package on the supercomputers at the Texas Advanced Computing Center to perform molecular mechanics (MM), quantum mechanics (QM) and the hybrid QM/MM calculations. The systems were first equilibrated by molecular dynamics with the generalized Amber Force Field to the target experimental temperatures of 15K, 77K, and 300K for DBF, and 6K and 300K for tetracene and pentacene. The density functional theory calculations were performed with the DZVP basis set and GTH type pseudopotentials on the dimers. The electrostatic coupling scheme was chosen to treat the mutual polarization between the QM and MM subsystems. A total of eleven 2-picosecond thermodynamic integration windows were used to probe the free energy profile along spin separation that exhibits a driving force of  $\sim 2.7$  eV. In addition, the time-dependent DFT calculations yielded optical gaps of 3.26eV, 2.35eV, and 2.05eV for the DBF, tetracene, and pentacene dimers. These results all compare well to experimental UV-visible absorption spectra. Restricted open Kohn-Sham calculations were also used to obtain the on-site exchange interaction energy of a DBF molecule, which was subsequently used to determine the electronic coupling strength between its SN and SS diabatic states. Finally, by employing the semi-classical Marcus electron transfer theory, the rate of spin recombination was estimated to be  $\sim 10^{-21}$  s<sup>-1</sup>.

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## Function of TEPs in the immune response of *Drosophila* against entomopathogenic nematodes and their mutualistic bacteria

*Drosophila melanogaster* is an outstanding model to understand innate immune defense mechanisms. The fly employs different immune responses according to the type of pathogen it encounters. How the eukaryotic parasites such as insect pathogenic nematodes interact with the fly immune system is still not well understood. Recent studies on the entomopathogenic nematode *Heterorhabditis bacteriophora* and its mutualistic bacteria *Photorhabdus luminescens* have started to investigate the fly response to nematodes carrying the bacteria (axenic worms), nematode lacking the bacteria (symbiotic worms) and the bacteria alone. The advantage of using this model is that the immune response of the fly can be studied against each partner of the mutualistic interaction that allows comparative studies between antibacterial and anti-nematode defenses. Thioester-containing proteins (TEPs) are conserved throughout the animal kingdom. In insects they act as opsonins, binding to parasites recognition and promoting their phagocytosis or encapsulation. Recent studies in *Drosophila* have shown that TEPs are not involved in the immune defense against certain bacterial and fungal pathogens. Here we present data on the potential role of TEPs in the immune response of *Drosophila* against bacterial infection of *P. luminescens*. We infected the wild (W1118) flies and TEP mutants (TEP1, TEP2, TEP3, TEP5 and TEP6) with *P. luminescens* and recorded survival rate (every 12h) for a week. The TEP2 and TEP3 mutants showed slight resistance towards *P. luminescens* in comparison to wild type. We propose that these proteins may trigger some kind of sensitivity to the flies against this bacterial pathogen. Further experiments on TEP mutants against nematode infection (axenic and symbiotic) will shed light on their prospective role in the immune response.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### Cell-by-cell Tissue Imaging of Metabolites by Laser Ablation Electrospray Ionization Mass Spectrometry

Imaging mass spectrometry (IMS) is an emerging technology for the analysis of biomolecular distributions in tissues. Matrix-assisted laser desorption ionization, desorption electrospray ionization and laser ablation electrospray ionization (LAESI) IMS have shown imaging capabilities for metabolites, lipids and proteins in various biological tissues. In most of the existing studies, imaging is performed by sampling on an artificial rectangular grid that does not reflect the cellular pattern of the tissue. LAESI mass spectrometry (MS) coupled with an optical fiber enabled the direct analysis of single cells and subcellular compartments.<sup>1</sup> Cell-by-cell imaging was demonstrated using LAESI-MS, where individual cells were utilized as natural pixels for tissue imaging.<sup>2</sup> Here, we present a novel cell-by-cell LAESI imaging technique that automates cell coordinate recognition and ablation sampling. The cell recognition is carried out by image analysis software on microscope images of the tissue. Figure 1a shows the microscope image of *Allium cepa* epidermal cells. Cell edges are differentiated from the background by thresholding the grayscale levels in the image (see Figure 1b). Measurements of cell shape and size are performed on the resulting binary mask image. The centroid of each object provides the cell coordinates. An automated stage-control program uses these coordinates to sequentially position the cells under the ablation fiber and acquire LAESI mass spectra one cell at a time. This results in increased data acquisition efficiency allowing us to ultimately investigate extended tissue areas. Intensities of selected ions in the LAESI mass spectra are used to color code the individual cells indicating the levels of the corresponding metabolites. An example of cell-by-cell distribution of a disaccharide is shown in Figure 2.

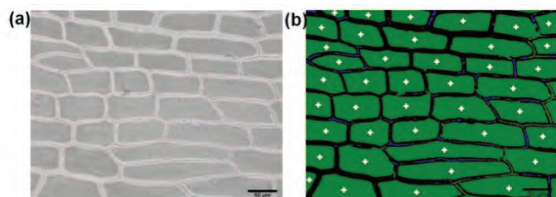


Figure 1. (a) Optical image and (b) thresholded image of *A. cepa* epidermal tissue.

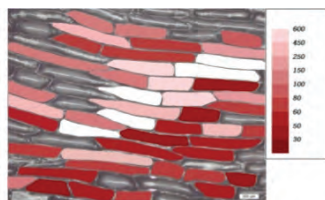


Figure 2. Cell-by-cell distribution of the ion  $m/z$  381 corresponding to a disaccharide.

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### Analysis of Ancient Volcanic Rocks in Southern Virginia: Implications for Modern Volcanic Systems

Accurate prediction of volcanic eruptions is a goal of modern volcanology because of the threat posed to communities living near active volcanoes. Understanding the dynamics of the magma systems that give rise to eruptions is an essential tool. Because the processes controlling magma ascent do not change, geologists study Precambrian volcanic rocks as an analog for modern systems. The 760 million-year-old Razor Ridge volcanic center is a particularly suitable system because of similarity to the currently active Yellowstone complex. These rocks were previously recognized as volcanic, but eruptive processes were unknown.

This study utilized petrographic and geochemical analysis to characterize eruptive mechanisms. Differences in these define into two distinct units: blue and red. The chemically evolved red unit displays high  $\text{SiO}_2$ , Nb and Ta concentrations, high Rb/Ba and K/Ba ratios, low Ti, Eu/Eu\*, Sc and Sr, and low Hf/Ta and Zr/Nb ratios. The less evolved blue unit exhibits lower silica contents, and trace element concentrations indicative of an unfractionated silicic magma. Variation in concentrations in blue contrasts with tight clustering red, indicating that the latter is likely a fractionation product from a common magmatic source. Mineralogical differences confirm the geochemistry with blue characterized by 1-9% plagioclase phenocrysts, whereas red contains none.

Increase in volatile content accompanied magma differentiation, causing pyroclastic eruptions. Pyroclastic origin is supported by evidence for abundant volatiles, as indicated by copious, pervasively embayed quartz phenocrysts, broken feldspar phenocrysts, accretionary ash pellets, and fiamme. The presence of the latter two suggest that both fallout and ash-flow mechanisms were involved.

These data from Razor Ridge indicate that (1) the magma differentiated, producing at least two chemical zones (2) high volatile component influenced the style and rate of magma ascent and (3) pyroclastic eruptions dominated. This study demonstrates how the characteristics of an ancient eruption can be deciphered from physical evidence and thereby could contribute to the prediction of a modern system.

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## The Global Gay: Modernity, State-Sponsored Homophobia, & a Ugandan LGBTI Rights NGO

This study investigated the perceptions of modernity and development that frame the actions of Sexual Minorities Uganda (SMUG), an indigenous LGBTI rights advocacy NGO that is the major voice of remonstrance to anti-homosexual legislation in Uganda's parliament. Within the context of NGO institutionality, this study examines how SMUG appropriates and defines 'gay identity' in relation to anti-gay sociopolitical sentiment. The primary research question centers on how SMUG constructs an identity and positions itself in this debate, and what narratives it employs to achieve this.

Bolstered by reviews of existing literature, ethnographic fieldwork was conducted through an internship with SMUG's Research Department in Kampala in June & July of 2012, and included 200+ hours of participant observation and nine semi-structured interviews. Data analysis evaluated the efficacy of development as a tool for affecting sociopolitical change, and concludes SMUG allies itself with an identity of gayness it perceived to be universal and inalienable. SMUG organizes its practice through the language of development and human rights, which allows SMUG to (inter)act on international and national stages. SMUG equates the realization of LGBTI rights with being more culturally enlightened, thereby placing Uganda on a hierarchical scale opposite fully 'developed' nations. SMUG positions LGBTI Ugandans as unable to be 'fully gay' in their current, repressive environment, thus linking their realization of rights to the Ugandan state's ability to achieve full modernity.

Furthermore, the study concludes these development practitioners are caught in a catch 22: SMUG must secure a global gay identity to accrue enough sociopolitical and economic capital to have the room to maneuver internationally and on a national scale. However, in demarcating themselves as gay, SMUG's membership assumes the status of a sociopolitical minority within Uganda, which limits them from participating in development on national and local scales to enact social change.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### Characterization of exchanger gene mutants in *Caenorhabditis elegans*

#### BACKGROUND:

$\text{Na}^+/\text{Ca}^{2+}$  exchange proteins (or NCX proteins) play integral roles in signal transduction and cellular homeostasis. Exchange proteins balance the levels of sodium and calcium ions in cells by exchanging  $\text{Na}^+$  ions from the outside of the cell, for  $\text{Ca}^{2+}$  ions inside the cell. In neurons, this results in the resetting of a negative charge inside the cell.<sup>1</sup> Similarly, in muscle cells,  $\text{Ca}^{2+}$  ions must be removed from the cytoplasm in order for them to relax. In both muscle cells and neurons, NCX proteins are involved in resetting the ionic balance to restore the appropriate charge. Dysfunction of NCX proteins has been linked to stroke, heart attack, and Parkinson's disease. Studying NCX proteins is a crucial component to better understanding and treating these ailments.

#### OBJECTIVES:

The O'Halloran lab is doing a genome wide analysis of exchanger proteins in the model organism, *C. elegans*. The purpose is to better characterize this understudied family of exchanger proteins.<sup>2</sup> My objective was to characterize NCX mutants, and describe the differences that are observed between mutants and wild type worms.

#### METHODS:

*C. elegans* with mutated proteins are available, and after outcrossing, they can be compared to wild type worms. Three experiments were run using the mutant strains. The first was a dye-filling assay. The worms were introduced to the lipophilic dye DiD and then examined under a microscope. The second experiment is a behavioral assay that examines changes in neuronal plasticity when compared to wild type worms. The final experiment examines axon guidance by determining if there are differences in the amount of commissures formed between the dorsal and ventral nerve cords when compared to the wild type control.

#### RESULTS:

At the moment, the dye-filling assay has been completed, and the other experiments are in progress. None of the mutant strains observed were found to be dye-filling defective.

#### CONCLUSIONS:

Mutant strains were not found to be dye-filling defective. This indicates that the primary sensory neurons of the mutants are intact. Additionally, it means that the cilia and sensory organs are functional. This is a phenotypic characterization, so it does not quantify the extent of the functionality of the sensory neurons. The other experiments will provide more information in determining the functionality of neurons in mutants.

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## Schrodinger Equation: Journey from Uncertainty to Certainty

As Richard Feynman said: Where did we get that (equation) from? Nowhere. It is not possible to derive it from anything you know. It came out of the mind of Schrödinger.

In 1927, Erwin Schrödinger constructs a wave equation for de Broglie's matter waves. And along with Schrodinger we entered the world of Uncertainty. Schrödinger was quite puzzled by the nature of the wave function. What is the physical meaning of  $\psi(x,t)$ ? It doesn't give you a precise location for your particle at a given time  $t$ , so it doesn't give you the trajectory of a particle over time. Late in 1927, Max Born, proposed that the wave function is a kind of information wave. It provides information about the probability of the results of measurement, but does not provide any physical picture of "what is really going on." This probabilistic nature links with a rather shocking consequence of de Broglie's formula for the wavelength and momentum of a particle, discovered by Werner Heisenberg in 1927. This result is now known as Heisenberg's uncertainty principle. So, Schrödinger's equation does not make it any easier to "visualize" what these waves looked like. They are not "real waves", like water waves, but rather mathematical waves described by a mathematical function. Our goal is to step into the world of certainty and study the non-linear Schrödinger equation (NLS) which is a non-linear partial differential equation of dispersive category. In mathematics a partial differential equation is called dispersive if waves of different wavelength travel at different phase velocities. To study the solutions or even the existence of solutions over small time for non-linear Schrödinger equation (non-linear PDE) requires special care and techniques related to Fourier and Functional Analysis. To analyze the properties of dispersive PDEs we study some recent developments associated with Semi Linear Schrödinger equation.

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### Effects of Copper Induced Degradation on DNA Recovery Time From Unfired Cartridge Casings

#### OBJECTIVES/BACKGROUND:

In the presence of Copper, DNA has been shown to degrade. A majority of cartridge casings are made from brass. Since one of the major components of brass is copper, we experience copper induced DNA degradation. To show the effects of this copper induced degradation, different cartridges were spotted with cells for extraction to determine the time in which DNA can no longer be recovered.

#### METHODS:

Four different cartridges were used to evaluate the effects of copper induced degradation; brass, nickel, aluminum, and steel. While the brass and nickel contain amounts of copper, the aluminum and steel do not. A time series of 30 minute increments up through 150 minutes were used on the brass cartridges, while a time series of 1 day, 2 days, 5 days, 7 days, and 2 weeks were used on the nickel, aluminum and steel cartridges. A known amount of cells were spotted onto the cartridges and allowed to dry according the timetable for that cartridge. Once dry, the DNA was extracted and the samples quantified to for analysis.

#### RESULTS TO DATE:

We are observing the recovery times for unfired brass cartridges, which is still being investigated. Currently, we have observed some recovery of DNA on nickel, aluminum, and steel after 4 weeks time.

#### CONCLUSIONS:

DNA can be successfully recovered from unfired cartridge casings composed of nickel, aluminum, and steel. Further analysis will lead to observing this copper degradation effect on DNA recovery time.

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### The Sp185/333 proteins from the California purple sea urchin opsonize microbes and augment phagocytosis

The California purple sea urchin, *Strongylocentrotus purpuratus*, is used to study fundamental functions and principles of innate immunity. The Sp185/333 gene family of *S. purpuratus* is estimated to have 40 to 60 loci, which are upregulated in response to immune challenge, and produce highly diverse mRNAs encoding a wide range of membrane-associated protein variants. The deduced Sp185/333 proteins are composed of blocks of sequences called elements that are present in mosaics of recognizable element patterns (e.g. E1 and E2). Individual sea urchins can express  $\geq 260$  distinct Sp185/333 protein variants upon immune challenge. The diversity of the Sp185/333 proteins suggests that different variants may have different immune effector functions. Native Sp183/333 proteins, nickel-isolated native Sp185/333 proteins (Ni-natSp185/333) as well as a recombinant Sp185/333 protein, rSp0032 (E1 element pattern), bind to the Gram-negative marine bacterium *Vibrio diazotrophicus*. Microbial binding is the first step in the process of phagocytosis, thus we tested whether *Vibrio* opsonized with Sp185/333 proteins would augment phagocytosis. To determine whether Sp185/333 proteins augment phagocytosis, we calculated the phagocytic stimulation index (PSI) after opsonizing *Vibrio* with 1) Ni-natSp185/333, 2) rSp0032, 3) cell-free coelomic fluid (positive control), and 4) artificial coelomic fluid (negative control). While the rSp0032 variant did not augment phagocytosis, *Vibrio* opsonized with Ni-natSp185/333 showed a PSI value between those of the positive and negative controls. This suggested that some Sp185/333 proteins have a moderate ability to augment phagocytosis. This is the first antimicrobial function identified for the Sp185/333 proteins. Future work will involve using insect cells to express E2 Sp185/333 protein variant (the most predominant variant identified from coelomocytes) for opsonization and its ability to augment phagocytosis. Understanding the putative immune activities of the Sp185/333 proteins will advance our knowledge of protein diversity and functions as well as its importance for innate immunity in invertebrates.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Feeding Ecology Dispersal of Leaf-Tying Caterpillars

Leaf-tying caterpillars are ecosystem engineers in that they build shelters between overlapping leaves that are utilized by other arthropods, increasing species richness and diversity of arthropods at the whole tree level. While some leaf-tiers have been observed to leave their ties and create new shelters (and thus additional microhabitats) the factors affecting shelter fidelity have not been investigated. For this study, I explored the effects of resource limitations and occupant density on shelter fidelity. First I quantified the area of leaf material required for a caterpillar to fully develop for two of the most common species of leaf-tying caterpillars that feed on white oak. On average, *Psilocorsis cryptolechiella* required 21.87 cm<sup>2</sup> leaf material and *Psilocorsis quercicella* consumed 19.97 cm<sup>2</sup> leaf material. I also measured the area of natural leaf ties found at our study site, to determine the amount of resources available to caterpillars in situ. Of 158 natural leaf ties, 46.8% were too small to sustain even one caterpillar throughout development. Finally, I manipulated caterpillar densities in artificial ties on potted trees to determine the effects of cohabitants on the likelihood of a caterpillar to leave its tie. I used densities of 1, 2, or 4 caterpillars in ties of a standard size and monitored the trees twice daily to track the movement of the caterpillars. In ties with more than one occupant, caterpillars show a significantly greater propensity to leave their tie. These findings suggest that both food limitation and interactions with other caterpillars influence patterns of caterpillar dispersal.

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## Concordant integrative analysis of multiple gene expression data sets

Microarray is an experimental method by which tens of thousands of genes can be printed on a small chip. This technology enables us to measure genome-wide expression profiles. The cost of a microarray experiment is still relatively high. Therefore, the sample size of a microarray experiment is still relatively small. For some important disease studies, microarray data have been collected by different laboratories. We expect to obtain more efficient analysis results if different data sets collected for the same or similar study can be integrated. However, due to many complicated experimental issues, it is necessary to evaluate the genome-wide concordance among these data sets before their integrative analysis. If the underlying behavior of a gene is consistent among different experiments, then the related expression profiles in different data sets will be concordant. Statistically, mixture models have been widely used to accommodate unobserved heterogeneities in a study population. A mixture model based method has been proposed for the integrative concordant analysis of two microarray data sets. It is necessary to extend this approach for an integrative analysis of multiple data sets.

The general statistical framework for our integrative analysis is the partial concordance/discordance (PCD) model. Its related statistical estimation difficulty is that its parameter space increases exponentially with the number of data sets. Since the complete concordance model (CC) and the complete independence (CI) model are two basic statistical frameworks that can be derived from the PCD model, we propose a two-level mixture model to approximate the PCD model. It combines the basic CC and CI models and its parameter space increases linearly with the number of data sets. We have implemented an expectation-maximization (E-M) algorithm for the model parameter estimation. Simulation studies have been conducted to understand the performance of our method. We have also applied our method to a collection of microarray gene expression data sets for a lung cancer study.

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# NATURAL SCIENCES

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## A Textual Analysis of Nucleophiles and Nucleophilicity in Organic Chemistry Textbooks

Previous studies have revealed that students have difficulties understanding organic chemistry, especially the mechanisms that are taught. The main components of the mechanism are the nucleophile and electrophiles that are part of the reaction. Without proper understanding of those concepts, it is difficult to understand what is going on in any mechanism. Our hypothesis is that the understanding of nucleophiles can lead to better understanding of organic chemistry. The main goal of this study was to analyze how nucleophiles were introduced in different organic chemistry textbooks, in what context they were introduced, and if they were reinforced throughout the book. Data from the text analysis will be presented and implications for teaching organic chemistry will be discussed.

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## A *Drosophila* infection model for studying bacterial and nematode pathogenicity

The fruit fly *Drosophila melanogaster* is a powerful genetic model to study the innate immune response in eukaryotic organisms. The fly immune system includes a variety of immune defense mechanisms against infection by pathogenic organisms. To date, most information on the innate immune response in *Drosophila* derives from studies that involve bacterial, fungal and viral pathogens. However, our understanding of the molecules that participate in the host immune response to entomopathogenic (or insect pathogenic) nematodes remains incomplete. *Steinernema carpocapsae* nematodes and *Xenorhabdus nematophila* bacteria form a mutualistic complex that is extremely pathogenic to a broad range of insects and are therefore used as biological agents in pest control. A major advantage of this model is that *Steinernema* nematodes are viable in the absence of their mutualistic *Xenorhabdus* bacteria. Consequently, each player in the mutualistic relationship can be separated and studied in isolation or in combination enabling host immune responses to be studied for the nematode alone, for the bacteria alone, and for the nematode-bacteria complex. We have recently started to use the *Drosophila*-*Steinernema*-*Xenorhabdus* model to understand the molecular basis of the insect immune response to a combined insult of both parasitic nematodes and their mutualistic bacteria. We have initially infected *Drosophila* wild-type flies with different numbers of *Xenorhabdus* bacteria and found that these pathogens are significantly more virulent to flies compared to the related insect pathogenic bacteria *Photorhabdus*. These preliminary results suggest that *Xenorhabdus* possibly employs distinct strategies to overcome the host immune response and establish infection in the fly. Future studies will include the identification of the minimum number of *Xenorhabdus* cells that are capable of conferring pathogenicity to *Drosophila* as well infections with the nematode partner carrying or lacking the bacteria.

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## Cotton Swabs vs. 4N6FLOQSwabs™: A Comparative Study for Optimal Recovery of DNA from Simulated Forensic Evidence

In forensic laboratories, moistened cotton swabs are often used to collect DNA evidence. These swabs are made of cotton fibers tightly wrapped around the tip of a wooden stick. While highly absorbent, the dense inner core can trap cellular materials within its fibers. An alternative type of swab, called 4N6FLOQSwabs™ (Copan Italia, Brescia, Italy), is instead made of thousands of parallel short nylon strands that are flocked onto a plastic stick. Due to this unique feature, these swabs lack an inner core that can trap cellular materials. The first objective of this study was to compare the DNA recovery obtained when the swabs were used to collect DNA samples deposited on various substrates simulating forensic evidence, such as a knife handle or gun grips.

Copan Italia has also developed a specialized spin basket called a Nucleic Acid Optimizer (NAO) that may increase recovery of nucleic acids. The NAO consists of a semi-permeable basket, which retains fluid until placed in a centrifuge. The second objective of this study was to determine the effect of the NAO on nucleic acid recovery.

DNA recovery was evaluated with two different extraction kits: PrepFiler® Forensic DNA Extraction Kit (Life Technologies) and DNA IQ™ System (Promega). To determine the amount of DNA extracted, the Quantifiler® Human DNA Quantification Kit (Life Technologies) was used and quantification was performed on an ABI PRISM® 7000 Sequence Detection System.

Results indicated that in our experiment, the best recovery occurred when DNA was collected from a substrate with nylon swabs and extraction was performed using the NAO and PrepFiler® kit. Also, the NAO increased DNA recovery by 34%. Finally, it was determined there was an incompatibility between the DNA IQ™ System and the nylon swabs and a modified protocol was successfully developed to overcome the problem.

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## Gamma-ray bursts: a bridge between the electromagnetic and gravitational wave skies

Gravitational waves, ripples on space-time predicted by Einstein's theory of general relativity, have never been observed directly. Starting from 2015, LIGO - the Laser Interferometer Gravitational Wave observatory - will likely detect the elusive gravitational waves emitted during some of the most energetic stellar explosions in the universe: Gamma-Ray Bursts (GRBs). The search for gravitational wave signals in LIGO data depends on two critical factors: knowledge of the astrophysical source that produces them, and expected properties of the signals in question. The former is largely based on electromagnetic observations. The latter governs whether we use highly sensitive but strictly model-dependent searches, or less sensitive but more robust detection techniques. We examine two paths towards improving the searches for gravitational waves in coincidence with GRBs: (i) nailing down of the key astrophysical parameters through the creation of a literature-informed database of GRB candidates; (ii) the development of a novel search for intermediate-duration gravitational wave signals, for which none of the traditional gravitational waves searches are well suited. The detection of these signals, besides proving directly Einstein's theory, would allow us to answer some of the most intriguing questions on the nature of GRB progenitors.

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## <sup>40</sup>Ar/<sup>39</sup>Ar Dating in Paleoanthropology: Advantages and Pitfalls

<sup>40</sup>Ar/<sup>39</sup>Ar dating in the Pliocene/Pleistocene (between 5.332 million years and 11,700 years ago) is a useful technique because potassium (K) is an abundant naturally occurring element in the Earth's crust and K bearing minerals are commonly found in fossil bearing volcanic ash deposits. One of the isotopes of K is radioactive and decays to <sup>40</sup>Ar. In the initial application of the K-Ar geochronometer, the concentrations of <sup>40</sup>K and <sup>40</sup>Ar are measured on two separate splits of the sample raising concerns about sample homogeneity. With the development of the <sup>40</sup>Ar/<sup>39</sup>Ar variant, K and Ar are measured on the same material even on samples as small as a single mineral grain. Even though the <sup>40</sup>Ar/<sup>39</sup>Ar method offers significant improvements, there are still possibilities of errors, especially if more than a single grain is tested at a time. Another difficulty with argon dating is possible site contamination caused by different geological processes, which mix older volcanic components in with primary ones. Other sources of error are both excess argon and argon loss. However, most issues with <sup>40</sup>Ar/<sup>39</sup>Ar dating can be examined through incremental laser heating and single grained analysis, making this dating method applicable to many fields. In the field of paleoanthropology <sup>40</sup>Ar/<sup>39</sup>Ar dating has been instrumental in the dating of sites and in understanding human evolution. The <sup>40</sup>Ar/<sup>39</sup>Ar dates for Java, Indonesia demonstrate how argon dates have assisted in both developing and correcting human evolutionary theory. Java dates allowed paleoanthropologists to refine their theories on dispersion of hominids out of Africa into Asia. The key importance of <sup>40</sup>Ar/<sup>39</sup>Ar dating to paleoanthropologists is that it allows the assignment of numerical ages to various anthropologic events allowing them to understand when there was movement and at what rate, which leads to a better understanding of human evolution.

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## Combinatorial Heegaard Floer Homology and Ribbon Diagrams

Heegaard Floer homology is a collection of invariants for closed oriented three-manifolds, introduced by Ozsvath and Szabo in 2004. The simplest version is defined as the homology of a chain complex coming from a Heegaard diagram of the three manifold. In the original definition, the differentials count the number of points in certain moduli spaces of holomorphic disks, which are hard to compute in general.

More recently, Sarkar and Wang (2008) and Ozsvath, Stipsicz, and Szabo (2010) have determined combinatorial methods for computing this homology with  $\mathbb{Z}_2$  coefficients. Both methods rely on the construction of very specific Heegaard diagrams for the manifold, which are generally very complicated.

In 1988 Matveev and Piergallini introduced the concept of branched spines as efficient and powerful descriptors of three-manifolds. We show that a branched spine gives rise to a natural Heegaard diagram. By comparing this construction with the above constructions we have found a more streamlined combinatorial description of the Heegaard Floer homology for certain manifolds. The nature of our construction allows for a convenient graphical representation as a “ribbon diagram,” obtained by cutting open the Heegaard surface along what Ishii calls the e-cycle.

Our construction’s main advantage is a very large “marked region” (containing the e-cycle) which touches all other regions. Because the “marked region” does not contribute to the differential map, this has the effect of greatly simplifying the combinatorial complexity associated with counting differentials in our chain complex as well as restricting the total number of generators.

We will also show applications of our method to some calculations for specific manifolds.

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## Rivised Black-Scholes Model for Option Valuation with Transaction Cost

This project discusses ways of valuating European options based on a delta-hedge strategy in a risk-neutral financial market.

In the first part, we review the Black-Scholes-Merton (BSM) model and basics of stochastic calculus, which allows us to set up the stock price model via rigorous mathematical approach. In particular, we discuss one of the assumptions that there is no transaction cost enforced, which turns out to be impractical in modern market.

In the second part, the delta-hedge strategy is introduced for the BSM model. This allows us to deduce rigorously the corresponding BSM equation for option valuation and obtain the analytic solution for the modified equation.

In the third part, the assumption of no transaction cost is abandoned in order to get a better simulation of a real financial market. To this end, we first examine the situation when a transaction fee is charged only once in a certain period of time for as many transactions as desired. Secondly, we suppose that there is a transaction fee for each transaction (the case of a real financial market). This second assumption is considered together with the Leland model approach for the price estimate, which requires adjusting the amount of stocks at a fixed time interval. It explains why the option price can only be estimated rather than determined exactly. Finally, we show how to calculate the expectation of the option price. We note, however, that even though the expectation can be calculated, the corresponding variance diverges. This indicates that a straightforward application of the delta-hedge strategy with the transaction costs can be extremely risky. We discuss several examples by numerical approach.

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## Turing Categories

Computability theory is one of the revolutionary ideas of the 20th century, and has gone on to become one of the pillars of the foundations of mathematics. It explores the idea of what can be done by any powerful-enough agent.

Category theory studies objects and the connections between them. It was originally developed for use in topology, but has come to be seen as a fundamental part of mathematics. Today, it is recognized that much, if not all, of mathematics can be done in category theory.

However, computability theory is just starting to be codified in category theory. We explore this codification, using the techniques of logical analysis. We find that we can find more general versions of some results.

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## Determination of optical band gaps for PAH and soot in a N<sub>2</sub>-diluted, ethylene/air non-premixed flames

Simultaneous visible absorbance and scattering measurements were made at a height of 20 mm above the fuel tube exit in a nitrogen-diluted, ethylene/air, non-premixed flame and this data was used to determine the optical band gap, as a function of radial position in the flame. In our previous work, analysis of the Raman spectrum suggested the source of the scattering was PAH species with a molecular mass range of 500 -1000 Da. In a recent manuscript from our group, light from a light emitting diode, with center emission wavelength of 445 nm, was used to make line of sight absorption measurements in the flame. After tomographic reconstruction of the radial extinction field, the optical band gap was derived from the near edge absorption spectrum using a Tauc analysis. The optical band gap,  $2.38 \pm 0.08$  eV, was then compared with calculations of the electronic structure of a series of D<sub>2h</sub> PAH using time-dependent density functional theory. HOMO-LUMO gaps for these PAH were correlated with the number of aromatic rings in the molecules. From this correlation, the measured band gap suggested that the source of the extinction could be a PAH with as few as 10 aromatic rings. In the current work, a super continuum light source is used to make simultaneous line of sight absorbance and scattering measurements. The current system allows for adjustment of the scattering angle, wavelength, and polarization, while also allowing for the scattering to be accounted for in the Tauc analysis of the absorbance data. Initial results using the super continuum source are consistent with the results from the LED source, while offering better spectral resolution, more intensity, an extended spectral coverage, and additional information from scattering data.

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### Analysis of Linked NSF Survey Data on the Scientific Workforce

The National Science Foundation's Survey of Doctorate Recipients (SDR) is conducted every two or three years and collects detailed information on thousands of individuals receiving PhDs in science and engineering in the U.S. and some others with PhDs from abroad in these areas. A significant portion of the sample (e.g., 60% on 3 or more surveys from 1993-2006) appears in multiple survey years and can be linked across time. Most institutions in the SDR can be linked to institutions in the NSF-NIH Survey of Graduate Students and Postdoctorates in Science and Engineering (GSS) through IPEDS numbers. The GSS is a yearly near census of institutions awarding PhDs and MS degrees. This poster presents linkage rates by survey year, measures of mean and spread in characteristics over time by field, and results of testing for significant differences in subgroups. This research is funded by a cooperative agreement from the NIH National Institute of General Medical Sciences (NIGMS) on modeling the scientific workforce in health and medical sciences. The NSF, NIH, and GWU are not responsible for the content of this poster.

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### Three regions of a recombinant Sp185/333 protein from the purple sea urchin have different functions.

The California purple sea urchin, *Strongylocentrotus purpuratus*, possesses a sophisticated innate immune system that functions without adaptive immune capabilities. It responds to pathogens effectively by expressing a highly diverse array of Sp185/333 proteins, suggesting that these proteins are involved in immune responses against pathogens. Individual sea urchins can express more than 260 distinct Sp185/333 proteins and one speculation on the advantages of this level of diversity is that different versions may have different immune functions. Although diverse, the deduced proteins share an overall organization and structure with a hydrophobic leader, a glycine-rich N-terminal region with a RGD motif (integrin binding), a histidine-rich region, and a C terminal region. There is no transmembrane region and no cysteines in the deduced sequences. The amino acid composition suggests that the proteins are intrinsically disordered and thus may not have any stable secondary folding. The lack of homology with known proteins precludes any functional predictions, but the conserved leader and RGD motif provide clues that these proteins may be secreted and interact with cell surface integrins. A recombinant Sp185/333 protein (rSp0032 with E1 element pattern) shows specific, non-reversible and high affinity binding against the marine Gram negative bacterial species, *Vibrio diazotrophicus*. We have employed three fragments of the rSp0032 protein to determine which region of the protein is responsible for bacterial binding. These fragments are the 1) glycine-rich N-terminal region, 2) RGD motif, and 3) histidine-rich region. Preliminary results suggest that the N-terminal glycine-rich region and histidine-rich region function in bacterial binding, and that the RGD motif mediates protein-protein multimerization. Our results provide preliminary insight into how the full length rSp0032 proteins bind to bacteria and has laid the groundwork for future Nuclear Magnetic Resonance studies to evaluate the rSp0032 structure.

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## Simple Structures with Complicated Properties

We use a sophisticated diagonal method, called the priority method, to construct computable mathematical structures with non-computable relations on their domains. We satisfy infinitely many mutually conflicting requirements by fitting together opposite strategies in a step-by-step construction. Computable relations are those for which there exist algorithms requiring no external knowledge to compute them. Non-computable relations are further classified into an infinite hierarchy, based on the amount of external knowledge needed to perform the computation. This level of external knowledge is called the Turing degree. We study how a specific computable relation on a computable structure changes under an isomorphic transformation of the structure. We are especially interested when the transformation encodes a computable relation into a relation of certain higher Turing degree while preserving the computability of the transformed structure.

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### Laser Heterodyne Radiometry for the Detection of CO<sub>2</sub> in the Atmospheric Column

Laser heterodyne radiometry (LHR) is a spectroscopic technique that allows for the detection of weak signals via technology that is adapted from radio receivers. A weak input signal is mixed with a stronger local oscillator resulting in a beating frequency (beat signal) at a lower, easier to measure frequency (in the RF region). In the case of LHR, the weak signal is sunlight that has undergone absorption from trace gases in the atmospheric column and the local oscillator is a distributive feedback (DFB) laser tuned to a frequency close to an absorption feature of the gas of interest. DFB lasers are desirable for use as local oscillators as they are not only cost-effective but they are commercially available in frequencies that can be tuned to specific features in the rotational spectra of many of the significant greenhouse gases of interest. In conjunction with NASA Goddard Space Flight Center, measurements of CO<sub>2</sub> were taken by mixing sunlight with laser light while scanning the laser(s) across two absorption features in the CO<sub>2</sub> spectrum – one centered at 1573.6 nm and another centered at 1611.5 nm. The two beams of light are combined on single mode fibers and mixed on a fast photodetector. This results in an RF beat signal which has an amplitude that is related to absorbance. From the absorbance measurement, concentration of CO<sub>2</sub> can be calculated. Since the LHR instrument collects sunlight as it passes through the atmosphere, the total column CO<sub>2</sub> concentration is measured. The sensitivity of the LHR instrument is estimated to be ~8 ppmv. Future efforts will focus on further miniaturizing the instrument, de-convolving gas concentration as a function of altitude and expanding the instrument to measure other atmospheric gases such as methane (CH<sub>4</sub>) and carbon monoxide (CO).

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### Subcellular near-field biomolecule sampling using a biosensor

The study of temporal and spatial distribution of biomolecules, such as metabolites and proteins in cell samples is significant for understanding biological functions, how molecules interact with others, migrate in the cell, and respond to the stimulation. Current methods of identifying and profiling biomolecules in biological samples use mass-spectrometry based, soft ionization techniques, and so far can only achieve 40-micron lateral resolution. In order to improve the resolution for subcellular study (dimensions on the order of several microns) and keep the sensitivity, we couple near-field ablation with an optic-fiber biosensor.

As the initial test towards integrating the near-field technique with a biosensor, the near-field ablation on *Arabidopsis thaliana* leaf samples and spectra data from crushed leaf solutions using optic-fiber biosensors will be reported. Lateral resolution of 2 microns was achieved in these experiments. We functionalize the biosensor probe with certain crosslinkers so that the biosensor can identify specific biomolecules from the near-field ablation. These functionalized biosensor probes are capable of detecting biomolecules with various ranges of molecular weight.

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## Identifying and Counting Ion Hits on the MCP/ Phosphor Screen in ALPHA

**BACKGROUND:**

The Antihydrogen Laser Physics Apparatus (ALPHA) collaboration aim is the stable trapping and study of antihydrogen atoms, the antimatter counterpart of the hydrogen atom. The series of electric coils surrounding a Penning-Malmberg catching trap confine charged particles. Here, a series of potential drops heated electron plasma until it was energetic enough to ionize residual gases (i.e. hydrogen, helium, and nitrogen) left in the vacuum chamber. Once ionized and dumped from the vacuum chamber onto the multichannel plate (MCP)/phosphor screen, these ions could be detected and imaged.

**OBJECTIVES:**

Ion hits on the phosphor screen need to be identified from background noise and other extraneous particle hits, and then counted, in order to determine vacuum quality in the trap. As a secondary objective, the program should be able to identify and count antiproton hits.

**METHODS:**

A routine written in MATLAB analyzes the images, distinguishes actual ion hits from other noise, and most importantly (in addition to gathering other data) counts the hits. The program was tested on sparse images and compared to manual counts done by eye.

**RESULTS:**

The program works very well for what it was intended to do - count sparse ion hits. In 15 separate test images, it made accurate counts with a relative error of  $0.05 \pm 0.05$  hits. It had a slight tendency to undercount. However, without modification and fine-tuning, the current program cannot reliably count antiproton hits.

**CONCLUSION:**

With more tests and data, this program could be refined to accurately count both ion (ionized gas) hits as well as antiproton hits, and to more accurately distinguish them from noise, annihilation products, and other extraneous hits. At present, because of particle stacking (multiple particles striking the same point on the screen) and high multiplicity particle production from antiproton annihilation, the program becomes less accurate as images become less sparse and more intense.

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## Computable Binary Trees and Their Paths

A tree is a partially ordered set closed under initial segments. A countable tree is computable if there is an algorithm that decides which nodes belong to the tree. In computability theory, much research has been done on computable trees and computability theoretic properties of their paths. Infinite computable binary trees have infinite paths, but not necessarily computable ones, not even computably enumerable ones. On the other hand, using the topological properties of trees, Jockusch and Soare established that every infinite computable binary tree has an infinite path with the same Turing jump as any computable set. We will demonstrate the proof of this result. We will show how this and other results about computable trees can be applied to a variety of important problems in computable model theory by transforming them to problems about finding infinite paths through certain computable trees. Thus, computable binary trees are a useful tool for solving seemingly diverse problems in computable mathematics.

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## In-vitro near-field metabolite sampling of biological samples with sub-micron resolution.

Chemical analysis of metabolites directly from cell samples in ambient conditions is essential to understand the functions of living organisms. Currently the identification and structural characterization of metabolites in tissue samples and large cells ( $\sim 100 \mu\text{m}$ ) is possible through mass-spectrometry-based, soft-ionization techniques. In order to probe the role of metabolites in smaller cells such as myoblast, fibroblast, etc., a method with a higher resolution is needed. In particular knowing the spatial distribution of metabolites at the sub-cellular level in such cells helps in elucidating the biochemical pathways. In order to achieve this, we attempt to combine near-field ablation with mass spectrometry.

As a first step towards the integration of near-field ablation with mass spectrometry, we will report preliminary results of the chemical analysis of *arabidopsis thaliana*. In order to map out the spatial distribution of the metabolites, it is necessary to have a spot size which is a fraction of the cell size. In these experiments we were able to achieve a resolution as high as  $1.5 \mu\text{m}$ . A difficulty which arises when using such a small spot size is the relatively small amount of ablated material, which is on the order of only a few hundred zepto moles. Currently we are unable to directly analyze the ablated material with the mass spectrometer. To address this issue, we introduce an intermediate step using nanopost arrays in combination with near-field ablation.

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## Fiber Optic Nanobiosensor

Protein sensing is critical to medicine, biology and several other research areas. In general, protein sensing methods fall into two major classes: labeled and label-free. Both methods have advantages and disadvantages. In short, labeled methods require a complex bioengineering process before an interaction can be tested. Label-free methods do not require such an engineering process; however, yield more convoluted results. In both schemes, conventional equipment is bulky, requires a large sample volume and renders in vivo measurements impossible. Our work centers around the development of a miniaturized portable immunoassay, which utilizes the optical properties of gold nanoparticles to perform highly sensitive molecular recognition. Due of their unique plasmonic properties, metallic nanoparticles are being utilized as multi-functional platforms in new chemical and biological sensing apparatus. In the context of biology, gold colloids are especially intriguing because of their proven durability in biological media.

Although engineering advances are steadily improving the efficacy of such sensors, progress in the field is hampered due to a lack of standardized results and tools for characterization. In other words, it is very difficult to objectively compare nanobiosensors across research groups, and also difficult to predict sensor behavior a-priori. In an effort to overcome these limitations, we are constructing a calibration schema to relate a sensor's optical response to its surface particle deposition as characterized by scanning electron microscopy. In conjunction, we have developed open-source software for both modeling a wide range of nanobiosensors, as well as a new toolkit for exploratory analysis of UV-VIS spectroscopy in general. We feel strongly that such efforts will equip the academic biosensing community with software and calibration tools comparable to those already afforded to commercially invested sensing apparatus.

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# NATURAL SCIENCES

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## Representability of the Regular Language by the Corresponding Nerve Nets

The regular language is a concept in mathematical logic and theoretical computer science. Each word in the regular language, including all formulas in the associated predicate calculus, can be represented as a corresponding element in a partially ordered set. This is the main result by McCulloch and Pitts. The namesake MCP model of the neural network in human brains employs some simple but accurate assumptions describing anatomical facts about the neural network. This model became the foundation of computational neurology. I will explain some fundamental facts about the human neural network and its associated mathematical model, a nerve net. I will present a mathematical proof showing the representability of the regular language by this model.

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## Efficient Computation of Jones Type Invariants

Jaegera, Vertigana and Welsha (1990) showed that computing the Jones polynomial of an alternating link diagram is  $\#P$ -hard. We are looking into a family of truncations discussed by Przytycka & Przytycki (1993) which can be computed in polynomial time. We have implemented some of their ideas in Mathematica and eventually hope to reproduce their ideas in the more general setting of Khovanov Homology.

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# SOCIAL SCIENCES



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## COLLEGE OF PROFESSIONAL STUDIES

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### The United States Congress and the Digital Age

#### BACKGROUND:

According to a 2009 report from the Pew Research Center, “wireless connectivity has drawn many users more deeply into digital life.”<sup>1</sup> The word hyper-connected has even been coined to describe the extent to which humans are now digitally interconnected.<sup>2</sup>

#### OBJECTIVE:

The purpose of undertaking this project on Congress and its policymaking role in the digital age is to:

- 1) Explore the symbiotic relationship between (a) Congressional actions pertaining to communications technology and (b) the growth and use of all this technology.
- 2) Understand the legislative challenges in the area of communications technology.

#### METHODS:

This research paper is a collective review of five literary works on laws and policies pertaining to communications technology:

- Cohen, E.S. (Ed.). (2007). *Broadband Internet: Access, Regulation, and Policy*.
- Postigo, H. (2012). *The Digital Rights Movement: The Role of Technology in Subverting Digital Copyright*.
- Smith, M.S., Noteff, J.D., Kruger, L.G., McLoughlin, G.J., Seifert, J.W. (2002). *Internet: An Overview of Key Technology Policy Issues Affecting Its Use and Growth*.
- Solove, D.J., & Schwartz, P.M. (2011). *Privacy, Information, and Technology* (3rd ed.).
- Thurber, J.A., & Campbell, C.C. (Eds.). 2003. *Congress and the Internet*.

It is an assessment of the authors’ arguments about the legislative actions that have impacted the World Wide Web.

#### RESULTS:

This paper is a work in progress. Currently its author is reviewing the history of the Internet and the legislative history of communications technology.

#### CONCLUSION(S):

Because this work is only in its early stages, a definitive conclusion has yet to be reached.

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#### SOURCES

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Identifying the Real Effects of Loan Supply Shocks

This paper investigates potential long run relationships between the health of lending banks, as measured by CAMEL5 data and the FDIC Problem Bank series, and components of real economic growth. Federal Reserve Greenbook forecasts and Society of Professional Forecasters estimates are used as a catch-all variable for all information that could possibly be demand-driven, and the CAMEL5 bank health variable is used to determine any supply-side effects. The simple model by Peek et al. (2003b) may continue to have contemporaneous cross correlations in the error terms, however there is an attempt to create an orthogonalized measure of the loan supply shock. I also investigate long run relationships in the data using vector error correction models. I extend this paper using data from FDIC Quarterly Banking Profiles as the CAMEL5 data is confidential.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Effects of Fictional Political Television

Over the course of the past decade, television viewers have been treated to a number of series depicting life inside politics. Several scholars have argued that fictional television shows about politics can have an impact on how citizens view their system of government and its key players in a similar way to the news media. The principal objective of the study is to examine the way in which fictional political television series portray female politicians and the impact these portrayals have on public opinion. Specifically, the study will look at whether television series featuring female politicians prime viewers to think more positively about women in politics. After exposure to either an episode of *Commander in Chief*, which features a positive portrayal of a female president, an episode of *The West Wing*, or no entertainment content, participants will be asked to evaluate the male and female candidates described in a fictional newspaper article. Analysis of these responses will allow for assessment of whether watching an episode of *Commander in Chief* results in a change in the characteristics that hold the greatest importance in viewers' overall evaluation of the female candidate. Additional analysis will seek to determine whether or not a change in these characteristics results in a more positive overall evaluation of the female candidate on the part of viewers of *Commander in Chief* as compared to viewers of *The West Wing* and participants who did not view any entertainment content. Overall, the study will seek to add support to previous research on effects of fictional entertainment content. It will also seek to expand the research related to television portrayals of gender roles beyond the previous studies of the effects of stereotypical portrayals of female characters.

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# SOCIAL SCIENCES

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### An Examination of the Intrinsic Logic of Cities and LGBT Cultural Identity through a Case Study of German LGBT Pride Festivals

What makes a city unique? In her recently published book, Martina Löw (2008) presents a concept that seeks to address this question while providing a theoretical basis with which to examine the twenty-first century city: die Eigenlogik der Städte or the intrinsic logic of cities. While acknowledging the homogenizing effects of living in an increasingly globalized society, Löw argues that each city nevertheless retains its own unique nature that both influences and reflects the rituals, habits and norms of everything within and pertaining to the city. This includes daily interactions but also the organization and carrying out of celebrations and special events such as festivals. Beginning in early summer and ending in fall each year, "Christopher Street Day" (CSD) festivals, Germany's version of lesbian, gay, bisexual and transgender (LGBT) pride festivals, take place in nearly every city in Germany. Over the past three decades, Christopher Street Day has grown ever larger in Germany, expanding from its original purpose to commemorate the anniversary of the Stonewall riots in New York in which many LGBT people rioted against an oppressive justice system. Against the backdrop of research on festivals as public rituals that reflect and reinforce the social norms, order and rituals of their community, this study examines how three German cities' CSDs (Berlin, Cologne, and Hamburg) reflect the intrinsic logic of those cities. Specifically, through research of CSD festival resources, such as the official festival publications and websites, and through observations gathered onsite at the 2012 festivals in the three cities, the study analyzes the three festivals in, among others, the areas of festival scope, interaction rituals and parade composition with the aim of providing insight into LGBT identity while also rendering more tangible evidence for Löw's concept of Eigenlogik.

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#### SOURCES

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# SOCIAL SCIENCES



## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

### Family-Centered (FACE) Advance Care Planning: Acceptability for Teens with Cancer

#### STATEMENT OF THE PROBLEM:

Cancer is the leading cause of death due to disease among youth aged 15 to 24 years. While many pediatric cancer patients survive their primary cancer, a subset dies prematurely secondary to their curative cancer therapy. Lack of advance care planning creates significant problems for families and providers when conflict emerges at the time of medical crisis. Research in this area has been hampered by fears that adolescents/families will be harmed.

#### SUBJECTS:

Adolescents with cancer aged 14-21 (n=19) and their 22-62 year old family members (n=19) were recruited from a hospital-based outpatient clinic and inpatient unit. Adolescents mean age was 16.6; 63% were male; 58% Black, 11% at or below poverty level. Diagnoses were 47% leukemia, 26% brain tumor, 16% solid tumor, 11% lymphoma.

#### PROCEDURE:

A two arm randomized control clinical trial of experimental Family Centered (FACE) Advance Care Planning condition and standard of care control was conducted. Of 43 individuals screened for eligibility, 1 could not identify a surrogate, 6 were interested but not ready, 1 did not know diagnosis, 1 was clinically depressed and 15 declined. Of eligible participants 19 adolescent/family dyads (N=38) were available for analysis.

The intervention is conducted in a dyadic interview format with a trained/certified facilitator and consists of Session 1 (Lyon Advance Care Planning Survey); Session 2 (Respecting Choices Interview & Completion of Statement of Treatment Preferences); Session 3 (Completion of Five Wishes, an advance directive). Sessions of 60 minutes each were scheduled one week apart, followed by completion of process measures. The same weekly intervals were used for the standard of care control condition assessment. A research assistant, not the interviewer, administered the questionnaires which were read aloud. Referrals are given as need to providers, chaplain or ethicist.

#### ANALYSIS:

Data were collected in 2011. Descriptive statistics and t tests were used to test for significance at 0.05 level.

#### RESULTS:

Both adolescents and families were highly satisfied with participation in the study. In Session 2 families rated their satisfaction as higher than adolescents (p=0.0443).

Adolescents and families rated the quality of the interviewer/facilitator highly. In Session 2 families rated "the overall quality of the discussions" as higher than adolescents did (p=0.0254).

#### CONCLUSIONS:

Palliative care conversations were worthwhile and not harmful to teens, an underserved population. FACE demonstrated feasibility and acceptability.

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# SOCIAL SCIENCES

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Contemporary Psychoanalytic Theory: Navigating Complicated Trauma during the Psychotherapy Process

In 1968, Stephen Karpman introduced the psychoanalytic community to a new way of understanding trauma. His model, the Karpman Triangle, proposed that traumatized individuals switch between the interchangeable, archetypal roles of Persecutor, Rescuer and Victim. He believed that both patients and therapists can fulfill these roles at different times, and a process of role reversals can lead to unique enactments throughout the course of psychotherapy. This poster will examine this process, especially as it relates to factors that initiate a transition between the aforementioned roles. Additionally, it will suggest ways in which contemporary psychoanalytic theories can be useful in furthering an understanding of this process. Literature on both attachment theory and rupture and repair will be utilized to illustrate the clinical importance of the Karpman Triangle. In particular, this presentation will analyze an in-depth, qualitative, case study of a college-aged female who had a remarkable history of childhood trauma. Her case is further complicated, as this patient sought treatment at a training clinic after her only living sister was diagnosed with a terminal illness. Due to the clinical rotation of her initial psychotherapist, her therapy was time limited, and it became necessary for her to transfer to a new clinician. However, this transfer occurred only days after the death of her sister. Instead of providing a stabilizing environment during an episode of grief and loss, this patient experienced psychotherapy as disruptive and re-traumatizing. Instead of being Rescuers and the Rescued, both she and her therapists entered into a cycle of powerful role reversals, and, at times, they each felt as if they were the Victim, Rescuer, and Perpetrator. This poster concludes that the Karpman Triangle can be a useful tool in understanding the psychotherapy process, but will also highlight ways in which modern psychoanalytic theories can further explain pivotal moments in treatment.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Ideation and Coalition: Examining Shifts in Sentencing Policy through Policy Ideation and Coalitions

#### OBJECTIVES/BACKGROUND:

This study examined emerging trends in criminal justice, and specifically sentencing, policy. While alternatives to the standard ‘tough on crime’ position have become increasingly popular, the question of the ability of sentencing policy reform to gain traction either as a conservative or bipartisan issue increasingly came into focus. This study assessed the transition away from a ‘tough on crime’ status quo and investigates if and how sentencing reform gains traction, who the prevalent actors are, and what strategies are used to advance sentencing reform not only rhetorically, but also in practice.

#### METHODS:

The study combined a review of literature, an analysis of the content of two conservative publications, and interviews with policymakers and advocates of sentencing reform. The analysis of publications and interviews targeted the importance of the issue to specific political ideologies, and specifically focused on the role that conservatives have, and the political ideations that they bring to the issue. Analysis of the publications involved a three person, independent review of articles identified as pertaining to sentencing reform in order to categorize issues within sentencing reform and rank the stance of each article.

#### RESULTS TO DATE:

Data from both parts of the study supported the fact that potential policy coalitions are dependent on bipartisanship and consensus-creation across policy ideations. The interviews identified bipartisan support for reform legislation; the analysis of publication content identified drugs, criminalization, and public safety as high priority issues within sentencing reform, and the cost of criminal justice and sentencing as a “most important” issue for many of the articles. Moreover, an analysis of the literature evinces a buildup of legislative success to initiate policy reform in the 2000s and 2010s, seen in the passage of the Prison Rape Elimination Act (2003), the Second Chance Act (2008), and especially in the Fair Sentencing Act (2010).

#### CONCLUSIONS:

The results suggest that policymakers are serious about changing the way the criminal justice system operates. The potential for change and reform has reached levels not seen since before the beginning of the escalation of crime policies in the 1960s. While policy entrenched over the course of nearly four decades cannot be expected to change overnight, or even over the course of a year, the possibility for reform exists - in large part due to newfound conservative support. While conservative support reform is far from unanimous, the results suggest that reform is an increasingly viable possibility, significantly more than could have been said as late as the early 2000s.

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## Why do Solvent Countries Default?

Simple indicators of sovereign default risk, such as debt-to-GDP, are often used alone to characterize the sustainability of a country's debt burden. Research by Reinhart, Rogoff, and Savastano (2003), as well as Manasse, Roubini, and Schimmelpfennig (2003) and Manasse and Roubini (2009) have sought to better explain the failure of simple indicators. By highlighting the heterogeneity of default episodes these authors have proposed highly nonlinear relationships between different types of indicators. This paper expands on the work of these authors by formally incorporating a theoretical basis for distinguishing between different types of sovereign defaults. A benchmark model is used to distinguish "atypical" defaults from "typical" defaults. This distinction is made ex ante, before the model is estimated, rather than ex post, after the model is estimated (as in Manasse and Roubini (2009)). The paper then examines "atypical" defaults using both case studies and more general quantitative analysis in order to evaluate which expanded theories of sovereign default, if any, can better explain the causes of "atypical" defaults.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Workplace Discrimination: We've come a long way... Or have we?

Current research suggests that workplace discrimination has become increasingly subtle in recent years, with greater awareness of so-called "microaggressions" - that is, commonplace ambiguous indignities directed at minority group members that may be intentional or unintentional, and which may occur outside of the awareness of the perpetrator. The present study examined workplace microaggressions ranging in severity from mild to blatant, and how these actions are perceived by members of different ethnic groups. There has been little empirical work on microaggressions, mostly limited to undergraduate samples rather than working adults. We address this need for a diverse workplace sample to assess perceptions of microaggressions, hypothesizing that African Americans and women will perceive microaggressions more often than Caucasians at all levels of severity, with the difference being most pronounced at the more subtle levels of discrimination.

The study included 30 African Americans, 131 Caucasians, 25 Asian Americans, and 18 Hispanics, recruited through the website Mechanical Turk. Microaggressions were assessed using standardized vignettes validated in previous research. Hypothesis 1, which predicted that African Americans would perceive greater microaggression than Caucasians, was supported, with  $M_s = 12.92$  and  $11.98$ , respectively ( $F = 3.20, p < 0.01$ ). T-tests broken down by severity level revealed that African Americans perceived significantly greater microaggression than Caucasians in both the microinvalidation condition,  $M = 3.18$  vs  $2.81, t = 3.77, p < 0.01$ , and the microinsult condition,  $M = 3.60$  vs  $3.28, t = 2.51, p < 0.01$ . African Americans also perceived more microaggressions than Caucasians in the most blatant microassault condition,  $M = 4.05$  vs  $3.88$ , however this result was not significant. Significant racial differences in a control condition were neither predicted nor found.

Hypothesis 2 predicted that members of all minority groups would perceive more microaggressions than Caucasians. The overall  $F$  was significant ( $F=10.46, p < .01$ ), with means and t-tests indicating that Caucasians were significantly less likely to perceive microaggressions at all levels of severity (from subtle to blatant) than were members of any of the other three groups. Hypothesis 3 predicted and found a significant interaction effect between race and gender in the perception of microaggressions ( $F= 2.87, p < .01$ ), where Caucasian men were least likely to perceive incidents as microaggressions, followed by Caucasian women. As predicted, African American women perceived the most microaggression, followed by Hispanic and Asian American men.

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### Observational Learning of Romantic Relationship Behavior in Emerging Adults

#### BACKGROUND:

Those who fail to achieve intimacy by young adulthood experience lower empathy, higher egotism, and feelings of isolation (Berk, 2008). Positive romantic relationships help individuals find a sense of identity, security, and bar against anxieties and depression (Brown et al., 1999). Previous studies show that positive parent-child, friendship, and sibling relationships serve as a basis for positive romantic relationships (Scharf & Mayseless, 2001; Rauer & Volling, 2007). This study hypothesizes that the observation of healthy behaviors in other's romantic relationships will be correlated with a higher frequency of healthy behaviors in one's own relationships.

#### PARTICIPANTS AND PROCEDURE:

120 primarily Caucasian college students (ages 18-25) who have had a romantic relationship within the last two years completed online questionnaires measuring the frequency of positive and negative relationship behaviors for themselves, as well as in an influential adult couple's relationship, their siblings' relationships, and their peers' relationships. The Conflict Tactics Scale (Strauss 1979), Mother's Expression of Affection Scale (Koblinsky and Palmeter, 1984), and Network of Relationships Inventory-Behavioral Systems Version (Furman and Buhrmester, 2009) were used.

#### RESULTS:

Data were analyzed using Pearson-product moment correlations.

Observed relationship behaviors were positively correlated with current relationship behaviors. A moderately positive correlation existed between observed and performed behaviors measured by both the NRI ( $r=.42$ ) and MEA ( $r=.20$ ). Correlations were also found between observed peer relationships and own relationship behaviors for several subscales of the NRI: the tendency to seek security through a relationship ( $r=.37$ ), antagonize a partner ( $r=.64$ ), and criticize a partner ( $r=.58$ ). The only significant correlation found between observed sibling relationship behaviors and current relationship behaviors was on a subscale of psychological aggression ( $r=.79$ ).

Counter to our hypothesis, significant negative correlations were found between the observation of detrimental CTS behaviors in adult relationships and one's own performance of these detrimental behaviors ( $r=-.24$ ). Two subscales were significant: partner-injury behaviors ( $r=-.46$ ) and physical assault ( $r=-.34$ ).

#### CONCLUSIONS:

Although we cannot determine causality, these results suggest that positive relationship behaviors witnessed in a caregiver-child relationship tend to be modeled; however, extreme negative behaviors are not. Conversely, negative relationship behaviors seem to be learned most readily by observing peer relationships. While these behaviors were studied in the context of short lived relationships in emerging adulthood, these relationships form the basis for long-term relationships; therefore, these results should provide both hope that individuals can break the cycle of abuse learned at home, and a warning to understand the impact one's peers negative choices can have.

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# SOCIAL SCIENCES



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### Effective Methods for Improving Perceived Self Control and Their Impact on Substance Use Cognitions

High self-control is associated with positive outcomes, including lower drug and alcohol abuse, whereas low self-control is a risk factor for negative outcomes. Furthermore, higher self-control buffers against the consequences of negative life events such that increases in self-control are associated with decreases in substance use. The current study was designed to determine an effective method for improving perceived self-control and to examine how improved self-control impacts substance use cognitions. Undergraduate students who reported prior substance use ( $n = 137$ ) were randomly assigned to one of five conditions that manipulated perceived self-control. The conditions were: exposure to an aversive noise either with control over the volume and duration or no control over noises, an essay writing task about a time participants felt in control or powerful, a word completion task that primed feelings of power or control, and a neutral condition. Self-reported feelings of control, substance use willingness, and an indirect measure of substance use attitudes were assessed post-manipulation. Stroop task response latency measured post-manipulation inhibitory control. An overall ANCOVA comparing all five conditions, controlling for gender and negative mood, revealed that the writing condition had the strongest effect on perceived self-control. When compared to the neutral condition, respondents in the essay condition reported higher feelings of control ( $\mu_{\text{essay}} = 3.89$ ,  $\mu_{\text{neutral}} = 3.13$ ,  $p < .02$ ), lower response latency in the Stroop incongruent trials ( $\mu_{\text{essay}} = 1445.08\text{ms}$ ,  $\mu_{\text{neutral}} = 1657.19\text{ms}$ ,  $p < .02$ ), and lower willingness to use substances ( $\mu_{\text{essay}} = 2.54$ ,  $\mu_{\text{neutral}} = 3.74$ ,  $p < .03$ ). Respondents in the word completion task also reported lower response latencies in Stroop incongruent trials ( $\mu_{\text{neutral}} = 1659.18$ ,  $\mu_{\text{wordcompletion}} = 1422.52$ ,  $p < .02$ ). The findings demonstrate that the essay writing task is an effective way to enhance perceived and inhibitory control, and is negatively associated with risky substance use cognitions. The word completion task is an effective method for enhancing only implicit inhibitory control.

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#### SOURCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Perceived causes of and responsibility for Anorexia Nervosa and Binge-Eating Disorder

Although perceived causes of anorexia nervosa (AN) have been studied, less is known about perceptions of binge-eating disorder (BED), newly recognized as a psychiatric disorder, or about the implications of causal beliefs about either disorder for perceptions of responsibility for both its cause and solution. In this study, influenced by Brickman's (1982) model of responsibility, college students ( $n = 206$ ) read vignettes describing a female with AN or BED, then completed scales assessing seven causal beliefs and perceptions of self and other responsibility for causing and solving the disorder.

Participants emphasized life stressors and poor emotion regulation over genes, metabolism, and negative family influences as contributors to both disorders. Compared to AN, BED was viewed as caused more by genetics, metabolism, and lack of self-control and less by life stressors and negative cultural influences. Affected women were also perceived as more personally responsible, and others as less responsible, for causing and solving BED.

Relationships between causal factors and responsibility scales were examined through multiple regressions. Lack of self-control strongly predicted perceived personal responsibility for causing both disorders and, for BED, responsibility for solving it. For AN, participants also associated poor emotion regulation with high personal responsibility, life stress with low responsibility. For both disorders, participants associated genetic causes with others' responsibility for recovery. Participants affected by eating disorders (through self, family, friends) placed more emphasis on external contributors (family, culture, stressors) and less on personal responsibility for the problem than unaffected participants, suggesting an actor-observer bias (Jones & Nisbett, 1971). Personal experience did not affect perceived responsibility for recovery. Overall, a strong perception that individuals with binge-eating disorder, like obese individuals, lack self-control appears to increase their perceived responsibility for both causing and resolving their disorder. Future research, drawing on attribution theory, should examine implications for stigmatization.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Evaluating the effect of central banks' ability to achieve economic stability through inflation-targeting in developing countries

In recent times, many developing countries have switched to inflation-targeting monetary policy frameworks, in many cases from an exchange rate targeting framework or implicit stability targeting framework. Inflation targeting entails setting medium-term inflation targets and holding the central bank accountable to meet these targets through transparent and broad-based monetary policy actions. The theory behind this is that central banks with a single, theoretically very obtainable objective will be better able to achieve economic stability. This study seeks to examine a corollary to the unproven but well-supported notion that inflation-targeting frameworks are more successful than the variety of other frameworks previously used in developing countries. Essentially, this research is looking for empirical evidence to suggest that central banks that more consistently meet targets are, or are not, producing economies with greater macroeconomic stability. Since price stability measured by inflation is directly related to whether central banks meet their targets, this study will focus on output stability, the other core component of overall macroeconomic stability. Empirically, this study will examine the potentially causal relationship between the ability of central banks to meet inflation targets and output stability in these developing countries. Taking publicly available data on inflation targeting frameworks in twelve countries and World Bank data for macroeconomic conditions, the study will evaluate the statistical significance of regression models that seek to explain the number of standard deviations from each country's average growth rate for the period as dependent upon the difference between observed inflation and the target in the prior year. While there is some evidence of the relationship, it is not as strong as expected. Furthermore, conditions exogenous to the model have a tremendous impact on output stability. Developing countries are very susceptible to shocks, and bringing inflation in line with targets is not sufficient to ensure macroeconomic stability.

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#### SOURCES

Inflation targets and bands sourced from the websites of the central banks of the countries in the study (Brazil, Botswana, Chile, Colombia, Dominican Republic, Indonesia, Kazakhstan, Mexico, Peru, South Africa, Turkey, and Uruguay)

Inflation, GDP, GDP per capita, GDP growth, GDP per capita growth, and other macroeconomic indicators sourced from the World Bank's global dataset



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# SOCIAL SCIENCES

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## The Correlation between Reproductive Health and Economic Development: Contraceptive Prevalence and Female Life Expectancy

The positive relationship between public health and economic development is fairly common knowledge; healthy workers are more productive and higher incomes allow for better healthcare. But the more nuanced and specific relationships between specific health and development indicators are often less obvious. One such relationship that has not been the subject of much economic research is the correlation between contraceptive prevalence, an indicator of reproductive health, and female life expectancy, an indicator of economic development and overall population health. This paper will examine the relationship between contraceptive prevalence and female life expectancy using a panel data set spanning a decade and encompassing data from fifty countries. This data was gathered from published World Bank and UN Data sets; the sample size was chosen based on data availability. The data will be put into EViews, an econometric software, in order to obtain several regressions and robustness checks.

The expected results of the study are that contraceptive prevalence and female life expectancy are positively related. As more women have access to birth control, fertility should decline and with it, the risk of dying in childbirth. Additionally, contraceptive prevalence is an indicator of reproductive health which greatly contributes to overall health, so increased contraceptive prevalence means women who are healthier overall. Further, contraceptive prevalence also serves as an indicator of female autonomy, and greater female autonomy increases life expectancy for women. However, it is not expected that changes in life expectancy will be entirely predicted by contraceptive prevalence, and will thus need to use fixed effects and control variables to prevent my results from suffering from omitted variable bias. I expect that both fixed effects and control variables will be necessary.

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## Age as a moderator of the impact of perceived racial discrimination on African American adults' diet and exercise cognitions

Discrimination has been positively associated with risky health behaviors (Pascoe & Smart Richman, 2009; Stock et al., 2011). In studies of substance use and risky sex among African Americans, this association was mediated by cognitions such as behavioral willingness (Gibbons et al., 2010; Roberts et al., 2012). The present analyses extended this work to diet and exercise. African Americans have lower diet and exercise behaviors compared to Whites (August et al., 2011) and higher rates of health conditions linked to these behaviors, such as heart disease and obesity (Mays et al., 2007). The present study examined whether perceived racial discrimination predicted African American adults' diet and exercise cognitions and whether this relationship was moderated by age.

African Americans (N = 117; M age = 38.75; 53% male) completed a computer-based survey on perceived discrimination, willingness to diet and exercise, prototypes of the typical person who eats healthy and exercises, and worry about associated health conditions. Regressions showed significant interactions between age and discrimination (controlling for sex, health insurance, education, and past behavior) on: exercise prototypes, willingness to diet and exercise, and worry ( $\beta$ 's  $\geq .27$ ,  $ps \leq .01$ ). Among older adults, discrimination predicted higher worry and lower willingness ( $\beta$ 's  $> .51$ ,  $ps < .01$ ), and marginally less favorable exercise prototypes ( $\beta = -.27$ ,  $p < .10$ ). However, among younger adults, discrimination did not predict either willingness or worry ( $\beta$ 's  $\leq .12$ ,  $ps > .26$ ), and was associated with more favorable prototypes ( $\beta = .24$ ,  $p < .03$ ). Efforts to promote diet and exercise among African American adults should promote factors that protect against the effects of discrimination and consider the impact of age.

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# SOCIAL SCIENCES

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## Are Fare Cards Like ATM Cards? Investigating Possible Indirect Network Effects in Public Transit Payment Systems

Network effect theory suggests that increasing incompatibility between systems, such as the addition of surcharges to the ATM transactions of non-members, discourages people from utilizing an otherwise compatible network. This study uses data from the Washington D.C. area to examine whether the use of a common smart card for transit fare payment, which reduces incompatibility between transit systems, affects the overall utility of the network. Holding all else constant, ridership should increase due to the reduction in incompatibility. A model of Metrorail ridership serves as the base of the analysis, with explanatory variables that control for fare price, employment and other common determinants of transit ridership. The results of this analysis may be useful to transit system planners, especially in municipal systems that connect to a larger metropolitan network. With various fare collection options available in the market, accurate assessment of network effects will be important in determining the cost and benefit of joining a larger network such as SmarTrip.

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### Influences of Object Properties to Attentional Guidance

Recent studies suggest that target-to-object relationship (whether the target appears to be a part of the object or is perceived as placed on top of an object) is the primary factor that determines whether attentional guidance is influenced by object representations (Chen & Cave, 2006; Richard, Lee, & Vecera, 2008; Hollingworth, Maxcey-Richard, and Vecera, 2012). Others, however, suggest that object-based selection is largely driven by spatial uncertainty of target location (Shomstein & Yantis, 2002; Drummond & Shomstein, 2010). Here, we re-evaluate the contribution of spatial uncertainty to object-based attentional guidance as well as examine the interaction between spatial uncertainty and target-to-object relationship. In a series of five experiments, object-based effects were measured as a function of whether the target location was known in advance (certainty manipulation) and whether the targets were perceived to be as concavities of the object (bites), floating on top of the object (floaties), or part of an object (parts). We observed object-based effects only when target location was uncertain, independent of whether the targets were interpreted as being part of the object (bites), or simply placed on top of the object (floaties). There was an exception, however, with parts failing to elicit object-based effects. These results re-instate the importance of location uncertainty in object-based attentional guidance, and suggest that object representations, placed within the boundaries of an attended object, benefit perceptually regardless of whether they are perceived to be an integral part-of or on-top-of the object.

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### Arts Integration in DC Public Schools

#### BACKGROUND:

Arts integration is a teaching pedagogy that uses the arts (including music, dance, drama, and visual arts) to teach other academic subjects while increasing students' understanding of the art form. Urban public schools often struggle to keep the arts in the face of budget cuts and high-stakes standardized testing, especially in an underachieving environment. As such, arts integration is an increasingly important teaching method, as it can be students' only access to the arts. Further, arts integration has been proven a successful teaching method, using both academic and artistic standards to engage students who struggle with traditional teaching styles.

#### OBJECTIVES:

The purpose of this case study is to explore an arts integration program at an underperforming public elementary school in Washington, DC. The research is intended to understand how one school engages students while maintaining a focus on the schools' external priorities.

#### METHODS:

In order to understand the experience in this school, the researcher interviewed two teachers and two administrators at the school. Each interview focused on the participants' experience with arts integration. The interviews were transcribed and coded for emergent themes. This was triangulated to determine what the experience of an arts integration program is like for the variety of stakeholders in the public school. To determine the success of the arts integration, the interviews and their conclusions were compared to the bodies of knowledge that already exist in the fields of arts integration and arts education.

Results and conclusions will be discussed pending completion of data analysis.

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## The role of personal choice in promoting college men's sun protection cognitions

Young adult men engage in fewer sun protection behaviors than women (Kasparian et al., 2009), which likely contributes to older White men having higher skin cancer rates than women (e.g., Skin Cancer Foundation, 2012). However, sun protection interventions for men are limited. The present study examined one way that informational interventions for men may be designed to have a maximum impact on sun protection cognitions - by promoting feelings of personal choice. The focus on enhancing personal choice was based on past research on the importance of individual choice and autonomy in health, as well as literature suggesting that health promotion efforts for men include themes of choice and independence (Sloan et al., 2010).

White male undergraduates (N = 68) were randomly assigned to read information on sun protection behaviors framed as either recommendations to follow or personal choices to make. This information was presented either in an electronic brochure or in a way that required an active response from participants. ANCOVAs, controlling for past behavior, showed that those who received choice-promoting information reported greater perceptions of choice,  $F(1, 62) = 3.86, p = .05$ , and autonomy support  $F(1, 62) = 8.56, p = .005$ . However, these effects were only significant for men who received the active format ( $ps < .04$ ). Further analyses with this group showed that men who received the active format choice-promoting information reported higher willingness to protect their skin,  $F(1, 30) = 5.87, p = .02$ . Autonomy support and/or perceptions of choice were positively correlated with sun protection willingness, intentions, and prototypes of the typical male who protects his skin ( $ps < .05$ ). Findings demonstrate that perceptions of choice over sun protection can be affected by brief informational manipulations, are associated with men's sun protection cognitions, and should be considered in future interventions.

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### Spiritually Rich, Economically Poor: Religious Culture in Central Appalachia

Someone driving through the rolling hills of Eastern Kentucky can see at least ten churches in less than five minutes. The presence of so many churches suggests a strong role of spirituality in traditional Central Appalachian culture. Little research has been done on how spirituality influences economic disparity, another major cultural aspect of Central Appalachia. The purpose of this research is to understand how spirituality influences the experience of rural poverty in the mountains of Central Appalachia. To understand this experience, the researcher conducted five in-depth, qualitative interviews in Harlan County, Kentucky, and Mercer County, West Virginia, in January 2013. Initial findings from the interviews indicate that spirituality is a saving grace and beacon of hope for many Appalachians. The researcher identified that harmful substances tend to serve as a numbing outlet before individuals turn to religion and scripture as another method of support. On a communal level, the researcher found that the spiritual experience churches provide is secondary to the community it fosters for its attendees. The economic hardship Appalachians face is distinct to other poverty experiences in America because of the rural landscape of the region and its unique history. Churches generate a supportive and empathetic community where difficult experiences may be shared and understood. Members of the respective churches also rely on this community to receive financial support because federal assistance and non-profit outreach programs are unknown and unheard of in Appalachian communities. Further results, findings, conclusions, and implications will be discussed upon completion of data analysis.

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### Interpretation of Emoticons in Computer-mediated Communication

#### BACKGROUND:

Computer-mediated communication is a vital part of our lives today. From text messaging, to email, to Facebook, it is yet to be determined if emoticons play a significant role in computer-mediated communication as they have potential to convey nonverbal behaviors and help establish tone in text-based communication. Emoticons, popular among millennials, are a very new topic of research and it is necessary to understand how they are used and interpreted in order to understand what kind of role emoticons play in a world of increasingly computer-based communication.

#### OBJECTIVES:

This study aims to examine how GW students interpret emoticons in a variety of examples of computer-mediated communications. Examples will showcase the most frequently used emoticons in a variety of ways ranging from happiness to sadness to joking and sarcasm. Analysis will examine similarities and differences among interpretations of messages involving emoticons to assess the effect emoticons have on creating meaning of a message. Ultimately, conclusions of the study may lead to a greater understanding of emoticons in relation to nonverbal communication or behavioral and emotional communication.

#### METHODS:

Open-ended surveys will be distributed to a group of approximately 30 GW students that will feature sample computer-mediated communication messages using emoticons. Participants will be asked to interpret the samples as well as answer some questions about how they regularly use emoticons.

#### RESULTS:

Results are in the process of being analyzed and will be complete by April 1st. It is anticipated that results will show common interpretations of emoticons among a randomly selected participant group.

#### CONCLUSIONS:

Conclusions are being gathered and will be complete by April 1st. After data has been analyzed, conclusions will be drawn detailing common interpretations of emoticons as well as cataloging differences between sender and receiver interpretations. This study will contribute to the emerging amount of research about emoticons and their purpose in computer-mediated communication.

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## Measuring and Forecasting World Income Inequality

**BACKGROUND:**

Most of the attention in Development Economics has been placed on economic growth and poverty, though there is much to be said about inequality. While we understand growth to be desirable and poverty to be undesirable, inequality is ambiguous.

**OBJECTIVES:**

In this paper I estimate inequality in the world using different indices: Atkinson, Generalized Entropy, and Gini. Furthermore, I decompose the Generalized Entropy measurement into “within” and “between” country inequality, and I forecast the measures out for two years.

**METHODS:**

To address missing data, I employ Sala-i-Martin’s estimation technique from previous papers. He classifies countries into three groups depending on data availability. Group A countries are those with more than one year of data available in the time series. I have chosen to focus only on Group A countries as they compose almost 90% of the world’s population in all years from 1980-2012. To fill in missing data points, I use: linear interpolation/extrapolation and linear regression. By doing so, I hope to show that regardless of which estimation technique is employed, the results will be similar enough to deem estimation errors negligible. Lastly, using auto-regression, I forecast all measurements out for two years.

**RESULTS & CONCLUSIONS:**

Preliminary results show that income inequality in the world has declined and is likely to continue to do so. Additionally, the preliminary results of my decompositions show that while inequality between countries has been decreasing, within-country inequality has in fact been rising.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Intonation and Gender Perception: Applications to Transgender Speakers

Early guidelines for voice feminization therapy with a speech-language pathologist were limited to elevating speaking fundamental frequency (pitch) from the male range toward the female range or gender-neutral range. Recent studies indicate that changing pitch alone is insufficient to change perceived gender of the voice. Wolfe et al. (1990) suggest that male-to-female (MTF) speakers who pass as female use a higher percentage of upward intonation patterns and downward shifts than speakers judged to be male, but Gelfer and Schofield (2005) also studied intonation in MTF speakers and found no differences. Therefore, it remains unclear whether intonation is influential to gender perception and applicable to transgender communication treatment.

Audio-recorded descriptions of a Norman Rockwell painting as described by 12 male, 12 female, 14 MTF and 6 female-to-male (FTM) speakers were presented to 14 listeners who then judged the speaker's gender as well as the speaker's femininity level. Acoustic analysis of all speech samples was collected on several measures of intonation.

When the speakers were divided and compared across the 4 gender groups, there were no significant differences for duration of utterance, semitone range, pitch slope, or percentage of utterances with upward, downward, or neutral pitch shifts. However, when the groups were formed according to perceived gender of the speaker, comparisons revealed statistically significant differences with medium-large effect sizes. Speakers perceived as female used a greater ST range and more upward intonations compared to the group perceived as male. The differences in ST slope, percent downward intonations, and percent utterances within 2 ST were not significant and had very small effect sizes. The MTF speakers who passed as female ( $n=4$ ) used a greater ST range and considerably more upward intonations and less downward intonations compared to those who did not pass ( $n=10$ ), yet these differences did not reach statistical significance.

Data indicate that use of a large semitone range and frequent upward pitch shifts are associated with female voice, and therefore may benefit MTF speakers who want to be perceived as female. This conclusion is guarded, however, because the results were not replicated in a smaller sub-group of male-to-female transgender speakers. A larger population of speakers might have helped to determine intonation significance in the role of femininity, specifically more MTF individuals who passed as feminine. However, the current findings of this research warrant the inclusion of intonation measures in future studies of gender perception and in development of treatment protocols.

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### Changing Diagnostic Criteria for Autism Spectrum Disorders: Perceptions of Personal Impacts

The purpose of this study is to understand ways in which family members of children with autism, Asperger's syndrome, or Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS) perceive changes being made to the diagnostic criteria and labeling of these disorders. When the American Psychological Association publishes the fifth edition of the Diagnostic and Statistical Manual (DSM-V), autism, Asperger's syndrome, and PDD-NOS will no longer be distinct diagnoses, but will be subsumed by the diagnosis of Autism Spectrum Disorder. The proposed content for the DSM-V has been released, prompting much speculation on the part of researchers and advocacy organizations about the possible impacts on families. While several studies have been published about the anticipated impacts on individuals and families, no study has sought to understand the family members' perceptions of the changes. This situation also offers a unique chance to study both the process of how perceptions of change are formed and the content of those perceptions, prior to the change occurring. Qualitative interviews were conducted with five adult family members of children with a diagnosis of Asperger's, PDD-NOS, or autism, or who are in the process of obtaining a diagnosis. Initial findings reveal that family members of children with a diagnosis of Asperger's syndrome have high levels of knowledge of the changes and negative reactions to them. One parent of a child in the process of obtaining a diagnosis was unaware that any changes were being made to the diagnostic criteria, and one family member of a child with autism knew that changes would be made, but did not know the nature of the changes. None of the participants indicated that their children's doctors had spoken to them about the DSM-V. Further findings and implications will be discussed.

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### Economic Democracy and Building the Better City

For the first time in nearly 50 years, Americans are moving back into urban areas. This shift necessitates an examination of the current urban scheme in creating a “good” urban life. A “good” city must ensure social equity and environmental sustainability without diminishing economic efficiency. Despite the need for a more efficient, more empowering city, traditional practices in business, government, and community organizations do not seem to create sustainable results. Urban dwellers, whose lives are constantly dictated by traditional top to bottom authoritative structures, can often fall prey to feelings of oppression and inability to change the system in which they live. Cooperative businesses offer an alternative to traditional business models by providing a foundation upon which social empowerment, environmental sustainability, and economic efficiency can occur simultaneously. In the scope of this research, cooperative businesses are defined as democratically governed businesses, in which members have an equal opportunity to influence the business decisions. This project focuses on three cooperative case studies in three cities along the East Coast: New York, Philadelphia, and Washington, DC. Interviews with members of these cooperatives as well as professionals in the field have illuminated that urban cooperatives primarily serve to offer choices. These businesses empower employees and consumers to adopt a bottom-to-top organizational structure and play a more active role in determining which jobs and products they feel best suit their needs. By shifting business’ bottom lines from profit maximization to concern for members and their broader community, cooperatives become more fertile grounds for creating socially just and environmentally sustainable business practices.

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### Understanding the Service-Learning Experience of Racial Minorities at Predominantly White Universities

Service-learning, a method of pedagogy that incorporates and connects community service with class curriculum, has recently gained popularity in higher education. Many studies have been conducted concerning the benefits and practices of service-learning; however, few have looked into how students of color experience service-learning. Though service-learning has been seen as a tool to expose White students to the issues present in racial minority communities, little research has focused on how service-learning is experienced by those students who identify with those communities. As universities - especially those that are predominantly White - become increasingly racially diverse, understanding how racial minority students experience service-learning becomes essential in ensuring that service-learning programs are accommodating of students of color. The purpose of this study seeks to describe and understand the service-learning education experience for racial minority students at a predominantly White university. In order to address this research, qualitative interviews were conducted with six current racial minority students who have all had experience with service-learning courses at The George Washington University, a predominantly White university located in Washington, D.C. These interviews were then coded for various themes in the data. Initial results reveal themes relating to how students of color perceive themselves, the people they serve, and their White colleagues in the context of service-learning. Results also highlight how students of color feel they are benefitting from participation in service-learning and their perception of how this compares with other White students. Such results can be utilized to further develop service-learning curriculum to be more accommodating of students from diverse racial backgrounds.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Community and DC: How Undergraduate Students' Involvements Shape Their Sense of Place

As 98% percent of The George Washington University undergraduate students come to the university from different regions, many are creating novel impressions of the District of Columbia as new residents of the city. Community involvements are an essential component of an individual's impression of the environment around them and may shape how students create their sense of their new place of residence. This study therefore seeks to provide insight into how student activities influence the manner in which they perceive DC to better inform what contributions they make to the city and region.

This qualitative study included semi-structured interviews with five undergraduate GW students on how their activities shape perceptions of the city as a social and physical place. Purposeful sampling ensured the interviewees represented a range of experiences and backgrounds. Initial data analysis suggests that the communities students join can have a foundational influence on how they perceive the city, thus creating views of DC centered on particular interests and schemas. The findings identify how further study can better conceptualize way in which students engage the District and how their perceptions may shape their interactions with the city.

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Gender Moderates the Relationship between Perceived Racial Discrimination and African Americans' Hopelessness and Risky Health B

African Americans experience health disparities are partially explained by experiences of racial discrimination (Williams & Mohammed, 2009). Research has demonstrated that African Americans who perceive greater racial discrimination engage in higher levels of substance use (Gibbons et al., 2010). Less research has examined gender as a moderator of the association between perceived racial discrimination (PRD) and health. The present study examined whether PRD among African Americans is associated with hopelessness, alcohol use, and sex under the influence of alcohol; and tested whether these effects were moderated by gender.

Participants were 300 African American young adults (157 females; ages 18-25) who completed a survey that assessed PRD, hopelessness, alcohol use, sex under the influence of alcohol, and demographics.

PRD was related to greater hopelessness ( $\beta = .19; p < .01$ ) and a PRD by gender interaction emerged ( $\beta = -.20; p = .02$ ). PRD was also associated with greater alcohol use ( $\beta = .23; p < .001$ ) and a PRD by gender interaction emerged ( $\beta = .17; p = .04$ ). For both hopelessness and alcohol use, the relationship between PRD and health was significant for men only. For sex under the influence of alcohol, PRD was related to greater risky sexual behavior ( $\beta = .20; p = .01$ ) and a PRD by gender interaction emerged ( $\beta = -.17; p = .04$ ), but for sex under the influence of alcohol the relationship with PRD was significant only among women.

Results suggest that discrimination's influence on health behaviors is moderated by gender. Among African Americans, the relationship between PRD and hopelessness and alcohol use was stronger among men compared to women. African American men may experience racial discrimination in a unique way and may be more likely to cope with psychological outcomes through engaging in distinct health behaviors (Gibbons et al., 2012).

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### The invisible man: The presence of men in an all women's psychotherapy group

Women's groups can be of great therapeutic value to female patients, particularly among those with histories of trauma. By joining women who share similar experiences, such as rape, molestation, alcoholic parents, and traumatic losses, female patients can create an environment of safety, trust, and empathic regard (Gagerman, 2004). Particularly when women have suffered physical, sexual, or emotional abuse that was perpetrated by a man, an all women's group can provide female members with an added layer of safety and understanding to support them in achieving their treatment goals.

Men, however, can never be completely excluded from a women's group. They are present in the members' lives, and at the very least, in their unconscious. Acknowledging and discussing men is something that each all women's group will navigate differently, but engaging in candid discussion about men has the potential to be a healing experience as the women are able to make space to reflect on the roles men have played in their lives, and consequently to form healthier and more compassionate internal representations of them.

This presentation will present a qualitative case study of a women's group of trauma survivors, conducted at The George Washington University Center Clinic. It will explore the fact that for many months, men were rarely spoken about, and it will examine how men were introduced into the dialogue of the group: at first in more unconscious and indirect ways, for example, in the co-leaders' male supervisor, in one of the co-leader's pregnancy, and in talk of (a male) God, and gradually, as relationships and sex were discussed in a more explicit way. The presentation will explore how this group's relationship with men evolved over time, and it will consider the healing benefits of making space for men in a safe and supportive environment.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### National Survey of College Graduates Estimation using the American Community Survey

The National Survey of College Graduates (NSCG) has been conducted by the Census Bureau for the National Science Foundation (NSF) since the 1960s. It is the nation's only source of detailed statistics on the science and engineering (S&E) labor force. The NSCG is a longitudinal survey, designed to provide data on the number and characteristics of experienced individuals with education and/or employment in science and engineering (S&E) living in the United States. The sampling frame for the NSCG is undergoing change. The past design selected NSCG sample from the decennial census long form sample augmented by the National Survey of Recent College Graduates. The decennial census in 2010 only included a short form and is no longer available as a frame for selecting the NSCG. The American Community Survey (ACS) is the replacement for the decennial census long form. This poster presents opportunities to be studied for improving NSCG estimation using current ACS survey data and for predicting NSCG variables in non-survey year using the current year ACS.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Effect of Faculty Development on Service Learning at GW

Service learning, a method of teaching that brings together formal instruction and related service in the community, has become a larger part of university life, especially at The George Washington University (GW), with an increasing number of professors incorporating service learning into a wide variety of disciplines. Throughout the existing research on service learning, there is a lot of theories and empirical findings available on how to implement a course and the benefits that service learning has to students, but how does faculty development effect service learning? Learning more about the effects of faculty development on service learning at GW specifically came through interviews with seven members of GW faculty and a staff member at the Center for Civic Engagement and Public Service who are involved in service learning. The interviews shed light on what resources have been available in the past, what is currently available, and what services are planned to be available to all professors who are currently involved in and those who are interested in becoming involved in service learning courses at GW. As professors reflected on their time as a service learning professor, the true diversity of class outcomes, both desired and actual, varied with the professors' backgrounds. The results can inform practice and may be important for the advancement of service learning with The George Washington University community and the development of resources available for faculty and their development as service learning professors.

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Empowering Victims of Bullying Through Participation in the Solution-Oriented Art Therapy for Bullying Victims Intervention

Peer victimization characterized by malicious intent, a power differential, and repeat occurrences is commonly referred to as bullying. The topic of bullying is gaining media and research attention as the associated consequences are becoming more overt and prevalent. Bullied individuals tend to respond by internalizing their feelings, enabling their needs to easily go unnoticed. The lack of interventions of victims of bullying is reflected in the lack of research in this area. Before victims of bullying develop a detrimentally low self-esteem, seek revenge or choose to end their lives, their mental health needs must be addressed. The intervention tested in this study, developed by the author, consists of 10 one-hour sessions and is based on the main principles of Solution-Focused Brief Therapy and solution-focused, cognitive-behavioral and supporting art therapy experientials. The purpose of this explanatory mixed-methods study is to test the efficacy of the Solution-Oriented Art-Therapy for Bullying Victims (SOAT-BV) intervention at increasing participants' global self-esteem and peer-relations self-esteem as well as decreasing incidences of endured bullied. Currently, the first group of participants is participating in SOAT-BV, and data will be analyzed in April and May after the curriculum and posttests have been completed.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Visual Rhetoric at the Ballots: Internet Memes and the American Political Stage

#### BACKGROUND:

The Internet as a communicative tool has empowered visual rhetoric, or the ways in which visual images communicate and persuade. This research study focuses on two brand-new phenomena, the GIF and meme, and how these visual formats mock and satirize American politics and politicians.

#### OBJECTIVES:

Given the known impact and theoretical frameworks behind visual rhetoric, it is safe to assume that fast-spreading GIFs and memes targeting American politics change the ways we view issues and politicians. The ultimate objective of this study is to determine the ways in which GIFs and memes construct perceptions of the American political stage.

#### METHODS:

This study is a rhetorical criticism using Internet GIFs and memes as isolated artifacts meant to satirize its subjects. Using the method of generic criticism, this study seeks to discover commonalities in rhetorical patterns within the framework of Internet GIFs and memes.

#### RESULTS TO DATE:

Research indicates that there exist certain patterns and themes within these satirical artifacts that may leave its consumers with unrealistic perceptions of politicians, political issues, and political events.

#### CONCLUSIONS:

The significance of this study lies in the pervasiveness of the subject matter. Given that GIFs and memes reach millions of Internet users across all demographics, a distorted understanding of the American political stage has real-life consequences. As a brand-new and ubiquitous visual rhetoric, Internet memes should be regarded as powerful tools of persuasion.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Old Groups, New Media

From government agencies to politicians and the President, elite American political institutions are harnessing digital communications technology and interactive “social” media platforms like Facebook and Twitter to connect with citizens, with important implications for American democracy. Yet just because these technologies create more opportunities for interaction between citizens and government does not mean these opportunities are seized in practice. This research studies social media adoption by influential legacy advocacy organizations to ask whether these groups are using social media in a way that increases citizen participation in political processes. The organizations studied are the American Association of Retired Persons (AARP), the American Civil Liberties Union (ACLU), the Humane Society of the United States (HSUS), Planned Parenthood and the Sierra Club. Data was gathered via a content analysis of each organization’s social media platforms including Facebook, Twitter, email newsletters, blogs, YouTube, Tumblr and Pinterest. This was followed by in-person interviews with each organization’s digital communications staffer. Results show that while these groups have developed robust digital communications strategies using a variety of social platforms, true interaction between average followers and group leadership remains limited and weak. Past research has demonstrated that advocacy organizations are significant influencers of American policy, as well as important avenues for American civic engagement. Because democratic government relies on an engaged and informed citizenry, understanding how elite institutions are or are not using social media to foster greater engagement will shed light on the ongoing quest to understand just what this new technology means for American democracy.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Federal Reserve Greenbook Forecasts: Can Informational Rigidity Explain Biases?

#### BACKGROUND:

Since 1965, the staff of the Board of Governors of the Federal Reserve has been publishing forecasts of GDP, inflation, unemployment plus other macroeconomic variables. Their forecasts are made eight times a year for the current quarter and the next few quarters. While, many studies have examined the quality of these forecasts, none have examined the process by which the new information is incorporated into their forecasts.

#### OBJECTIVES:

My research undertakes an in depth analysis of the mechanism by which the Federal Reserve utilizes information. This research is a cutting edge analysis of the properties of economic forecasts. It is particularly important because the Fed forecasts are used in setting monetary policy.

#### METHODS:

I rely initially on a study of informational rigidity, i.e., not including the latest information in forecasts, by Coibion and Gorodnichenko (2010). Coibion and Gorodnichenko (2010) estimate a regression in which the forecast errors are regressed on the forecast revisions to obtain a metric for informational rigidity. The model is a test of whether informational rigidity can explain forecast biases.

#### RESULTS:

I find that the Fed forecasts are both bias and irrational. Informational rigidity cannot explain this bias.

#### CONCLUSIONS:

My results are not in accord with the interpretations provided by the Coibion and Gorodnichenko (2010) model. The Fed frequently revises their forecasts in the wrong directions, potentially indicating that they do not use information appropriately. I am continuing my research to investigate other explanations for the bias in Fed forecasts.

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#### SOURCES

Coibion, O., and Y. Gorodnichenko, 2010, "Information Rigidity and the Expectations Formation Process: A Simple Framework and New Facts," working paper.

# SOCIAL SCIENCES



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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### When Thinness and Drinking Pressures Collide: Self-Objectification, Gender Roles, and Drunkorexia

#### BACKGROUND:

“Drunkorexia”—restricting caloric intake before drinking alcohol to avoid weight gain and/or facilitate intoxication—is related to greater chances of being physically hurt, taken advantage of sexually, having unprotected sex, and memory loss while drinking, especially among women. “Drunkorexia” may be pertinent to female college students with simultaneous (and somewhat incompatible) pressures to drink and be thin.

#### OBJECTIVES:

This research aimed to identify correlates of self-reported drunkorexia.

#### METHODS:

Participants were 271 female college students aged 18-22. Students completed a two-part online study for course credit. Measures of body mass index (BMI), body surveillance (McKinley & Hyde, 1996), passive acceptance of traditional gender roles (Fischer et al., 2000) and drunkorexia (Giles et al., 2009) were interspersed with other health and political measures. We expected the more women viewed their bodies as objects, the more episodes of drunkorexia they'd report. We predicted this positive relation between body surveillance and drunkorexia would be moderated by passive acceptance of traditional female gender roles, which may emphasize thinness.

#### RESULTS:

Controlling for BMI, a linear regression showed a significant main effect for body surveillance and a marginal main effect for traditional gender roles in predicting drunkorexia episodes in the past month; these were qualified by a significant two-way interaction [ $R^2 = .11$ ;  $F(4, 267) = 8.58$ ,  $p < .001$ ]. At low body surveillance, women who were low and high in passive acceptance reported approximately two episodes of drunkorexia in the past month. However, at high body surveillance, women who endorsed traditional gender roles averaged four episodes, whereas women who rejected them averaged two-and-a-half.

#### CONCLUSIONS:

Results showed that higher body surveillance in college women is related to a risky drinking behavior, especially when they endorse traditional female gender roles. We will discuss implications for change at the individual, social, and policy levels to try to improve this public health problem.

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#### SOURCES

- Fischer, A.R., et al. (2000). Assessing women's feminist identity development. *Psychology of Women Quarterly, 24*, 15-29.
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- McKinley, N. M., & Hyde, J. S. (1996). The objectified body consciousness scale. *Psychology of Women Quarterly, 20*, 181-215.

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# SOCIAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Utilization of the LEED Certification System in Municipal Green Building Legislation

The US Green Building Council LEED (Leadership in Energy and Environmental Design) certification system is a recognition system designed to encourage and recognize environmental best practices in building construction and design. Although LEED is a voluntary program, over 200 municipalities now require and/or incentivize the use of LEED certification in public and/or private building construction. The aims of this study were to 1) analyze the temporal and spatial adoption of city legislation mandating LEED certification for publically-funded buildings and 2) explore the rhetoric establishing the motivations and intentions of these requirements. These objectives were met through coding of motivating language from all legislative documents concerning the municipal use of LEED from the 25 cities with the highest number of public LEED certified buildings in 2010. Municipalities appear to be emulating each other in policy structure and language. While the primary rationale for LEED policies is generally environmental protection, strong cases are often made for the economic benefits of these policies, while social motivations are understated. Legislation accentuated the importance of policies to address generic global issues such as resource depletion and greenhouse gas emissions more commonly than specific, local issues like providing green-collar jobs or protecting a specific regional water body. These findings provide a point of reference from which to assess the efficacy of green building policies in addressing established objectives.

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#### STATUS

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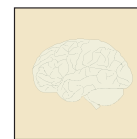
Dr. Melissa Keeley

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### X-ray Absorption Spectroscopy Investigation on High Activity De-alloyed Pt<sub>3</sub>Co Cathodic Catalysts

In-situ XAS measurements were performed on de-alloyed Pt<sub>3</sub>Co/HSC for use in PEM fuel cells developed by General Motors. TEM data showed the average particle size to be around 2.8 nm with a morphology of a Pt<sub>3</sub>Co core with Pt shell, but also a significant number of particles with several Pt<sub>3</sub>Co cores surrounded by a Pt rich layer or "blanket".

A method that can provide adsorbate coverages in an operating fuel cell on real catalysts is x-ray absorption spectroscopy (XAS) using the  $\Delta\mu$ -XANES analysis technique. Comparing the XANES results with theoretical FEFF8 results provides adsorbate coverage and binding site information. It is possible to follow the OH and O coverage on the cathode in either N<sub>2</sub> or O<sub>2</sub> saturated electrolyte (0.1 M HClO<sub>4</sub>), by plotting the magnitude of the  $\Delta\mu$ , reflecting the relative adsorbate coverage.

Using the  $\Delta\mu$ -XANES analysis technique we observed that the O or OH coverage, when saturated with N<sub>2</sub>, arises just from water activation; that in O<sub>2</sub> from water and the oxygen reduction reaction (ORR). We also observed that the de-alloyed Pt<sub>3</sub>Co exhibits relatively high OOH coverage below 0.8 V, while in contrast the pure Pt, and a non-de-alloyed Pt<sub>3</sub>Co catalyst revealed OH coverage during the ORR. This large OH coverage is supported by the  $\Delta\mu$  on both the Pt and the Co.

The results explain the increased reactivity of the de-alloyed Pt<sub>3</sub>Co. It has been suggested that the increased rates in de-alloyed Pt<sub>3</sub>Co arise from a reduced Pt-Pt distance in the Pt skin, and as the Pt-Pt distance decreases the activation energy from OH removal decreases. The presence of the non-dissociated OOH on the de-alloyed Pt<sub>3</sub>Co is consistent with this picture. Further studies are in progress to determine which de-alloyed Pt<sub>3</sub>Co particle morphologies, the core-shell or multi-core shell/blanket structures are primarily responsible for the increased rate effects.

Support from a DOE-EFRC/GM grant

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**ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS**

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## The Effect of Female Executives on Firm-Level Gender Wage Gaps in Ecuador

What is the effect of a female executive on the size of a firm's gender wage gap (GWG)? This paper tests the effect of female CEOs on the firm-level wage gap of more than 5,000 Ecuadorian firms. The study exploits a panel of data for these firms over a period of six years (2003-2008) to control for firm and time fixed effects. Ordinary least squares regressions are used to test the effect of the binary variable "ceofemale", which records the gender of the firm's CEO, on the size of the firm's GWG. I test, for a developing country, the findings of Cardoso (2007), that in Portuguese firms (i) female CEOs reduce the average gender wage gap at the firm and (ii) that this effect is greater at the upper tail of the wage distribution. Initial model specifications without fixed effects suggest that a female CEO decreases the wage gap between men and women at the mean and at each quartile. When firm fixed effects are included in the models, however, the effect of CEO gender disappears except for smaller firms and firms in certain sectors, suggesting that unobserved heterogeneities in firms' wage-setting processes play a large role in determining the GWG.

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## ELLIOTT SCHOOL OF INTERNATIONAL AFFAIRS

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### World Heritage Designation as a Tool for Sustainable Urban Development: A Case Study of the Historic District San Felipe, Panama

Urban revitalization projects are often hotly contested for promoting gentrification and displacing low income populations. Conversely, many researchers note that revitalization projects can serve as a tool for positive growth in the community. In the developing world there has been a great deal of research attention focused sustainable revitalization. Sustainable revitalization brings economic development opportunities to a community while allowing for social, environmental, and economics sustainability for current and future generations. UNESCO has outlined guidelines of sustainable revitalization and encourages communities to develop management plans that create a balance between the positive and the negative. In particular, UNESCO World Heritage designation is offered to sites throughout the world which are considered to be of outstanding value to humanity. Our study focuses on the linkages between UNESCO World Heritage Site designation and sustainable urban development. This paper utilizes the case study of the historic district of Panama World Heritage Site in analyzing the relationship between UNESCO World Heritage designation and sustainable revitalization. The paper reviews the historical development of the region, and the current revitalization projects being implemented in the San Felipe district as of June of 2012 in the context of environmental, social and economic impacts. Preliminary findings suggest that many of the development issues in San Felipe are related to the disparity between the populations that benefit from the restoration efforts and those who do not. Although development progress in San Felipe appears to be promoting gentrification and accelerated social disintegration, the UNESCO World Heritage Site designation may nonetheless usher in sustainability so long as careful and holistic planning and policymaking is conducted.

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## The Good, The Bad, and The Ugly: Investigating and redefining public health campaigns for safe drinking water

The lack of safe drinking water in many communities is a major problem. Drinking water is used for drinking, cooking, domestic household purposes, and for personal hygiene and basic sanitation. Public health campaigns focused on water are conveying a message of individual and collective change within a country to see a change. The role of safe drinking water is imperative in developing, emerging, and even developed countries. The object of this study is to analyze public health campaigns with a focus on safe drinking water in Bangladesh (Low-income country), India (Lower-middle income country), and Singapore (High-income country). In each country, a new campaign will be proposed, based on a set of communication criteria and the particular problems faced by each country. The communication criteria is based on Edward Maibach's framework of public health. The results determined that each country can improve its public health campaigns with recommendations. Further, based on these recommendations, a new mock-up of the campaign will be created for each country to make these campaigns better. It will understand the data about different countries, environmental communication strategies, water problems and solutions, and links to climate change. Each country can work at the government, regional, and local levels to implement a positive change and to save lives. With the collaboration of public-private partnerships, sponsors, and donors this change can be made possible. The quality of water and a greater awareness needs to be implemented.

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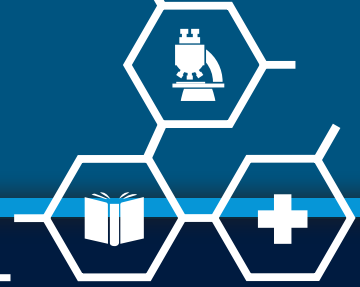
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Michael Svoboda



**START OF DAY 2**



# GW RESEARCH DAYS

## 2013

## HEALTH & MEDICINE RESEARCH DAY

WEDNESDAY, APRIL 3, 2013

### MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

8:00-9:00 a.m. Posters Setup (Grand and Continental Ballrooms)

### MEDIA AND PUBLIC AFFAIRS BUILDING JACK MORTON AUDITORIUM

805 21ST STREET, NW

8:00-9:00 a.m. Registration and breakfast

9:00-9:05 a.m. Welcome & Introduction of Keynote Address

**Jeffrey S. Akman, MD**  
Vice President for Health Affairs and Dean, School of Medicine and Health Sciences

9:10-10:00 a.m. Keynote Address

**Dr. Gary Simon, MD, PhD**  
Director, Division of Infectious Diseases; Vice Chairman, Department of Medicine; Walter G. Ross Professor of Medicine and of Microbiology & Tropical Medicine; Professor of Biochemistry and Molecular Biology, School of Medicine and Health Sciences  
"AIDS: The Fourth Decade"

10:00-10:05 a.m. Introduction of Keynote Speaker

**Lynn Goldman, MD**  
Dean, School of Public Health and Health Services

10:05-10:55 a.m. Keynote Address

**Alan Greenberg, MD, MPH**  
Professor and Chair, Department of Epidemiology and Biostatistics, School of Public Health and Health Services  
"HIV/AIDS: Enhancing Prevention Research in Washington, DC"

10:55-11:15 a.m. Coffee break

11:15 a.m.-12:00 p.m. Panel Discussion: "HIV/AIDS: Prevention and Treatment Looking Forward"

**Moderator: Vincent A. Chiappinelli, PhD**  
Interim Associate Vice President for Health Affairs and Associate Dean, School of Medicine and Health Sciences

**Gary Simon, MD, PhD**

**Alan Greenberg, MD, MPH**

**Natella Rakhmanina, MD, PhD**  
Associate Professor of Pediatrics, School of Medicine and Health Sciences; Childrens National Medical Center

**Erin Athey, DNP, FNP**

Assistant Professor, School of Nursing

**Manya Magnus, PhD, MPH**

Associate Professor of Epidemiology and Biostatistics, School of Public Health and Health Services

**Amanda Castel, PhD, MPH**

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### MARVIN CENTER

800 21ST STREET, NW, 3RD FLOOR

12:30-2:00 p.m. Distribution of Box Lunches (Rms. 310 and 311)

12:30-3:00 p.m. Poster Presentations and Judging (Grand and Continental Ballrooms)

3:00-4:30 p.m. Award Ceremony and Oral Presentations (includes 10 min presentations by winners of oral competition awards from each School) (Rm 309)





# GW RESEARCH DAYS

APRIL 3, 2013

3:00–4:30 p.m.

## AWARD CEREMONY

### SCHOOL OF MEDICINE AND HEALTH SCIENCES

Moderator: **Vincent A. Chiappinelli, PhD**  
*Interim Associate Vice President for Health Affairs and Associate Dean, School of Medicine and Health Sciences*

**Dipti Chhajwani:**  
*"Determining the Impact of External Stressors on Laparoscopic Skills and Performance"*

### INSTITUTE FOR BIOMEDICAL SCIENCES

Moderator: **Linda Werling, PhD**  
*Associate Dean for Graduate Education, School of Medicine and Health Sciences; Director, Institute for Biomedical Sciences*

**Claire Hoptay:**  
*"Aging Is Sufficient To Induce Progenitor Cell Mitotic Dyssynchrony"*

### SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Moderator: **Lynn Goldman, MD**  
*Dean, School of Public Health and Health Services*

**Sarah. B. Namugenyi:**  
*"Prevalence and Genotype Distribution of HPV in Atypical Glandular Cell-Grade Liquid-Based Cytology Specimens: Case-Control Study"*

### SCHOOL OF NURSING

Moderator: **Brenda Sheingold, PhD, RN**  
*Assistant Professor, Coordinator Healthcare Quality MSN, School of Nursing*

**Commander Ann Marie Matlock:**  
*"Family Caregiver Training - Results from a Literature Review"*

### RESIDENT ORAL PRESENTATION

Moderator: **W. Scott Schroth, MD, MPH**  
*Associate Dean for Administration, School of Medicine and Health Sciences*

**Hope T. Jackson, MD,**  
**Department of Surgery:**  
*"The Use of an Adapted FAST Protocol in Pregnant Patients with Hemodynamic Collapse"*

### 2013 DORIS DEFORD SPECK AND GEORGE SPECK, MD ENDOWED PRIZE

Presenter: **Vincent A. Chiappinelli, PhD**

**Hesham Zakaria:**  
*"Mitochondrial Quality Control in Neurons Mediated by the Parkinson's Disease Protein Parkin"*

### 2012 ELAINE H. SNYDER CANCER RESEARCH AWARD

Presenter: **Vincent A. Chiappinelli, PhD**

**Sidney Fu, MD, PhD**  
*Associate Director of Genomic Medicine, Professor of Medicine*

### 2013 DISTINGUISHED RESEARCHER AWARD

Presenter: **Vincent A. Chiappinelli, PhD**

**Fred Gordin, MD**  
*Professor of Medicine, Section Chief, Washington VA Hospital*

### POSTER AWARD WINNERS ANNOUNCED

School of Medicine and Health Sciences

Biomedical Engineering

School of Nursing

School of Public Health and Health Services



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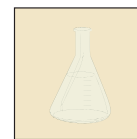
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# BASIC BIOMEDICAL SCIENCES

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COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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## Targeting Transcription Factors in Zebrafish Cardiogenesis using Transcription Activator-Like Effector Nucleases (TALENs)

The cardiovascular system remains one of the most profoundly affected systems in the human bodies. An average of 600,000 people die of heart disease in the United States every year. In order to tackle this realm of diseases and the underlying genetic factors, the conducted research aims at modeling heart disease in zebrafish (*Danio rerio*). Heart development and its transcriptional regulation play a major role in elucidating the genetic basis of malfunctions of the cardiovascular system. Using the zebrafish model is an efficient way of understanding and manipulating genes involved in heart development and therefore can bring insight into some of the causative agents of heart disease.

Specifically, transcription activator-like effector nucleases (TALENs) has proven as a useful method to disrupt genes in the developing embryo. This novel technique evolved from the discovery of such regulatory elements in bacterial pathogens (*Xanthomonas*) of plants. Such TALENs were specifically constructed to interfere with expression of certain transcription factors that are known to be crucial in heart development. TALENs bind specifically to genes via proteins that recognize the DNA sequence and then the attached nuclease will cut the sequence, which disrupts the gene. After a series of steps used to construct the DNA elements coding for a variety of transcription factors, an mRNA transcript thereof is injected into one-cell stage zebrafish embryos. Subsequent sequencing of the affected DNA regions can verify whether targeted genes were disrupted. Phenotypic studies using fluorescent microscopy can further assist in understanding heart development. Using the idea of transcription activator-like effectors (TALEs), another construct that aims at inserting external genetic material into the genome and thus tracking or otherwise affecting gene expression in the heart was built.

Little data have been collected, but the results so far suggest that this novel system of genetic manipulation will assist in understanding heart development and tackling heart disease as it pertains to humans.

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# BASIC BIOMEDICAL SCIENCES

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Elucidating Bacteriophage's Strategy of Viral Genome Delivery to Bacteria: the Roles of Electrolytes

Using  $\lambda$  phage with dsDNA genome as a model system, we aim to unravel the molecular mechanisms utilized by bacteriophage to deliver its genomic dsDNA into bacteria hosts, a critical event during a phage's life cycle.

In our experimental approach of the plaque assay, bacteria are infected with varying concentrations of bacteriophage, incubated and plated to allow for sufficient incubation and growth. The cultures are then analyzed via the number and size of the phage plaques to determine the success rate and propagation speed of viral infection. To probe the roles of electrolytes in the phage infection of bacteria, we systematically vary salt concentrations and monitor the changes in viral infection. It has been observed that with increasingly more dilute electrolytes, more viral bursts occur due to the hypotonic surroundings, an interesting phenomenon, that is correlated with the reduced infection of bacteria by bacteriophage in our plaque assays. It is hoped that with more trials and analysis, this combined research will enhance the understanding of bacteriophage and their lifecycle, from which practical, medical, and scientific applications may arise.

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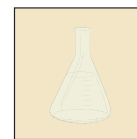
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# BASIC BIOMEDICAL SCIENCES

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Exploring the effects of fullereneol on human amylin aggregation

The fibrillization of human islet amyloid polypeptide (hIAPP) or amylin into proteinaceous plaques, a hallmark of type 2 diabetes mellitus (DM2), is linked to  $\beta$ -cell death and insulin deficiency. While the mechanisms behind hIAPP cytotoxicity remain unresolved, the actual aggregation process, as well as amylin-induced oxidative stress are thought to play key roles in the decline of pancreatic  $\beta$ -cell secretory function. This causes insulin insufficiency in the body, which leads to DM2. As such, strategies focusing on reducing amylin aggregation and amylin-induced oxidative stress may prove to be beneficial in combating DM2. In recent years, research has indicated that fullerene-derivatives are effective free-radical quenchers that may also possess anti-amyloid capacity against the  $\beta$ -amyloid peptide of Alzheimer's disease. However, there has been insufficient investigation of such properties in relation to DM2. Hence, this project focuses on fullereneol  $C_{60}(OH)_{24}$  as a potential agent against hIAPP aggregation. Using a classic Thioflavin T (ThT) fluorescent assay, amylin fibril growth curves, reflecting the kinetics and extent of amylin aggregation, were obtained in the presence and absence of varying fullereneol concentrations (0.1-9.0  $\mu\text{g/ml}$ ). The possibility of spectral overlap between ThT and fullereneol was ruled out before performing the aggregation assay by determining the emission spectra of ThT and fullereneol at varying concentrations. The ThT assay revealed an inverse relationship between fullereneol and hIAPP, wherein rising concentrations of fullereneol impede overall hIAPP aggregation and aggregation kinetics in a dose-dependent manner. Current efforts are aimed at strengthening this conclusion through the use of dynamic light scattering techniques. Overall, this research is important in identifying potential therapeutic agents for DM2. Future results pertaining to the antioxidative activity of fullereneol on diabetic cells may clarify the relationship between amyloid aggregation and oxidative stress.

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## DEPARTMENT OF UROLOGY & DEPARTMENT OF BIOPHYSICS

### Genomic Landscape of Benign Prostatic Hyperplasia

#### INTRODUCTION:

Benign prostatic hyperplasia (BPH) is one of the most common diseases among aging men. It was estimated that more than 50% of men will have histologic evidences of BPH by the age of 60, and ~90% of men will be affected by BPH by the age of 85. BPH is generally considered as a progressive disease, and previous studies have suggested that prostate volume/size is related to the progression of BPH. The enlarged prostate volume is correlated with negative clinical outcomes such as acute urinary retention, response to therapy and need for surgery. Despite the high prevalence of this disease, little is known regarding the genomic profile and/or molecular mechanism associated with the BPH progression.

#### METHODS

To investigate the genetic alterations during BPH progression, we compared mRNA expression profiles of BPH specimens derived from prostate glands with normal volume (n=19) and enlarged volume (n=19). Affymetrix human exon ST1.0 arrays was used to analyze the global mRNA expression profiles of the BPH specimens, and the statistical analysis of array data has identified 898 genes which were differentially expressed (FDR< 0.1, fold change> 1.5) between the BPH samples from normal prostates and enlarged prostates.

#### RESULTS

Our pathway analysis results further revealed that the differentially expressed genes were overrepresented in 33 canonical signaling pathways, including Oxidative Phosphorylation, Mitochondrial Dysfunction, VEGF, Growth Hormone, Leukocyte Extravasation, Wnt/beta-catenin, Nitric Oxide Signaling, Protein Kinase A, Pentose Phosphate Pathway, Ubiquinone Biosynthesis, Complement System and Integrin Pathway.

#### CONCLUSION

BPH is a complex disease likely resulted from multiple alterations in gene expressions. Our study provided the genomic landscape of BPH and elucidated the molecular pathways related to the progression of BPH. Further study of the identified genes and associated signaling pathways will facilitate our understanding of BPH etiology and the development of novel therapeutic strategy of this disease.

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# BASIC BIOMEDICAL SCIENCES



**GW CENTER FOR MICROSCOPY AND IMAGE ANALYSIS, OFFICE OF VP FOR RESEARCH**

## Confocal imaging using linear spectral un-mixing – overcoming present challenges and advantages for non-invasive tissue imaging

### BACKGROUND:

Confocal imaging with fluorescence labeling has been a major tool to investigate systematic changes in various organs and tissues subjected to experimental paradigms or pathological processes. However, imaging of fluorescence labeled tissues is of particular challenge due to interference of multiple optical and linear or non-linear quantum processes such as auto-fluorescence, non-elastic light scattering, and sum-frequency generation.

### OBJECTIVES:

Confocal spectroscopy in principle can surmount these problems while at the same time, by acquiring a better understanding of the contribution of these collateral optical phenomena and their relation with the targeted fluorescence detection can transfer into valuable noninvasive approaches for anatomical identification. Routinely, several optical processes, such as coherent light elastic scattering or second harmonic generation might be combined with auto-fluorescence and targeted fluorescence labeling to build a comprehensive multichannel image of a given tissue. Here we present our most recent R&D effort to apply spectral confocal imaging with linear and non-linear excitation.

### METHODS:

We utilized Carl Zeiss 710 Confocal system equipped with Quazar 32 channel spectral detector. All the light deriving from the samples is spectrally separated by a diffraction grating and directed to the 32-channel PMT array. Thus a simultaneous 32 channel confocal spectral data could be registered at 9.6nm spectral resolution. Spectral data is either further offline separated by applying linear spectral un-mixing algorithm, or separated online by using experimentally acquired emission curves.

### RESULTS:

Using liver tissues presenting GFP-tagged blood derived cells and excitation with IR pulsed laser tuned at 920 nm, we separated SHG deriving from the collagen, auto-fluorescence signal of the hepatocytes and GFP-tagged blood deriving cellular elements. In samples from the skin, we show separation of two distinct classes of auto-fluorescence – deriving from the red blood cells and lipids using excitation with 488-laser line. While using 920 nm line clearly revealed the dermal layers by the presence of collagen (SHG) and various forms of auto-fluorescence. Auto-fluorescence and SHG could be readily separated from GFP-tagged cellular structures. We have built a robust set of quality controls that further strengthen the approach and made it transferable to other systems.

### CONCLUSIONS:

Our data indicates that with the presently available infrastructure, we can routinely and consistently overcome a major problem in the confocal imaging, and to turn these problems into an advantage. The approach has major advantages over the conventional confocal imaging allowing combining minimum and non-invasive optical techniques for vital confocal imaging and rapid identification in fixed samples.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Regulation of MUC5B Gene Expression by the Glucocorticoid Dexamethasone in Human Lung Epithelial Cells

#### BACKGROUND:

Secretory mucins are very large, highly O-glycosylated proteins and the major macromolecular components of epithelial mucus in the respiratory tract. They provide a barrier that protects against pathogens and toxins and are part of the innate immune system. MUC5AC and MUC5B are the major respiratory tract mucins and are overproduced in acute lung exacerbations and in chronic airway diseases such as asthma, chronic obstructive pulmonary disease and cystic fibrosis. Glucocorticoids are a commonly used drug for treating lung diseases. We have shown previously that the glucocorticoid Dexamethasone (Dex) transcriptionally represses expression of the *MUC5AC* gene in lung epithelial cells *in vitro* and that Dex-activated Glucocorticoid-receptor binds to two Glucocorticoid Response Elements in the *MUC5AC* promoter (Chen YA et al., 2006, 2012). Dex also reduces abundance of MUC5B mRNA and protein (unpublished data). Since overproduction of MUC5B mucin contributes to morbidity and mortality in lung diseases and MUC5B mucin is overproduced in the middle ear secretions of patients with chronic otitis media (Preciado D et al., 2010), we investigated whether Dex represses *MUC5B* gene expression at the transcriptional level.

#### METHODS:

We transfected A549 human lung epithelial cells with a full length *MUC5B* promoter (4.1 kbp) and deletion-luciferase(Luc) constructs. Cells were also transfected with the 1.5 MUC5AC promoter-Luc construct. Cells were exposed to 1uM Dex for 24 hours. Cell lysates were isolated and analyzed for chemiluminescent activity and protein content. Data were normalized for promoter activity (*MUC5B*- or *MUC5AC* promoter-Luc/PGL3-Luc/protein). In a subsequent experiments, cells were or were not transfected with full length *MUC5B*-Luc or *MUC5AC*-Luc plasmids in the presence or absence of Dex and mRNA levels were determined by RT-PCR.

#### RESULTS:

Dex decreased the promoter activity of *MUC5AC*, but did not alter the promoter activity of the full length *MUC5B*(4.1kb)-luc construct. However, Dex increased the activity of the 2140 deletion construct, which has several GRE sites.

#### CONCLUSIONS:

Promoter analyses with the full length *MUC5B* plasmid indicate that Dex does not regulate *MUC5B* expression transcriptionally, in contrast to *MUC5AC*. However, Dex increased the activity of the 2140 deletion construct, which has several GRE sites, indicating that Dex further studies are warranted.

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# BASIC BIOMEDICAL SCIENCES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Outpatient Ketamine Infusions Reduce Visceral Hyperalgesia in Chronic Abdominal Pain

#### INTRODUCTION:

We present two cases of intractable chronic abdominal pain. Patient A, a 37 year old male diagnosed with idiopathic chronic pancreatitis and patient B, a 47 year old female diagnosed with Type II diabetes mellitus and gastroparesis. Both presented with severe abdominal hyperalgesia refractory to treatment. Both underwent multiple outpatient ketamine infusions on consecutive days with significant improvement of symptoms.

Patient A initially complained of a sharp 7/10 pain with occasional flare-ups that required ER visits for pain control. He exhibited tenderness to palpation and allodynia to light touch in the epigastrium. Patient B described an aching pain rated 6-7/10 and was exacerbated by eating. Her past relevant surgical history included Gastric Stimulator placement, Nissan fundoplication, Appendectomy and Cholecystectomy. She had significant discomfort with palpation and light touch of the epigastrium.

#### MATERIALS AND METHODS:

Both patients underwent prognostic celiac plexus blocks, which provided some relief. Patient B requested a neurolytic celiac block that did not give her the relief as anticipated. Patient A was on high dose opioids with suboptimal pain control. They consented for consecutive multi-day outpatient ketamine infusions for interim pain relief.

#### RESULTS:

Both patients underwent ketamine infusions on consecutive days with no adverse side effects. Patient A had a significant reduction in allodynia, 5/10, in the epigastrium. Patient B had significant improvement for five weeks, citing pain 3/10 and nausea associated with eating. The infusions were repeated with some improvement but with less of an impact as previous infusions.

#### DISCUSSION:

Ketamine is a NMDA receptor antagonist that has been administered as an anesthetic and/or analgesic for many years. Subanesthetic doses of ketamine have been administered for analgesia and opioid-sparing effects in chronic pain as well as in refractory cancer pain. Recently, ketamine has been used increasingly to help manage chronic non-cancer pain, neuropathic pain, and complex regional pain syndrome.

Patients with chronic abdominal pain frequently present with chronic abdominal and or visceral hyperalgesia. These patients are difficult to treat and often end up on high dose opioid analgesics which exacerbate some of their abdominal symptoms leading to more pain. Patients with chronic abdominal and visceral hyperalgesia may benefit from consideration of outpatient ketamine infusions as a multimodal approach to their pain control. More research is needed to evaluate the role of ketamine infusions in patients with chronic abdominal and visceral hyperalgesia.

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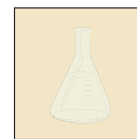
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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Multicopy Crystallographic & Biophysical Analyses of the N-terminal Domain of NBCe1-A: Illumination of the Human R298S Mutation

#### BACKGROUND:

NBCe1-A membrane-embedded macromolecules cotransport sodium and bicarbonate ions across the bilayers that serve to maintain acid-base homeostasis throughout the body. Defects are linked to a number of disorders, including proximal renal tubule acidosis, mental retardation, dental defects, and cataracts. Previously, we demonstrated the N-terminal domain of NBCe1-A (Nt) is in pH-sensitive monomer-dimer equilibrium. At neutral pH, bicarbonate ions bind the Nt, stabilizing dimerization and intermolecular self-associations of dimers.

#### METHODS:

We determine and analyze the X-ray crystal structure of the Nt as a dimer at 2.4-Å resolution using molecular-replacement methods, and a multicopy crystallographic structure of the monomer using 5 atomic models and strict 4-fold NCS constraints in refinement procedures. We measure the pH-sensitivity of a truncated Nt mutant by light-scattering techniques, and bicarbonate, bisulfite, mutant self-association bindings by surface plasmon resonance techniques.

#### RESULTS:

The structures reveal that R298 implicated in the disorders is part of a putative conduit that transverses the Nt. The conduit opens to the transmembrane domain (TMD) on one end and an apparent foyer entrance on the opposite end. The naturally occurring mutation R298S disrupts an electrostatic pocket within the conduit that disables substrate binding. We also report similar conducts in family member AE1 (Band 3) when exploring its crystal structure. Further, we identify by biophysical analyses on a truncated Nt that the autoregulatory domain (ARD) at the N-terminus of the Nt is responsible for self-associations.

#### CONCLUSIONS:

The Nt responds to changes in pH or bicarbonate fluctuations. In proximal tubule cells, we propose a model where the ARD is a gate for the foyer. When self-associated, the foyer entrance is accessible, allowing substrate entry into the conduit. During acid loads, the gates close entry into the foyer, preventing bicarbonate from leaving the cell. The R298S defect similarly prevents bicarbonate ions from being transported to blood, giving rise to metabolic acidosis that results from the renal tubule acidosis.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Epigenetic Regulation of Soluble Guanylyl Cyclase Subunit Beta1 in Cancer

The nitric oxide (NO) receptor soluble guanylyl cyclase (sGC) is an obligate heterodimer composed of two subunits  $\alpha_{1,2}\beta_{1,2}$  that catalyzes the formation of second messenger cGMP in response to NO stimulation. NO-cGMP signaling plays a critical role in numerous processes, and loss of NO signaling by way of limited NO bioavailability, or decrease in expression or activity of sGC correlates with several disease states including hypertension, neurodegenerative disorders, inflammation as well as in cancers of the brain, and breast. Restoration of NO-cGMP by treatment with NO donors, or sGC activators have been successful in the treatment of many pathologies but are ineffective in the treatment of diseases, such as cancer, where expression of sGC is lost. We have recently shown that restoration of sGC $\beta_1$  levels through enforced expression in glioma cell lines significantly reduced cell growth, and proliferation. Additionally, orthotopic implantation of glioma cells transected with constitutively active mutant form of sGC (sGC $\alpha_1\beta_1^{\text{cys105}}$ ) in athymic mice increased survival time 4-fold over the control. Thus, developing means to restore sGC expression offers a novel therapeutic option for some particularly intractable diseases states.

Here we report that expression of the sGC subunit, sGC $\beta_1$ , can be elevated up to 10-fold above control in breast cancer cell lines by treatment with histone deacetylase inhibitor, Panobinostat. Panobinostat has gained notoriety as an effective, and targeted anti-neoplastic treatment and is approved for treatment in lymphoma and is undergoing Phase II testing for the treatment of breast and prostate cancer. Our discovery of the effect that HDAC inhibition has on the expression of sGC not only provides insight into the potential mechanism underlying the efficacy of HDAC inhibition in the treatment of cancer, but also provides novel therapeutic options for the treatment of diseases marked by decreased expression of sGC $\beta_1$ .

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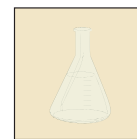
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# BASIC BIOMEDICAL SCIENCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### HEART-BREAK Study - Using $\gamma$ H2AX as a biomarker to study and reduce genotoxicity from low levels of diagnostic ionizing radiation

Coronary artery disease(CAD), also know as coronary heart disease(CHD), is the leading cause of mortality amongst women and men in the United States. Frontline testing comprises of cardiac imaging to identify blockage(s) involved in the disease of the heart. However, most cardiac imaging modalities utilize radiation(IR). This includes the gold standard, the invasive coronary angiography(ICA), as well as myocardial perfusion scintigraphy(MPS) and cardiac computed tomographic angiography(CCTA). How much transient DNA damage occurs has never been studied within the parameters of cardiac imaging. This study will evaluate the levels of  $\gamma$ H2AX, a specific biomarker for double strand breaks in DNA, induced by cardiac imaging in patient lymphocytes and hair follicles. Analysis of  $\gamma$ H2AX levels will reveal the degree of genotoxicity from cardiac imaging radiation, since  $\gamma$ H2AX foci counts and/or intensities are directly correlated to radiation dose. Although normal healthy individuals repair minor DNA damage on a daily basis, it is still unknown if accumulation of DNA damage from repeated exposure to low levels of medical radiation can lead to increased cancer risk. As a sub-focus in this study, women receiving cardiac imaging with or without a breast shield are being evaluated since breast tissue is at the focal point of cardiac imaging.  $\gamma$ H2AX is a marker for radiation damage and analysis of  $\gamma$ H2AX is an efficient way to evaluate relative safety of imaging techniques.

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# BASIC BIOMEDICAL SCIENCES

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### The Effect of Non-Thermal Plasma on Blood Coagulation

Plasma is a partially ionized gas, where electrons are free rather than being bound to an atom. Because the positive and negative charges can move somewhat freely, plasma is electrically conductive so that it responds strongly to electromagnetic fields. Plasma is therefore sometimes referred to as “the fourth state of matter”<sup>2</sup>. Recent research in the field of physics has allowed for development of plasma at room temperature and atmospheric pressure called “non-thermal” or “cold” atmospheric plasma. In addition to its usage for tumor ablation, recent research has shown that non-thermal plasma can be used to enhance blood coagulation. Current instrumentation primarily utilizes a dielectric barrier discharge method, that is not applicable or practical in the clinical setting. This study was undertaken to determine if a handheld operated system could enable hemostasis and coagulation.

#### METHODS:

The procedure included 4 separate experiments with plasma treatment at 8.2mV: (1) TRIS buffered, purified human fibrinogen treated with plasma for 30s, 1 minute, 2m, and 5m and non-treated, followed by objective analysis of changes in viscosity. (2) Citrated, heparinized, EDTA (anticoagulants) and whole human blood treated ex vivo with plasma for 30s, 1m, 2m, and 5m and objective analysis of changes in viscosity. (3) Heparinized mouse mesenteric vessels treated in vivo with plasma at 2min, 3min, 5min and compared to an untreated control. Tissue and vessels were harvested and examined for damage and thrombus formation by histology. (4) Heparinized mouse aorta treated in vivo with plasma, cauterization, and no treatment for 5m and examined for tissue damage and thrombus formation by histology.

#### RESULTS:

Results indicated an increase of viscosity with a gel like/semisolid quality at 5min following treatment of human fibrinogen. Similarly a coagulum was noted in heparinized treated blood in 4min. Results for both experiments (3) and (4) showed no tissue damage from the plasma treatment (as oppose to the cauterization in experiment (4)), and thrombus formation adhering to endothelial lining of vessel walls with 5min treatment. Those vessels that received no treatment did not show signs of thrombus formation.

#### CONCLUSIONS:

Non-thermal plasma appears to induce coagulation by converting fibrinogen to fibrin. Its added advantage over diathermy cauterization is the minimal tissue damage observed. As the data collected was primarily observational, mechanistic studies determining the effects on coagulation are needed. Current efforts are underway to utilize scanning electron microscopy (SEM) to visualize changes in fibrinogen post-plasma treatment.

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# BASIC BIOMEDICAL SCIENCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Nuclear envelope laminopathies: Evidence for developmentally inappropriate chromatin-nuclear envelope interactions

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#### BACKGROUND:

During terminal differentiation of cells, there is typically a transition of the nuclear envelope from the Lamin B to Lamin A/C proteins. This is commensurate with exit from the cell cycle, and maintenance of the transcriptional programs associated with the terminally differentiated cells. Dominant missense mutations in Lamin A/C cause a broad spectrum of human genetic disorders, where specific point mutations are associated with defects in specific organs or tissues. We have previously presented a model where Lamin A/C mutations disrupt developmentally appropriate interactions between chromatin and the nuclear envelope and lead to poor coordination of E2F cell cycle pathways and terminal differentiation pathways. One of the phenotypes caused by Lamin A/C mutations is Emery Dreifuss Muscular Dystrophy (EDMD). An X-linked recessive phenocopy of EDMD is caused by loss of function of emerin - a binding partner to Lamin A/C at the nuclear envelope.

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#### OBJECTIVE:

Here we tested the hypothesis that emerin plays a role in chromatin remodeling via stabilizing nuclear lamina-heterochromatin interactions necessary for appropriate and time dependent muscle differentiation.

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#### MATERIAL AND METHODS:

We used WT and emerin null mouse myogenic stem cells to study transcriptional and epigenetic changes during *in vitro* exit from the cell cycle and differentiation to the myogenic lineage. Specific cell cycle (E2F) and myogenic genes were analyzed by qPCR and ChIP-qPCR to determine mRNA timing and H3K9me3 enrichment on gene promoters. Nuclear lamina-chromatin colocalization was determined and quantified by confocal imaging and Matlab.

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#### RESULTS:

Our results showed that TK1 and other cell cycle genes are inappropriately persistently expressed in emerin null cells during differentiation causing delayed exit from cell cycle. Transcripts marking commitment to the myogenic lineage (myogenin and Mef5A) showed delayed activation on both mRNA and protein level. Epigenetic imprints predicted observed deviations from transcriptional timing in emerin null cells, with persistent suppressive chromatin state on myog promoter upon myogenic induction and failure to appropriately establish repressive histone marks (H3K9me3) on Tk1 promoter (cell cycle). Finally, we showed that the early cell cycle exit and terminal differentiation of emerin null myoblasts were accompanied by decreased H3K9me3 staining at the nuclear periphery (lamin A/C immunostaining).

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#### CONCLUSIONS:

Myogenic cells lacking emerin exhibit perturbations in terminal commitment to the myogenic lineage. Our transcriptional, chromatin remodeling and gene promoter accessibility data show that both exit from cell cycle and terminal commitment to myogenesis are disrupted due to inappropriate heterochromatin-nuclear lamina interactions in EMD myogenic cells.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Mitotic Dyssynchrony Induces TGF- $\beta$ 1 in Airway Epithelial Progenitor Cells

#### BACKGROUND:

Mitotic behaviors are likely important for maintaining and restoring homeostasis in lung diseases with epithelial injury. We showed previously that while normal airway epithelial cell populations progress in synchrony through the cell cycle ( $G_1, S, G_2, M$ ), asthmatic progenitor cells proliferate with a more even distribution in each cell cycle phase. As evidence of homeostatic importance, asthmatic mitotic dyssynchrony was coincident with elevated basolateral secretion of TGF- $\beta$ 1, a mediator of lung fibroproliferation and matrix deposition and other pro-fibrotic cytokines with the potential to affect asthma pathology. The purpose of the current study was to establish the directionality of the hypothetical cause (mitotic dyssynchrony) and effect (secretion of TGF- $\beta$ 1).

#### METHODS:

In vitro experiments were performed wherein airway epithelial progenitor cell mitosis was mitotically dyssynchronous due to disease state (i.e. asthma) and then resynchronized by capture of the  $G_1/S$  checkpoint via two-hour daily pulse exposure to dexamethasone, simvastatin, or aphidicolin. Further experiments utilized a novel method we developed for inducing mitotic dyssynchrony in normal progenitors.

#### RESULTS:

Upon mechanical injury, human asthmatic fully-differentiated air-liquid interface airway epithelial mitosis was dyssynchronous ( $G_1$ [mean $\pm$ SEM],  $S, G_2, M$ : 47.4 $\pm$ 3.8, 23.9 $\pm$ 6.3, 28.7 $\pm$ 5.7%) relative to normal epithelia (71 $\pm$ 1, 12 $\pm$ 2, 17 $\pm$ 2%). Mitotic capture increased the percentage of progenitors in  $G_1$ . This resynchronization in the proliferating asthmatic epithelia reduced basolateral TGF- $\beta$ 1 secretion, in particular at the 24-hour peak where TGF- $\beta$ 1<sub>PBS</sub>=285 $\pm$ 74pg/mL but decreased to 45 $\pm$ 17pg/mL with dexamethasone, 81 $\pm$ 26pg/mL with simvastatin, and 77 $\pm$ 50pg/mL with aphidicolin. If this and other inflammatory signals are downstream, rather than upstream, of abnormal mitotic behavior, the contents of the conditioned media would not alter the mitotic synchrony of co-cultured proliferating airway epithelial progenitors. Results revealed no change in the mitotic synchrony of these progenitor cells. We next examined whether inducing mitotic dyssynchrony in normal epithelial cells would result in TGF- $\beta$ 1 secretion. Mitotic dyssynchrony was induced in parallel cultures of normal proliferating epithelial cells via transient, staggered serum starvation. The mixed samples showed moderate dyssynchrony at 6 and 12 hours that resolved spontaneously by 24 hours. The cells grown in mixed conditions show elevated TGF- $\beta$ 1 secretion at 12 hours compared to either cell population in isolation.

#### CONCLUSION:

We used a series of mitotic experiments wherein airway epithelial mitosis was desynchronized and resynchronized via  $G_1/S$  checkpoint manipulation. Cumulative analysis shows mitotic synchrony is the homeostatic state in airway epithelial progenitor populations and poorly-synchronized mitosis (as in asthma) induces TGF- $\beta$ 1 secretion and a pro-inflammatory/pro-fibrotic airway. This finding establishes rationale for targeting progenitor cell mitotic behavior rather than immune-mediated inflammation in fibrotic disease.

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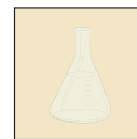
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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Rapid molecular diagnostics and discovery of novel genes in myopathy: a next-generation sequencing approach

#### BACKGROUND:

Myopathy forms a clinically and genetically heterogeneous group of diseases. Clinically different phenotypes of myopathy are due to different genes causing similar disorders (genetic heterogeneity) and different mutations in the same gene causing different phenotypes (allelic heterogeneity). With more than a hundred genes known to cause myopathy, diagnosis of the disease-causing mutation can be especially arduous (increased time, cost) using single-gene testing. With the advent of newer next-generation sequencing technologies, all candidate myopathy genes can be sequenced in parallel through targeted sequencing or whole exome sequencing approaches in a timely and cost-effective manner.

#### OBJECTIVE:

The purpose of this study is to use next-generation sequencing technologies to provide molecular diagnostics and discovery of novel genetic loci for patients with previously un-explained myopathies. We also compare the efficacy of targeted and whole exome sequencing strategies towards diagnosing disease-causing genes in myopathy.

#### METHODS:

Sequence enrichment for targeted sequencing was performed using microdroplet emulsion PCR (RainDance Tech). The target library consisted of 45 genes that are known to be responsible for causing myopathies (1851 amplicons). Exome enrichment was carried out by whole exome hybrid capture kits by Illumina that target all protein coding genes in the genome. Next-generation sequencing was done using either Illumina HiScan SQ or Illumina MiSeq sequencers.

#### RESULTS:

We have sequenced 65 samples by targeted sequencing and 42 samples by exome sequencing. Targeted sequencing showed lower exon drop-out rates compared to exome sequencing (2% instead of 10%). Depth of coverage varied from 50X - 5000X for targeted sequencing and 20X - 50X for exome sequencing depending on the number of samples pooled, and instrument used for sequencing. We showed an example of a case where a homozygous mutation in dysferlin gene (known muscular dystrophy gene) was missed by exome sequencing and detected by targeted sequencing. On the other hand, we were able to identify mutations in a novel gene through exome sequencing: GDP-mannose pyrophosphorylase B (GMPPB) associated with congenital and limb girdle muscular dystrophy.

#### CONCLUSIONS:

Both targeted and exome sequencing panels effectively deliver molecular diagnostics for myopathy patients at substantially reduced cost and time compared to single gene testing. Our pilot data suggests a strategy moving forward, where targeted sequencing is used as a first pass screening approach for confident exclusion of known myopathy causing genes. When no detectable mutations are found through targeted sequencing, whole exome sequencing approaches are then performed for discovery of novel genes associated with myopathy.

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# BASIC BIOMEDICAL SCIENCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Development of a 3D Co-Culture System for the Study of Submucosal Gland Morphogenesis

#### INTRODUCTION:

Chronic rhinosinusitis (CRS) is a ubiquitous upper airway disease, characterized by inflammation, mucus hypersecretion, and obstruction of the sinonasal outflow tracts. Although the pathophysiology of CRS is not well understood, the mucus hypersecretion characteristic of CRS has been demonstrated to be a byproduct of submucosal gland proliferation. A current model of CRS pathophysiology postulates that an environmental insult, such as a toxin or pathogen, leads to secretion of inflammatory mediators that stimulate upregulation of growth factors by mesenchymal cells, which in turn facilitate progenitor cells to proliferate and differentiate into submucosal glands. Previous studies from the lab have identified these submucosal progenitor cells as basal cells from nasal epithelium (HNE) and sinus epithelium (HSE). We hypothesize that when HNE basal cells are stimulated by growth factors secreted by mesenchymal cells, they will proliferate and differentiate into submucosal glands. To test this hypothesis, we developed an *in vitro* 3D glandular model wherein HNE basal cells were co-cultured with human lung fibroblasts in Matrigel®.

#### METHODS:

We prepared a series of 3D co-cultures, in which human lung fibroblasts were overlaid with Matrigel® and HNE basal cells were seeded onto the top layer. The ratio of fibroblasts to HNE cells was varied between cultures, as was the thickness of the Matrigel® layer. A control culture with HNE cells seeded in Matrigel® alone was also prepared. Spatial and temporal changes in morphology were monitored via bright field microscopy over the course of 7-10 days. The cultures were subsequently fixed, sectioned by cryostat, and further analyzed via hematoxylin and eosin staining.

#### RESULTS:

Morphology and growth kinetics of co-cultures varied dramatically depending on the ratio of fibroblasts to HNE cells. In co-cultures with fibroblasts and epithelial cells seeded in equal amounts of 100,000 cells, we detected the most rapid formation of acini with vast networks of tubular connections. In the control cultures, in which HNE cells were seeded in Matrigel® alone, only glandular acini were formed. These results suggest that HNE basal cells were prompted to differentiate into more complex networks of acini and tubules due to the influence of growth factors secreted by fibroblasts.

#### CONCLUSION:

The *in vitro* 3D co-culture is a useful model for evaluating the effects of growth factors secreted by mesenchymal cells on the differentiation of HNE cells into glandular structures. In future studies, we hope to further probe the nature of submucosal gland differentiation by evaluating temporal changes in gene expression.

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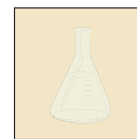
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# BASIC BIOMEDICAL SCIENCES

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SCHOOL OF MEDICINE AND HEALTH SCIENCES

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## The Effect of Non-Thermal Plasma on Blood Coagulation

Plasma is a partially ionized gas, where electrons are free rather than being bound to an atom. Because the positive and negative charges can move somewhat freely, plasma is electrically conductive so that it responds strongly to electromagnetic fields. Plasma is therefore sometimes referred to as “the fourth state of matter”. Recent research in the field of physics has allowed for development of plasma at room temperature and atmospheric pressure called “non-thermal” or “cold” atmospheric plasma. The ability to produce plasma at ambient conditions allows the ionized gases to be directed towards cancerous cells or tissues, which are more sensitive to the reactive oxygen species than non-tumor cells are, that appear to be resistant. Plasma medicine is a rapidly growing field, with different disciplines of medicine using the technology for various innovative purposes. In addition to its usage for tumor ablation, recent research has shown that non-thermal plasma can be used to increase the rate for the natural process of blood coagulation as well as induce blood coagulation in blood samples that have been treated with an anti-coagulant. The current theory is that the plasma induces a conversion of the clotting factor fibrinogen to fibrin, bypassing the clotting cascade. Current instrumentation primarily utilizes a dielectric barrier discharge method, which is not applicable or practical in the clinical setting. This study utilized a handheld operated system, which relies on slightly different application of the plasma stream but similar mechanisms of plasma creation. For these experiments, an electrical discharge was applied to helium gas to create the non-thermal plasma. The procedure included 4 separate experiments with plasma treatment at 8.2mV: (1) TRIS buffered, purified human fibrinogen treated with plasma for 30s, 1 minute, 2m, and 5m and non-treated, followed by objective analysis of changes in viscosity. Results indicated an increase of viscosity with a gel like/semisolid quality at 5m (2) Citrated, heparinized, EDTA (anticoagulants) and whole human blood treated ex vivo with plasma for 30s, 1m, 2m, and 5m and objective analysis of changes in viscosity. The same results were seen as with the purified fibrinogen experiment. (3) Heparinized mouse mesenteric vessels treated en vivo with plasma at 2m, 3m, 5m and no treatment for 5m and examined for tissue damage and thrombus formation by light microscopy. (4) Heparinized mouse aorta treated en vivo with plasma, cauterization, and no treatment for 5m and examined for tissue damage and thrombus formation by light microscopy. Results for both (3) and (4) showed no tissue damage from the plasma treatment (as oppose to the cauterization in experiment (4) which showed significant injury), and thrombus formation adhering to endothelial lining of vessel walls with 5m treatment. Those vessels that received no treatment didn’t show signs of thrombus formation. Although many of the results are promising, this experiment is still in the active process. Due to the implications of objective data analysis and objective hypothesis, a more concrete method of data analysis should be sought. Current efforts are being made to utilize scanning electron microscopy (SEM) to visualize changes in fibrinogen post-plasma treatment.

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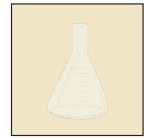
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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Variant in SLC30A8 Gene is Associated with Skeletal Muscle Size and Damage in Young Men

Exercise plays a major role in the prevention and management of Type 2 Diabetes (T2D) by increasing the rate at which skeletal muscle cells take up glucose. Boulé et al. found that individuals with T2D participating in exercise interventions greater than eight weeks duration had significantly lower HbA1c levels than the individuals who did not exercise - highlighting the importance of regular exercise for T2D patients. Recent genetic studies examining T2D have implicated genes involved in several potential therapeutic pathways. One variant (rs13266634) highly associated with T2D, is a non-synonymous change in the SLC30A8 gene that encodes for the Zinc Efflux Transporter 8 protein (ZnT-8) expressed mainly in the  $\beta$ -cells of the pancreas—responsible for zinc efflux and the proper storage and release of insulin. In the absence of a properly functioning ZnT in vesicles, insulin cannot be synthesized and stored appropriately, disrupting glucose uptake and ATP formation downstream. We hypothesized that this variant in the SLC30A8 gene may help explain differences in muscle response to exercise, possibly due to insufficiency in glucose uptake and ATP synthesis. Two cohorts with a total of 1,025 participants were subjected to one of two exercise interventions to determine the effects of resistance-training on muscle. Our results indicated that variant is strongly associated with several different muscle phenotypes in men but not in women. Male carriers of the common allele were more likely to demonstrate greater post-workout strength loss and soreness. Increased markers of muscle damage - creatine kinase and myoglobin - were also strongly associated with the common allele. Furthermore, we recorded decreased baseline strength and muscle size in men with the common allele. In this era of increasing interest in personalized medicine, there is a search for genetic markers that can be used to prevent and manage T2D. Clinically, the outcome of our study may help identify patients for whom resistance-training is an optimal first-line therapy in the management and treatment of T2D. We have demonstrated that the rs13266634 variant in SLC30A8 may be used as an indicator for those individuals who may not respond to exercise as the first-line therapy for T2D, and thus may require an alternative method to manage their impaired glucose tolerance. Additional research is needed to determine if the presence of this SNP and predisposition to post-exercise soreness leads to a decreased desire to be active, thus, promoting a more sedentary lifestyle, further amplifying their risk of developing T2D.

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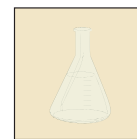
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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Identifying Directional Secretomes of In Vitro Differentiated Primary Normal Bronchial Epithelium

#### BACKGROUND:

Airway epithelium is polarized and secretes signals directionally, simultaneously responding to airborne pathogens and environmental challenges at the apical surface while creating local and systemic changes in the basal lamina based on these external stimuli. Maintaining this barrier and its polarity is vital to preserving directional signaling between the apical and basolateral compartments and is responsible for homeostatic lung function.

#### OBJECTIVE:

Our aim is to establish an in vitro airway secretome model for normal epithelium as a tool to study relevant global protein changes that occur in lung diseases.

#### DESIGN/METHODS:

Normal primary human bronchial epithelial (HBE) cells were differentiated into respiratory tract epithelium (n=3) under air-liquid interface conditions. Apical and basolateral secretions were collected from each compartment at 24h under homeostatic conditions and processed for secretome profiling by LC-MS/MS analysis after SDS-PAGE and tryptic digestion of eluted bands. Only proteins present in all 3 HBE secretions and unique to compartment or differentially expressed between compartments (paired Student t-test; p<0.05) were included in final analysis. Bioinformatic analysis included Uniprot, SignalP, and Panther Database. Results of secretome profiles were validated by Western blot and ELISA.

#### RESULTS:

A total of 246 proteins were identified in all HBE secretomes. Based on protein abundance, 51% were classified as secreted proteins (35% secreted, 16% exosomal). A total of 67 unique apical, 8 unique basolateral and 14 differentially secreted proteins were identified in apical and basolateral secretomes. Bioinformatic analysis identified unique patterns of apical and basolateral biologic processes. Expression of annexin A4 (apical) and desmoglein-2 (basolateral) were validated.

#### CONCLUSIONS:

This is the first study demonstrating proteomic analysis of in vitro airway epithelial apical and basolateral secretomes and reinforces that protein networks consistent with homeostatic function are present in normal epithelium. Applying this directional secretome model to future lung disease studies may lead to candidate biomarkers identification of functional epithelial abnormalities.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Variant in the ADCY5 gene is Associated with Whole Muscle Volume and Subcutaneous Fat Volume Phenotypes

#### BACKGROUND:

The fetal insulin hypothesis states that common genetic variants predisposing to insulin resistance also reduce fetal birth weight since fetal insulin acts as a key growth factor. A recent genome wide association study identified two single nucleotide polymorphisms (SNPs), rs9883204 in ADCY5 and rs900400 near CCNL1, that were associated with fetal birth weight.

Interestingly, the weight-lowering C allele of the rs9883204 SNP is in high linkage disequilibrium with allele A of the rs11708067 SNP which has been associated with a high risk of type 2 diabetes and elevated fasting glucose. Likewise, CCNL1 may be involved in insulin secretion as well. The bio-mechanism behind insulin resistance genetic variants causing lower birth weight has yet to be elucidated. Furthermore, neither ADCY5 nor CCNL1 have been shown to be associated with adult phenotypes, including adult height and BMI.

#### OBJECTIVE:

Our study sought to further expand our understanding of the relationship between the ADCY5 and CCNL1 genes and human development by examining associations between the birth weight-associated SNPs and a range of adult musculoskeletal phenotypes such as muscle volume, subcutaneous fat volume, and bone density.

#### METHODS:

We genotyped rs900400 SNP near CCNL1 and rs9883204 SNP in ADCY5 in a cohort of 753 healthy college-aged Caucasian men and women enrolled in a supervised resistance-training program of the non-dominant arm (18-40 yrs, mean 24 yrs) for the "Functional Polymorphism Associated with Human Muscle Size and Strength" study. Mean quantitative muscle measurements were compared in relation to SNP genotypes using analysis of covariance (ANCOVA) methods. The ANCOVAs used Sidak post hoc tests to control for multiple comparisons.

#### RESULTS:

Our results were sexually dimorphic for the rs9883204 SNP in ADCY5. In females, the T allele in rs9883204 was associated with increased baseline whole muscle volume (CC: N=169;  $432082 \pm 11637 \text{ mm}^3$  vs. CT/TT: N=137;  $488964 \pm 12906 \text{ mm}^3$ ;  $p=0.0012$ ) and increased baseline subcutaneous fat volume (CC: N=172;  $238736 \pm 8107 \text{ mm}^3$  vs. CT/TT: N=138;  $270594 \pm 9036 \text{ mm}^3$ ; 0.0091).

#### CONCLUSIONS:

Our study suggests that variation in the ADGY5 gene may impact not just fetal growth, but may also impact muscle and fat development in women; the same allele associated with decreased birth weight was shown to be associated with lower measures of skeletal muscle and subcutaneous fat volume. Further research is needed to elucidate the mechanism behind the interaction of fat and skeletal muscle with the ADCY5 rs933294 SNP.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Tgf- $\beta$ 1 Up Regulates The Expression Of Pdgf- $\beta$ Receptor Mrna And Induces A Delayed Pi3k, Akt And P70s6k Dependent Proliferative Response In Activated Hepatic Stellate Cells

#### BACKGROUND

TGF- $\beta$ 1 is a pleiotropic cytokine that activates hepatic stellate cell (HSC) proliferation, but inhibits parenchymal cell proliferation. Therefore, we hypothesize that TGF- $\beta$ 1 regulates HSC proliferation and elucidated its molecular action. Methods: In order to elucidate the molecular mechanism whereby TGF- $\beta$ 1 up regulates PDGF- $\beta$  receptor mRNA and induces a delayed proliferation of HSC, we used proliferation and apoptosis assays as well as RT-PCR, western blot analysis, immunostaining and flow cytometry in mouse and rat HSC. Results: We show that TGF- $\beta$ 1 markedly induces the proliferation of mouse HSC in culture with concomitant 2.1 fold ( $p < 0.001$ ) stimulation in 3H-thymidine incorporation into cellular DNA. This induction is maximal between 24-30 hours post cytokine exposure that is triggered by 7.6-fold ( $p < 0.001$ ) up-regulation of PDGF- $\beta$  receptor mRNA and associated increase in PDGF- $\beta$  receptor protein after 48h. TGF- $\beta$ 1-dependent HSC proliferation is mimicked by H<sub>2</sub>O<sub>2</sub> that is inhibited by catalase implying TGF- $\beta$ 1 action is mediated via reactive oxygen species (ROS). HSC proliferation is blunted by PDGF- $\beta$  receptor neutralizing antibody as well as by specific inhibitors of PI3K, AKT and p70S6K, indicating that the action of TGF- $\beta$ 1 involves activation of PDGF- $\beta$  receptor via the PI3K/AKT/p70S6K signaling pathway. TGF- $\beta$ 1 also induces a reorganization of actin and myosin filaments and cell morphology leading to the formation of palisades although their myosin and actin contents remained constant. These findings suggest that TGF- $\beta$ 1-mediated oxidative stress causes the trans-differentiation of HSC and primes them for extracellular matrix (ECM) deposition and scar contraction.

#### CONCLUSION:

We conclude that liver injury up regulates TGF- $\beta$ 1 that inhibits parenchymal cell proliferation, but stimulates HSC proliferation leading to production of ECM and type I collagen resulting in fibrosis.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Adipocyte Exosomal miRNAs May Mediate The Effects Of Obesity On Lung Disease

#### RATIONALE:

With rates of comorbid asthma and obesity steadily increasing, identifying the mechanisms by which obesity affects asthma is critical. Obesity results in a systemic inflammatory state and our group has shown that adipocytes from obese patients can produce numerous mediators, including TGF $\beta$  which is central to asthma pathobiology. Exosomes are actively secreted endocytic vesicles that contain and transport mRNAs, miRNAs and proteins among cells, both in the microenvironment and over larger distances within the body. Adipocytes have been shown to release exosomes and in obese patients these can contribute to the development of insulin resistance. Thus we hypothesize that adipocyte exosomes from obese patients spread dysfunction to other organ systems, including the lungs and particularly through the TGF $\beta$  pathway.

#### METHODS:

We isolated exosomes from surgically-acquired lean (L) and obese (Ob), paired visceral (v) and subcutaneous (sq) adipose depots (n=3L/5Ob). A novel bead-based flow cytometry assay we developed was used to confirm exosome size and quantity. Exosomal miRNA expression was measured using Affymetrix GeneChip miRNA 3.0 arrays on amplified samples. Data were analyzed in Partek Genomics Suite. T-test was used to compare miRNA expression between L and Ob groups, using  $p \leq 0.1$  and fold change  $\geq |1.2|$ .

#### RESULTS:

Adipose donors were African American or Caucasian females between the ages of 12 and 19 years of age. The diameters of the isolated exosomes were within the 50-90 nm range typical for exosomes. Because visceral fat is most associated with obesity-related disease, we first focused our analyses on vOb vs. vL exosomes. We found 39 miRNAs (with 5,862 confirmed or putative mRNA targets) differentially-expressed between these conditions. Using Ingenuity Pathways Analysis, TGF $\beta$  signaling was ranked the second of the top canonical pathways reflecting our data with 49 out of 89 predicted mRNA targets. In particular, downregulated miRNAs included mir-379, mir-133, miR-654, miR-376, miR-142, and miR-4438. Downregulation of these miRNAs is predicted (and confirmed in the cases of mir-379 and mir-133) to increase TGF $\beta$  signaling in target tissues.

#### CONCLUSIONS:

Adipocytes from obese individuals release exosomes that contain miRNAs that are downregulated compared to those from lean individuals. This is associated with increased TGF- $\beta$  signaling in target tissues. Adipose exosome-derived stimulation of TGF $\beta$  signaling may be a mechanistic link between adipose and lung and this could lead to novel therapeutic targets.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### $\beta$ -defensin-inducing plant extracts and their effects on both $\beta$ -defensin and inflammatory marker production in canine keratinocyte

This study was funded by Virbac

#### BACKGROUND:

Beta defensins are antimicrobial peptides that are part of the innate immune system and produced by the skin to combat skin infections.<sup>1</sup> The skin of atopic dermatitis patients is deficient in these peptides and it is believed that this may have a direct effect on the increased susceptibility of these patients to recurrent skin infections which occur due to the significant barrier disruption, chronic skin inflammation, and impaired innate immune response that are all characteristics of the disease.<sup>2</sup> Compounds that induce the production of beta defensins in the skin without concurrently inducing inflammatory cytokines have potential use in atopic dermatitis therapy and screening methods have been developed to screen plant extracts with this profile.<sup>3</sup>

#### OBJECTIVES:

The purpose of this study was to evaluate the effects of two such plant extracts (Extract A and B) on the production of  $\beta$ -defensin (cBD103), which is analogous to human beta defensin 3 (hBD3), in canine keratinocyte cultures, while also assessing their effect on pro-inflammatory cytokines (IL-8 and TNF- $\alpha$ ).

#### METHODS:

Keratinocytes were extracted from the skin biopsies of 5 atopic and 5 normal beagle dogs. These keratinocytes were grown to confluence and then treated with Extract A (1%, 0.4%, and 0.2%) and Extract B (2%, 1.5%, 1%, 0.4%, and 0.2%). Cell cultures were done in duplicate. The negative control was Dulbecco's Phosphate-Buffered Saline and the positive control was IL-1 $\beta$ . Quantitative real-time PCR was used to quantify the mRNA expression of cBD103 from cell lysate, and IL-8 and TNF- $\alpha$  were evaluated from supernatant by ELISA.

#### RESULTS:

Analysis of the PCR and ELISA results was done through independent paired t-testing on mean values to determine statistical significance ( $P < 0.05$ ). Extract B at 2% showed a significant increase in TNF- $\alpha$  in atopic keratinocytes compared to baseline and normal keratinocytes. At 1.5%, Extract B showed a significant increase in cBD103 in atopic keratinocytes compared to baseline, while also showing a significant decrease in IL-8 in atopic keratinocytes compared to baseline. Extract A at 1% showed in both atopic and normal keratinocytes a significant increase in IL-8 compared to baseline, as well as at 0.4% in atopic keratinocytes compared to baseline.

#### CONCLUSIONS:

In conclusion, Extract B at 1.5% should be further looked at in *in vivo* trials as a potential treatment adjunct for patients suffering from atopic dermatitis, while it appears Extract A had the opposite effect of what was intended.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A functional variant in the SPP1 Promoter Affects Global Methylation in Skeletal Muscle from Males

A genetic variant in the promoter of the secreted phosphoprotein 1 (SPP1) gene (rs28357094) has been shown to affect disease progression in Duchenne muscular dystrophy. It is suspected that global methylation patterns in skeletal muscle are different with the mutant allele (G) compared to the wild type allele (T).

#### PURPOSE:

To identify global methylation patterns in skeletal muscle of males with the mutant (G) and wild type (T) alleles.

#### METHODS:

DNA was extracted from the vastus lateralis muscle of 17 healthy males (20-26yrs) and analyzed for methylation using the Infinium HumanMethylation450 Beadchip. Genotypes for rs28357094 were obtained using a TaqMan allelic discrimination assay to detect a fluorescent reporter signal generated during PCR reactions. PCR was performed with 10 minutes at 95°C and 44 cycles of 15 seconds at 92°C and 1 minute at an annealing temperature of 60°C. PCR reactions were analyzed using an ABI 7900HT Quantitative Real Time PCR system.

#### RESULTS:

Allele frequencies were 0.82 (T allele) and 0.18 (G allele) with 14TT and 3 TG. Analysis of methylation differences showed 18,100 CpG sites that had higher beta values of TT genotypes and 5,362 CpG sites with lower beta values for the TT homozygotes ( $p < 0.05$ ). 455 CpG islands shared the following parameters: 620bp (270bp to 2000bp) size, 10 probes in regions, and p-value for the region of  $< 0.005$ . The top CpG site ranked by p-value is located within 200bp of the transcription start site for the gene *SCNN1G* (sodium channel, non-voltage-gated 1, gamma;  $P = 2.74E-11$ ). The GG genotype showed 93% higher beta value than GT genotype. We detected 104 CpG islands ( $p < 0.0007$ ) on 20 different chromosomes with the number of CpG sites located in these islands ranging from 10 (sites located in *SPON1* gene) to 51 (sites located in *MEST* gene).

#### CONCLUSION:

Polymorphisms at rs28357094 in *SPP1* influence global methylation patterns in the skeletal muscle of healthy males.

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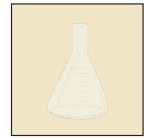
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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Effects of In-vivo Application of Cold Atmospheric Plasma on Corneal Wound Healing in New Zealand White Rabbits

#### BACKGROUND:

Cold Atmospheric Plasma (CAP) has been shown to reduce corneal infection but little is known about the impact of CAP on healthy corneal tissues and their ability to respond to injuries.

#### OBJECTIVE:

To examine the effect of Cold Atmospheric Plasma (CAP) on wound healing after corneal epithelial and basement membrane ablation in New Zealand white rabbits.

#### METHODS:

Twelve New Zealand white rabbits were assigned into two groups, Group A (7 rabbits) and Group B (5 rabbits). Five rabbits from each group underwent surgical intervention to the right eye, a 6 mm central corneal ablation to the epithelium and stroma using an Alger brush with 0.5 mm burr. After ablation, all rabbits in group A received 120s application of CAP. Two rabbits in Group A received CAP application without ablation. Eyes monitored for haze, inflammation, and reepithelialization with slit lamp examination. 24 hours after ablation, two corneas were harvested from each group. The 20th day, the remaining corneas were harvested, fixed in formalin and stained with H&E. In addition, immunofluorescence microscopy was performed to assess scar formation using antibodies against fibronectin and smooth muscle actin.

#### RESULTS:

Corneal reepithelialization on day 1 showed that rabbits in group A (treated) had an average epithelial defect of 9.25 mm<sup>2</sup> and group B (untreated) had a defect of 12.05 mm<sup>2</sup>, not a statistically significant difference. H & E stained sections showed the expected responses of stromal fibroblasts to debridement injury in both groups. Epithelial thickness and stromal cell counts on both groups 20 days after injury showed no significant statistical differences. At 24 hours and 20 days after injury, analyses show that CAP-treatment increased fibronectin deposition in the anterior stroma and aSMA localization within stromal fibroblasts; quantitative analysis of immunofluorescence data will be needed to determine whether these differences are significant.

#### CONCLUSION:

CAP treatment following corneal injury does not interfere with rate of wound closure or induce increased inflammation. CAP treatment did affect corneal tissues since aSMA and fibronectin localization within stromal fibroblasts appears to increase slightly after CAP treatment regardless of whether corneas have been wounded. More studies are needed to evaluate the potential effects of CAP on the cornea and its possible applications in the field of Ophthalmology.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Effect of SFRP1 on Wnt Pathway & Glandular Hyperplasia in CRS

Understanding of the mechanism that regulates the development and distribution of submucosal glands in human airway is crucial for an improved treatment of Chronic Rhinosinusitis (CRS). This research project studies the wnt pathway in relation to submucosal gland morphogenesis in order to reveal the molecular mechanism of glandular hyperplasia in Chronic Rhinosinusitis (CRS). Dr. Wu has previously shown that SFRP1 and GSK3 $\beta$  genes are down-regulated in CRS sinus mucosa. These genes are key components of wnt pathway that contribute to the degradation of beta-catenin, a protein that enters the nucleus to turn on transcription factors such as TCF/LEF potentially leading to cell proliferation and ultimately glandular hyperplasia. Hence, Dr. Wu and I investigate in this research the association between wnt signaling and submucosal gland growth by observing the effects of SFRP1 and SFRP1 inhibitor on CRS glandular hyperplasia. Furthermore, we aim to determine if SFRP1 has a dose-dependent effect on the wnt pathway. In order to test our hypothesis, we cultured normal HNE cells on Matrigel and treated the cells with SFRP1, SFRP1 inhibitor, SFRP1 +LiCl (inhibitor of GSK3B), SFRP1+Cyclosporin A (inhibitor of NFAT). We have run western blot (and plan to run real time PCR in the future) to determine how gene expression is regulated under the different conditions. Our current data have demonstrated that SFRP1 does affect the wnt pathway as we anticipated, subsequently resulting in gland growth - SFRP1 treatment resulted in an increased production of GSK3  $\beta$  protein and reduced cell proliferation. This supports our initial hypothesis that GSK3  $\beta$  is part of the destruction complex that degrades  $\beta$ -catenin which can lead to glandular hyperplasia. In conjunction with Dr. Wu's previous findings, we can demonstrate in this research the role of SFRP1 on WNT pathway and its relation to glandular hyperplasia observed in CRS patients, which may potentially lead to beneficial treatment available for CRS.

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# BASIC BIOMEDICAL SCIENCES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### FTO variant is associated with differences in Global Methylation in Skeletal Muscle

Single Nucleotide Polymorphisms (SNPs) in the FTO (fat mass and obesity-associated) gene have been linked to obesity through a number of pathways, including hypothalamic regulation of energy homeostasis. SNPs in FTO gene have been associated with changes in DNA methylation pattern in whole blood and associated with response to exercise.

#### PURPOSE:

To determine the effect of an FTO SNP on differential genetic methylation patterns in skeletal muscle in males and females.

#### METHODS:

Methylation patterns were generated in 31 subjects (16 males and 15 females) with an average age of 23 years and a healthy BMI ( $24.8 \pm 3.70$ ). DNA was extracted from the vastus lateralis muscle, treated with sodium bisulfite, and analyzed for methylation changes using the Illumina HumanMethylation450 BeadChip (485,577 CpG sites). Genotyping of the FTO SNP rs9939609 (T/A) was performed using a Taqman assay. CpG sites were removed from analysis if a SNP was present at the CpG site or within the probe site. Statistical analysis was completed on 395,899 CpG sites using Partek Genomics Suite (version 6.6) with a dominant model (TT versus TA/AA). Any CpG sites with an average Beta values less than 0.1 were removed due to the sensitivity of the BeadChip assay.

#### RESULTS:

Genotypes for the FTO SNP did not violate the Hardy-Weinberg Equilibrium with allele frequencies in males (T=0.69; A=0.31) similar to females (T=0.70; A=0.30). Females showed 13,282 CpG sites that were significantly different with hypomethylation occurring at 3,575 sites with the TT genotype and 10,071 CpG sites were hypermethylated in females with the TT genotype. The top ranked CpG site by p-value ( $p = 7.0 \times 10^{-6}$ ) for females was cg16929692 located in the gene *DSCAML1*. Males with the TT genotype showed 6,564 CpG sites that were hypomethylated and 2,778 CpG sites that were hypomethylated. The top CpG site in males by p-value was cg16385448 in the *JAG2* gene ( $p = 2.1 \times 10^{-7}$ ). Males and females shared 2,335 methylation sites when analyzed by FTO genotype.

#### CONCLUSIONS:

FTO genotype has been associated with body mass index and type 2 diabetes. In this study we show that FTO genotype affects whole genome methylation differently in males and females. This work provides new insight into the interaction of genetics and methylation in skeletal muscle and may reveal novel pathways for analysis of the causes of obesity.

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# BASIC BIOMEDICAL SCIENCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Maternal Determinants of Neural Fate in *Xenopus laevis*

The purpose of my ongoing research project in the Moody laboratory is to discover whether maternal mRNAs influence embryonic cells to become part of the nervous system. I am testing whether three maternal mRNAs that are normally enriched in the animal blastomeres of the frog (*Xenopus laevis*) embryo are required for the development of the embryo's neural plate. The neural plate is the embryonic precursor of the central nervous system. In many organisms, important developmental events are regulated by mRNAs that are synthesized in the egg and locally stored for later use in embryonic development. These are referred to as maternal factors. In the frog, several maternal mRNAs are highly localized in the animal embryonic cells (called blastomeres) that give rise to the non-neural ectoderm, which will become the skin, and the neural ectoderm, which will become the neural plate. Previous research in the Moody lab has determined that three transcription factors (regulators of gene expression) have important roles in the formation of the neural plate after gastrulation (FoxD4L1, Gem, Zic2). My project is to determine whether they also have a function before gastrulation.

A problem in studying the maternal function of these three maternal transcription factors is that manipulating their expression levels subjects them to events in the embryo that can confound the interpretation of the results. Therefore, to study the function of these maternal factors, the Moody lab developed a culture system that removes cells from the embryonic environment prior to the onset of embryonic (zygotic) gene transcription and gastrulation. Previously, gain-of-function experiments in non-neural isolated ventral cells have resulted in the expression of neural genes - indicating a direct correlation between these maternal factors and neural gene expression. My work in the Moody lab is to determine whether the maternal factors are required for zygotic neural gene expression in isolated dorsal animal blastomeres using gain-of-function experiments. Currently, my experiments have focused on the Zic2 maternal factor and have demonstrated that heightened levels of Zic2 enhance the expression of neural genes in dorsal cells.

Understanding how neural stem cells are formed in the embryo will provide critical information about how to create and manipulate neural stem cells for therapeutic uses. Additionally, it is important to establish whether these genes are evolutionarily conserved, particularly in humans. These are future goals that I will pursue in coming months.

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# BASIC BIOMEDICAL SCIENCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Mesenchymal cell phenotype in an epithelialized tissue-engineered vocal fold

#### PURPOSE:

To characterize mesenchymal cell phenotype within tissue engineered bi-layered vocal fold tissue via immunofluorescence, and compare those constructs against the human vocal fold tissue cell phenotype.

#### METHODS:

Frozen sections of tissue constructs, produced by the UCLA Head and Neck Department, were exposed to antibody markers specific for vimentin and pro-collagen, as well as to histologic stains, Oil Red O and von Kossa, respectively. Oil Red O is specific for lipid and von Kossa stains calcium. A control tissue engineered specimen, without an epithelial layer, was stained with the same markers for comparison. All construct sections were contrasted against similarly stained human vocal fold tissue

#### RESULTS:

Constructs were comparable to human vocal fold tissue in density and distribution of vimentin and pro-collagen, which are both intracellular proteins characteristic of fibroblastically differentiated mesenchymal cells. Pro-collagen, the precursor form of collagen, which is produced by fibroblasts, was most concentrated in the middle and at the base of the tissue constructs. The constructs also stained positive for lipid and calcium deposits.

#### CONCLUSION:

The presence of vimentin and pro-collagen within tissue constructs indicated the presence of mesenchymal cells with characteristics similar to human vocal fold fibroblast cells. However, the occurrence of lipid and calcium deposits within the constructs did not mimic the cellular phenotype of normal human vocal folds. Although lipid is unlikely to alter the functional capability of the constructs, calcium deposits may be indicative of osteoblast differentiation and could alter vibration functionality of the tissue. Further work must be done using markers specific for the various sources of calcium to characterize the nature of the deposits and identify potential bone producing cells.

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# BASIC BIOMEDICAL SCIENCES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Osteopontin modulates myostatin expression via AKT1 - FOXO1 pathways

#### OBJECTIVE:

Osteopontin (OPN, also secreted phosphoprotein 1 [SPP1]) is a multifunctional cytokine associated with many pathological states. An OPN promoter polymorphism in humans has recently been shown to be associated with muscle hypertrophy and strength phenotypes in Duchenne muscular dystrophy (DMD) and normal volunteers. We sought to understand the role of OPN in muscle remodeling using the dog model of DMD and in vitro assays. We hypothesized that OPN could inhibit the most potent negative growth regulator of muscle mass known as myostatin.

#### METHODS:

Cranial sartorius (CS) muscle circumference was measured surgically in golden retriever muscular dystrophy (GRMD) dogs at 6 months. Osteopontin and myostatin mRNA was subsequently measured in CS muscle samples taken from biopsies at 4-9 weeks and 6 months. H-2kb-tsA58 wild-type myoblasts and myotubes were treated with recombinant OPN protein and outcome measures were assessed, including myostatin, AKT1, and FoxO1 levels.

#### RESULTS TO DATE:

There was an age-related increase and decrease in OPN and myostatin in the hypertrophied CS muscle of GRMD dogs, respectively. Use of recombinant OPN protein on H-2kb-tsA58 wild-type myoblasts showed a dose-dependent induction of AKT1 hypertrophy pathways, including AKT1 phosphorylation, increased FoxO1 phosphorylation, and inhibition of myostatin (MSTN) expression. The effect of OPN on this hypertrophic pathway was blocked by an AKT1 inhibitor. OPN has been shown to bind integrin  $\alpha 3$  and we show that this receptor is present on myoblasts. Recombinant OPN protein treatment decreased myostatin in myotubes as well. Finally, AKT1 phosphorylation and myostatin were positively and negatively correlated with CS muscle size in GRMD dogs at 6 months, respectively.

#### CONCLUSION:

Thus, we propose a molecular model where OPN serves as a ligand for AKT1 to inhibit myostatin. We suggest that OPN promotes muscle hypertrophy in normal muscle, whereas this molecular function is overshadowed by inflammatory roles in dystrophic muscle.

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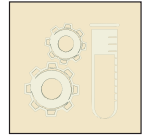
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCES

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### Echogenicity and release characteristics of folate-conjugated ELIPs for cytosolic delivery of cancer drugs

Echogenic liposomes (ELIPs) are specially prepared liposomes that encapsulate both aqueous and gaseous phases. The presence of gas makes them echogenic. Since, ELIPs retain all the favorable properties of normal liposomes they can be used for simultaneous ultrasonic imaging and drug delivery applications. These liposomes are polymerized on the external leaflet using a disulphide linker. Disulphide bonds are reversibly broken in presence of thiol above a critical concentration. Therefore, the liposomes are stable in the plasma (thiol concentration 10  $\mu\text{M}$ ) but release its content inside the cell (thiol concentration 10 mM). The liposome also expresses folate group on its surface which allows its entry into the cancer cells. The release can be controlled by diagnostic frequency ultrasound. Therefore, these ELIPs hold promises for ultrasound image-guided cytosolic delivery for cancer drugs. We will report on their acoustic properties and ultrasound-mediated release characteristics. Their implications on design and development of these novel contrast agents will be discussed. (Supported by NSF CBET-0651912, CBET-1033256, DMR-1005283).

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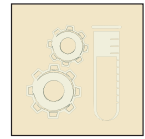
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Detection and Tracking of Secondary Flow Structures in Model Curved Arteries

#### RESEARCH QUESTION:

The overarching goal of our research is to present an efficient and automated method of quantifying secondary flow structures in blood flow through curved arteries. The results from application of this method will deepen our understanding of the dynamics of arterial blood flow and eventually help improve stent design.

#### MOTIVATION FOR THE RESEARCH:

Cardiovascular disease is the leading cause of death in the US, and as such, is an important problem. The biological mechanisms that affect cardiovascular diseases such as atherosclerosis, thrombosis, and aneurysms, are known to be influenced by the behavior of secondary flows in curved arteries, and their interactions with stents. As such, a better understanding of this type of flow is necessary. This need, coupled with the richness in fluid dynamics and the kaleidoscope of secondary flow structures encountered in blood flowing through curved arteries serves as motivation for this research. Terabytes of data are generated from running the in vitro experiments for relatively short periods of time. This has necessitated the development of an automated method for efficient analysis of the data.

#### RESEARCH METHOD / APPROACH:

Arterial blood flow was studied in an experiment using a bent pipe as a model for a curved artery. Carotid artery flow rate was generated using a physiological waveform input in a programmable pump. Flow visualization was performed using particle image velocimetry (2C-2D PIV) technique, which yielded velocity vector fields. Vorticity fields were acquired and then post-processed using continuous wavelet transforms to detect coherent structures (vortices) in the secondary flow. At this stage, 'Boundary Tracing', a new automated method of detecting and isolating coherent vortical structures based on 'Otsu's Method', was used to further process the data. In addition to isolating the structures, the method also generated metrics such as count of structures detected, scale of these structures, and information about circulation. This process was repeated at different instances of time across the physiological waveform, allowing characterization of the evolution of the periodic secondary flow, as a function of time.

#### RESEARCH RESULTS:

Various metrics for the flow were generated across the entire physiological waveform. These data were used to create histograms and plots, helping visualize the behavior of the flow as a function of time. Significant activity was observed in the flow during its acceleration and deceleration phases. High vortical structure counts were also observed during the deceleration phases.

#### RESEARCH CONCLUSIONS:

The research has provided new insight into the dynamics of arterial flow. The automated method was successfully developed and implemented, leading to efficient processing of large amounts of PIV data, and generation of useful metrics that help characterize the flow. This method also enables generation of more accurate regime maps, plots that help visually characterize the flow. These improved regime maps have the potential of improving stent design.

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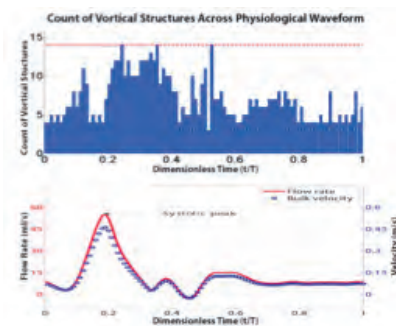
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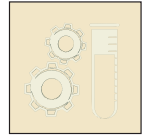
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# BIOMEDICAL ENGINEERING

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Biomimetic and Biphasic Nanocomposite Scaffold with Growth Factor-Encapsulated Nanospheres for Repairing Osteochondral Defects

Osteoarthritis is defined as the progressive degeneration of hyaline cartilage leading to structural and functional failures at the bone-cartilage interface.<sup>1</sup> People with this disease experience reduced joint mobility and severe pain due to the gradual loss or traumatic injury to the articular cartilage and subchondral bone which is collectively known as osteochondral tissue. As the osteochondral tissue degrades, the connective tissue holding the joint together stretches, further increasing the pain felt by patients. Compounding the damage, articular cartilage is not highly vascularized, and depends on diffusion of gases and nutrients from the subchondral bone.<sup>3</sup> Current treatment methods used to address these defects include autografts, allografts, and mosaicplasties. Each of these methods contain their own inherent limitations, including donor site morbidity, infection, poor tissue integration, and neovascularization<sup>4</sup>, which continue to prevent the clinical success of these traditional methods and lead researchers to consider alternatives. This research investigates the validity of biomimetic materials to better simulate the osteochondral site. Due to the complex mechanical nature of the osteochondral site, single-material constructs lack the dynamic range necessary to repair the interface. For example, osteochondral sites are often subject to repetitive, complex compressive loads which prove difficult for any single biomaterial to respond to appropriately as the natural material does. The sheer complexity of engineering an interface between vastly different tissues leads one to believe that only a nanocomposite material can adequately reproduce the physiological and mechanical properties of the osteochondral site. Highly porous poly(caprolactone) (PCL) with bone morphogenetic protein-2 (BMP-2)-encapsulated poly(dioxanone) (PDO) nanospheres as well as nanocrystalline hydroxyapatite is fabricated via porogen-leaching through the combination of water soluble poly(ethylene glycol) diacrylate (PEG-DA) and sodium chloride salt particles, serving as the bone layer of the biphasic scaffold. The cartilage layer is composed of PEG-DA with transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1)-encapsulated PLGA nanospheres and is cast on the porous PCL bone layer then cured under ultraviolet (UV) radiation physically joining the two layers by crosslinking of infiltrated PEG-DA. In this manner, a biomimetic nanoscale osteochondral scaffold with sustained chondrogenic and osteogenic growth factor distributions is created. Human bone marrow derived mesenchymal stem cells will be seeded onto each layer and evaluated for directed osteogenic and chondrogenic differentiation in vitro. We expect that sustained growth factor release in combination with a more biomimetic biphasic nanostructured construct will yield a more clinically relevant tissue-engineered construct for improved osteochondral regeneration.

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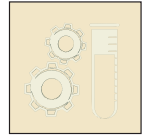
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Regime Maps and the Role of Centrifugal Forces on Multi-scale Secondary Flow Structures in Curved Arteries

#### BACKGROUND:

An arterial network consists of branches and curvatures that are present ubiquitously in the human vasculature. Endothelial cell lining on the inner arterial walls respond to the shear stresses generated from the pulsatile blood flow profiles. Pulsatility of blood flow and shear stress distribution are closely linked to the onset of atherosclerosis, thrombosis, restenosis and activation of sensitized platelets. Under steady and oscillatory inflow conditions in curved arteries, unlike in the straight pipe analog, symmetric secondary flow (vortical) structures develop in planar cross-sections due to imbalances in pressure gradients and centrifugal forces<sup>[1,2]</sup>. The analytical procedures to predict secondary flow structures are complicated, requiring solution of governing Navier-Stokes equations in toroidal co-ordinates and asymptotic theories<sup>[2,3]</sup>.

#### MOTIVATION AND OBJECTIVE:

This study is inspired by our experimental observation of multiplicity of secondary flow structures in curved arteries possessing a variety of scales, swirl magnitudes (strengths) and morphologies. The overarching goal of this study was to understand the driving mechanisms that govern this loss in coherence in arterial secondary flow structures. Under physiological (pulsatile) inflow conditions, complicated effects, e.g. asymmetry and spatio-temporal distributions arise, that cannot be predicted from simple theories.

#### METHODS:

A rigorous *in vitro* experimental investigation of secondary flow structures with a bent tube model of a curved artery was performed using phase-averaged, two-component, two-dimensional, particle image velocimetry (2C-2D PIV) technique under physiological inflow conditions. By means of continuous wavelet transform algorithms, vorticity ( $\bar{\omega}$ ) fields characterized secondary flow structures quantitatively.

#### RESULTS:

We developed regime maps based on two nondimensional parameters, dimensionless pumping power ( $B_p$ ) and secondary flow Reynolds number ( $R_s$  [3]) to explain the evolution of large-scale coherent structures viz., deformed Dean-, Lyne- and Wall-type (D-L-W) vortices. Results suggest that D-L-W vortices evolved during the systolic acceleration phase, followed by the predominant loss in coherence during systolic deceleration phase. We examined the role of streamwise ( $F_\theta$ ) and cross-stream centrifugal force ( $F_\varphi$ ) terms, that were derived from Navier-Stokes equations in toroidal co-ordinates.

#### CONCLUSION:

Our main conclusion is that cross-stream centrifugal forces ( $F_\varphi$ ) are driving mechanisms for the overall loss in coherence of large scale secondary flow structures during deceleration phases. Our experimental analysis of arterial secondary flow structures will stimulate fresh insights into onset of atherosclerosis, thrombosis, restenosis and activation of sensitized platelets.

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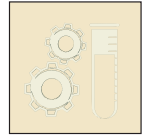
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# BIOMEDICAL ENGINEERING



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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### The influence of transmural fiber orientation on epicardial conduction in the heart

#### BACKGROUND:

Active tissue properties such as heterogeneity of action potentials duration (APD), APD restitution, and conduction velocity restitution are commonly used to investigate the reentrant electrical activity during arrhythmia. Passive tissue properties such as fiber orientation, gap junction distribution, and tissue curvature can also contribute to modulating wavefront loading of arrhythmia. Previous studies have shown that curved fibers impose directional loading, where fibers curved away from a wavefront causes dispersed current and an increase in electrotonic loading. While fibers curved toward a wavefront causes current to be concentrated and the electrotonic loading to reduce.

#### OBJECTIVE:

Our goal is to study how transmural fiber gradients distort epicardial wave front velocities. Our hypothesis is that epicardial wave front direction and speed in an intact heart will be different than what would be predicted by only considering epicardial fiber orientation.

#### METHODS:

Langendorff perfused rabbit hearts were stained with a voltage-sensitive dye (di-4\_ANEPPS) to reveal action potentials via fast changes in dye fluorescence. Fluoresced light (>590nm) was imaged using a high speed CCD camera (128x128 pixels, 750 fps). Fluorescence signals at each pixel were analyzed to measure wave front position and velocity. Hearts were studied before and after a cryoablation procedure, which removed the electrotonic load of transmural tissue. The result of cryoablation was the destruction of Purkinje fibers, endocardial tissue, and mid-myocardial tissue while all epicardial tissue was preserved. The average surviving thickness was 1-3mm, resulting in a 2D sheet of epicardial tissue with anatomic fiber orientations intact.

#### RESULTS/CONCLUSION:

Epicardial point stimulation before cryoablation created elliptical wave fronts. The major axis of the ellipse was oriented along the local epicardial fiber orientation. This result is generally consistent with cardiac anisotropic conduction theory. However, cryoablation resulted in changes of the long and short axis lengths of elliptical wave fronts as well as differences in wave front velocities along and across fibers. Our results suggest that the electrotonic loading of sub-epicardial tissue layers significantly influences the speed and direction of epicardial wave fronts. This highlights the importance of 3D electrotonic loading as well as the potential dominating influence of local fiber orientation on the formation of reentry during local ischemic injury. Data analysis is still in progress.

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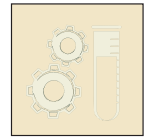
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#### SOURCES

This project was supported by  
NIH R01 HL095828

# BIOMEDICAL ENGINEERING



## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### 3D Fabrication of Biomimetic Nanocomposite Scaffolds for Tissue Interface Engineering and Regenerative Medicine

#### RESEARCH QUESTION:

This research sought to explore whether or not a construct could be created for osteochondral tissue regeneration that could support and encourage stem cell growth and differentiation, while also maintaining structural integrity, and even produce improved mechanical strength.

#### MOTIVATION FOR THE RESEARCH:

The osteochondral region of the knee or other articulate joints consists of several layers of cartilage consisting of different material orientation and structure and a bone layer. In native tissue these layers form a strong, continuous tissue interface. In the field of regenerative medicine, efforts to create tissue engineering scaffolds for osteochondral repair have encountered problems with replicating the bone-cartilage interface. These scaffolds consist of materials of different internal structure, or of different materials altogether, and often such scaffolds fail at the interface region. This research is intended to present a design solution to this problem by utilizing 3D printing to print anisotropic, yet continuous structures that have two distinct, biomimetic layers and additional support features to improve compressive and shear strength.

#### RESEARCH METHOD/APPROACH:

For the 3D printed osteochondral scaffolds, constructs were designed using Rhinoceros 3D modeling package. Scaffolds were then printed in groups of six using a PrinterBot 3D printing system modified with a 347  $\mu\text{m}$  diameter nozzle, and a spool of 1.75 mm diameter Poly lactic acid (PLA) polymer. 3D models were converted into a gcode instruction file using Slic3r, and then used to instruct the printer via the Proneerface software package. There were a total of six experimental groups designed: (1) homogenous cross-hatched structures; (2) bi-phasic structures consisting of a cross hatched pattern and an intersecting rings structures; and (3) biomimetic bi-phasic structures with key features; each of the structure with large and small pore features. In addition, we applied a collagen type II coating on the printed scaffolds to further improve their cytocompatibility properties. A protocol for chemically functionalized attachment known as acetylation was utilized. As opposed to a chemical process, hydrogen-treated MWCNT used in previous study were also attached to scaffolds using absorption. All mechanical tests were done using an ATS axial tester, a 50 Newton load cell and compression placard. When 3D printed scaffolds were coated, the surfaces of poly-L-lysine nanotube and acetylated collagen constructs were also evaluated using a SEM. All cellular studies used human bone marrow derived MSCs cultured in cell culture media. Once all the scaffolds were fabricated and modified, a proliferation study was conducted.

#### RESEARCH RESULTS:

All of the scaffolds showed excellent mechanical properties similar to or exceeding cartilage (.75 to 1 MPa) and subchondral bone (30 to 50 Mpa) in human osteochondral tissue. Under compressive loading, the biphasic key models both in small and large feature have the highest modulus when compared to the homogeneous controls and the bi-phasic models. The proliferation study result showed on day one, with slightly greater cellular activity on bi-phasic scaffolds when compared to homogenous control groups. More importantly, our result shows that all of the biphasic scaffolds with small features can significantly promote MSC proliferation after 5 days. Based on table 4, these biphasic scaffolds with smaller feature attain increased surface area and greater feature density, thus providing a more advantageous environment for cellular growth. Furthermore, the scaffolds with acetylated collagen and poly-L-lysine coated H2 treated MWCNTs outperformed all other groups, which shows that nanostructured surface morphology and chemical modification can greatly increase MSC proliferation.

#### RESEARCH CONCLUSION:

This study yielded a series of biomimetic and bi-phasic constructs that had excellent mechanical properties, cytocompatibility and anatomical shape for musculoskeletal tissue engineering applications. This study showed that, through modification of the initial design parameters, the surface area, pore density and number of internal features could be easily controlled to yield desirable MSC activity. It was also demonstrated that the design of both a bi-phasic construct and that of a mechanically enhanced key structure increased cellular activity, and the addition of an internal key feature enhanced the mechanical characteristics of the scaffold when compared to homogenous control scaffolds. Finally, chemical and nano-constituent modification showed that the addition of collagen and poly-L-lysine coated MWCNTs further enhanced MSC proliferation *in vitro*.

#### STATUS

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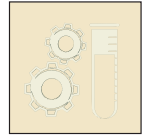
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# BIOMEDICAL ENGINEERING

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Automated Classification of Clinical Reports Using Natural Language Processing and Topic Modeling

With the recent emphasis on the use of electronic health records (EHRs), the importance of leveraging the large amounts of electronic clinical data have become clearer. These clinical reports embody important information about patients' health in various formats including free text. Efficient utilization of them is critical to improving health care quality, preventing medical errors, and reducing health care costs. There are, however, many challenges in developing such automated systems. Clinical reports include medical terms, that are not commonly used in daily language, in various forms. Those terms have to be coded into their standard forms defined in the medical dictionaries. Furthermore, coding by itself may not be sufficient for correctly identifying clinical conditions; reported conditions must be analyzed with their surrounding contexts to validate their temporal, certainty, and negation status.

Biomedical natural language processing (NLP) tools map medical terms are to dictionaries and analyze the conditions with their surrounding contexts. However, their output cannot be directly used for automated processes such as classification. In this research, we first investigated the best ways to extract features from the NLP output that can be used for automatic classification. Alternatively, we developed a framework for topic modeling based classification system. Representing reports according to their topic distributions is more compact and can be processed faster than raw text or NLP output in subsequent automated processes. Results show that the classification performance is significantly improved by using the NLP features over using the raw text. Topic based representation of reports gets comparable results with NLP; they also provide interesting insight into the themes that exist in the patient reports.

Machine learning techniques, such as NLP, topic modeling, and text classification, are shown to successfully classify patient reports into categories representing clinical conditions. This type of automated analysis of patient reports can help medical professionals make clinical decisions much faster with more confidence by providing predicted outcomes; e.g., recommending the need for a certain medical test while avoiding steps that would result in unwanted intrusion or medical costs.

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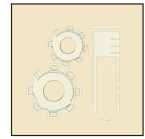
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Three-Dimensional Flow Separation Induced by a Model Vocal Fold Polyp

#### BACKGROUND:

The fluid-structure energy exchange process for normal speech has been studied extensively, but it is not well understood for pathological conditions. Polyps and nodules, which are geometric abnormalities that form on the medial surface of the vocal folds, can disrupt vocal fold dynamics and thus can have devastating consequences on a patient's ability to communicate<sup>1</sup>.

#### MOTIVATION AND OBJECTIVE:

A recent in-vitro investigation of a model polyp in a driven vocal fold apparatus demonstrated that such a geometric abnormality considerably disrupts the glottal jet behavior and that this flow field adjustment was a likely reason for the severe degradation of the vocal quality in patients<sup>2</sup>. The present investigation concerns the three-dimensional flow separation induced by a wall-mounted prolate hemispheroid with a 2:1 aspect ratio in cross flow, i.e. a model vocal fold polyp. Previous work on flow separation from a surface mounted protuberance has been primarily limited to steady free-stream flow conditions. Therefore, the flow structures produced by three-dimensional flow separation from a polyp in pulsatile flow conditions are not well understood.

#### METHODS:

In this work, unsteady three-dimensional flow separation and its impact of the wall pressure loading are examined using oil-film visualization and wall pressure measurements. Oil-film techniques enable the visualization of skin friction lines, high and low velocity regions, and separation and attachments points within a surface flow.

#### RESULTS:

Preliminary results have shown that the formation of a horseshoe vortex system upstream of the protuberance and hairpin vortices downstream of the protuberance results in spatial and temporal pressure variations in unsteady flow conditions. A representative skin friction line visualization image is displayed in Figure 1.

#### CONCLUSION:

Variations in aerodynamic loadings caused by the protuberance are assumed to be contributing mechanisms for producing irregular vocal fold dynamics observed in patients with polyps. Understanding the formation and propagation of vortical structures from a geometric protuberance, and their subsequent impact on the aerodynamic loadings that drive vocal fold dynamics, is a critical component in advancing the treatment of this pathological condition. Future work will include investigating the three-dimensional flow separation in unsteady flow conditions using particle image velocimetry.

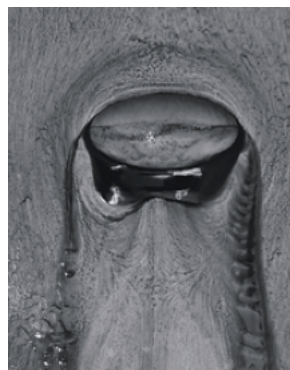


Figure 1: Skin friction line visualization image for a prolate hemispheroid in cross flow ( $Re=9,000$ ).

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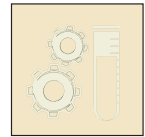
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#### SOURCES

Supported by the National Science Foundation, Grant No. CBET-1236351 and GW Center for Biomimetics and Bioinspired Engineering (COBRE).

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Investigating Contact Forces in a Model of the Human Vocal Folds to Understand how Cysts and Polyps Form and Evolve

#### BACKGROUND:

The formation of cysts (fluid-filled distensions) and polyps (more fibrous distensions) on the vocal folds is one of several causes of voice pathologies diagnosed by physicians in clinics each year. In the US alone, it is estimated that 28 million people suffer from voice problems, costing approximately \$2billion annually [Verdolini, 2001], and out of a sample of 1,262 patients, 11.4% were diagnosed with polyps and 1% with cysts (7.9% were diagnosed as normal) [Herrington-Hall *et al.*, 1988]. These pathologies present patients with significant, and in some cases chronic, difficulties with verbal communication and expression, causing a marked decrease in their quality of life.

#### OBJECTIVE:

It is our aim to measure the forces acting on the vocal folds during contact in an artificial model with physiological properties, which will be used to improve models of vocal fold tissue interaction and better understand the formation of cysts and polyps in patients.

#### METHODS:

Using a well-known and highly-published [Murray and Thomson, 2012; Pickup and Thomson, 2009; Drechsel and Thomson, 2008] *in vitro* self-oscillating model of the human vocal folds, a high-speed camera is used to capture the position of individual fiduciary marker particles within grids marked on the surface of the vocal folds. These positions are then calculated and quantified using a particle tracking algorithm, which is then used to calculate the strain acting on the surface of the vocal folds. The stress, and hence the forces, acting on the vocal fold surfaces are calculated from the strain.

#### RESULTS TO DATE:

Preliminary results like those shown in Figure 1 have been acquired. These results illustrate that it is possible to calculate the position of particles marked on a self-oscillating *in vitro* model of the vocal folds. In order to capture the position of all of the particles, further work will need to be undertaken to optimize the particle tracking algorithm and the strain then calculated.

#### CONCLUSIONS:

The measured results from this work will generate data describing the forces acting on the surface of the vocal folds. This information will then be used in conjunction with other data (e.g. velocity and pressure) for this type of model and provide insight into how cysts and polyps form and evolve.

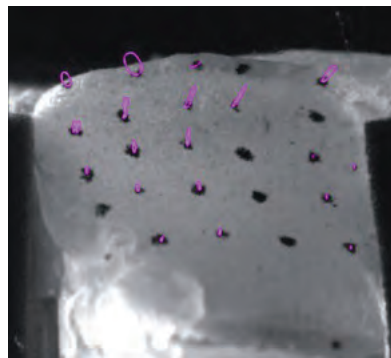


Figure 1: Image of one half of the *in vitro* model of the vocal folds with the detected particle tracks overlaid (in magenta).

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#### REFERENCES

[Drechsel and Thomson, 2008] Drechsel, J. S. & Thomson, S. L. (2008). Influence of supraglottal structures on the glottal jet exiting a two-layer synthetic, self-oscillating vocal fold models. *The Journal of the Acoustical Society of America*, 123: 4434-4445.

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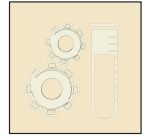
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[Verdolini, 2001] Verdolini, K., & Ramig, L.O. (2001). Review: occupational risks for voice problems. *Logopedics, Phoniatrics, Vocology*, 26 (1): 37-46.

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# BIOMEDICAL ENGINEERING

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Cold atmospheric plasma and gold nanoparticles interaction in cancer therapy

#### BACKGROUND:

Our research work is aimed at a novel method of cancer therapy. Gold nanoparticles (AuNP) have emerged as a promising cancer therapy, as it can enhance specificity via conjugation with antibodies. Recently, cold atmospheric plasma (CAP) demonstrated exquisite selectivity for cancer cells in pre-clinical models. Based on these results, we hypothesize a synergy of CAP and AuNP in cancer therapy.

#### OBJECTIVES:

This research is of great importance because cancer is the leading cause of death in the world according to the World Health Organization (WHO). Cancer has been challenged by the need for more specific therapies to improve outcomes.

#### METHODS:

Glioma U87 cells were cultured in vitro, and subsequently treated with CAP and AuNPs. The sequence of CAP and AuNPs applied to the cells were changed in order to find out the mechanism of the interaction.

#### RESULTS:

Our results show that CAP enhanced the migration rate of AuNPs. In specific, the number of nanoparticles penetrated into the cells was greater if AuNPs were applied after 60s plasma treatment.

#### CONCLUSIONS:

It can be concluded that CAP enhanced the migration rate of AuNPs. Moreover, cells were activated by CAP before incubated with AuNPs.

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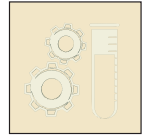
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#### FACULTY ADVISOR

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Flexible Integration of CMOS MAGFET Biosensor with Microfluidics for Magnetic Immunoassays

#### BACKGROUND:

Magnetic immunoassays (MIA) are novel medical diagnostic tools using magnetic beads as labels for detecting antibodies, antigens and proteins. Compared with conventional enzyme (ELISA), radioisotope (RIA) and fluorescent (FIA) labels, MIA offers much simplified workflow and cheaper reagents without sacrificing performance. However current MIA instruments are bulky and expensive which severely limit their utility in point-of-care or low resource settings.

#### OBJECTIVES:

In this work, we aimed to achieve a compact, low cost and semi-automated MIA system which can potentially lead to a handheld diagnostic instrument.

#### METHODS:

To achieve the objectives above, we proposed a novel CMOS magnetic sensor technology along with a new hybrid CMOS/Microfluidics packaging approach. In this system, a CMOS split-drain Hall Effect Magnetic Field Effect Transistor (MAGFET) was designed to measure the magnetic field generated by magnetic beads. The MAGFET was optimized using a numerical noise model to result in a highly robust SNR, and fabricated employing a fairly conventional CMOS 0.5 $\mu$ m commercial fabrication process to reduce the cost. The flexible packaging technology integrated the MAGFET sensor die on a soft polydimethylsiloxane (PDMS) substrate containing microfluidic channels. Those channels not only can precisely deliver liquid magnetic bead samples directly onto the MAGFET to obtain a larger signal, but also can deliver liquid metal to the contact pads on the chip to form electric connection in place of the conventional solid wires. Additionally, this technique gives the integrated device the ability to maintain full functionality under miscellaneous bending and stretching conditions.

#### RESULTS:

A low-cost easy-to-fabricate flexible CMOS/Microfluidic MIA device was fabricated and tested. With this device, we achieved magnetic nanoparticle detection sensitivity of  $\sim 100\mu\text{g/mL}$  from a sample volume of only  $1\mu\text{L}$ . In addition, the device was fully functional under bending curvature radius of one centimeter and uniaxial strain of 15%.

#### CONCLUSION:

This is, to our knowledge, the first experimental demonstration of a fully integrated CMOS/Microfluidic hybrid microsystem without performing any wire bonding or post-processing on the CMOS die. In addition, our novel packaging method provides a new way of making flexible (i.e. bendable and stretchable) electronic systems with high performances. The flexible integration technology demonstrated in this work holds great potential for wearable health monitoring, point-of-care diagnostics and environmental sensing among many other applications.

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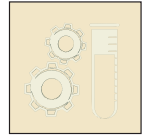
Zhenyu Li



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# BIOMEDICAL ENGINEERING

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### The Fluid Dynamics of Human Birth

This study investigates the fluid dynamics associated with the human birth process. Specifically, we investigate the role of the viscosity of the amniotic fluid in transferring force from the contracting uterus to the fetus during delivery. This experimental work uses a makeshift uterus and dilated cervix—fabricated with liquid latex—filled with a fluid of known viscosity and an oblong solid fetus. The force required to extract the fetus will be recorded for several values of amniotic viscosity. The study looks at both pull-out force values (where the fetus is pulled from outside the uterus) and push-out force values (where pressure in the experimental uterus is used to remove the fetus). In addition to the viscosity study, we also investigate the increased force required to deliver an offset fetus by tilting the major axis of the oblong fetus and repeating the pull-and push-out experiments. This study will provide knowledge about the fundamental fluid dynamic processes involved in human birth.

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#### STATUS

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Undergraduate Student

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#### AUTHORS

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Andrea Lehn

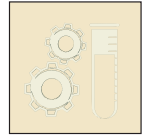
Megan C. Leftwich

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Changes in Cardiac Function Upon Light-Activated Release of Norepinephrine from Sympathetic Neurons Expressing Channelrhodopsin

#### BACKGROUND:

Release of norepinephrine (NE) from sympathetic neurons enhances heart rate (HR) and contractility through  $\beta$  receptors, but may also be a key player in the formation of cardiac arrhythmias<sup>1,2</sup>. As such,  $\beta$ -blockers, which target the  $\beta$ -adrenergic receptors in cardiac cells, have been long used as treatment for cardiac arrhythmias<sup>1</sup>. Although the connection between  $\beta$ -adrenergic stimulation and cardiac arrhythmias has been made, exact mechanisms remain elusive. This research presents and tests a novel methodology of light-activated endogenous NE release that can eventually be applied to controlled studies of  $\beta$ -blockers and the arrhythmic events that arise from  $\beta$ -adrenergic stimulation.

#### OBJECTIVES:

The main objectives of this study were to discover whether hearts from mice expressing a light-gated ion channel in cardiac neurons could be stimulated with light to release NE, and to observe the effects of NE on left ventricular pressure (LVP) and HR.

#### METHODS:

Hearts from mice expressing channelrhodopsin-2 (ChR2) in catecholaminergic neurons were isolated and Langendorff-perfused at 37°C with modified Krebs-Henseleit buffer and fitted with a balloon in the left ventricle to measure and record LVP. ECG electrodes captured signals for HR measurements. After hearts stabilized, a 470nm LED (Mightex, Pleasanton, CA) illuminated the epicardium in 5 msec duration pulses at a frequency of 1 and 2 Hz, for 10 seconds. After 10 seconds, the light was turned off and recordings were monitored. At the end of each study,  $\beta$ -adrenergic receptor agonist isoproterenol (1  $\mu$ M) was added to confirm that the  $\beta$ -adrenergic receptors were able to be stimulated in the excised heart.

#### RESULTS:

Mouse hearts were imaged to look at the distribution of nerve fibers. The investigator observed densely packed arrays of nerve fibers on the epicardial surfaces of heart slices up to 20  $\mu$ m deep, a finding which provided confidence that epicardial illumination would stimulate sympathetic neurons so close to the surface. An increase in HR (18 $\pm$ 9 bpm) as well as LVP (up to 75% increase) was observed in all three ChR2 hearts after stimulation with blue light. Addition of isoproterenol further increased HR (22 $\pm$ 2 bpm) and LVP (up to 21% increase).

#### CONCLUSIONS:

Blue light pulsing increased left ventricular pressure and heart rate, confirming the release of norepinephrine from catecholaminergic cells expressing ChR2 in isolated mouse hearts. This experiment introduces a new and physiologically relevant model for the study of cardiac arrhythmias that arise from the activation of intrinsic sympathetic fibers and local  $\beta$ -adrenergic stimulation in excised mouse hearts.

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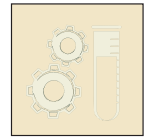
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### High-fidelity Modeling and Simulation of Hemodynamic Effect of Peripheral Arterial Stenoses

#### BACKGROUND AND GOAL:

Multiple subcritical stenoses can be a significant resistance to flow in the upper legs, but they are not generally treated by angioplasty because there is little understanding of the hemodynamic effects of multiple stenoses in the vasculature. We carry out numerical simulations to illuminate the subject further and provide guidance to vascular surgeons that will improve outcomes for patients with multiple subcritical stenoses in the peripheral vessels. I implement an in-house computational fluid dynamics (CFD) model to predict the cumulative effect of multiple mild to moderate stenoses in superficial femoral/popliteal arteries on blood flow distally. Our hypothesis is that, in diseased vessels, multiple mild stenoses can be equivalent to or effectively more occlusive than, a single critical stenosis.

#### APPROACHES:

We conduct a series of post-simulation analysis of hemodynamic effect of multiple stenosis using idealized geometries. Variables to be considered include percentage of stenosis and separation between stenosis. The computational model and numerical methods employ an in-house CFD solver developed by Dr. Liang. The program solves unsteady 3D incompressible Navier-Stokes equations on complex geometries. We use the Finite-Volume method based on hexahedral cells with unstructured meshes.

#### RESULTS:

Our preliminary results indicate that the effect of multiple stenoses is not simply additive, but depends on their severity. Comparing with moderate stenosis, i.e. <50%, critical stenosis, i.e. >60% would cause more severe pressure drop which was concerned as a major local parameter leading to diseases.

Num	Degree	Pressure drop
1	40%	279.354
3	40%	418.674
1	50%	908.499
3	50%	2676.048
1	60%	2085.197
3	60%	3817.019



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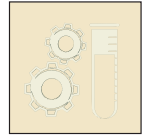
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# BIOMEDICAL ENGINEERING

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Generalized Focus + Context Framework for Improved Medical Data Exploration

In the everyday practice of medical diagnosis and surgical planning physicians rely on exploring multimodal 2D images of patients. Radiologists examine 2D orthogonal slices to create an accurate diagnosis and to plan a detailed intervention procedure. In contrast, surgeons examine the same dataset using 3D visualizations to get an overview of the dataset and to practice the surgical intervention. In our work we provide a solution to the problem of how to unify the above-mentioned two ways of examining multimodal medical datasets. This task requires a visualization that can display 1. 2D and 3D images simultaneously, 2. the whole dataset or only a subsection of it, and 3. the path taken to reach the target.

To create a unified framework for 2D, 3D and sub-3D volume visualizations in orthogonal and arbitrary planes we employ the Focus + Context visualization approach. The focus and context areas are assigned different dataset and rendering modalities. The focus area, referred to as a lens, can display a 2D slice visualization used by radiologists, while a surgeon can enable a 3D volume visualization. Using the lens as a drill and enabling 2D or 3D rendering inside it, a surgeon can simulate drilling.

Our generalized Focus + Context framework allows the user to visualize the target area as a 3D volume and then switch to a 2D slice visualization where the target area is explored by scrolling through the sequence of 2D slices. This gives the necessary detailed information about the anatomy while preserving the explicit spatial perception with the rest of the dataset. The problem of volume occlusion is addressed by allowing a sub-volume visualization within the focus region so that only important areas are displayed. The applicability of the lens to be used as a drill gives the user the flexibility to accurately plan the surgical intervention path and to explore the resulting 3D anatomy.

Our team has incorporated the requirements of both radiologists and surgeons for medical data exploration into one unified tool. This tool is a generalized framework that provides the necessary intervention plan information that multidisciplinary medical teams use in their work. The unified visualization approach provides other research teams with a way of qualitatively comparing 2D, 3D and Focus + Context techniques applied in the clinical domain. The next step in this work involves a user study that aims at showing the advantages of our approach in inner structure exploration.

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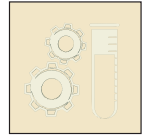
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Ultrasound-enhanced Delivery of Antibiotics and Anti-inflammatory Drugs into the Eye

#### BACKGROUND:

Millions of people suffer from variety of ocular diseases which in some cases lead to vision impairment and eventually blindness. Topical administration of drugs, for treatment of ocular inflammations and infections, through cornea is the preferred method for drug delivery, but cornea's barriers makes delivery of a sufficient amount of therapeutic drugs a challenging task.

#### METHODS:

Initial study was carried out using unfocused ultrasound transducers in ultrasound- and sham-treated rabbit corneas *in vitro* using a standard diffusion cell set-up. Ultrasound application (frequencies of 400 KHz-1 MHz, intensities of 0.3-1.0 W/cm<sup>2</sup>, and exposure duration of 5 min) was studied to investigate corneal permeability of ophthalmic drugs, Tobramycin, Dexamethasone Sodium Phosphate and Sodium Fluorescein. Overall exposure of cornea to drug solution was 60 min. Amounts of drug that penetrated through ultrasound and sham-treated corneas were examined using a spectrophotometer. Light microscopy observations of histology slides were used to determine ultrasound-induced structural changes in the cornea. Using the most effective parameters, a study was designed for *in vivo* rabbit corneas to investigate the effects of ultrasound on corneal permeability to ocular drugs. The eye-cup with drug solution (Dexamethasone Sodium Phosphate) was placed on corneal and under the eyelid. The tested ultrasound frequencies were 400 KHz and 600 KHz, at intensity of 0.8 W/cm<sup>2</sup>, and exposure duration of 5 min. Aqueous humor was sampled 60 min after the start of experiment, and drug concentration in samples was determined using chromatography methods. The animals were sacrificed immediately after the experiments, and corneas were dissected and fixed for histological observations using light microscopy.

#### RESULTS:

Our *in vitro* results showed that increase of 32-47% , 46-126% (p<0.05) and 32-109% (p<0.05) in corneal permeability for Tobramycin, Sodium Fluorescein, and Dexamethasone Sodium Phosphate, respectively, was achieved at different ultrasound-treatment parameters as compared to sham treatment cases. For *in vivo* study, increase in drug concentration in aqueous humor samples was 2.8 times (p<0.05) at frequency of 400 KHz and 2.4 times (p<0.01) using 600 KHz frequency, both at 0.8 W/cm<sup>2</sup> intensity and 5 min of ultrasound application, as compared to sham treated samples.

#### CONCLUSIONS:

Ultrasound appeared to be most effective at lower frequencies (400-600 kHz) and higher intensities (0.8-1.0 W/cm<sup>2</sup>). Some structural changes in the epithelial layer of the cornea were observed at all applied ultrasound parameter combinations. In general ultrasound has a potential to provide effective and safe method for ocular drug delivery in treatment of eye infection and inflammation.

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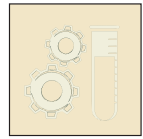
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCES

### Detection and Tracking of Secondary Flow Structures in Model Curved Arteries

#### RESEARCH QUESTION:

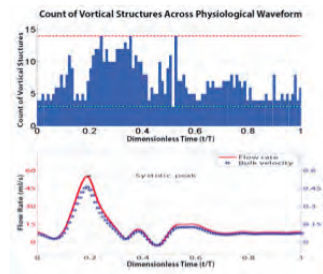
The overarching goal of our research is to present an efficient and automated method of quantifying secondary flow structures in blood flow through curved arteries. The results from application of this method will deepen our understanding of the dynamics of arterial blood flow and eventually help improve stent design.

#### MOTIVATION FOR THE RESEARCH:

Cardiovascular disease is the leading cause of death in the US, and as such, is an important problem. The biological mechanisms that affect cardiovascular diseases such as atherosclerosis, thrombosis, and aneurysms, are known to be influenced by the behavior of secondary flows in curved arteries, and their interactions with stents. As such, a better understanding of this type of flow is necessary. This need, coupled with the richness in fluid dynamics and the kaleidoscope of secondary flow structures encountered in blood flowing through curved arteries serves as motivation for this research. Terabytes of data are generated from running the in vitro experiments for relatively short periods of time. This has necessitated the development of an automated method for efficient analysis of the data.

#### RESEARCH METHOD / APPROACH:

Arterial blood flow was studied in an experiment using a bent pipe as a model for a curved artery. Carotid artery flow rate was generated using a physiological waveform input in a programmable pump. Flow visualization was performed using particle image velocimetry (2C-2D PIV) technique, which yielded velocity vector fields. Vorticity fields were acquired and then post-processed using continuous wavelet transforms to detect coherent structures (vortices) in the secondary flow. At this stage, 'Boundary Tracing', a new automated method of detecting and isolating coherent vortical structures based on 'Otsu's Method', was used to further process the data. In addition to isolating the structures, the method also generated metrics such as count of structures detected, scale of these structures, and information about circulation. This process was repeated at different instances of time across the physiological waveform, allowing characterization of the evolution of the periodic secondary flow, as a function of time.



#### RESEARCH RESULTS:

Various metrics for the flow were generated across the entire physiological waveform. These data were used to create histograms and plots, helping visualize the behavior of the flow as a function of time. Significant activity was observed in the flow during its acceleration and deceleration phases. High vortical structure counts were also observed during the deceleration phases.

#### RESEARCH CONCLUSIONS:

The research has provided new insight into the dynamics of arterial flow. The automated method was successfully developed and implemented, leading to efficient processing of large amounts of PIV data, and generation of useful metrics that help characterize the flow. This method also enables generation of more accurate regime maps, plots that help visually characterize the flow. These improved regime maps have the potential of improving stent design.

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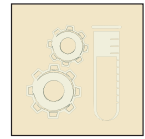
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# BIOMEDICAL ENGINEERING



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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Computer-Based Planning System for Mandibular Reconstruction Surgery

#### OBJECTIVE:

Mandibular reconstruction is typically performed for traumatic and may involve the use of autologous osteocutaneous fibula free flaps for large defects. Recreating the native contour of the mandible is challenging. This research addresses automated ways of optimizing the pre-operative planning of the mandibular reconstruction surgery. We are optimizing 1) the number, shape, and orientation of the osteotomies in order to best recreate the mandible in three dimensions 2) the position of the osteotomies in order to minimize injury to the perforator vessels and 3) the position of the osteotomies along the linear axis of the fibula in order to maximize the length of the pedicle for anastomosis.

#### METHODS:

Two CT scans of the patient's head and lower extremities are obtained. Our optimization pipeline consists of three stages. Stage one optimizes the lengths and the orientations of the needed wedge osteotomies with respect to the defective mandible. Second stage finds the best fibula osteotomies cut locations that match the needed wedge osteotomies by taking the perforator blood vessels into account. Stage three reconstructs the defected mandible with the suggested fibula osteotomies. A dynamic programming algorithm is used to find the optimal wedges length and orientation by minimizing the least square error between the mandible curve and the osteotomized fibula segments. And a greedy algorithm counts on the blood vessels locations to find the best osteotomies on the fibula. A case study was designed to evaluate the accuracy of the planned surgery using our system. The accuracy of the computer aided planning software was then assessed by evaluating the angles and lengths and the locations of the segments.

#### RESULTS TO DATE:

The surgical results using the virtual model were compared to the current gold standard of non-aided surgery. The recommended reconstruction met all the requirements of the standard reconstruction performed without using it.

#### CONCLUSIONS:

The surgeon would plan the surgical defect preoperatively based on the patient characteristics, and would identify the perforators to the skin based on preoperative angiograms of the lower extremities. Outcomes would be maximized, surgery would be more durable, and operative time would be dramatically reduced. The optimization process improves the mandibular reconstruction surgery by mapping the surgery accurately and by reducing planning and intra-operative surgery time. It appears from this study that computer aided planning software has great potential to reduce patient risk by cutting operative time, and to improve osteocutaneous flap survival rates by optimizing both bony and vascular parameters.

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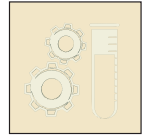
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Prof. James Hahn



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Strength Analysis of Single-Ridged Plaster of Paris Splints for Hand Surgery

#### INTRODUCTION:

Plaster-of-Paris (PoP) splints are frequently used postoperative in hand surgery for immobilization, decreasing the risk of injury to the structures repaired. PoP is widely used in the orthopaedic field because of its relatively cheap cost and its strength once it is applied. Currently, it is common practice for upper extremity splints to be formed without ridges.

One of the advantages of PoP is its ability to be molded with certain modifications. Theoretically, ridges and laminations should allow for stronger constructs with the same amount of PoP. Our current research is investigating the three-point bend strength of PoP splints made with a single, longitudinal dorsal ridge versus conventional, non-ridged splints and non-ridged fiberglass.

#### METHODS:

Plaster-of-Paris (POP) splints were made with 4"x12" slabs. The splints were made with 8, 10, or 12 layers of PoP and submerged in warm water for 5 seconds, with excess water wrung out by hand. Five ridged and five non-ridged splints were made for each layer group, with ridges measuring 1-cm in height and 2-cm in width. Both ridged and non-ridged splints were allowed to dry on 2-ply of webril on the volar surface, and 1-ply on the dorsal surface for 48 hours. The splints and webril were removed before further testing.

Fiberglass splints were made in a similar manner to the PoP splints. 4"x12" slabs of fiberglass were used for testing. The splints were submerged in water, wrung out by hand. None of the fiberglass splints were made with ridges. The splints were allowed to dry with webril placed on the dorsal and volar surfaces for 48 hours before testing was started.

Each splint as subjected to three-point bend testing using an MTS machine. Each splint was secured 1 cm from the longitudinal edges of the construct. Increasing dorsal pressure was applied at the middle of each splint to failure. The total pressure required for each splint to fail was recorded. The data compiled for the ridged PoP splints, non-ridged PoP splints, and non-ridged fiberglass splints and analyzed for statistical significance.

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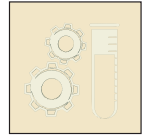
David Moss

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David Moss





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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### An Optimal Set of Landmarks For Metopic Craniosynostosis Diagnosis From Shape Analysis of Pediatric CT Scans of the Head

Craniosynostosis is a severe condition in which there is a premature fusion of the skull sutures and is present in one of every 2000 newborns. Craniosynostosis can result in severe and permanent head deformity as well as developmental delay if left untreated. Metopic craniosynostosis is specifically a premature fusion of the frontal (metopic) suture and accounts for 20-27% of cases. Currently metopic craniosynostosis is diagnosed qualitatively in terms of skull shape abnormality, a subjective call of the surgeon. In this paper we introduce a new quantitative diagnostic feature for metopic craniosynostosis derived optimally from shape analysis of CT scans of the skull. We built a robust shape analysis pipeline that is capable of obtaining local shape differences in comparison to normal anatomy. Spatial normalization using 7-degree-of-freedom registration of the base of the skull is followed by a novel bone labeling strategy based on graph-cuts according to labeling priors. The statistical shape model is built from 94 normal subjects and allows matching a patient's anatomy to its most similar normal subject model. Subsequently, the computation of local malformations from a normal subject allows the characterization of the points of maximum malformation on each of the frontal bones adjacent to the metopic suture, and on the suture itself. Our results show that the malformations at these locations vary significantly ( $p < 0.001$ ) between abnormal/normal subjects and that an accurate diagnosis can be achieved using linear regression from these automatic measurements with an area under the curve for the receiver operating characteristic of 0.97. Here we have proposed a computational model of local malformation in a craniosynostotic skull which, with further research and refinement, could help to assist in clinical decision making with quantitative data.

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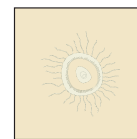
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#### SOURCES

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Kirmi, O., Lo, S., Johnson, D., and Anslow, P., "Craniosynostosis: A radiological and surgical perspective," *Seminars in Ultrasound, CT and MRI* 30(6), 492-512 (2009).

Branson, H. and Shroff, M., "Craniosynostosis and 3-dimensional computed tomography," *Seminars in Ultrasound, CT and MRI* 32(6), 569-577 (2011).



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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Nitric Oxide as a Novel Regulator of TP53

Nitric oxide (NO) has been shown to impact gene expression by cyclic GMP-dependent and independent modulation of transcription. However, the role of NO in alternative splicing has not been described. Our group is the first to show an effect of NO on splicing. Specifically, we identified a PTB-associated RNA splicing factor (SFPQ) as a mediator of NO-induced silencing of a TP53 alternative exon that leads to a decrease in the relative abundance of the TP53-beta isoform.

We found that NO decreases TP53-beta expression in cell lines that originated from leukemia, multiple myeloma, neuroblastoma and colorectal cancers. Pulse-labeling showed that NO does not affect stability of TP53-beta mRNA. Using a splicing reporter system we demonstrated that NO inhibits the inclusion of alternative exon 9. We analyzed the identified NO-responsive genomic sequence and determined whether any of the predicted binding factors are co-expressed with TP53 in cancer patients. The combined analysis implicated SFPQ as a potential splicing regulator of TP53. Accordingly, siRNAs targeting SFPQ abolished NO activity on the splicing reporter. Moreover, inhibition of the upstream activator of SFPQ, glycogen synthase kinase 3, induced TP53-beta expression. Interestingly, the concentration range of various nitric oxide donors and inhibitory analysis of the NO effect are consistent with a mechanism independent of the cGMP pathway. Recently glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was found to bind SFPQ in response to direct S-nitrosylation of a reactive cysteine thiol. Thus, GAPDH can link NO to SFPQ-mediated silencing of TP53-beta splicing.

The tumor suppressor TP53 orchestrates a variety of stress responses including cell cycle arrest, apoptosis and cellular senescence. Deregulation of TP53 splicing was suggested to be a prognostic indicator in various types of cancer. Thus, research into the mechanisms governing TP53 alternative splicing is expected to provide novel therapeutic strategies.

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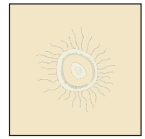
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma: An Epidemiological Comparison of Two Malignant Tumors that Arise

**BACKGROUND:**

Hepatocellular carcinomas (HCCs) and intrahepatic cholangiocarcinomas (ICCs) arise from the same organ and have the same embryologic derivation, yet are entirely different morphologically.

**OBJECTIVE:**

To determine whether HCCs and ICCs have the same pathogenesis from an epidemiological perspective by comparing the incidence and survival trends of liver and intrahepatic bile duct cancer between 1992 - 2009 by racial/ethnic group, age distribution, geographic location, and other epidemiological variables including age specific rates.

**METHODS:**

The Surveillance, Epidemiology, and End Results (SEER) Program was utilized to obtain incidence, mortality, and survival rates from Registry 13 and Registry 18 for patients aged 35 and older, Black or White, and had HCC or ICC from 1992 - 2009. Trends and log-log plots were generated to illustrate patterns. Unadjusted and adjusted odds ratios were calculated to determine the odds of ICC versus HCC.

**RESULTS:**

The trend for hepatocellular carcinomas among males has the highest incidence and increase in rate, peaking at nearly a 20.3% incidence rate in 2009. Log-log incidence rate plots for hepatocellular carcinomas and intrahepatic cholangiocarcinomas illustrate parallel lines from 1975 - 1985. This contrasts with the graph generated from years 1992 - 2009, where the incidence rate curve for hepatocellular carcinomas dips slightly near ages 70-85 whereas the one for intrahepatic cholangiocarcinomas continues to show an increase. Odds of ICC versus HCC are decreased among males (0.451) and Blacks (0.527). Five year survival is the worst for white males with ICC, at 5.00%

**CONCLUSION:**

There may be a new etiologic factor based on epidemiological observations that seems to affect the pathogenesis of HCC and ICC in the recent past. It provides a beginning for future researchers to find a cause for intrahepatic cholangiocarcinomas, after which improved diagnosis and clinical treatments can be implemented.

**STATUS**

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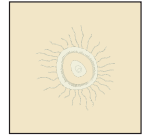
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Inhibiting Hepatocellular Carcinoma Metastasis Via Ion Channel Modulation

#### BACKGROUND:

Many types of metastatic cancers cannot be cured through current treatments, undermining the effectiveness of traditional therapies and contributing to the high mortality rate associated with drug resistance and tumor recurrence. Recent studies have investigated the characteristics of such tumors which contribute to their aggressive phenotype. Intriguingly, a number of findings point to cationic channel activation as a key contributor to cancer progression, though little is known about the role of anionic channels. In hepatocellular carcinoma (HCC), we have previously identified several cationic and anionic channels which are differentially expressed in advanced stages of the disease. The purpose of this study has thus been to explore the contribution of ion channel activation to HCC invasion, metastasis, and tumor growth, repurposing drugs traditionally used as ion channel modulators within the CNS to instead target and inhibit HCC spread.

#### METHODS:

Hep3B cells stably expressing an empty vector (Hep3B-EV) or glucagon receptor (Hep3B-GR) were analyzed for protein and mRNA expression of the cationic sodium channel SCN5A and anionic GABA<sub>A</sub> receptor subunit  $\beta$ 3 (GABRB3) using western blot, immunocytochemistry, and quantitative RT-PCR techniques. Chromatin immunoprecipitation assays were conducted to identify transcription factors which bind to the SCN5A and GABRB3 promoters to regulate gene expression, and invasion assays were completed to identify pharmaceutical agents that target the channels. Nude mice intrasplenically injected with Hep3B-EV cells were subsequently administered saline or drug treatments to examine the effect channel modulation had on HCC metastasis.

#### RESULTS:

SCN5A and GABRB3 proteins are highly expressed at the plasma membrane and in cell lysates of Hep3B cells, and mRNA expression is significantly decreased following knockdown with siRNAs. We identified putative transcription factor binding sites phosphorylated by ERKs (known to contribute to cancer aggression) on the SCN5A promoter or by PKA (which we have previously cited as a mediator of GR signaling in HCC) on the GABRB3 promoter using the PROMO virtual database. We additionally validated that these factors do bind and regulate SCN5A and GABRB3 transcription. Invasion and metastasis in cell lines and a mouse model were blocked using the antiarrhythmic drug flecainide, which specifically inhibits SCN5A activation, and with pregnenolone, which selectively activates GABA<sub>A</sub> receptors.

#### CONCLUSION:

We have shown that commercially available pharmacological agents can be repurposed from their traditional roles to prevent cancer metastasis. The alterations in ion channel expression represent novel gene targets that can be utilized as therapeutic alternatives with substantial translational potential.

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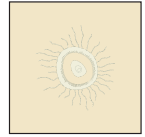
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# CANCER/ONCOLOGY

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### The effect of aldehyde dehydrogenases ALDH1A1 and ALDH3A2 on the tumorigenicity of human epithelial ovarian cancer

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#### OBJECTIVE

Ovarian cancer accounts for more than half of deaths due to gynecological malignancy due to a variety of poor prognostic factors. Most ovarian cancer patients are diagnosed in late stages, with 80% experiencing recurrence despite successful surgery and chemotherapy, and have a 5-year survival rate of only 30%. Understanding the molecular mechanisms underlying ovarian carcinogenesis and histological differentiation is of paramount importance for decreasing the mortality of ovarian cancer. The cancer stem cell (CSC) model hypothesizes the presence of a cellular hierarchy in the tumors such that a subset of tumor cells have the ability to self-renew and generate the diverse cells that comprise the tumor. Many studies have demonstrated an association between cancer stem cells and elevated ALDH1A1 enzyme activity. Aldehyde dehydrogenase (ALDH) proteins are a superfamily of 19 enzymes that are found to protect cells from cytotoxic and carcinogenic aldehydes. Deregulation of these enzymes has been linked to multiple cancers. Previous work by the Ng lab demonstrates overexpression of ALDH3A2 in ovarian tumors and tumor type-specific expression of ALDH1A1, which may indicate a role in histopathologic development of ovarian tumors.

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#### METHODS

To elucidate the roles of ALDH1A1 and ALDH3A2 isozymes in cancer stem cells and ovarian pathogenesis, a type of RNA interference (RNAi), short hairpin RNA (shRNA), was used to reduce the expression of ALDH1A1 and ALDH3A2 enzymes in cultured human ovarian mucinous cystadenocarcinoma (MCAS) cells. Commercially available DNA knock-down constructs were inserted into the MCAS cells using lentivirus. After generating three different clones for each gene, the extent of the enzyme knock-down was preliminarily established by Western Blot.

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#### RESULTS TO DATE

Initial phenotypic characterization of the cell lines suggested that, compared to unaltered MCAS cells, both the ALDH3A2 and ALDH1A1 knockdowns show reduced cell growth rates, altered spheroid formation in 3D culture, and no increase in cell apoptosis measured by immunofluorescent staining.

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#### CONCLUSION

More experiments are needed to clarify whether the observed phenotypes are due to reduced expression of ALDH3A2 and ALDH1A1, as opposed to artifact from the lentivirus shRNA constructs. The extent of the reduction of ALDH expression will need to be confirmed by both Western blot and RT-PCR. If these techniques both show reduction of the specific ALDH expression, then it would suggest that ALDH3A2 and ALDH1A1 play an important role in cancer cell growth, and CSC spheroid formation, but not in cell apoptosis.

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#### STATUS

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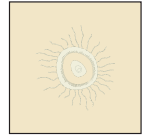
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### PI3K/AKT/mTOR pathway activation drives expression of the immune inhibitory ligand PD-L1 in lung cancer

Despite the development of targeted drug therapies, lung cancer remains the leading cause of cancer-related death worldwide. Targeting immune checkpoints altered in cancer, such as the T cell inhibitory proteins, PD-L1, PD-1 or CTLA-4, represent promising new approaches to lung cancer treatment. Here we investigate the relationship of the PI3K/Akt/mTOR signaling pathway to expression of the immune suppressive ligand, PD-L1, in lung cancer. Lung cancer cells lines with known mutations in KRas, EGFR, BRaf, ALK and RET exhibited PI3K/Akt/mTOR pathway activation as well as membrane and intracellular PD-L1 expression. In contrast, cell lines that lacked these mutations, with low PI3K/Akt/mTOR pathway activation, displayed diminished PD-L1 levels. In murine cell lines derived from tobacco carcinogen (NNK)-induced lung tumors, activation of PI3K/Akt/mTOR correlated with PD-L1 expression. *In vitro*, PI3K/Akt/mTOR pathway activation by treatment of lung cancer cells with EGF, NNK or PTEN siRNA induced PD-L1 expression within hours, while treatment of high PD-L1 expressing cell lines with inhibitors of PI3K, AKT and mTOR decreased PD-L1 expression in a similar time-frame. The most potent PD-L1 inhibitor, rapamycin, decreased PD-L1 protein levels, but did not alter PD-L1 mRNA in murine lung cancer cell lines. In addition, rapamycin-mediated PD-L1 loss was partially blocked by pre-treatment with a lysosomal, but not a proteosomal inhibitor. *In vivo*, PD-L1 expression and p-S6 levels increased in normal mouse lung following 3 weekly exposures to the tobacco carcinogen NNK, while a single dose of rapamycin blocked NNK-induced PD-L1 expression. PD-L1 was also expressed in mouse models of NSCLC with constitutive activation of Akt/mTOR driven by mutant KRas or EGFR. Additionally 95% of human lung adenocarcinomas and 80% of lung squamous cell carcinomas examined expressed PD-L1 in correlation with active mTOR signaling. To test the efficacy of systemically blocking PD1 while reducing the expression of PD-L1 ligand in tumor tissue, rapamycin and a murine anti-PD-1 antibody were administered to A/J mice bearing syngeneic lung tumor xenografts, both together and as single agents. Expectedly, the combination increased the amount of activated CD8+ T cells in the tumors, and decreased regulatory T cells. It also decreased the tumor growth rate to a greater degree than either agent alone and decreased mTOR pathway signaling, PD-L1 expression, and increased cleaved caspase 3 in the tumors. Our data support a relationship between activation of PI3K/Akt/mTOR signaling, PD-L1 expression and the development of an immune resistant phenotype in NSCLC. Combination regimens using PI3K/Akt/mTOR inhibitors may enhance the efficacy of immune therapies targeting PD-1.

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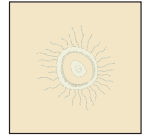
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Very Low Avidity Endogenous Memory CD8<sup>+</sup> T Cells Control Tumor Growth

#### BACKGROUND:

Endogenous Memory (EM) T cells are proposed to arise from naïve T cells in the absence of activation by foreign antigen. These EM-T cells have been documented in unprimed, germ-free, pathogen-free wildtype mice as well as in unmanipulated RAG<sup>-/-</sup> TCR transgenic mice. EM-T cells are a very rare population of cells and are estimated to occur at a frequency of 200 cells per animal per epitope. EM-T cells are thought to contribute to primary immune responses, but have not been studied in cancer models. In this study, we describe mice (TCR<sub>vlo</sub>) bearing a very low avidity TCR transgene specific for the melanoma antigen tyrosinase-related protein 2 (TRP-2<sub>180-188</sub>). Remarkably, more than 50% of the TCR<sub>vlo</sub> CD8<sup>+</sup> T cells express markers consistent with endogenous memory. These mice were tested for their ability to control B16 melanoma.

#### METHODS:

CD8<sup>+</sup> T cells from the TCR transgenic mouse strain TCR<sub>vlo</sub> were characterized by flow cytometry for markers associated with endogenous memory. C57BL/6 mice were compared to TCR<sub>vlo</sub> mice for their ability to control tumor challenge. In that study, mice were injected subcutaneously with B16 tumor cells and were subsequently injected with a TRP-2 pulsed dendritic cell vaccine. Tumor size was measured using a caliper.

#### RESULTS:

A majority (>50%) of TCR<sub>vlo</sub> CD8<sup>+</sup> T cells displayed a phenotype of CD44<sup>hi</sup>, CXCR3<sup>hi</sup>, Gr1<sup>hi</sup>, GITR<sup>hi</sup>, CD69<sup>lo</sup>, CD25<sup>lo</sup>, CD49d<sup>lo</sup> which is consistent with the marker pattern for endogenous memory T cells. This phenotype is not observed in the thymus, but occurs after thymic egress and was documented in peripheral tissues (spleen and lymph nodes), as well as in the bone marrow of these mice. Our preliminary tumor studies suggest that mice bearing TCR<sub>vlo</sub> CD8<sup>+</sup> T cells delayed subcutaneous B16 melanoma growth compared to wildtype animals.

#### CONCLUSIONS:

EM-T cells are a very rare population, and are incompletely understood. Our very low avidity TCR transgenic mice may provide a unique model for studying EM-T cells. On going studies are focused on characterizing the functional response of the TCR<sub>vlo</sub> CD8<sup>+</sup> T cells to antigen. Future studies will include the use of TCR<sub>vlo</sub> CD8<sup>+</sup> T cells in adoptive transfer models which will be used to examine the ability of these cells to avoid or delay tolerance induced by the tumor microenvironment. Overall, these preliminary studies suggest that endogenous memory T cells may provide a novel tool for use as cancer immunotherapeutics.

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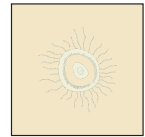
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Iris Melanoma in Children: Current Approach to Management

Iris melanoma is a rare condition, comprising 4% of uveal melanoma and having a prevalence of 5.1 cases per million population in the United States.<sup>1</sup> The mean age of presentation is 40-47 years, which is approximately 10-20 years younger than patients with other uveal melanomas.<sup>2</sup> Most patients are Caucasian (97.8%) with blue or green irides (97%), and males and females are affected equally.<sup>1,3</sup> Pediatric (Younger than 21 years of age) iris melanoma is especially rare, representing only 8% of iris melanoma cases.<sup>1</sup> The differential diagnosis of iris melanoma includes primary iris cyst (38%), iris nevus (31%), essential iris atrophy (5.7%), iris foreign body (4.5%), peripheral anterior synechiae (2.5%), and iris metastasis (2.5%).<sup>4</sup> Iris melanoma in children is characterized by smaller tumors, less seeding, and fewer cases of secondary glaucoma compared to adults.<sup>1</sup>

A 15-year old Caucasian male presented with one-month history of a brown nodule in the inferotemporal aspect of his left eye. Iris nevus was diagnosed and the patient was observed. Nearly two years later the lesion had grown in basal diameter and thickness, and the tumor was excised by partial lamellar scleral flap and sector iridectomy. Histopathology confirmed spindle cell iris melanoma. Two years post-operatively, tumor recurrence with anterior chamber angle involvement and secondary glaucoma developed. The presence of glaucoma in eyes with iris melanoma complicates treatment. Iris melanoma associated with glaucoma is more likely to be thicker, involve the angle, and demonstrate iris stromal seeding.<sup>5</sup> The patient was then treated with custom designed Iodine<sup>125</sup> plaque radiotherapy. Local tumor recurrence after resection in patients with iris melanoma ranges from 2% to 14%, depending on surgeon and surgical technique. The median time from resection to recurrence is 45 months.<sup>3</sup> Metastasis after local iris melanoma resection occurs in 0% to 9% of reported cases.<sup>3</sup> Older age, involvement of the anterior angle, elevated IOP and extraocular extension are all risk factors for metastasis.<sup>1</sup>

Resection and plaque radiotherapy for iris melanoma have remarkable local success rates but complications of therapy can lead to visual damage. Visual damage will be an unavoidable complication in this patient but treatments such as plaque radiotherapy need to be implicated in aggressive cases such as this to ensure tumor eradication and preservation of life. This case report outlines current management options for pediatric iris melanoma and also demonstrates the possibility of tumor recurrence that exists despite proper surgical management.



Figure. A 15-year-old Caucasian male with a pigmented iris lesion. The iris lesion was small at presentation (A) and showed growth over 2 years (B) visible on gonioscopy (C) and anterior segment optical coherence tomography (D). The lesion was excised by partial lamellar scleral flap and sector iridectomy (E). Later tumor recurrence in the anterior chamber angle with elevated intraocular pressure necessitated Iodine<sup>125</sup> plaque radiotherapy (F).

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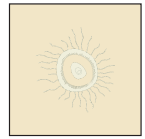
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#### SOURCES

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Philadelphia chromosome-positive precursor-B cell acute lymphoblastic leukemia in association with chronic lymphocytic leukemia

Chronic lymphocytic leukemia is occasionally associated with a spectrum of autoimmune diseases as well as higher susceptibility to other lymphoproliferative disorders. They usually represent clonal evolution of the CLL but can also arise de novo as part of the immune dysregulation associated with the disease. In this report we describe a case of Philadelphia chromosome-positive precursor B-cell acute lymphoblastic leukemia arising from a preexisting chronic lymphocytic leukemia.

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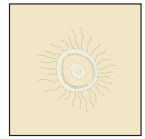
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## Utilization of Physical Therapy Services in Hospice and Palliative Care Settings

**BACKGROUND AND OBJECTIVES:**

The nature of palliative and hospice care has changed dramatically over the past decade. Despite the focus on interprofessional patient care, it is unclear if physical therapy (PT) is routinely provided in these settings. Therefore, the purpose of this study is to describe the utilization of PT services in palliative and hospice care settings and to identify barriers to service provision.

**METHODS:**

An online survey was developed by 2 PT faculty and 2 student PTs. A 23 item survey resulted using an iterative review process with content experts to ensure face validity. The survey was distributed electronically to the National Hospice and Palliative Care Organization listserv (~2,000). Respondents were asked to address utilization of PT services in the previous year.

**RESULTS:**

One hundred and sixteen agencies responded to the survey (5.8% return rate). Most respondents were hospice programs or combined hospice and palliative care programs. Approximately half were located in a mixed urban/rural setting, providing service in multiple venues. The majority were Medicare certified (95%) and independently owned (61%). The average daily census was 108. Most respondents (97.8%) provide PT services to their clients. Only 35% employ their own PTs, while 68% use contract services. Only half reported more than 10 patients received PT services in a given calendar year, with cancer, heart disease, dementia and lung disease cited as the most frequent diagnosis. A nurse identifies the need for PT services (94%), followed by a family member, and finally a primary care provider. Impaired mobility (85%) and safety concerns (82%) most frequently prompt a referral. More than half of those receiving PT receive less than 5 treatments. The most common barrier to providing PT services was insufficient payment to cover the cost (44%). Twenty-seven percent of respondents reported that PT services were not appropriate for the population and 24% stated that PTs were unavailable to provide needed services. Other barriers included lack of knowledge regarding benefits of PT or referrals too late in the care process.

**CONCLUSION:**

This is the first national survey describing utilization of PT services in palliative and hospice care settings. Although generalizability is limited due to the low response rate, it appears that agencies have the ability to provide PT services, but the number of clients receiving PT remains low. Reasons may include reimbursement issues, lack of knowledge regarding PT benefits, late referrals, and limited human resources to provide care. Additional studies are warranted.

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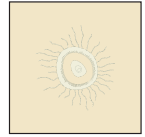
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Investigating the role of BMI1-regulated microRNAs in cellular senescence using human diploid fibroblasts

#### BACKGROUND:

After completing a certain number of divisions, normal cells enter a state of irreversible growth arrest and altered function, known as cellular senescence. Senescence results due to the shortening of DNA structures known as telomeres and various cell stress signals. Senescent cells are characterized by an accumulation of cell growth inhibitors such as pRb, p53, p21 and p16INK4a. Genes that counteract growth inhibitors can cause a cell to overcome senescence and to begin dividing again. Results from previous studies suggest that senescent cells have reduced levels of a gene regulatory protein BMI1, and conversely cells overexpressing BMI1 have an extended life span. This suggests that BMI1 regulates cellular senescence and replication. The exact mechanism of this regulation is currently unknown. This project examines if BMI1 regulates senescence by altering the expression of certain microRNAs (miRNAs).

#### METHODS:

In vitro, MRC5 human diploid fibroblasts were transfected such that BMI1 expression was knocked down: using the RNAi approach; or BMI1 was overexpressed: using a retrovirus. As a result, we developed four cell lines: MRC5-B0 (vector control); MRC5-BMI1 (BMI1 overexpressing); MRC5-Cntrl-I (control RNAi); and MRC5-BMI1-I (BMI1 shRNA expressing). These cells were analyzed for the expression of BMI1 to ascertain for overexpression or knockdown of BMI1. Next, we examined these cells for proliferation and senescence, the expression of various genes known to be altered in senescent cells, and the expression of a few representative miRNAs.

#### RESULTS AND CONCLUSIONS:

Cells overexpressing BMI1 had a higher proliferation rate, and a smaller proportion of senescent cells. Conversely, BMI1 knockdown cells had a lower proliferation rate and underwent senescence. BMI1 overexpressing cells had a lower expression of growth inhibitory protein p16INK4a. Consistent with the overexpression data, BMI1 knockdown cells significantly upregulated p16INK4a. Also, BMI1 overexpressing cells had increased levels of ubiquitinated and acetylated histone proteins H2A and H2B. The quantitative RT-PCR analysis showed that BMI1 may downregulate two microRNAs, miR-141 and miR-205, and upregulate miR-4436b. In summary, our new data suggest that in addition to regulating H2A ubiquitination, BMI1 may also regulate H2B ubiquitination and acetylation of both H2A and H2B. With respect to miRNA expression, BMI1 differentially regulated miR-141/205 and miR-4436. Currently, work is in progress to identify the targets of these miRNAs, and identify additional miRNAs regulated by BMI1. This work will help contribute to our understanding of the role of BMI1 in cellular senescence, aging and cancer, and will translate into a greater understanding of age related pathologies including cancer.

#### ACKNOWLEDGMENT:

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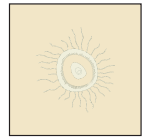
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### miR-671-5p Inhibits Cell Proliferation by targeting FOXM1 in Breast Cancer Cells

Recent studies have demonstrated that MicroRNA (miRNA) deregulation occurs in the majority of human malignancies including Breast cancer. Using miRNA microarray and LCM technologies from FFPE tissues in our previous study (Chen et. al, PLoS One. 2013;8(1):e54213), we identified a list of miRNAs that play an important role in breast cancer development and progression. Among them, miR-671-5p (Sequence: AGGAAGCCCUGGAGGGGCUGGAG) was significantly down-regulated in both atypical ductal hyperplasia (ADH) and invasive ductal carcinoma (IDC) when compared to normal epithelial cells. We hypothesized that miR-671-5p regulates target genes that are important in breast cancer tumorigenesis. We used several miRNA target prediction programs, such as Diana-Microt, MicroRNA.org, MiRDB, TargetMiner and TargetScan-Vert 6.2 to identify potential target genes for miR-671-5p to produce a list of overlapping target genes. In this study, we focus on one of the most prominent target genes, FOXM1. FOXM1 a transcriptional activator involved in cell proliferation and regulates the expression of several cell cycle genes, such as cyclin B1 and cyclin D1. Our microarray analysis compared miR-671-5p overexpressors to controls in both MDA-MB-231 and MCF-7 cell lines and showed FOXM1 down-regulation in miR-671-5p transfected cells. As expected, miR-671-5p transfected cells exhibit decreased proliferation via MTT assay. Luciferase analysis on miR-671-5p transfected MDA-MB-231 cells showed decreased levels of FOXM1 expression; approximately 1.6 times lower than the control. The expression of FOXM1 and Cyclin B1 was subsequently confirmed by the Western blot assay. Using LCM technology, we recently dissected nine FFPE tissue blocks in separating normal, ADH, DCIS and IDC cells. We are in the process of determining their expression levels via qRT-PCR to analyze the role of miR-671-5p during breast tumor progression. To conclude, we believe miR-671-5p is down-regulated in advanced breast lesions, such as ADH and IDC. miR-671-5p inhibits the proliferation of both MDA-MB-231 and MCF-7 cells, and could negatively regulate FOXM1 protein expression. As such, miR-671-5p could be potential therapeutic target for breast cancer treatment.

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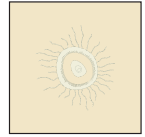
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### miR-638, a Novel Tumor Suppressor for ER-negative Breast Cancer

MicroRNAs (miRNAs) are endogenous non-coding RNAs of 19~25 nt in length, which regulate many protein-coding genes. miRNA dysregulation is observed in a variety of cancers, including breast cancer. miRNAs have emerged as an important set of biomarkers. miRNA profiling studies have led to the identification of miRNAs that are aberrantly expressed in human breast cancer, with miR-10b, miR-125b and miR-145 being down-regulated and miR-21, and 155 being up-regulated. In our previous miRNA expression profiling studies using microdissected FFPE tissues, we identified 8 clusters of miRNAs, which discrete the normal and breast lesions such as ADH, DCIS and IDC. miR-638 is one of the differentially expressed miRNAs during breast cancer progression. We first sought to determine the expression of miR-638 in different breast cancer cell lines such as MCF-7, Hs578T, T47D and MDA-MB-231 using qRT-PCR, which shows a very low expression compared to normal tissues. This led us to hypothesize that miR-638 may function as a tumor suppressor during breast cancer development. To determine the role of miR-638 in both ER+ and ER- breast cancer cells, we transfected miR-638 mimic oligos and scrambled oligo mocks into MCF-7 (ER+), T47D (ER+), MDA-MB-231 (ER-) and Hs578T (ER) cells. After 48 hours, we found that the proliferation rate was significantly down-regulated in ER- cells but not in ER+ cells by MTT assay. Our preliminary matrigel analysis shows that miR-638 overexpressing MDA-MB-231 cells had 3~4 fold invasiveness decrease compared to the control. Further, our TargetScan analysis revealed that BRCA1 is one of the direct targets of miR-638 among the 30 conservative target genes. We found that overexpression of miR-638 resulted in an upregulation of BRCA1 mRNA expressions in ER- cell lines, MDA-MB-231 and Hs578T but not in ER+ cell lines, T47D and MCF-7. Taken together, these findings showed that miR-638 may function as a tumor suppressor in ER- breast cancer, possibly in part by upregulating BRCA1 tumor suppressor gene. Further functional analysis is underway to decipher the exact role of miR-638 in ER- breast cancer, which could become a therapeutic target.

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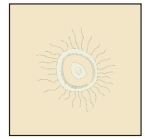
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### miR-141 Expression Increases during Breast Cancer Development and Progression

MicroRNAs (miRNAs) are non-coding RNA molecules, about 22 nucleotides in length that silence gene expression by binding to complementarity sequences of target genes. miRNAs cause either target mRNA gene to be degraded or prevent gene translation altogether. As a result of the prominent role miRNAs play in gene expression, miRNAs have been linked to cancer development and progression. Specifically, miRNA appears to be an essential part of breast cancer progression and metastasis. Breast cancer is believed to be developed from normal epithelial cells - hyperplasia - atypical ductal hyperplasia (ADH) - ductal carcinoma *in situ* (DCIS) and invasive ductal carcinoma (IDC). From our recent studies, we found that certain miRNAs, including miR-141, are differentially expressed during this process. miR-141 is a member of the miRNA-200 family and has been linked to breast cancer metastasis. We hypothesized that expression of miR-141 increases during the breast lesion progression. We aimed to prove this hypothesis and identify potential target genes for miR-141. Formalin-Fixed, Paraffin-Embedded (FFPE) tissues from 9 breast cancer patients, which included ADH, DCIS, IDC, and normal components, were analyzed for miR-141 expression levels. We found that miR-141 was expressed higher in ADH, DCIS, and IDC tissue samples as compared to normal tissue. We also transfected miR-141 mimic and its control miRNA into triple negative breast cancer cell line, MDA-MB-231, respectively. The expression of miR-141 was successfully verified by qRT-PCR. Target genes were predicted using bioinformatic techniques, such as TargetScan, and qRT-PCR was performed to determine the gene expression of potential target genes in the miR-141 transfected cells, including HOXB7, HOXB5, and FOXA1. These genes are all associated with cell proliferation, differentiation, and cell cycle regulation. The expression of HOXB7, HOXB5, and FOXA1 was much higher in the 141 transfected sample as opposed to the control. Data regarding cell viability and cell proliferation rate are still underway. These data indicated that miR-141 plays an important role in breast cancer progression and could serve as a biomarker for breast cancer management.

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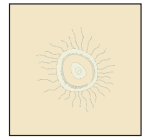
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Upper Extremity Lymphedema Rates Following Treatment for Breast Cancer: The role of radiation, surgery, nodal status, and node count

#### OBJECTIVES:

The rate of breast cancer related lymphedema (LE) in the published literature varies widely from < 5% to > 60% depending on type and extent of surgery and radiation therapy. In this retrospective chart review, we analyze the role of radiation therapy, surgical procedure, nodal status, and number of lymph nodes removed in the development of LE.

#### METHOD:

48 subjects who had bilateral circumferential forearm and upper arm measurements recorded were reviewed. Measurements were taken pre-operatively and 6, 12, and 24-months post-operatively to evaluate for LE, which was defined as  $\geq 2$  cm change in arm circumference compared to the contralateral arm. Records of radiation therapy (location, dose, and frequency), surgical procedure, pathologic nodal status, and number of lymph nodes removed were reviewed.

#### RESULTS

The rate of LE following radiation therapy the rate was 11.0% compared to 9% without (ns). Of those treated with radiation, the rates following treatment with a supraclavicular (SCLV) field, posterior axillary boost, and whole breast irradiation alone were 22.0%, 25.0%, and 5.0%, respectively. There was a trend level of significance ( $\phi$  coefficient = 0.18,  $p = 0.23$  for SCLV and  $\phi = 0.21$ ,  $p = 0.19$  for chest wall fields) for the more aggressive treatments. > 9 lymph nodes removed had an LE rate of 50.0% versus 3.0% with fewer nodes removed ( $\leq 9$ ) ( $p < 0.01$ ,  $\phi$  coefficient = 0.43). Patients without LE had an average  $5.7 \pm 5.5$  nodes removed versus  $14.8 \pm 9.6$  in those with LE ( $p < 0.01$ ). The total number of positive nodes and the percent positive nodes were not associated with the outcome of LE.

#### CONCLUSIONS

We report a rate of LE following radiation therapy that is not statistically different from those who were not treated with radiation. Of the factors evaluated, removing greater than 9 nodes from the axilla is most strongly associated with the subsequent development of LE. Although not statistically significant, there was a trend level of significance between the more aggressive radiation treatment (SCLV field) and LE. Nodal status was a not significant predictor of LE within our cohort. Larger studies are necessary to identify factors that may result in LE.

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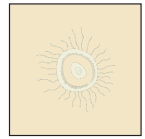
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Induction of CD8 T cell Tolerance by Pre-B Acute Lymphoblastic Leukemia

**BACKGROUND:**

Acute lymphoblastic leukemia (ALL) is the most common form of childhood cancer with relapse as the leading cause of mortality. A potential mechanism for leukemia immune evasion is the induction of regulatory CD8 T-cells, which induce active immunologic tolerance and suppress the immune response to leukemia. Regulatory B-cells, well-described in autoimmunity models, can induce regulatory CD8 by producing regulatory cytokines like IL10. Pre-B cell ALL, the most common form of childhood ALL, has been shown to act as a poor antigen-presenter though mechanisms of leukemia-associated immunologic tolerance are not well-understood.

**OBJECTIVES:**

To investigate leukemia immune evasion via the induction of regulatory CD8 T-cells, which induce active immunologic tolerance and suppress the immune response to leukemia by production of cytokines such as IL-10.

**METHODS:**

Immune responses to pre-B ALL were measured in an in vitro co-culture system using ELISA to measure levels of Interferon-gamma (IFN- $\gamma$ ) & IL-10 production. CD8 T cells whose T-cell receptors are transgenic for the male-specific antigen, HY, were used in all co-cultures.

**RESULTS:**

Male Dendritic cells in culture with HY specific CD8 T cells (positive control) induce high levels of IFN- $\gamma$  and low levels of IL10 as expected. Male B cells in culture with HY CD8 T cells (negative control) did not induce significant IFN- $\gamma$  or IL10 production. Male Pre-B ALL in presence of HY CD8 T cells induced significantly lower levels of IFN- $\gamma$ , but higher levels of IL-10. Female Pre-B ALL in culture with HY specific CD8 T cells does not induce significant IFN- $\gamma$  or IL10 production, suggesting the effect is antigen-specific.

**CONCLUSIONS:**

Pre B cell ALL induces less IFN- $\gamma$  and more IL10 production from CD8 T cells, which might result from poor antigen presentation. Though, ELISA assay cannot distinguish whether cytokines are produced by the APC or CD8 T cells.

Furthermore, there might be additional mechanisms of immune activation and regulation beyond IFN- $\gamma$  and IL10 secretion.

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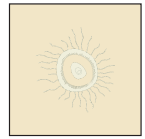
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Genomic Approaches to Identify Breast Cancer Signature Using an Isogenic Model

Numerous studies in the past decade have identified various breast cancer signatures associated with different subtypes. These studies, employing microarray and RT-PCR based technologies were derived from primary human tumor samples. However, owing to the heterogeneity of the samples, various signatures derived from similar subtypes are very divergent and have little or no overlap. Gene signatures derived from cell line based models also show similar tendency because of their diverse genetic backgrounds. Despite multitude of studies, obtaining a reliable signature of breast cancer subtype based on receptor status has been very challenging and the precise contribution of isogenic clones remains poorly defined.

Here we sought to identify the set of elements that distinguish triple negative breast cancer (TNBC) from other common forms of breast cancers namely, estrogen receptor alpha (ER) positive and human epidermal growth factor (HER-2) positive. We generated stable isogenic clones by introducing ER and HER-2 in MDA-MB-468, a TNBC cell line. The functionality of these receptors was investigated by treatment with hormones and anti-hormones and Herceptin. Gene expression profiling using microarrays with fold change  $\geq 1.5$  and p value  $\leq 0.05$  gave a comprehensive list of genes between TNBC and ER or HER-2 positive clones. We found 659 genes differentially expressed between TNBC and ER positive samples and 1090 genes between TNBC and HER-2 positive samples. Next, we compiled two different super datasets from various microarray studies from breast cancer patient samples from Gene Expression Omnibus (GEO) repository. Comparison of differentially expressed genes between TNBC and non-TNBC between our data and GEO super dataset gave various overlaps. We found 127 and 109 genes common when we compared TNBC and ER positive and TNBC and HER-2 positive samples respectively between GEO dataset and data from MDA-MB-468. Additionally, we also identified 1598 genes between TNBC and ER positive samples and 3527 genes between TNBC and HER-2 positive samples showing splicing deregulation.

In brief, the overlap between isogenic cell models and patient samples could potentially represent the true gene isogenic expression signature that distinguishes TNBC from ER positive and HER-2 positive breast cancer. Additionally, our studies also point to a possibility that breast cancer subtypes may differ in their splicing pattern. These findings could be of high value not only for diagnostic and therapeutic decision making but also for guiding treatment modalities in treating TNBC in general.

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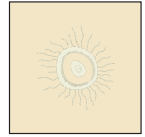
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### BP1, a Homeoprotein, Regulates Estrogen Receptor Alpha and Induces Estrogen Independence

#### BACKGROUND:

BP1 is a member of the homeobox gene family of transcription factors. Our recent studies have shown that BP1 may play a role in breast cancer cell survival, aggressiveness and metastasis. BP1 protein (pBP1) is expressed in 80% of invasive ductal breast tumors; 100% of ER $\alpha$  negative (ER-) tumors expressed BP1, while 73% of ER positive (ER+) tumors expressed BP1.

#### OBJECTIVE:

Our objective is to elucidate the mechanism(s) of ER-alpha regulation by BP1.

#### RESULTS:

MCF-7 cells overexpressing BP1 or control cells containing an empty vector were injected into nude mice. Approximately half of all the estrogen-supplemented mice developed tumors, regardless of the originating cells (MCF-7 overexpressors or empty vector controls). In general, MCF-7 cells require exogenous estrogen to form tumors in nude mice. However, approximately 20% of the mice implanted with cells overexpressing BP1 were able to form tumors in the absence of estrogen, in contrast to mice injected with cells containing an empty vector. Thus, high level BP1 expression can confer estrogen independence in mammary tumors in mice. To understand the molecular mechanisms of this observation, we carried out *in vitro* experiments. Our data suggest that BP1 regulates ER alpha via two mechanisms: (a) a direct transcriptional effect and (b) an indirect translational effect. (a) ChIP assays and EMSA assays showed that pBP1 binds to the first intron of the ER-alpha gene. MCF-7 cells engineered to overexpress BP1 exhibit increased ER-alpha protein compared with cells containing an empty vector. Increased ER-alpha protein levels correlated with increased expression of pS2, a known downstream target of ER-alpha. (b) The post-translational regulation of ER-alpha is attributed to BP1 regulation of BRCA1, p300 and BCAR1. We show that BP1 binds to and activates the EP300 gene, which encodes p300, a known histone acetyl transferase (HAT) which competitively binds and acetylates ER alpha and "rescues" it from degradation. We also show that cells overexpressing BP1 have higher survival and proliferation than empty vector containing cells when grown in 3 $\mu$ M tamoxifen. In addition, BP1 overexpressing cells have increased levels of breast cancer anti-estrogen resistance 1 (BCAR1) protein compared with empty vector containing cells.

#### CONCLUSIONS:

We hypothesize that pBP1 plays a major role in the transition from ER+ tumors to tamoxifen resistant tumors to ER- tumors, making it an important prognostic indicator in ER+ tumors, as well as a potential therapeutic target.

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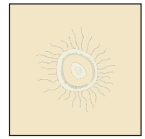
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Extramedullary Hematopoiesis in the Breast of a Woman with Myelofibrosis Secondary to Essential Thrombocythemia: Case report

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#### BACKGROUND:

In mammographic screening of the breast, pleomorphic calcifications can be a radiologic marker of both benign and malignant lesions. Mammographically detected non-palpable high-risk breast lesions such as atypical ductal hyperplasia (ADH), ductal carcinoma in situ (DCIS) and rarely lobular carcinoma in situ (LCIS) can often present as calcifications alone. Invasive carcinoma of lobular type can have equally as subtle findings on physical examination and mammography, presenting as an asymmetric thickening or in some cases as increased interval calcifications. If a soft tissue density is not identified, radiographic calcifications can be sampled by a stereotactic guided biopsy or a wire guided excision to remove the involved area. In these cases tissue biopsy or an excision is performed to exclude an occult invasive carcinoma, DCIS or LCIS. In most cases the diagnosis of invasive or in situ carcinoma is uncomplicated.

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#### OBJECTIVE:

Benign elements, such as extramedullary hematopoiesis (EMH), unusually located in the breast may be confused with a malignant process. Awareness of this pattern of EMH in the breast can prevent a potential misdiagnosis of infiltrating carcinoma.

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#### RESULTS:

A 54 year old woman presented to the Breast Center for surgical management of clustered pleomorphic calcifications in her left breast. The radiographic findings were classified as BI-RADS 4, suspicious for malignancy. There was no palpable mass, nipple discharge or dimpling of the breasts on physical examination. The patient underwent a wire-guided excision of the suspicious calcifications. The excision revealed stromal infiltrates of megakaryocytes, normoblasts and myeloid cells at various stages of maturation consistent with trilineage extramedullary hematopoiesis. The hematopoietic cells were not associated with a mass lesion or with microcalcifications and showed no relation to the vasculature. Additionally, there was an incidental focus of ADH. By immunohistochemistry, the megakaryocytes were reactive for CD61 but not for cytokeratin (MAK-6). The myeloid lineage was reactive for myeloperoxidase (MPO). Clusters of normoblasts were noted within the breast parenchyma.

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#### CONCLUSION:

Non-mass forming trilineage EMH in the breast is rare, but can occur with chronic myeloproliferative disorders. When this case was initially reviewed, the patient's medical history of essential thrombocythemia (ET) with secondary myelofibrosis was unknown. Pathologists should be aware that this phenomenon is a potential pitfall for misdiagnosing infiltrating mammary carcinoma especially in the setting of suspicious radiologic and clinical findings. Rendering the correct diagnosis requires knowledge of the patient's complete clinical history and judicious use of immunohistochemical stains within the appropriate morphologic context.

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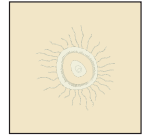
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Cross-regulation of polycomb group protein BMI1 and WNT inhibitors

#### BACKGROUND:

Polycomb group (PcG) proteins are evolutionarily conserved gene silencers, which determine cell fate decisions during development. These proteins are often aberrantly expressed in cancer cells. In particular, BMI1 and EZH2 are known to be overexpressed in a number of human malignancies including breast and prostate cancers. In vitro models of cancer development strongly support oncogenic role of overexpressed BMI1 in cancer and metastasis. BMI1 is known to be required for self-renewal of neural, hematopoietic, intestinal and mammary stem cells. In addition, BMI1 is downregulated in senescent cells, and this downregulation may contribute to age-related pathologies. BMI1 is also suspected to play a role in cancer stem cell development and increase stem cell-ness of tumors to promote drug resistance. Despite its role in cancer, stem cell phenotype, development and aging, very little is known about the signaling pathways that regulate the expression of BMI1. Here we report that BMI1 activates WNT pathway and upregulates its target genes such as Cyclin D1 and c-Myc. We also report that conversely, WNT inhibitors also regulate the expression of BMI1.

#### METHODS:

To study the role of WNT pathway in regulating BMI1 expression and vice versa, we generated BMI1- overexpressing and knockdown MCF10A cells. Using these cells, we performed quantitative RT-PCR, Western blot and promoter-reporter analyses for BMI1 and the various genes that are part of WNT pathway. We also determined expression of BMI1 and WNT inhibitors in breast cancer cell lines. Finally, the role BMI1 and WNT inhibitors was studied for cancer stem cell phenotype using mammosphere formation, Aldefluor assay and FACS analysis of CD44 and CD24 markers.

#### RESULTS AND CONCLUSIONS:

Our data suggest that BMI1 upregulated expression of c-Myc via activation of WNT pathway. Further dissection of this regulation revealed that BMI1 represses expression of WNT inhibitors, in particular DKK family of proteins such as DKK1, DKK2 and DKK3. Interestingly, we also found that DKK1 inhibits expression of BMI1. Thus BMI1 and WNT inhibitors such as DKK1 cross-regulate each other's expression. Our data also suggest that cross-regulation of BMI1 and WNT inhibitors is important for determination of cancer stem cell phenotype. Based on our results, we speculate that such regulation favor BMI1 overexpression in cancer cells via increased WNT activity and c-Myc expression. On the other hand, increased expression of WNT inhibitors such as DKK1 might favor BMI1 downregulation in senescent and aged tissues. Thus, a fine tuned cross-regulatory loop controls BMI1 expression via a WNT signaling pathway, which may be relevant to the role of BMI1 in cancer, stem cells and senescence.

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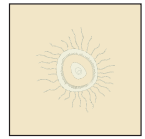
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Necdin Modulates Metastasis by Regulating Cell Behavior and Gene Expression

#### BACKGROUND:

Most cancer-related deaths are a result of metastasis. Studies in mouse mammary tumorigenesis and human breast cancer has demonstrated that dysregulation of extracellular matrix (ECM) genes is predictive of metastasis. There appears to be an intimate relationship between hereditary germ-line polymorphisms and tumor gene expression that affects the progression of metastasis. These variations in the DNA have been shown to influence dysregulation of the ECM. Crawford et al previously identified seven candidate genes (*Ndn*, *Pi16*, *Luc71*, *Rrp1b*, *Brd4*, *Centd3*, and *Csf1r*) by correlation analyses with ECM expression and known associations with metastasis. *NDN* previously has been shown to interact with p53 and has been shown to be involved in transcriptional repression, angiogenesis, and hematopoietic stem cell quiescence. Preliminary studies have suggest that over-expression of *Ndn* in the highly metastatic mouse mammary tumor cell line Mvt-1 induces a gene expression signature that predicts survival in breast cancer patients. A variant of *Ndn*, which has a polymorphism (T50C) that changes a Valine to an Alanine (V17A), was shown to distinguish the highly metastatic AKR strain mice from the low metastatic DBA strain. These previous studies lead us to hypothesize that *Ndn* modulates breast cancer metastasis through the regulation of gene expression.

#### METHODS:

To examine the role of *Ndn* in depth, we first established cell lines that over-expressed *Ndn* within the highly metastatic Mvt-1 cell line. Our goals were to observe the cells' behavior and to identify the possible genes that were either up-regulated or down-regulated with the over-expression of *Ndn*. To understand the cells' behavior, a proliferation assay was done which demonstrated the slower growth rates of the *Ndn* and *NdnV17A*-overexpressing cells in comparison to the control cell line. A soft agar assay was also performed to view the cells' behavior in an anchorage independent situation. Orthotropic injections of stable Mvt-1 cell with either an over-expression of either *Ndn* and *NdnV17A*-overexpressing cells, or a control were injected into nude mice. For identification of possible genes regulated by *Ndn*, we performed microarray analyses with three stable cell lines of *Ndn* and *NdnV17A*-overexpressing cells, as well as control cell lines. These results were validated by real-time PCRs.

#### RESULTS:

The proliferation assay demonstrated slower growth rates of *Ndn* and *NdnV17A*, -over-expressing cells in comparison to the control line. Interestingly, in an anchorage independent environment (soft agar), an accelerated growth rate of *NdnV17A* was observed, in comparison to the control and *Ndn* cell line. The tumors in the nude mice injected with an over expression of *NdnV17A* were larger and more pulmonary metastasis were counted.

#### CONCLUSION:

These studies help further our understanding of how *Ndn* functions as a modifier of breast cancer metastasis and what role the polymorphism (V17A) plays in this pathway. With future studies, we hope this knowledge can be applied to a clinical application for treatment purposes.

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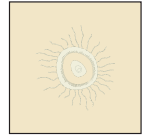
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Local Delivery 2-Deoxy-D-Glucose as a Possible Therapeutic Option: A Preclinical Study

**INTRODUCTION:**

The glucose analog, 2-deoxy-D-glucose (2-DG), has been shown to be an effective inhibitor of tumor growth through inhibition of the glycolytic pathway and subsequent halting of glycolytic ATP generation in tumor cells. Previous studies have shown that effective use of 2-DG in cancer treatment requires high systemic doses that can cause dose-limiting side effects. Therefore, clinical trials have been approved for only low dose systemic 2-DG. We postulate that these systemic side effects can largely be avoided by direct intracranial delivery of 2-DG. We implanted 2-DG-impregnated controlled release biopolymer wafers intracranially in rats and assessed efficacy. In this study, we explore the effectiveness of 2-DG as a monotherapy in treating intracranial 9L rat gliosarcoma in vivo.

**METHODS:**

Thirty rats were intracranially implanted with 9L rat gliosarcoma on Day 0. Control rats received no treatment. Rats in the 2-DG (Day 0) and 2-DG (Day 5) groups received intracranial 2-DG polymers on Day 0 or Day 5, respectively. Survival was compared across all three groups.

**RESULTS:**

Rats in the control group had a median survival of 11 days, while those in the 2-DG Day 0 and 2-DG Day 5 had median survivals of 18 days ( $p < 0.009$  vs. control) and 17 days ( $p < 0.0461$  vs. control), respectively.

**CONCLUSION:**

The results of this study show that 2-DG alone, when delivered locally, can cause a statistically significant increase in survival in rats with intracranial 9L tumors. Additionally, these results suggest that intracranial delivery of 2-DG may further enhance combination therapies that are limited by side effects of systemic 2-DG.

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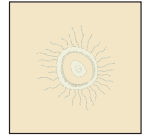
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Efficacy of Locally Delivered Rapamycin in a Rodent Gliosarcoma Model

**INTRODUCTION:**

In addition to its common use as an immunosuppressant in organ transplantation, the mTOR inhibitor rapamycin has also demonstrated potent anti-proliferative effects in the treatment of different types of cancers. Recent studies have demonstrated that gliomas express elevated levels of FKBP and NF- $\kappa$ B that are critical components of the mTOR- driven proliferation of tumor cells. Due to its inhibitory effects of these factors, rapamycin is a promising agent in mitigating cell proliferation in malignant gliomas. In this study, we evaluate the therapeutic effect of locally delivered rapamycin in a rodent intracranial gliosarcoma model.

**METHODS:**

Twenty-four rats were implanted with intracranial 9L gliosarcoma and were then divided into the following three groups: 1) no treatment, 2) 50% rapamycin treatment (5mg total of drug) at time of tumor implant (day 0), and 50% rapamycin treatment (5mg total of drug) 5 days after tumor implantation. Survival was the primary endpoint for this experiment.

**RESULTS:**

Control animals had a median survival of 13 days. The treatment group that received rapamycin five days after tumor implantation had a median survival of 18 days ( $p=.0003$  vs. control) with an increase in survival of 38%. The treatment group that received rapamycin on day 0 had a median survival of 27 ( $p<.0001$  vs. control), increasing survival by 108%.

**CONCLUSION:**

Our results show that rapamycin delivered intracranially exhibited a statistically significant survival benefit in a rodent gliosarcoma model. Further studies should examine its effect when delivered in combination with chemotherapy and radiotherapy in glioma models.

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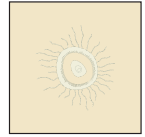
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Efficacy of the Orally Delivered, Anti-Parasitic, Mebendazole, in an Intracranial Rodent Gliosarcoma Model

**INTRODUCTION:**

Mebendazole (MBZ), methyl N-[6-(9-benzoyl)-1H-benzimidazol-2-yl] carbamate is an anti-parasitic approved by the FDA for treating roundworm, common hookworm, American hookworm, pinworm, and whipworm. Its mechanism of action is that it binds to the tubulin subunits in the gut epithelium of the parasite ultimately preventing growth. Mebendazole was previously shown to have survival benefits in two preclinical models of glioblastoma multiforme by the Ludwig Collaborative Laboratory at Johns Hopkins School of Medicine. We hypothesize that Mebendazole will have survival benefits delivered orally in Fisher 344 rats who have been previously implanted with intracranial gliomasarcoma.

**METHODS:**

Sixteen rats were divided into 2 groups: 1) Control-no treatment and 2) Daily oral treatment of Mebendazole. All rats were implanted with intracranial 9L gliosarcoma on day 0. On Day 5, the Oral Mebendazole group (n=8) began receiving Mebendazole by daily oral gavage. The control group (n=8) did not receive any treatment. Survival was the primary endpoint.

**RESULTS:**

Control animals had a mean survival of 11 days while the Mebendazole treatment group had a median survival of 15 days ( $p=0.0003$  vs. control).

**CONCLUSION:**

Our results show that daily oral gavage of Mebendazole increased survival in an intracranial gliosarcoma model. Fortuitously, this is an agent that has already been approved by the FDA for anti-parasitic treatment and has an extensive history of use in humans to date. We look forward to the upcoming clinical trial of this anti-parasitic compound.

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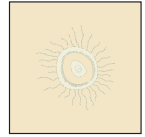
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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## Differential Incidence of Chronic Myeloid Leukemia by Age and Race in the United States: An Age-Period-Cohort Analysis

**BACKGROUND:**

Chronic myeloid leukemia (CML) is a myeloproliferative disease that comprises approximately 15-20% of all leukemias. Etiological factors for the development of CML are largely unknown. However, etiological clues may be obtained from incidence-related age-specific and racial differences. Given that age at diagnosis is an important risk factor for cancer, we designed a study to assess the effects of age and race after accounting for calendar-period and birth-cohort interactions.

**METHODS:**

Incidence data were obtained from the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) program for Black and White adults (25-84 years) diagnosed with CML (Philadelphia Chromosome + or Not Otherwise Specified) between 1975 and 2009 (15,037 cases). Standard descriptive analyses were complemented with age-period-cohort (APC) models that adjusted for year of diagnosis (calendar-period) and year of birth (birth-cohort).

**RESULTS:**

Blacks developed CML more than 7 years earlier than Whites with markedly different age distributions at diagnosis. Black Males exhibited a bi-modal distribution with an early (peak at 40 years) and late onset CML (peak at 58 years) while White Males had an early peak (37 years) followed by a more pronounced peak at age 73. Blacks had higher age-adjusted incidence rates corresponding to a Black:White incidence rate ratio of 1.10 (95% CI, 1.02-1.08) for males and 1.08 (95% CI, 1.00-1.17) for females. We observed interactions between race and age; age-specific incidence rates were higher among Blacks diagnosed between the ages of 25 and 49 after which rates were higher for Whites. The incidence rate cross-over between Blacks and Whites was robust to adjustment for calendar period and birth cohort effects (Black vs. White female:  $p=0.0220$ ; Black vs. White male:  $p=0.0125$ ).

**CONCLUSIONS:**

Black males and females are diagnosed with CML at an earlier age as compared to their respective White counterparts. An effect modification (or interaction) by race and age is consistent with etiologic heterogeneity for early- and late-onset CML. Therefore, stratification of age and race should be considered in future analytic studies designed to explore the earlier age at diagnosis and increased incidence among Blacks.

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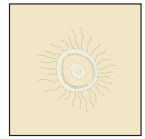
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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Lung Cancer among Workers in Chromium Chemical Production

#### BACKGROUND:

The carcinogenic and mutagenic activity of chromium is primarily associated with hexavalent salts. Occupational exposure is one of the main sources of human exposure to hexavalent chromium. In 1984 and 1986, the International Agency for Research on Cancer (IARC) and the Environmental Protection Agency (EPA), classified hexavalent chromium (Cr6) as Group I (Carcinogenic to Humans) and Group A (Human Carcinogen), respectively. The study was first described by Gibb et al. (2000). Our goal was to conduct a follow-up study on a cohort of chromate workers to examine the relationship between Cr6 exposure and lung cancer.

#### METHODS:

This follow-up study examined a cohort of 2,357 chromate workers employed from August 1, 1950 through December 31, 1974. For each member of the cohort, the cumulative exposure was based on the job history and annual average exposure estimates of Cr6. The exposure was stratified into 52 time frames to account for time varying exposure for each worker. The risk of lung cancer from Cr6 was assessed using bivariable and multivariable Cox proportional hazards (PH) regression models that took into account relevant covariates including smoking status, duration of employment and age at hire. Only significant two-way interactions were included in the final multivariable model. The outcome was the time until death or last date of contact measured in years. The relative risk of cancer was computed for different durations of exposure (30 days, 6 months, 1 year and 5 years) in smokers and non-smokers.

#### RESULTS:

During the 89,458 person years of observation, there were 169 deaths due to lung cancer. The number of deaths due to lung cancer has increased by 47 since Gibb et al (2000). Bivariable Cox PH models revealed a positive association between covariates- age at hire, smoking, work years and lung cancer. In the multivariable Cox PH model analysis, Cr6 yielded a significant hazard ratio of 1.9 (95% CI 1.44-2.209), after controlling for smoking, age at hire and work years.

#### CONCLUSIONS:

The findings from this study support the previous analyses demonstrating a dose - response relationship between Cr6 exposure and lung cancer and the effect of covariates on this relationship. The positive association between age at hire and lung cancer risk was contradictory to the negative association observed previously. Short period cumulative exposure results in higher risk of lung cancer compared to same longer duration cumulative exposure of Cr6.

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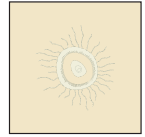
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## UROLOGY

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### Gene Network Associated with the Prostate Cancer Disparities in African American and Caucasian American Populations

Prostate cancer (PCa) is a disease conferred by multiple gene mutations, numerous alternations in gene expression and aberrant changes in genome composition/architecture. An area of research that continues to garner attention is PCa health disparities, wherein the African American (AA) population exhibits higher incidence and mortality rates compared to Caucasian Americans (CA). Although accumulating evidences have suggested that the widespread microRNA deregulation may play crucial role in cancer development, the relationship between population-specific microRNAs and PCa disparities remains largely unknown. To identify the genetic predispositions and oncogenic networks associated with the observed PCa disparities, we applied a systems biology approach by combining mRNA expression profiling, microRNA profiling and microRNA target searches to characterize the genetic portraits of PCa in AA and CA populations. Affymetrix human exon ST1.0 arrays and Agilent human miRNA V2 arrays were used to analyze the global mRNA and microRNA expression profiles in AA and CA prostate tissue samples. A 4-way statistical analysis (AA cancer vs. CA cancer; AA cancer vs. AA normal, CA cancer vs. CA normal, AA normal vs. CA normal) of mRNA and microRNA gene profiles have revealed hundred of mRNAs and dozens of microRNAs were differentially expressed (FDR < 0.1, fold change > 1.5). mRNA-microRNA pairing, resulted from computational integration of mRNA and microRNA data, and the canonical pathway analysis suggested that up-regulation of several cancer-associated pathways were involved in AA cancers. Our study has demonstrated that the differential mRNA-microRNA regulatory networks and downstream gene expressions may account for part of the PCa health disparities in AA and CA. This work was supported by NCI grant 5U01-CA-116937 and ACS-IRG-08-091-01.

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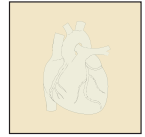
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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

### Dichloroacetate Increases Cardiac Mitochondrial NADH and Improves Function

#### BACKGROUND:

Following a heart attack, oxygen is limited so the function of the mitochondrion is severely depressed and the capability to produce ATP from NADH is severely hindered. Without mitochondrion, cells have to result to anaerobic glycolysis, yielding very small amounts of NADH and ATP and only for a very short period of time. It is impossible to yield any ATP from fat anaerobically, therefore only carbohydrate can be used. The amount of ATP the heart has available is very low and the mechanical function is depressed significantly even after resuscitation and restoration of oxygen. Dichloroacetate (DCA) is a compound that has previously been shown to increase ATP production in muscle cells.

#### OBJECTIVE:

Use NADH imaging in order to understand the underlying mechanism of DCA and its improvement on cardiac function after cardiac arrest.

#### METHODS:

A balloon was inserted into the left ventricle of whole rat hearts and pre-loaded to 10 mmHg to measure LV pressure (isovolumic contraction). The direct effect of administering DCA was measured by ECG, left ventricular pressure, and the fluorescence of NADH. NADH was easily imaged using its natural fluorescent property. After excitation by UV (365nm), the NADH of the mitochondrion fluoresced blue light (450nm) that was filtered by a band pass filter and acquired using a high sensitivity CCD camera.

#### RESULTS:

Addition of DCA to perfusate when oxygen and ATP were *non-limiting* (i.e. no ischemia) significantly increases NADH intensity with no changes in pressure (n=4). On the other hand, addition of DCA to perfusate when oxygen and ATP were *limiting* (i.e. ischemia) did not change NADH intensity, but pressure development was significantly increased (n=6).

#### CONCLUSIONS:

The accumulation of NADH after the addition of DCA in the non-ischemic scenario suggests there is more available NADH that can be used to produce ATP if needed. However, given that the heart is not recovering from ischemia, the additional NADH that is produced is not utilized for ATP, resulting in an accumulation. In a heart where ATP is limited, as in following cardiac arrest and ischemia, DCA did not show any increase in NADH but did show functional improvement. This suggests that DCA can have a beneficial effect to produce additional NADH that is then immediately utilized in order to overcome an ATP deficit and ultimately increase cardiac function for improved recovery.

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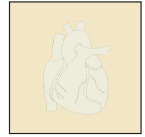
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**SCHOOL OF ENGINEERING AND APPLIED SCIENCE**

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## Visualization of epicardial cryoablation lesions using endogenous NADH fluorescence

**BACKGROUND:**

Percutaneous cryoablation is a commonly used procedure to treat atrial fibrillation and other cardiac rhythm disturbances. One of the major limitations of the procedure is the inability to directly visualize tissue damage and functional gaps between the lesions.

**OBJECTIVE:**

To aid the development of a new generation of cryoablation catheters capable of real-time visualization of tissue necrosis during ablation procedures.

**METHODS:**

Adult rats underwent thoracotomy, followed by point cryoablation of epicardial surface. Experiments were conducted both in situ and using excised hearts. Excised hearts were continuously Langendorff perfused with either saline or blood containing media. Lesions were visualized by using 365/50 nm wavelength UV LED illumination and by acquiring the emitted fluorescence within 460/40 nm wavelength range.

**RESULTS:**

Cryoinjury was associated with a marked decrease in NADH fluorescence that closely correlated with the degree of triphenyl tetrazolium (TTC) staining. Time course of the NADH decrease had strong temperature dependence, with higher temperatures leading to a faster rate of post-ablation NADH loss. Presence of the blood within coronary circulation did not interfere with the appearance of the lesions on NADH channel.

**CONCLUSIONS:**

The results confirmed feasibility of live visualization of cryoablation lesions in blood-perfused cardiac preparations.

**STATUS**

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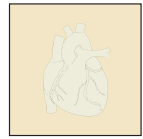
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Clinical significance of left atrial anatomic abnormalities identified by CT- correlations with stroke, atrial fibrillation, and palpitations

#### INTRODUCTION:

The clinical significance of newly identified left atrial anatomic abnormalities (LAAA) - accessory appendages, diverticuli, septal pouches - by CT remains unclear. Similar anatomical outpouchings, i.e., the left atrial appendage, have been associated with cardioembolisms and arrhythmia. To test the hypothesis that LAAA is associated with increased risk of these events, we performed a retrospective analysis to examine the prevalence of LAAA in patients undergoing CT and assess their history of embolic events and arrhythmia.

#### METHODS:

Complete clinical histories were available for 173 patients who had CT coronary angiography at our institution from 2007 to 2010 performed on GE Lightspeed 64 VCT, and images were independently reviewed for the presence of LAAA. Correlation of events-CVA, TIA, atrial fibrillation, and palpitations - to LAAA was determined by ( $\chi^2$ ) analysis of each outcome vs. the presence of each LAAA to measure an odds ratio (OR) with 95% confidence interval (CI); mean square contingency coefficient ( $\phi$ ) was also determined to measure association. Statistical significance was assumed by  $p < 0.05$ .

#### RESULTS:

The incidence of LAAA and clinical events are found in **Table 1**. OR for palpitations in patients with accessory appendage was 2.7 (CI 1.3-5.2,  $p < 0.05$ ). OR for atrial fibrillation or palpitations in patients with accessory appendage was 2.2 (CI 1.0-6.3,  $p = 0.05$ ) and barely did not meet predefined statistical significance, but  $\phi$  did demonstrate a weak but significant association (0.15,  $p < .05$ ). No statistically meaningful associations were seen with left atrial diverticuli.

**Table 1**

<b>LAAA</b>	<b>Patients (%)</b>
Accessory Appendage	49(28)
Diverticulum	36(21)
Septal Pouch	62(36)
<b>Events</b>	
CVA	18(10)
TIA	9(5)
Palpitations	60(35)
Atrial Fibrillation	14(8)

#### CONCLUSION:

We found accessory appendages to have significant clinical correlation with palpitations and atrial fibrillation. The association between septal pouches and accessory appendages with CVA or TIA was borderline significant; this retrospective study may have been underpowered to detect this suggestive finding. Further investigation of these newly identified anatomic abnormalities by CT is warranted.

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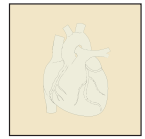
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Electrical Cardiometry Compares Favorably with Thermodilution for Post-Operative Hemodynamic Monitoring

#### INTRODUCTION:

Pulmonary artery catheters and thermodilution (PAC-TD) remain the gold standard for hemodynamic monitoring, particularly after cardiac surgery. However, the invasive nature of PAC-TD, combined with its lack of clinical efficacy, calls for the use of non-invasive hemodynamic monitoring techniques. Electrical cardiometry (EC), a form of thoracic electrical bioimpedance, provides completely non-invasive hemodynamic monitoring. This study evaluated the reliability of EC compared to PAC-TD for continuous hemodynamic monitoring in post-operative patients.

#### HYPOTHESIS:

EC provides reliable continuous cardiac index (CI) monitoring compared to PAC-TD in post-operative patients.

#### METHODS:

Post-operative patients with indwelling PACs (Continuous Cardiac Output catheters, Vigilance monitor, Edwards) underwent simultaneous, continuous hemodynamic monitoring with EC (Aesculon monitor, Cardiotronic). Comparisons were made between hourly PAC-TD and EC determinations of CI. EC CI values were averaged from one minute readings  $\pm$  6 minutes centered on the hour. Bland-Altman analysis was performed for each individual patient's data. Bias (mean difference between PAC-TD- and EC-derived CI) and percentage error (2SD of bias/mean CI) for each patient was calculated. Variance (coefficient of variation) over the entire monitoring period for each patient was calculated. Data are mean $\pm$ SD.

#### RESULTS:

30 patients (cardiac surgery 29, vascular surgery 1) were monitored for  $33\pm 19$  hours. Bias was  $-0.7\pm 1$  L/min/m<sup>2</sup> and percentage error was  $39\pm 12\%$ . Seven (23%) of 30 patients had a percentage error  $< 30\%$ . Coefficients of variation for PAC-TD and EC were  $0.6 \pm 0.1$  and  $0.4 \pm 0.1$ , respectively (P = NS).

#### CONCLUSIONS:

EC monitoring of CI demonstrated good correlation with PAC-TD in post-operative patients. While a percentage error  $< 30\%$  represents the ideal, clinically-acceptable limit of agreement between two hemodynamic monitoring techniques (Critchley and Critchley), many studies report values up to 40%. Our relatively small bias would generally be considered clinically insignificant and the low variance indicates reliable measurements. Our study supports EC as a reliable non-invasive method of hemodynamic monitoring.

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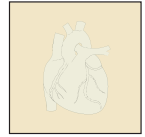
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# CARDIOLOGY/CARDIOVASCULAR RESEARCH

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Pilot Clinical Evaluation of a Miniaturized Extra Corporal Membrane Oxygenator (ECMO) System in Swine (*Sus Scrofa*)

#### BACKGROUND:

ECMO has been used as a rescue therapy for severe respiratory failure and cardiogenic shock since the early 1970's. In addition, it has been used to treat Acute Respiratory Distress Syndrome (ARDS), influenza, cardiac failure, massive pulmonary emboli, and trauma.

ECMO is a modification of cardiopulmonary bypass (CPB) with several important differences. It has no venous reservoir, normal body temperature is maintained, and cannulation is usually performed through more accessible extrathoracic vessels (venoarterial or venovenous). This enables ECMO to be performed at bedside in the ICU.

Due to the complexity of the ECMO setup and the high acuity of patients requiring its assistance, ECMO is usually performed within specialized centers with trained physicians, nurses, and technicians. However, recent developments in the ECMO equipment, including the miniaturization of components, and the introduction of a pumpless extracorporeal lung assist, have made the transport of patients on ECMO feasible.

During the transport of patients at different altitudes, the stability of the system must be maintained, including flow rates, efficacy of the membrane oxygenator, and microemboli detection and prevention. This novel mobile ECMO system can have a significant life-saving potential, especially in the military operations.

#### METHODS:

To clinically evaluate this novel miniaturized ECMO system in a swine model that replicates the pulmonary function of injured and non-injured lungs. This protocol is aimed to analyze the efficiency in cannulation, emboli detection and classification, and pump management. It will be considered a success if 50% of the subjects can be successfully be managed and monitored for three hours on pump after successful cannulation and lung injury induction. This experiment will use eight 80-90 kg pigs. The subjects will be properly anesthetized and monitored (cardiac monitor, temperature probe, and oxygen saturation monitor). After lung injury induction, labs (TEG, ABG, CBC, CMP, lactate, coags) will be drawn, and they will be placed on ECMO. For 3 hours, the team will conduct the routine management of the circuit, troubleshoot problems, and collect data with the ultrasonic microemboli detector. In addition, labs will be drawn from the arterial line every 45 minutes. At the end of a 3-hour period on ECMO, the pig will be euthanized.

#### CURRENT STATUS:

In progress

#### RESULTS:

Pending

#### CONCLUSIONS:

Pending

#### STATUS

Graduate Student

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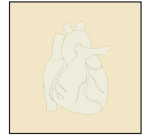
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Spectral profiles of acute and healed myocardial radiofrequency ablation lesions

**BACKGROUND:**

Radiofrequency ablation (RFA) is an established treatment for atrial fibrillation and other arrhythmias. RFA eliminates abnormal sources of electrical activity and pathways that lead to reentry. A shortcoming of the procedure is a lack of real-time visualization of the lesions. This leads to an incomplete treatment and repeated clinical applications. To improve the outcomes of both immediate and repeated RFA procedures, a spectral approach was explored as a tool to differentiate between acute and healed myocardial lesions.

**METHODS:**

The epicardial surface of excised Sprague-Dawley rat hearts was illuminated by continuous wavelength spectrum via an optical fiber coupled to a spectrofluometer. Emitted, scattered, and reflected light was acquired by a high sensitivity CCD camera. Spectra were analyzed for three tissue conditions: unablated tissue, acute RF lesions, and healed RF lesions. Structure of the lesions was confirmed by cytopathology.

**RESULTS:**

Spectra between all three groups differed significantly throughout the 300-800nm range. The largest difference was observed in the 300-400nm illumination range due to the loss of endogenous NADH fluorescence in acute lesions, but not in the healed tissue. In the 400-620nm illumination range both acute and healed epicardial lesions exhibited higher intensity of scattered and reflected light compared to the surrounding unablated tissue. In the 620-800nm range, the differences between the three groups diminished.

**CONCLUSIONS:**

The results suggest that visualization of acute and chronic lesions is possible based on the spectral differences in reflected and emitted light. The sensitivity and specificity of lesion identification can be further increased by ratiometry of the images acquired at various illumination wavelengths. This spectral information offers the option for improving the efficacy of both acute and repeated RFA procedures. This method could be implemented by adding an excitation/emission fiber-optic waveguide to the tip of an RFA catheter.

**STATUS**

Graduate Student

**AUTHORS**

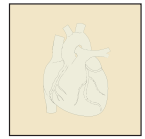
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Metabolic impact of extracorporeal membrane oxygenation on myocardial protein synthesis in the immature pig

#### BACKGROUND:

Extracorporeal membrane oxygenation (ECMO) is the primary method of providing mechanical circulatory support to pediatric patients suffering from cardiopulmonary failure. However, normal metabolic function can be impaired in patients on ECMO, resulting in total body wasting and protein loss. Thus, metabolic modulation plays a critical role in the recovery of cardiac contractile function. Our previous studies using <sup>13</sup>-Carbon isotopomer analysis by gas chromatography-mass spectroscopy have shown ECMO decreases amino acid oxidative metabolism while post-wean ECMO significantly increases protein synthesis in the immature heart. This study evaluates the changes in metabolic pathways involved in protein synthesis in piglets having undergone various ECMO loads.

#### METHODS:

Immature pigs (age: 27-36 days) were subjected to veno-arterial ECMO biventricular unloading. Piglets with normal circulation (Control: n=4) were compared with piglets placed on ECMO (ECMO: n=4) as well as piglets placed on ECMO and weaned off (WEAN: n=4) in order to identify differences in the metabolic pathways leading to protein synthesis in the left ventricle. ECMO was carried out for 8 hours at 80-100 ml/kg/min flow rate. Perfusion flow of ECMO was decreased gradually for 30 minutes and then ECMO was weaned.

#### RESULTS:

Immunoblot analysis from left ventricular tissues at the end of the protocol was performed in order to identify differences in the metabolic pathways leading to protein synthesis such as the mammalian target of rapamycin signaling (mTOR) pathway. Phosphorylation of mTOR was 2.5 times greater in WEAN protocols than ECMO and Control ( $p < 0.05$ ). AMPK, an inhibitor of mTOR is also upregulated in WEAN and ECMO protocols (WEAN:Control  $p < 0.05$ , ECMO:Control  $p < 0.01$ ). eIF-4E, one of the downstream components of mTOR, was activated in WEAN ( $p < 0.05$ ). AKT was upregulated in WEAN compared to ECMO ( $p < 0.05$ ). EEF and 4EBP1 did not significantly differ among the groups.

#### CONCLUSION:

Ventricular unloading by ECMO induced metabolic shifts in the left ventricle in both the ECMO and WEAN conditions as compared to normal piglet circulation. The impact on protein synthesis varied between particular regulatory molecules and ECMO protocol. The recovery of AKT activation, significant upregulation in eIF-4E phosphorylation and mTOR induction in the WEAN protocols as compared to ECMO suggests an environment that facilitates protein synthesis initiation. AMPK activation may be representative of inhibition of protein synthesis, it may also indicate the stimulation of fatty acid oxidation to help meet myocardial energy needs. These findings suggest that the mTOR pathway is an important regulator of metabolic change in the left ventricle during ECMO.

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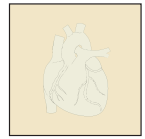
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# CARDIOLOGY/CARDIOVASCULAR RESEARCH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Next-generation, single-molecule RNA sequencing identifies novel TGF- $\beta$ target genes, including IER3

#### BACKGROUND:

Transforming growth factor- $\beta$  (TGF- $\beta$ ) comprises a small family of highly potent and pleiotrophic factors that regulate development, wound repair, immune function, cell cycle, and apoptosis. These factors are known to be critical modulators in cardiovascular diseases and many types of cancer. However, the pathways affected by TGF- $\beta$ s are far from understood despite being one of the most studied groups of factors.

#### OBJECTIVE:

The purpose of this study was to more fully elucidate TGF- $\beta$ 1 target genes in order to help understand the diverse actions of this key cytokine in cardiovascular disease, cancer, inflammation, and immunity.

#### METHODS:

Vascular smooth muscle, derived from both normal arteries and atherosclerotic lesions, keratinocytes, and breast cancer lines MDA231 and MCF7, were profiled by Helicos single-molecule RNA sequencing in the presence or absence of TGF- $\beta$ 1 (1 ng/ml, 24 hours). After treatment with TGF- $\beta$ 1, total RNA was purified and then depleted of ribosomal RNAs by RiboZero so that sequencing reads would not be consumed on rRNA. Short reads were aligned to the human transcriptome, counted as reads per thousand bases of exon (K) per million total reads per sample (RPKM), and differential expression determined by a triple filter for expression level ( $>0.01$  RPKM), fold-change ( $>2.0X$ ), and p-value ( $p < 0.05$ ). A meta-analysis of 20 prior microarray studies on TGF- $\beta$  targets was conducted and assembled in LOLA: Lists of Lists Annotated (<http://lola.gwu.edu/>).

#### RESULTS:

The results confirmed 43 known targets including SERPINE1 (PAI1), CTGF, and SMAD7, and identified 99 novel targets including amelotin (AMTN), LBH, AMIGO2, CLEC2A, and IER3. Among the 99 transcripts, 19 belong to known or putative non-coding RNAs, including long intronic non-coding (LINC) RNAs, such as EGOT. The effect of TGF- $\beta$ 1 on IER3 was confirmed by Western blotting, and Transfac promoter analysis revealed a SMAD-binding element near the transcriptional start site, as also suggested by prior chromatin IP studies.

#### CONCLUSIONS:

As many as two-thirds of the targets of TGF- $\beta$  have been missed by prior microarray studies. Novel targets include potentially important non-coding RNAs and the key apoptotic/cell cycle regulator IER3. IER3 has diverse actions on apoptosis by regulating the functions of MCL1, and is a key element in the DNA damage response by interactions with p53. IER3 can have a major impact in the inflammation pathways by regulating the NF- $\kappa$ B system, which makes IER3 a potentially important target of TGF- $\beta$  that has been largely missed by prior studies.

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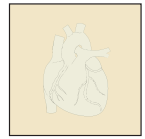
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Epidermal Growth Factor Receptor-tyrosine Kinase Inhibition by Erlotinib Causes Hypomagnesemia, Oxidative Stress and Cardiac Dys

**BACKGROUND:**

Clinical studies have documented persistent hypomagnesemia in cancer patients treated with cetuximab (EGFR-blocking antibody). Our prior studies with a non-clinically used EGFR-TKI agent, tyrphostin AG1478 (21 mg/kg/day), showed hypomagnesemia, oxidative stress, elevated plasma substance P and cardiac dysfunction after 5 weeks of treatment (Can. J. Physiol. Pharmacol. 2012, 90:1145-1149).

**OBJECTIVE:**

We sought to assess if rats treated with the clinical EGFR-TKI drug, erlotinib (Tarceva), at a lower dose (10 mg/kg/day) for a more prolonged (9 weeks) period, also displayed cardiac dysfunction (echocardiography) and associated hypomagnesemia.

**METHODS:**

Six to 7 week old (150-185 g) Sprague-Dawley male rats were placed on a Mg-normal diet (100% RDA) supplemented with essential vitamins and nutrients for up to 9 weeks. Tarceva (erlotinib) was administered to the rats in custom prepared diets to approximate a dose of 10 mg/kg/day. The effects of erlotinib on hypomagnesemia were monitored by assessing plasma Mg from tail bleed samples. All rodents were kept under a 12/12 h light/dark cycle with food and deionized water ad libitum. Transthoracic echocardiography (echo) determined the progression of cardiac dysfunction during treatment.

**RESULTS:**

We observed significant progressive hypomagnesemia ( $P < 0.05$ ) at 5 and 9 weeks, when a 3-fold elevation ( $P < 0.05$ ) of neutrophil superoxide production was seen. Moderately decreased ( $P < 0.05$ ) cardiac LV ejection fraction and % fractional shortening were observed by 7 weeks, and diastolic dysfunction (lower mitral valve E/A ratio) achieved significance ( $P < 0.05$ ) at 9 weeks of erlotinib treatment.

We conclude that EGFR-TK inhibiting agents also cause hypomagnesemia and this may partly underlie the oxidative stress and impaired cardiac contractility observed in our rodent model. The clinical relevance of these findings with the increasing use of EGFR-TK inhibiting drugs remains to be determined.

**SUPPORTED BY:**

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A new syndromic association: pituitary adenomas, paragangliomas and pheochromocytomas

We recently reported a potentially new syndromic association, that of a GH-secreting pituitary adenoma and pheochromocytoma/paraganglioma (PHEO/PGL)<sup>1</sup>. Prompted by this observation, we interrogated our International Registry of mostly pediatric sporadic pituitary adenomas, as well as adult and pediatric syndromic pituitary tumors for the occurrence of pituitary adenomas with PHEO/PGL. A total of 161 cases were investigated: 16 were identified as familial/syndromic and 145 as sporadic. Among the syndromic cases 4 were diagnosed with Cushing's disease and 12 with GH- and PRL-secreting adenomas. Among the sporadic cases 117 were diagnosed with Cushing's disease, 8 with GH-secreting adenomas, 5 with prolactinomas, 5 with non-secreting tumors, 1 with craniopharyngioma and 9 with hormonal syndromes and no obvious tumor. Out of the 145 sporadic cases 2 presented with the new syndromic association; 1 case had a GH/PRL pituitary adenoma and PHEO/PGL, and the other one an ACTH-producing adenoma and PGLs. In the second case, mutation screening for *SDHB*, *SDHC*, *SDHD*, and *SDHAF2* genes was negative, whereas mutation screening for the first case is pending. None of the syndromic cases had any PHEO/PGL association, and all were due to other mutations including 2 in *AIP* and 3 in *MEN1* genes or were due to yet unknown molecular defects. In addition to the two kindreds with pituitary adenomas and PHEO/PGLs and the previously reported family with acromegaly and PHEO/PGLs, we also identified four previously reported polymorphisms, including His50Arg and Gly12Ser in *SDHD*, as well as, 170A>G,p.His57Arg and 163Ser>Pro in *SDHB* in the sporadic adenoma population. This represents an unexpectedly higher frequency from what has been reported in the general population for these variants; screening of our own control group is ongoing. Both *SDHB* 163Ser>Pro and *SDHD* His50Arg have been associated with mitochondrial dysfunction in a subset of PTEN mutation-negative Cowden and Cowden-like syndrome individuals<sup>2</sup>. We conclude that as we speculated first, when we described the *SDHD* mutation in connection with a pituitary tumor and PHEO/PGL, there might be an association of these tumors that may constitute a new syndrome. However, it is rare among sporadic pituitary adenomas, although functional SDHx variants may play a role there, too. This discovery may lead to new therapies targeting mitochondrial oxidation in aggressive pituitary tumors.

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## REFERENCES

- 1 Xekouki et al. J Clin Endocrinol Metab 2011
- 2 Ni et al. Am J Hum Genet. 2008

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Developing a Surgical Access Staging System for Endoscopic Approaches to the Infratemporal Fossa

Many Infratemporal fossa (ITF) lesions can directly arise from structures within the ITF, but more often, are extensions of neoplasms from neighboring structures. Due to the location of the ITF and its close proximity to other structures, the surgeon must consider various factors when resecting the lesion. The selected approach will be dependent on the anatomical location of the target, the type of lesion, and the goal of the surgery. The approaches that are employed in endoscopic surgeries are: transnasal, transseptal, endoscopic anterior maxillotomy (EAM) approach and sublabial transmaxillary. These different approaches have various advantages and drawbacks. Some increase the working angle of the surgeon, which allows better access to the lesion, but may be more invasive. Selecting the appropriate technique will be a critical component to better patient outcome. A clinical chart review of approximately 100 charts, which includes 40 patients was evaluated and the lesions were assigned a stage using the following anatomical categorization:

**Type A Lesion:** Lesion is anterior to the posterior wall of the Eustachian Tube, medial to the Lateral PTG Plate.

**Type B Lesion:** Lesion is anterior to posterior edge of Lateral PTG Plate (medial border). Posterior edge is from the lateral PTG muscle (lateral border) to mandibular head/wall.

**Type C Lesion:** Lesion is in the flat plane behind Carotid Artery. Lesion is posterior and lateral to Lateral PTG muscle. In the Sagittal view, the lesion is superior to the Eustachian Tube. The Temporal Mandibular Joint will be the lateral margin.

**Type D Lesion:** Below the Palate line

Clinical chart reviews and radiographic images were analyzed and assigned a stage according to this system. The type of endoscopic approach employed was analyzed with regression analysis against the lesion stage in order to determine whether our staging system accurately predicts what is clinically encountered. We also analyzed whether the approach gave complications after surgery (Paralysis of cranial nerve, Trismus, facial defect, ocular injury, CSF leak), whether the surgery was successful (complete or subtotal resection), surgical time, and blood loss. At this point, our ultimate goal is to extrapolate whether our anatomically based staging system will correlate surgical techniques with better outcomes. Ultimately, our goal is to help direct future surgeons in selecting the appropriate surgical approach based on the location of the lesion and thus leading to better outcomes.

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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Enhanced Depth Imaging Optical Coherence Tomography of Optic Nerve Head Drusen

#### OBJECTIVE:

To assess the value of enhanced depth imaging optical coherence tomography (EDI OCT) in diagnosing and evaluating optic nerve head drusen (ONHD) compared to conventional diagnostic methods.

#### DESIGN:

Prospective, comparative, cross-sectional study

#### PARTICIPANTS:

Thirty-four patients with clinically-visible or suspected ONHD in either eye based on dilated optic disc examination and/or optic disc stereophotography and without ocular comorbidity.

#### METHODS:

Spectral-domain OCT of the optic nerve head in both conventional (non-EDI) and EDI modes, ultrasound B-scan, and standard automated perimetry (SAP) were performed on both eyes of all participants.

#### MAIN OUTCOME MEASURES:

Detection and findings of ONHD between EDI OCT and conventional diagnostic methods.

#### RESULTS:

Sixty-eight eyes were clinically classified into 3 groups: 32 eyes with definite ONHD, 25 eyes with suspected ONHD and 11 normal-appearing fellow eyes. In the definite ONHD group, EDI OCT, non- EDI OCT, and ultrasound B-scan were positive for ONHD in all eyes and visual field was abnormal in 24 eyes. In the suspected ONHD group, EDI OCT, non-EDI OCT, ultrasound B-scan, and visual field were positive in 17, 14, 7, and 3 eyes, respectively; 8 eyes had no evidence of ONHD in any of the tests. In normal-appearing fellow eyes, EDI OCT, non-EDI OCT, ultrasound B-scan, and visual field were positive in 3, 1, 1, and 0 eyes, respectively; 4 eyes had no evidence of ONHD in any of the tests. EDI OCT had a significantly higher ONHD detection rate than ultrasound B-scan in all eyes (52/68 eyes vs. 40/68 eyes;  $p < 0.001$ ), in eyes with clinically suspected ONHD or normal-appearing fellow eyes (20/36 eyes vs. 8/36 eyes;  $p < 0.001$ ), and in eyes with clinically suspected ONHD (17/25 eyes vs. 7/25 eyes;  $p = 0.002$ ). EDI OCT detected ONHD appeared as signal-poor regions surrounded by short, hyper- reflective bands or isolated/ clustered hyper-reflective bands without a signal-poor core. In non-EDI OCT, posterior surfaces of the ONHD and deep-seated hyper-reflective bands were invisible or less clear than in EDI OCT.

#### CONCLUSIONS:

EDI OCT is better than conventional tests at detecting ONHD and assessing their structure.

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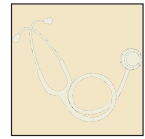
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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Skinning the Surface of Trichothiodystrophy *More Than Skin Deep: Bone Abnormalities in Trichothiodystrophy*

#### KEYWORDS:

Trichothiodystrophy; Bone Abnormalities; DNA Repair; Transcription Disorder

#### ABBREVIATIONS:

TTD—Trichothiodystrophy  
AVN—Avascular Necrosis

#### OBJECTIVE(S):

The purpose of the study conducted is to characterize the qualitative and quantitative features of the bone abnormalities present in patients diagnosed with Trichothiodystrophy (TTD), a DNA repair and transcription disorder. An additional goal of the study is to identify TTD patients at risk for rapidly progressive bone abnormalities in order to improve diagnosis and treatment for TTD patients.

#### STUDY DESIGN:

A retrospective study conducted at the National Institutes of Health (NIH) examining the bone abnormalities present in a study population comprised of 32 patients between the ages of 1 and 29 years of age diagnosed with TTD. Radiographic images, acetabular angle, walking ability and stage of avascular necrosis (AVN) were evaluated to assess changes in bone structure.

#### RESULTS:

Delayed bone age, central osteosclerosis, peripheral osteopenia, hip degeneration or coxa valga were present in 31 (97%) of 32 TTD patients. All TTD patients with hip abnormalities on radiographic images exhibited progressive degeneration and difficulty walking, over a 2-6 year period. Acetabular angle measurements did not correlate with the clinical and radiological findings for 4 (80%) of 5 TTD patients with hip abnormalities on radiographic images. Abnormalities in mean corpuscular volume (MCV), hemoglobin A2 (HbA2), red blood cell morphology and hormone and nutrient levels (calcium, parathyroid hormone and Vitamin D) were not associated with the onset of bone abnormalities present in the 32 TTD patients.

#### CONCLUSION(S):

Bone abnormalities are a common clinical feature of TTD that have been shown to significantly impact the quality of life of a TTD patient. Thus, analysis of the predictive factors and events preceding the onset of bone abnormalities is clinically important in improving the diagnosis and treatment of TTD.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Hypogonadism in Men Referred for Borderline Testosterone Levels

#### BACKGROUND:

In an era of increased measurements of serum testosterone in men, clinicians are encountering the common clinical scenario of men with “borderline” testosterone levels which are close to the lower limit of the normal reference interval. There is little literature on this population.

#### OBJECTIVE:

Our study seeks to clinically characterize men who are referred for borderline testosterone levels and to determine the prevalence of hypogonadism in this population using repeat testosterone measurements.

#### METHODS:

We performed a retrospective chart review of 162 adult men referred for borderline testosterone levels, defined as a total testosterone between 200 and 350 ng/dL (6.9-12 nmol/L). The main outcome variable was hypogonadism as defined by various interpretative models using repeat measurements of total and bioavailable testosterone and symptoms.

#### RESULTS:

As compared to men from the general population, men referred for borderline testosterone levels had higher rates of sexual dysfunction, overweight/obesity, and depression. In men with initial borderline total testosterone measurements, 48% had a repeat low total testosterone and 25% had a low bioavailable testosterone using the lower limits of the reference intervals for the assays used.

#### CONCLUSIONS:

Clinicians are advised to repeat testing for men with initial borderline testosterone levels as fewer than half had confirmed hypogonadism. Given the high prevalence of overweight/obesity, sleep disturbances and depression in this population, clinicians should consider treatment of these conditions that are likely contributing to the lower concentrations of testosterone. Randomized controlled trials are needed regarding testosterone therapy in this group of men.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Using The Ten-Point Clock Drawing Test As A Tool For Assessing Cognitive Dysfunction In Patients Undergoing Outpatient Ketamine Infusions For Chronic Pain

#### BACKGROUND:

Chronic pain patients with severe refractory pain may benefit from Ketamine infusions. Ketamine is an NMDA antagonist. The NMDA receptor plays an important role in central sensitization and in CNS functions such as learning and memory. Using Ketamine infusions in the chronic pain population could potentially affect memory systems, leading to cognitive dysfunction.

#### OBJECTIVE:

The objective of this study is to use the 10 point clock drawing test, a validated instrument for assessing cognitive dysfunction, to evaluate whether Ketamine infusions result in cognitive dysfunction. We compared 10 point clock scores before and after Ketamine infusions over three consecutive days.

#### MATERIALS AND METHODS:

Following approval from the Institutional Review Board, we completed a retrospective chart review for patients who were administered outpatient Ketamine infusions along with the 10-point clock drawing test between July 2011 and June 2012. Data reviewed included dose of Ketamine infusion, with age, gender and weight as static covariates, and 10 point clock score pre- and post- infusion on three consecutive days.

#### RESULTS:

We identified 31 patients receiving 88 outpatient Ketamine infusions for chronic pain syndromes including complex regional pain syndrome (CRPS), neuropathic pain, migraine headaches and chronic abdominal pain. We found no effect of infusion number, age, gender, or weight on the clock scores. The Ketamine dose ranged from 0.2 mg/kg/hr to 1 mg/kg/hr over four hours. Pearson's correlation (r) for the doses each day did not show significant associations with clock scores.

#### CONCLUSIONS:

Outpatient Ketamine infusions on three consecutive days in chronic pain patients did not affect cognitive function as assessed by the 10 point clock drawing test.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Anesthetic Management of a Parturient in Acute Respiratory Distress Syndrome (ARDS)

#### OBJECTIVES:

This is a case report discussing the anesthetic management of a parturient with acute respiratory distress syndrome (ARDS).

#### BACKGROUND:

A 36-year-old female, in her third trimester of pregnancy, presented to the intensive care unit for symptoms of acute respiratory distress syndrome (ARDS). The patient had no significant medical history and pregnancy was uncomplicated until this point. Initially the patient had presented with fever and cough but subsequently developed shortness of breath. She was transferred to the intensive care unit and soon required intubation. The patient required sedation while intubated because of agitation. Initial studies were inconclusive as to causation of her illness, and treatment with antibiotics and anti-viral medication were not improving her clinical situation. It was determined that a semi-elective caesarean section was the most appropriate course of action for both mother and the fetus.

#### RESULTS:

The patient successfully underwent caesarean section, and the baby was born without complications. The baby required continuous positive airway pressure briefly after delivery but did not require intubation. The mother's symptoms resolved after the caesarean section.

#### CONCLUSIONS:

There are special anesthetic concerns when sedating the parturient. Drug choice is especially important as it can affect fetus viability after delivery.

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# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Where Should Intratesticular Resistive Index be Measured?

#### INTRODUCTION:

Resistive Index (RI) calculated by Spectral Doppler ultrasound of the testis, is a non-invasive indicator of the intratesticular microcirculation. The current body of literature has shown that RI is related to spermatogenesis, with an elevated RI indicating dyspermia. However, the literature does not specify where in the testis the RI is best measured. It is the goal of this study to evaluate measurement of RI from multiple areas in the testes to determine if significant differences exist.

#### METHODS:

A retrospective review of all testicular ultrasounds performed at our clinic for one year (September 2011 through August 2012) yielded 214 patients and 418 testicles (10 patients with solitary testis). Spectral Doppler interrogation of a single centripetal or recurrent rami artery from the upper, middle and lower portions of each testis was performed using a BK medical Flex focus ultrasound with an 18 mHz linear array transducer by a single sonographer.

#### RESULTS:

The average RI for the right was 0.56 and for the left was 0.56. When comparing the right and left testis there was no statistical difference (p-value of 0.86). In the right testis, there was no statistical difference when comparing the upper and lower values (average RI 0.56 and 0.56, respectively) to the mid-testis (average RI 0.56) with p-value of 0.68 and 0.79, respectively. There was also no statistical difference when comparing the right upper to the right lower testis, with p-value of 0.48. In the left testis, there was no statistical difference when comparing the upper and lower values (average RI 0.56 and 0.57, respectively) to the mid-testis (average RI 0.56) with p-value of 0.95 and 0.70, respectively. There was also no statistical difference when comparing the left upper to the left lower testis with p-value of 0.73.

#### CONCLUSION:

Spectral Doppler ultrasound is a safe, non-invasive technique that adds unique real-time information about the intratesticular microvasculature and testicular function. This study has found that the RI measurements are not statistically different when measured from the upper, mid, or lower testis. Therefore, as the use of RI as an assessment of testicular function increases, this work indicates that measurement of the RI can be taken from any area in the testis with equivalent results. The process of identifying an intratesticular artery and calculating the RI in the upper, middle, and lower pole of each testis can be time consuming. Therefore, the ability to use a single measurement of RI from anywhere in the testis might encourage more Urologists to obtain this measurement as an independent marker of testicular function.

#### DOES IT MATTER WHERE TESTICULAR RESISTIVE INDEX IS MEASURED?

Intratesticular Arteries from All Areas of the Testis May be Used to Assess the Resistive Index

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Corrosion and Fretting of Modular Taper Junctions in Total Hip Arthroplasty

In Total Hip Replacement (THR), it has been documented that Metal-on-Metal (MoM) articulations have three times the failure rate of Metal-on-Polyethylene (MoP) components. Moreover, it has been suggested that this observation is related to fretting and release of corrosion products at the head taper junction. This study tested the hypothesis that (i) MoM implants exhibit higher rates of corrosion and fretting than MoP implants, and that (ii) the severity of corrosion and fretting is greater in components of larger head diameter. Our study included 41 MoM and 49 MoP implants (with modular head diameter >32mm) retrieved from revision hip arthroplasty. Taper surfaces were examined and scored for both corrosion (using modified Goldberg scoring system) and fretting (using standard Goldberg scoring system). Overall, there was no difference between the severity of corrosion or fretting damage of the femoral head taper surface, or fretting of the stem trunnions of the implants examined as a function of : (i) MoM vs MoP articulation (p values ranged from 0.245 to 0.733), or (ii) head size (p values: 0.333 to 0.680). However, corrosion damage of the stem trunnions did vary with the type of articulation (p= 0.0069), and with head size (p=0.0145). MoP trunnions were found to have significantly more corrosion damage than MoM trunnions at head diameters greater than 40mm (p = 0.005). This result contradicts our first hypothesis above, regarding articulation types. However, the finding that trunnion corrosion correlates with head size alone supports the second hypothesis. These results are preliminary, and further research is needed. Future investigation may include a chart review to gather, for each implant, the indications for revision, length of time *in-vivo*, and manufacturer. It may also be worthwhile to investigate third-body abrasion as a possible source of friction.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### An Observation of Bispectral Index Scores in Three Patients Undergoing Outpatient Ketamine Infusions

#### OBJECTIVES/BACKGROUND:

Ketamine, an NMDA receptor antagonist, helps reduce severe debilitating neuropathic pain in patients unresponsive to conventional treatment. Potential ketamine side effects include sedation, hallucinations, hypertension and tachycardia. Bispectral Index (BIS) is a relatively recent technology used to measure depth of anesthesia. BIS is a form of processed EEG which uses a 4 electrode strip placed on the patient's forehead and gives a score ranging from 0 to 99. Scores below 60 typically correlate with general anesthesia. We report the BIS values in three patients undergoing ketamine infusions at subanesthetic doses in an outpatient setting.

#### METHODS:

With IRB approval, we have enrolled 3 patients undergoing outpatient ketamine infusions for intractable chronic neuropathic pain. Each patient underwent 3 consecutive 4 hour infusions with increasing dosage each day. BIS scores were recorded every 5 minutes during the course of the 4 hour infusion and for 1 hour following conclusions of the infusion.

#### RESULTS:

All 3 patients tolerated the 3 daily infusions without significant side effects. Patient's 1 and 3 had baseline scores in the upper 90's which did not decrease beyond 70 during any point of the infusions. Patient 1 had a lowest value of 77, while Patient 3 had a lowest value of 73. There was no visible correlation between increasing dose and amount of decrease from baseline. Patient 2 showed substantially lower scores with multiple BIS scores in the 40's, and was recorded as low as 44 multiple times. (Baseline BIS for patient 2 was low to begin with). This however was only seen on day 1 of the 3 day infusions and again showed no visible correlation between increased dose and lower scores. All of our patients, including Patient 2 who had much lower scores even at baseline, returned to their baseline BIS score at within an hour of infusion conclusion and being sent home.

#### CONCLUSIONS:

In these three patients the BIS scores appeared to decrease during outpatient ketamine infusion at subanesthetic doses. The BIS score in each patient returned to baseline within one hour after the ketamine infusion was discontinued. Moreover, these are very preliminary results for which more conclusions cannot be made until we have recruited and enrolled more patients.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### A Case Report of A Disappearing Lesion on Breast Specific Gamma Imaging Following an Ultrasound Guided Core Needle Biopsy: A Lesson to Learn

#### OBJECTIVE:

We report an initial false negative Breast Specific Gamma Imaging (“BSGI”) finding in a patient with diagnosed invasive breast cancer in whom the anesthetic used during minimally invasive biopsy performed immediately prior to BSGI imaging contained a vasoconstrictive agent. Repeat BSGI several days later demonstrated a clearly positive BSGI.

#### BACKGROUND:

Mammography is an effective screening modality for the diagnosis of breast cancer. The sensitivity of mammography in women with dense breast tissue decreases significantly. Therefore additional imaging modalities are needed to improve cancer detection. While the performance of mammography together with sonography can raise the overall breast cancer detection rate, these two modalities both rely on the anatomic differences between breast cancer and normal breast tissue.

Alternative imaging modalities which are based on the physiologic differences between breast cancer and normal breast tissue, such as MRI and BSGI have the ability to detect additional breast cancers not identified by anatomic based imaging modalities. Breast Specific Gamma Imaging (BSGI) is based on angiogenesis, mitochondrial activity and cellular proliferation. BSGI has been shown to reliably detect breast cancers with sensitivities ranging from 78.6 to 100%. Its specificity has also been shown to be high, 59.5% to 93.3%, comparable to breast MRI.

#### DESIGN:

Case study.

#### METHODS:

An US guided core needle biopsy was performed utilizing a 14 gauge spring loaded device.

Prior to the biopsy 1% lidocaine with 1:100,000 epinephrine was injected intradermally as well as the deeper tissues. Immediately following the biopsy, the patient was escorted to the Breast Center’s Nuclear medicine suite. The patient was injected with 20.0 mCi of Technetium-99m- Sestamibi in the right antecubital.

#### RESULTS:

Imaging was performed on a high resolution gamma camera to evaluate the extent of disease and for evaluation for additional, occult foci of cancer. Rapid 1 minute and delayed images were obtained.

Results of the BSGI demonstrated no focal area of radiotracer uptake inconsistent with the mammographic and sonographic findings. Repeat BSGI performed one week later demonstrated 1 single focus of increased uptake in the upper outer left breast consistent with the mammogram and ultrasound images.

#### CONCLUSIONS:

Avoiding vasoconstrictive agents immediately prior to BSGI imaging or allowing sufficient time between minimally invasive biopsy and imaging with BSGI will allow for optimal diagnosis of cancer as well as improve patient care.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Assessing the effectiveness of an information fact sheet in reducing patient anxiety

#### BACKGROUND:

Obstetrical patients have various concerns about epidural placement that may increase their anxiety during labor. Misunderstanding the risks and complications of epidural placement might increase anxiety. Relief of pain and anxiety is an important issue for both women and health professionals.

#### OBJECTIVE:

To ascertain whether providing pregnant women with information fact sheet about epidural will decrease anxiety and improve their overall epidural experience.

#### METHODS:

The research team consented patients who met study criteria: primigravida, pain score less than 4/10, English-speakers. Consented patients were randomized to control group (-EIS) or intervention group (+EIS). -EIS group received a brief demographic questionnaire, pretest Speilberger State and Trait Anxiety Inventory, which is a validated tool to measure anxiety. +EIS group the same baseline inventories and received an Epidural information sheet created by the American Society of Anesthesiologists (ASA) prior to epidural placement. The anesthesiology team provided a standardized consent and answered subject's questions regarding epidural placement. All subjects completed a posttest Speilberger State and Trait Anxiety Inventory and a survey about overall satisfaction with pain management on the day after delivery in the Postpartum Unit.

#### RESULTS:

During the course of the study, 20 patients were approached to complete the survey. Out of these patients, only 17 completed the pre and posttest. Of the subjects who had a graduate education level, 41% of the +EIS subjects had a mean change of anxiety score equal to 11.9 compared to 32% of the patients who had undergraduate degree (mean=7) and 15% of subjects with a high school diploma (mean=5).

#### CONCLUSIONS:

The early results did not show a significant difference between the intervention group and the control group; we will continue the study to have more subjects for more accurate results.

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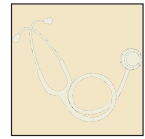
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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### The Effect of Outpatient Ketamine Infusions on Patient Hemodynamics, Level of Sedation, and Pain

#### OBJECTIVES/BACKGROUND:

Ketamine, an NMDA receptor antagonist, helps reduce severe debilitating neuropathic pain in patients unresponsive to conventional treatment. Potential ketamine side effects include sedation, hallucinations, hypertension and tachycardia. There have been no published studies to date examining these side effects in outpatient ketamine infusions. Our goals are to determine 1) the safety of outpatient ketamine infusions and 2) the effect of ketamine infusions on pain.

#### METHODS:

With IRB approval, we reviewed the vital signs, sedation assessment and pain scores of 46 patients diagnosed with severe chronic neuropathic pain. Each patient underwent 3 consecutive days of 4 hour ketamine infusions. Ketamine doses ranged from 0.2 mg/kg/hr to 1.2 mg/kg/hr for a total of 4 hours. In general, doses were incrementally increased from Day 1 to Day 3. Vital signs and Sedation-Agitation Scale (SAS) scores were recorded at baseline, every 15 minutes during the infusion, and 1 hour after infusion completion. Pre-infusion and post infusion pain scores were obtained each day.

#### STATISTICAL ANALYSIS:

The percent change in systolic and diastolic blood pressure (SBP, DBP), heart rate (HR), respiratory rate (RR), and oxygen saturation was computed for each patient on each day, for the highest increase and decrease from baseline. Ketamine dose was categorized into 5 dose ranges (0.2 to 0.3, >0.3 to 0.5, >0.5 to 0.7, > 0.7 to 0.9, and >0.9). Chi square was used to evaluate the association between dose and largest increase and decrease in the above variables. A paired t-test was used to examine changes in pain scores over time.

#### RESULTS:

A total of 138 ketamine infusions were administered to 46 patients with severe neuropathic pain. The total dose of ketamine infused ranged from 36 mg to 510 mg. The vast majority of patients showed small (<20%) changes in hemodynamic, respiratory and oxygenation parameters. 40 patients showed SBP increases of less than 20% from baseline and 32 showed SBP increases of less than 10% from baseline. There was a strong association between ketamine dose and highest SBP increase ( $p < 0.01$ ). An increase of greater than 20% from baseline was seen in 6 patients, 3 of which were in the highest dose group (>0.9 mg/kg/hr). Increased HR was associated with higher doses ( $p < 0.05$ ). Patients in the highest dose range had a maximum HR increase of 20% or more. However, across all dose ranges, 78% of patients experienced less than 10% increase above baseline and 84% (36 patients) had less than 20% increase. All patients had a baseline SAS score of 4 (calm, cooperative). The lowest SAS score for all patients during the infusions was 3 (sedated, easily arousable). Pain scores decreased from  $6.5 \pm 2.4$  on Day 1 pre-infusion to  $3.1 \pm 2.2$  on Day 3 post-infusion. The 95% confidence interval was 2.8 to 4.1 points on the pain scale ( $p < .0001$ ).

#### CONCLUSIONS:

Consecutive multi-day outpatient ketamine infusions have been shown to reduce pain in patients with refractory neuropathic pain and complex regional pain syndromes. We examined the safety profile of outpatient ketamine infusions with respect to hemodynamic changes, respiratory rate, oxygenation and level of sedation over a wide range of ketamine doses. There was little deviation from baseline in the majority of our patients. Increased SBP and HR were associated with higher ketamine doses. RR and oxygen saturation were not significantly altered during the infusions, across all doses. Sedation level decreased during ketamine infusions although patients were easily arousable. All patients returned to pre-infusion sedation level upon discharge. There was a significant decrease between the mean pain scores measured pre-infusion on Day 1 and post-infusion on Day 3. Continuous 4 hour infusions of ketamine at subanesthetic doses significantly decrease pain scores and may be safely administered to outpatients for management of severe chronic neuropathic pain.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### The Pediatric Critical Care Family Conference: An audiotaped analysis

#### OBJECTIVE:

To understand physician-parent communication patterns during Pediatric Intensive Care Unit family conferences.

#### DESIGN:

Prospective, cross-sectional study

#### SETTING:

Urban tertiary medical center

#### METHODS:

Family conferences between a parent and PICU attending physician to discuss a critical treatment decision were audio-taped.

#### RESULTS

Ten family conferences were audio-taped, representing 10 unique patients, 17 parents and 5 physicians. Both parents were present in 7/10 (70%), other family members in 3/10 (30%), social work in 9/10 (90%), case management in 4/10 (40%), bedside nurse in 9/10 (90%), another physician in 9/10 (90%), palliative care team member in 1/10 (10%), and chaplain in 1/10 (10%). Four conferences discussed goals of care, 3 tracheostomy placement and 3 resuscitation status. The mean duration of the family conference was 37 min (SD 15 min). On average, family members spoke 6 ½ min (15%) and the clinical team spoke 30 min (80.83%), of which the attending physician spoke for an average of 26 min (87%). The mean number of beeper interruptions per conference was 2.1 while phone interruptions averaged 3.1 per conference. There was full concordance between what the physician leading the conference anticipated discussing and what was subsequently discussed (10/10). However, the concordance between what was discussed in the conference and what the parents reported was discussed after the conference was full in 3/10 (30%) cases, partial in 5/10 (50%) cases and discordant in 1/10 (10%) cases.

#### CONCLUSIONS

The medical team spent significantly more time talking during the PICU family conference as compared to the families. Family's understanding of the purpose of the conference frequently did not fully match the content of the conference. Future studies should explore the association between the balance of communication and family involvement in the discussion with family satisfaction.

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# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Radiation Dose variability from CT-guided procedures at three teaching hospitals

#### INTRO:

A March 2009 report from the National Council on Radiation Protection and Measurements showed that nationwide exposure to ionizing radiation has nearly doubled during the past 2 decades, with the increase largely attributable to CT, nuclear medicine studies, and fluoroscopy. According to the FDA, the 3 techniques only account for 26% of imaging procedures involving radiation but contribute 89% of the annual exposure that patients have from medical imaging.

#### PURPOSE:

The purpose of this retrospective study was to evaluate the variability of radiation doses associated with CT-guided interventional procedures using data obtained from three academic centers.

#### MATERIALS AND METHODS:

Radiation dose information from nine types of CT-guided procedures including biopsies, drain insertions, and ablations in the chest, abdomen and pelvis were contributed from three teaching hospitals (Memorial Sloan Kettering Cancer Center, UNC Chapel Hill, and SUNY Syracuse). Participating institutions retrospectively identified up to 20 consecutive instances of each procedure type between 10/15/2009 and 4/15/2010. Aggregate data included 370 CT-guided procedures performed on 168 females and 202 males, including 50 chest biopsies, 22 thoracic drain insertions, 45 lung ablations, 50 abdominal biopsies, 50 abdominal drain insertions, 42 abdominal ablations, 50 pelvic biopsies, 41 pelvic drain insertions and 20 pelvic ablations. Effective Dose/Dose Length Product (E/DLP) values taken from the literature were used to convert the dose-length product to effective dose. Descriptive statistics were used to characterize the dataset.

#### RESULTS:

Lowest doses occurred for CT-guided biopsy, where median DLP was 268, 302 and 296 mGy-cm in thoracic, abdominal and pelvic biopsies, respectively. Highest median DLPs occurred in abdominal and pelvic ablations, where median doses of 1223 mGy-cm (range 229-8472) and 3302 mGy-cm (range 282-8427) were observed, respectively. For biopsies and drainages, more dose was accumulated from pre- and post-procedure scanning than from scanning during the procedure. For ablations, more dose was accumulated from scans obtained for procedural guidance. The mean effective dose for all cases was 8 mSv with a range of 1 to 160 mSv. Across institutions, the least variable doses were observed for thoracic drainage (11-fold variability) while the most variable doses were for abdominal drainage (74-fold variability).

#### CONCLUSION:

Huge variability in radiation dose is seen in CT-guided procedures, with an average 38-fold difference between minimum and maximum DLPs for the 9 different procedure types. More study is required to identify the modifiable sources of such variability. Further research is required to establish recommendations for protocol optimization, and reduction in dose variability. Future research should target specific strategies for dose economy of localization, procedural guidance, and post procedure evaluation scans.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Transition to Adult Care

In the field of Maternal and Child Health, there is increasing awareness of modifiable health conditions that appear early in the life course and impact development and wellness throughout the life span. Special opportunities exist in vulnerable populations with chronic illness to better understand what life course events can facilitate attainment of optimal health and development. One such opportunity arises during transition from pediatric to adult health care, referred to as “health care transition,” in the understudied and highly vulnerable patient population of adolescents and young adults with special health care needs (AYA-SHCN).

With improving medical care, children with many chronic health conditions are living well into adulthood. Experts generally agree that health care transition (HCT) is often unsuccessful and associated with a variety of adverse outcomes. (1-8) The National Survey of Children with Special Health Care Needs (NS-CSHCN) documents some limited improvement in HCT services, but national policy goals are yet to be realized. (9-12) For example, in the 2005-2006 NS-CSHCN, less than half of US children with special health care needs received needed HCT services and supports. (13,14) **Adverse outcomes of unsuccessful HCT include foregone or delayed medical care and having no identified adult medical home following HCT.** (15) Such foregone and delayed care can result in **potentially preventable costly utilization of hospital emergency and inpatient services.** (16,17) Particularly concerning is increasing evidence that for some youth, transition from pediatric to adult medical care is a high-risk period for mortality. (18,19) In addition to the adverse effects on individuals, unsuccessful HCT also likely has economic consequences, particularly given that the majority of health care spending is already allotted to individuals with chronic conditions. (20) These problems are even greater for low income and minority youth, (21,22) **with the District of Columbia (DC) having the highest level of unmet HCT needs in the U.S. (76% in 2006).** (12)

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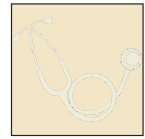
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# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Treatment of Hip Subluxation in Skeletally Mature Patients with Cerebral Palsy

#### BACKGROUND:

Hip subluxation in children with spastic cerebral palsy (CP) is common. While there is agreement that intervention is needed to maintain hip reduction in young children with CP, controversy exists in the treatment of skeletally mature patients with CP. Our goal was to assess the efficacy and complications of surgical interventions for hip subluxation in skeletally mature patients with spastic CP.

#### METHODS:

We performed a retrospective review of all patients with CP who underwent hip surgery for subluxation between 2005 and 2011. 20 patients were found to be skeletally mature and composed our study group. Charts were reviewed for the procedure performed and the pre-operative and most recent radiographs were reviewed to measure the acetabular index (AI), migration index (MI), and neck shaft angle (NSA). We also compared those patients who had all of their abnormal pre-operative radiographic findings addressed at surgery (acetabular osteotomy for AI > 25, open reduction for MI > 50%, and proximal femoral varus osteotomy for NSA > 135) vs those who did not, to evaluate the success of their procedure (defined as MI < 25% at final follow up).

#### RESULTS:

All patients had a GMFCS score of  $\geq 4$ . The average follow up was 2.2 years. The average MI for the entire group improved from 57 to 20 ( $p < 0.0001$ ). Of those patients who had all radiographic abnormalities addressed at surgery, 91% had a final MI of < 25%. In those patients who did not have all radiographic abnormalities addressed, only 33% had a MI < 25% at final follow up. There were no intra-operative complications, however 13 patients had at least one post-op complication (6: persistent hip pain, 5: skin ulceration, 2: heterotopic ossification, 1: post-op fracture).

#### CONCLUSION:

Hip subluxation in skeletally mature patients with cerebral palsy is difficult to successfully treat and is associated with a significant incidence of post-operative complications. We found the likelihood of a successful outcome was directly related to the appropriateness of the surgical procedure performed. When all pre-operative radiographic abnormalities were addressed during surgery the chance of a successful outcome at final follow up was much higher than when a less comprehensive surgical intervention was performed.

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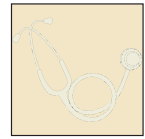
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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Evaluating the Prevalence of Depressive Disorder Among Emergency Department Patients Presenting with Nonspecific Abdominal Pain

#### BACKGROUND:

Nonspecific abdominal pain is one of the most common complaints in the Emergency Department (ED). With the time constraints in the ED and the nonspecific presentation of pain, CT scans can serve as a powerful diagnostic tool. However it is well recognized that unneeded CT scans have negative aspects that include excessive radiation exposure, expensive medical bills, and a longer waiting time in the ED. Nonspecific abdominal pain can have a variety of causes that do not require a CT scan, one of which is depressive disorder. This study investigates the presence of this subgroup of patients who were given, but did not need, a CT scan to evaluate their abdominal pain. To do this, the study measured the prevalence of depressive disorder among ED patients with nonspecific abdominal pain and among patients who receive an abdominal CT to evaluate their nonspecific abdominal pain.

#### METHOD:

Patients complaining of nonspecific abdominal pain in the ED were approached as asked to complete a two question Patient Health Questionnaire (PHQ-2) screening for depression. The PHQ-2 asks patients to rate their level of anhedonism and to rate their mood on a 0-3 scale. A total score of three or more from the two questions indicates a positive test and that further screening for depressive disorder is needed. PHQ-2 scores were analyzed using chi-square test to look for an association between a positive depression test and nonspecific abdominal pain. A separate analysis looked for an association between a positive depression test and abdominal CT scans ordered.

#### RESULTS:

624 patients with abdominal pain filled out PHQ-2 questionnaires. From this group, 62 patients scored a 3 or higher, which indicates a positive test for the depressive disorder. A chi-square analysis found no association between depression and nonspecific abdominal pain. A similar analysis found no association between depression and receiving an abdominal CT to evaluate nonspecific pain.

#### CONCLUSION:

No association was found between depression and nonspecific abdominal pain and depression and abdominal CT scans. Further research can be done to identify other specific subgroups of patients who could be spared unnecessary CT scans. Short surveys were an economical and fast tool for screening ED patients; a similar instrument could be used in future studies.

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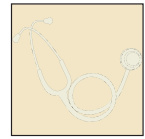
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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Inferior Vena Cava Filter Retrieval Rate at The George Washington University Hospital

#### BACKGROUND:

Inferior vena cava (IVC) filters have been used in a number of settings to prevent pulmonary embolism (PE). In the past, permanent filters have been used for patients at risk for venous thromboembolic events (VTE). However, filters left in place have a significant risk of causing caval thrombosis. For this reason, retrievable (or optional) filters have now replaced the use of permanent filters. However, these filters have their own risk. Their long-term complications are: filter migration, fracture, penetration/protrusion, and embolization. It is recommended that the filters be retrieved if clinically feasible.

#### OBJECTIVES:

To determine the retrieval rate of ICV filters at The George Washington University Hospital. To determine the occurrence of complications during retrieval of IVC filters. To determine the reasons that IVC filters were placed and which patients were more likely to return to have their filter removed.

#### METHODS:

All of the patients that had IVC filters inserted at GW from 2003-2012 were identified. For each filter that was inserted, the following data was collected: reason for filter, date filter inserted, and type of filter. If the filter was retrieved the following data was also collected: reason for removal, indwelling time and any complications that were noted during the removal.

#### RESULTS:

During the time period studied, 1099 filters had been inserted and 272 filters were removed for an overall removal rate of 24.75%. The highest retrieval rate was in 2010 in which 34.25% of the filters inserted were removed. The retrieval rates of filters inserted in 2011 and 2012 will continue to increase as patients have enough time to come back in and get them removed. The most common reason for filter placement was future gastric bypass surgery, which accounted for 44.45% of the filters inserted. Other common reasons for filter insertion were: pre-operative, post-operative, injury, and current PE or deep vein thrombosis. Out of the 272 filters that were removed, 44 were noted to be tilted, 20 had been endothelialized, 11 had fractured, 8 had migrated and 8 had perforated the IVC. There were also 10 unsuccessful filter removals due to severe endothelialization within the IVC.

#### CONCLUSIONS:

The results from the study will help target the various patient populations and how likely they are to return to have their filters removed. The next step will be to create a follow-up plan with the patients and see if the retrieval percentages increase.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Analysis of Critical Limb Ischemia Using MRA with Contrast-Enhanced MR Perfusion Scans

#### BACKGROUND:

Critical Limb Ischemia (CLI) defines the progressive evolution and end stage manifestation of peripheral arterial disease (PAD). Approximately 500-1000 new cases of CLI per million in the population are estimated to occur annually in North America and Europe; the condition exists at a population prevalence of 40/100000 individuals. CLI is characterized by rest pain and ischemic ulceration or gangrene of the forefoot or toes that results from chronic hypo-perfusion below resting metabolic demands. In the absence of intervention and revascularization, the prognosis of CLI carries a high risk of limb amputation and death.

#### OBJECTIVES:

To determine the perfusion deficit in CLI patients with non-healing wounds of the lower extremity using magnetic resonance angiography (MRA) in combination with 3-dimensional contrast-enhanced MR perfusion.

#### METHODS:

Patients with CLI underwent conventional physiologic lower extremity testing; prior to treatment, patients underwent conventional T1-weighted MRA with 3D reconstruction for anatomy. This study was supplemented with 3D gadolinium-enhanced MR perfusion imaging. All scans were performed on a high field strength 3T Siemens TrioTim MRI scanner. Image acquisition and analysis was performed using Siemens Tissue 4D software, which measures contrast agent concentrations. Perfusion (pharmacokinetic) parameters that were investigated included:

1.  $f_{pv}$  = plasma blood volume fraction
2.  $K^{trans}$  = transfer rate reflecting contrast delivery (perfusion) and transport across the vascular endothelium (permeability)
3.  $k_{ep}$  = contrast agent efflux/clearance from the extracellular space

#### RESULTS:

8 ischemic limbs were evaluated in patients with documented CLI. Average ankle-brachial index (ABI) values = 0.48 (S.D. = 0.23). Qualitative analysis of perfusion revealed focal hypoperfusion at the site of tissue injury (Fig. 1).  $f_{pv}$  (unitless, %) increased from control (0.0103±0.0004) to diseased (0.03728±0.0011) ( $p < 0.0001$ ).  $K^{trans}$  (1/min) shows no change between control (0.0143±0.0007) and injured (0.149±0.0006) ( $p > 0.05$ ). Lastly,  $k_{ep}$  (1/min) decreased from control (2.4514±0.0573) to diseased (0.80993±0.0414) ( $p < 0.0001$ ).

#### CONCLUSIONS:

MRA supplemented with 3D contrast-enhanced MR perfusion allows further assessment of the perfusion deficit in patients with CLI. Preliminary data is promising for using this novel technique for qualitatively and quantitatively evaluating the perfusion deficit in the lower extremities of patients with non-healing wounds. This information may be particularly useful to guide therapeutic intervention when physiological parameters are unreliable, such as elevated ABIs, and to assess the impact of angiosome-related ischemia.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Evaluation of General Abdominal Pain in Emergency Department

#### BACKGROUND:

Abdominal pain is the most common complaint seen in the Emergency Department (ED) and represents 10% of all ED visits. There is no standard of care when it comes to abdominal pain and non-specific abdominal pain is one of the most common diagnoses for serial visits to the ED. Advanced imaging for abdominal pain has increased in the ED setting, however there has not been an increase in diagnoses of major conditions. Since there are so many different underlying conditions that can cause abdominal pain, and diagnostic tests often lack sensitivity and specificity, it is a challenge for ED providers to determine the cause of the abdominal pain. To date, there have not been comprehensive surveys evaluating the causes of ED visits due to abdominal pain and variation in provider care.

#### OBJECTIVES:

The purpose of this study was three fold: (1) to describe the nature and severity of the abdominal pain seen in the ED, (2) to measure the outcome two weeks after the ED visit and (3) to measure the extent of provider variation in the management of abdominal pain.

#### METHODS:

Criteria to enroll patients with abdominal pain in the ED were developed. Patients were excluded if they were Non-English speaking, had altered mental status, had abdominal pain due to trauma, had major abdominal surgery in the past 3 months, or were known to be pregnant or gave birth in past 3 months. Enrolled patients were provided with a survey evaluating their pain characteristics, use of pain relievers, risk factors, and patient characteristics. Providers were also given two surveys, one prior to ordering a diagnostic test and another after receiving diagnostic test results. Patients received follow-up phone call two weeks after their ED visit to assess their current pain, medication prescription, and satisfaction with care after their original ED visit.

#### RESULTS:

856 patients were screened with and 521 patients were enrolled with abdominal pain in the ED over a six-month period. The data is still being finalized at this time.

#### CONCLUSIONS:

Pending data analysis.

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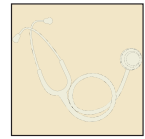
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# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Assessment of the clinical utility and indications for posterior based spinal osteotomies in the correction of AIS

#### BACKGROUND:

The goals of surgical treatment of adolescent idiopathic scoliosis (AIS) are to prevent further curvature progression and improve the alignment of the spine in the sagittal, coronal, and axial planes. Use of posterior based spinal osteotomies has been suggested as a technique to improve the flexibility of spinal deformities which may lead to improved three dimensional deformity correction. Despite the advancement of these complex surgical techniques, limited insight, based on clinical data, exists for both the efficacy of osteotomies in the treatment of AIS as well as indications for when osteotomies should be performed. The purpose of the present study was two-fold: 1) to assess the clinical utility of Ponte osteotomies (PO) in the correction of coronal and sagittal deformities in idiopathic scoliosis and 2) determine indications for the use of POs in the correction of adolescent idiopathic scoliosis.

#### METHODS:

A retrospective review of all patients who underwent posterior spinal fusion for AIS between January 2007 and January 2012, a total of 198 patients, was performed. Patients were classified based on their pre-operative xrays using the Lenke classification system. Cobb angles were recorded for the proximal thoracic, middle thoracic, thoracolumbar curves and the sagittal T5-T12 angle on all patients pre-operatively and at the first follow-up. Operative notes were reviewed for levels of instrumentation, use of POs, levels of osteotomies, estimated blood loss (EBL), and presence of surgical complications. Curve flexibility and surgical effectiveness were assessed based on: correction rate, flexibility rate, and correction index. Only the major structural curve was used for comparison between patients. Comparisons were made between the groups for those with major thoracic curves and those with major lumbar curves. Additionally, groups were compared based on curve size and curve flexibility

#### RESULTS:

There was no difference in absolute coronal curve correction between the two groups regardless of the location of the curve. Additionally, there was no difference in the degree of post-operative thoracic sagittal kyphosis. However, there was an improved correction index in the PO group in thoracic curves and when all of the major curves were analyzed together. Regardless of curve location, the PO group had a higher amount of EBL. In curves with a pre-operative measurement of  $>65^\circ$  the osteotomy group had a larger pre-operative curve magnitude and less pre-operative flexibility but a significantly larger correction index. There was no difference in EBL between the groups in curves  $> 65^\circ$ . In curves  $< 65^\circ$ , there were no significant differences between groups, except increased EBL in the osteotomy group. In the stiffer curves (flexibility index  $< 0.55$ ) the PO group had a higher pre-operative curve magnitude and a lower flexibility index. This subgroup demonstrated an improved correction index in the osteotomy group that was associated with a significantly increased EBL. No patients underwent an osteotomy when the curve flexibility was  $> 0.55$ .

#### CONCLUSION:

The data presented here support the indications that osteotomies are best utilized in AIS patients with combined larger ( $>65^\circ$ ) and stiffer (flexibility index  $< 0.55$ ) curves. In these cases the use of POs was able to loosen the curve to achieve a maximum correction unattainable with posterior spinal fusion and instrumentation alone without leading to an increase intra-operative blood loss.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Peripheral iris configuration as imaged by the anterior segment spectral domain optical coherence tomography (AS/SD-OCT) in patients with and without angle closure glaucoma

#### OBJECTIVE:

Patients with angle-closure glaucoma experience iris swelling upon dilation of the pupil, which consequently causes blockage of the trabecular meshwork. The trabecular meshwork contains the Schlemm's Canal and is the means of exit from the eye for the aqueous humor. This pathology obstruction will ultimately result in an increase of intra-ocular pressure. Patients who have undergone treatment with laser peripheral iridotomy (LPI) for this disease process will still experience iris swelling, however the degree of closure at the anterior angle should be reduced and thus decrease the amount of trabecular meshwork blockage. The objective of this study is to examine the anterior chamber of the eye and determine the risk of angle-closure in patients with angle-closure glaucoma that have received LPI compared to the risk in patients that have not undergone such a procedure with open-angle glaucoma and patients with healthy eyes.

#### METHODS:

Thirty eyes of 15 patients with Primary Angle Closure Glaucoma (PACG) with prior LPI will be included in this observational case-control study along with 30 eyes with Primary Open Angle Glaucoma (POAG) and 30 healthy eyes, neither of which has received LPI. All patients are examined using AS/SD-OCT prior to and post dilation of the pupils using neo-synephrine, a phenylephrine analogue. Images of the anterior chamber angle are taken at 12, 3, 6, and 9 o'clock positions in each eye. The parameters measured prior to and post dilation in each of the 90 total eyes are iris volume, Anterior Chamber Angle (ACA), and Angle Opening Distance at 250 and 500 um from the scleral spur (AOD250 and AOD500).

#### RESULTS:

Ongoing research with no results at this time.

#### CONCLUSIONS:

Ongoing research with no conclusions at this time.

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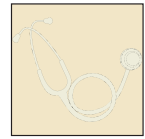
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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Prevalence of Myofascial Tender and Trigger Points in Patients Presenting with Cervico-Thoracic and Lumbo-Sacral Spine Related

#### BACKGROUND:

Spinal pathology may predispose to the development of tender (TP) and trigger (TrP) points. To correlate specific spinal diagnoses with associated TP and TrPs, we quantified the prevalence of those points based on referral patterns in patients with cervico-thoracic and lumbo-sacral spine pain.

#### DESIGN/METHODS:

Following IRB approval, we performed a prospective, observational study of 50 subjects presenting with cervico-thoracic or lumbo-sacral spine pain. Algometry was used to obtain pain-pressure threshold measurements of 10 muscles of the upper extremity (UE) and neck and 6 muscles of the lower extremity (LE).

#### RESULTS:

Of patients with cervico-thoracic pain, 61% were found to have TP and/or TrP in specific muscles. Patients with lesions in C3-C4 presented more commonly with both TP and TrP located in the deltoid, trapezius, pectoralis major and triceps brachii; C5-C6 lesions with TP in the latissimus dorsi; C5-C6 lesions with TrP in biceps brachii and pectoralis major; and C6-C7 lesions with TP in the pectoralis major, latissimus dorsi and triceps brachii. Of patients with lumbo-sacral pain, 58% were found to have TP and/or TrP in specific muscles. Patients with lesions in L4-L5 presented more commonly with both TP and TrP located in the gluteus maximus; and L5-S1 lesions with both TP and TrP in the gluteus maximus. The majority of diagnoses included spondylosis, degenerative disc disease, disc bulging, and spinal stenosis.

#### CONCLUSION:

TP and TrP of selected UE and LE muscles appear to correlate to spinal pathology. We expect to enroll a minimum of 100 subjects in this trial.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### The Effect of Trauma Team Size on Advanced Trauma Life Support (ATLS) Task Completion

#### INTRODUCTION:

Modification of trauma team size based on the likelihood of a severe injury is a common approach used to limit resource utilization. While lack of personnel may delay treatment of life-threatening injuries, large teams may worsen care because of role confusion and interference. The purpose of this study was to determine the effect of team size on task completion during ATLS and identify factors associated with team size during trauma resuscitation.

#### METHODS:

Video-recorded resuscitations of 205 trauma patients occurring over four months at a level I trauma center were reviewed for completion of 24 essential resuscitation tasks. The number of trauma team members was recorded upon patient arrival and at one and two minutes. Univariate and multivariate linear regression were used to assess which resuscitation characteristics were associated with variation in team size.

#### RESULTS:

The average number of people present in the trauma bay over the first two minutes of resuscitation ranged from 2.7 to 10.0 (mean(SD) = 6.5(1.7)). The number of team members present was greater for the highest acuity level activations (+2.2,  $p < 0.001$ ) and for patients with a penetrating injury (+1.0,  $p = 0.02$ ), while lack of pre-arrival notification was associated with fewer people present (-1.2,  $p < 0.001$ ). The number of tasks completed in the first two minutes ranged from 4 to 19 (mean(SD) = 11.7(3.8)). A best fit curve applied to these data showed that the maximum number of tasks was performed by seven member teams, while teams that were smaller or larger completed fewer tasks.

#### CONCLUSION(S):

Completion of trauma resuscitation tasks varies by team size, showing a non-linear association between number of team members and number of completed tasks. To optimize resuscitation performance, management of team size should be a priority during the highest acuity level resuscitations, those without prior notification, and those in which the patient had a penetrating injury.

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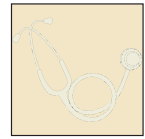
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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### The Effect of Alendronate on Subsidence after Lateral Transpsoas Interbody Fusion (LLIF): Preliminary Report

#### INTRODUCTION:

Success after minimally invasive transpsoas interbody fusion (LLIF) procedure partially depends on avoidance of subsidence to maintain spinal alignment and indirect neural decompression. Techniques for prevention of subsidence have largely focused on surgical and biomechanical properties of spinal reconstruction, however, medical management may also affect subsidence rates as well. Contrary to prior publications, alendronate has been shown in recent basic science and clinical studies to not adversely affect spinal fusion. One study examined the use of alendronate in post-operative TLIF patients and found that alendronate both promoted fusion and limited subsidence. The purpose of this study is to examine the effect of alendronate on LLIF patients with regard to radiographic and catastrophic subsidence.

#### METHODS:

A retrospective review was performed on all patients in the past two years who underwent an LLIF by one surgeon. Fifty patient's charts were reviewed to obtain data. Data points included alendronate use, cage size, the use of bone morphogenic protein. Catastrophic subsidence was defined as the need for posterior instrumented fusion after the index LLIF due to subsidence. Additionally, radiographs were reviewed to obtain measurements of subsidence. Subsidence was evaluated by measuring subsidence at the four corners of the cage. Due to the small sample size a Wilcoxon-rank-sum test was used for data analysis.

#### RESULTS:

AS = anterior superior corner. AI = anterior inferior corner. PS = posterior superior corner. PI = posterior inferior corner.

19 patients received alendronate and 31 patients did not. The cohorts were similar with regard to age, gender, and other demographic data. Due to lack of final follow on some patients (non compliance, date of surgery), the cohort size with data at final follow up (10-18 months) is 8 patients receiving alendronate and 10 patients who did not. Three patients had catastrophic subsidence in the control group versus none in the alendronate group.

#### CONCLUSION:

Preliminary data indicate that alendronate may decrease subsidence and prevent the need for reoperation due to catastrophic subsidence after LLIF. Analysis demonstrated an average decrease of 70% subsidence in patients receiving alendronate after LLIF at L4-L5 versus the control group. These data indicate the need for further study on the role of alendronate in the prevention of subsidence after LLIF.

#### RESULTS:

	L3-L4			L4-L5	
	Control	Alendronate		Control	Alendronate
AS	1.7mm	.5mm		1.8mm	.8mm
AI	1.0mm	1.0mm		2.0mm	0mm
PS	2.2mm	1.6mm		1.7mm	.6mm
PI	1.8mm	1.7mm		2.2mm	.9mm

AS = anterior superior corner. AI = anterior inferior corner. PS = posterior superior corner. PI = posterior inferior corner.

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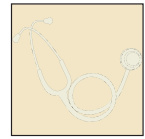
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# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Redo carotid endarterectomy in asymptomatic patients has a higher complication rate

#### BACKGROUND AND PURPOSE:

The risks and benefits of re-do carotid endarterectomy (r-CEA) in patients presenting with recurrent asymptomatic carotid stenosis has not been as well studied compared to primary carotid endarterectomy (p-CEA). This study compares and analyzes morbidity and mortality outcomes after both r-CEA and p-CEA.

#### METHODS:

Data from asymptomatic patients undergoing CEA in participating institutions of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) from 2005 to 2010 were analyzed. 31,838 asymptomatic patients underwent p-CEA for asymptomatic stenosis and 175 patients underwent r-CEA for recurrent asymptomatic stenosis. 30 day morbidity and mortality were compared between both groups. Patients with concomitant associated procedures (coronary artery bypass graft and any non-endarterectomy cerebrovascular operation) were excluded from this study.

#### RESULTS:

Overall 30-day post-operative stroke, myocardial infarction, and death were not statistically different (4.0% for r-CEA vs 2.6% for p-CEA,  $p = .022$ ). Upon multi-variate analysis, cranial nerve injury was five times higher after r-CEA (1.1% r-CEA vs 0.2% p-CEA; OR 5.05 CI 1.21 - 20.97,  $p = .026$ ) and wound complications (dehiscence and deep and superficial wound infections) were four times higher after r-CEA (2.3% r-CEA vs 0.6% p-CEA; OR 4.01 CI 1.46 - 10.97,  $p < 0.001$ ).

#### CONCLUSIONS:

These results suggest that surgeons should exercise caution before recommending r-CEA for asymptomatic patients.

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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Influence of APOL1 Haplotype on Forearm Fracture Risk and Vitamin D Status in African American Children

#### INTRODUCTION:

African Americans develop chronic kidney disease up to 4-5 times more often than individuals from other racial groups. Hypertension, HIV-associated nephropathy, and Focal Segmental Glomerulosclerosis are all manifestations of kidney disease seen at dissimilar rates among African Americans. Until recently, the genetic basis for this disparity was unknown. Recent research, however, strongly suggests a link between the *APOL1* gene and the predisposition to kidney disease in African Americans.

A genomic region on chromosome 22, located 14 kbp downstream from the *MYH9* gene, explains much of the differences seen between people of African vs. European ancestry for nondiabetic end stage kidney disease. In this genomic region lies the *APOL1* gene that encodes apolipoprotein L-1, whose known activities include powerful trypanosome lysis, autophagic cell death, lipid metabolism, and cellular senescence. The *APOL1* gene in African American populations contains two distinct haplotypes G1 and G2. The G1 haplotype contains two nonsynonymous coding sequence single-nucleotide polymorphisms (SNPs) that replace serine at residue 342 with glycine (S342G) and isoleucine at residue 384 with methionine (I384M). The G2 haplotype is defined by a 6-nucleotide deletion that leads to an in-frame deletion of two amino acids, asparagine-388 and tyrosine-389. Examination of the *APOL1* genotype in the Dallas Heart Study, a population-based cohort, demonstrated that most individuals with the G1 haplotype were at increased risk for developing chronic kidney disease compared to those with the WT haplotype. It has been shown that the G1 haplotype has persisted in the population because it also confers protection against sleeping sickness.

It is known that the kidneys play a pivotal role in maintaining and regulating the skeletal system. Parathyroid hormone (PTH) increases calcium reabsorption by the kidney while calcitonin inhibits calcium reabsorption. The kidneys also produce the active form of vitamin D. With that in mind, we sought to investigate whether haplotype variation in the *APOL1* gene might also influence measures of bone health.

Studies evaluating genetic factors, which contribute to fracture risk and vitamin D levels have been performed in adults but remain limited in children. In this study, we explored the relationship between *APOL1* G1 haplotypes and fracture risk and vitamin D levels in healthy African American children.

#### MATERIALS AND METHODS

**Study Participants:** Study subjects were part of an IRB protocol designed to study the influence of bone density and vitamin D level on fracture risk in African American children. Subjects included children aged 5 to 9 years, with forearm fractures (n=60) as well as fracture-free controls (n=70). Case patients were recruited through

*Continued on next page*

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# CLINICAL SPECIALTIES

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*Continued from previous page*

the outpatient Orthopaedic Clinic and the Emergency Department. Control patients were recruited through the Emergency Department, outpatient clinics, and using hospital- and community-based posted flyers.

Bone health evaluation included measurement of 25(OH)D level and bone mineral density by dual energy x-ray absorptiometry (DXA) scan. Body mass index (BMI) measurements and percentiles were calculated using the Centers for Disease Control Body Mass Index Percentile Calculator.

**SNP Selection:** We tested two variants that make up the G1 haplotype. This haplotype consists of the two derived non-synonymous coding variants rs73885319 (S342G) and rs60910145 (I384M) in the last exon of APOL1.

**Genotyping:** The genotypes were determined with assay-by-design Taqman genotyping assays (Applied Biosystems, Foster City, CA, USA) using allele discrimination assays that employ the 5' nuclease activity of Taq polymerase to detect a fluorescent reporter signal. Both alleles are detected simultaneously using SNP-specific oligonucleotides labeled with different fluorophores, and genotypes automatically determined by the ratio of the two fluorophores. The polymerase chain reaction (PCR) for the each genetic variant contained a minimum of 10 ng of DNA, 900 nM primers, 200 nM probes, and TaqMan Genotyping Universal PCR Master Mix (Applied Biosystems) in a final volume of 10  $\mu$ L. PCR was performed on ABI thermocyclers (9700 or 2720) using the following PCR profile: 10 minutes at 95  $^{\circ}$ C (denaturation), 44 cycles of 15 seconds at 92  $^{\circ}$ C, and 1 minute at an annealing temperature of 60  $^{\circ}$ C. The post-PCR allele calling was completed using an ABI 7900HT (genotyping software SDS ver. 2.3) and checked manually.

**Statistical Analysis:** Hardy Weinberg Equilibrium was tested for the SNP using a chi square test with one degree of freedom. The normality of each quantitative phenotype was confirmed using the Shapiro-Wilk normality test. Associations between the SNP and fracture status were tested using logistic regression with BMI and 25(OH)D levels as covariates. Associations between the SNP and 25(OH)D levels were tested using ANCOVA models, with BMI and fracture status as covariates. Post-hoc pair-wise comparisons were performed for those ANCOVAs showing a significant genotype effect F-test, and the resulting p-values were adjusted for multiple comparisons using the Sidak method. All regression models used a full genetic model comparing homozygous common allele individuals to heterozygotes to homozygous rare allele individuals. The nominal p-value for significance was 0.05. All statistical analyses were performed using Stata V11 (College Station, TX).

## RESULTS

Individuals with the APOL1 G1 haplotype did not show any statistically significant relationships with any measured phenotype in this study. We performed an unadjusted analysis of fracture status and found that populations with the APOL1 G1 haplotype did not demonstrate an increased fracture risk. Similarly we did not find a significant correlation for G1 haplotype when we adjusted fracture status for BMI and vitamin D levels. Finally, we analyzed

vitamin D levels and DXA scores adjusted for BMI and fracture status. Populations with the APOL1 G1 haplotype did not show any significant association to measured vitamin D levels ( $p=0.33$ ) or measured whole body DXA z-scores ( $p=0.48$ ).

## DISCUSSION

Because **little is known about the genetic factors that influence forearm fracture risk in children, we explored genetic associations between APOL1 G1 haplotype recently demonstrated to be associated with kidney disease.**

In the United States, African American children have significantly higher rates of obesity than non-Hispanic. Additionally, a high prevalence of vitamin D insufficiency and dietary calcium and vitamin D deficiencies are reported in African American children, and these factors are known to negatively impact bone mineral density. **The kidney is known to regulate many of these factors.** Since APOL1 has been found to contain variants that confer a greatly increased risk of kidney disease in African Americans, we sought to investigate the relationship between these variants and fracture risk and vitamin D levels in healthy African American children.

We failed to find a statistically significant relationship between fracture risk/vitamin D levels and the high risk APOL1 haplotype in healthy African American children. However, these negative results may be attributable to our relatively small cohort size.

## SIGNIFICANCE

Kidney function is critical to bone health. We sought to determine whether variation in the APOL1 gene, known to influence renal function, might also influence measures of bone health in children.

# CLINICAL SPECIALTIES



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Ganglion Cell Layer-Inner Plexiform Layer Thickness and Vision Loss in Young Children with Optic Pathway Gliomas

#### PURPOSE:

To evaluate if measures of macular ganglion cell layer-inner plexiform layer (GCL-IPL) thickness can discriminate between children with and without vision loss (visual acuity or field) from their optic pathway glioma (OPG) using spectral-domain optical coherence tomography (SD-OCT).

#### METHODS:

Children with OPGs (sporadic or secondary to Neurofibromatosis type 1) enrolled in a prospective study of SD-OCT were included if they were cooperative for vision testing and macular SD-OCT images were acquired. Manual segmentation of the macular GCL-IPL and retinal nerve fiber layer (RNFL) was performed using an ETDRS-like grid at 1.5, 3.0 and 4.5mm diameter. Logistic regression assessed the ability of GCL-IPL and RNFL thickness measures (microns) to differentiate between the normal and abnormal vision groups.

#### RESULTS:

Forty-seven study eyes (normal vision = 31, abnormal vision = 16) from 26 children with OPGs were included. Median age was 5.3 years (range, 2.5 - 12.8). The thickness of all GCL-IPL and RNFL quadrants differed between the normal and abnormal vision groups ( $P < 0.01$ ). All GCL-IPL measures demonstrated excellent discrimination between groups (area under the curve,  $AUC > 0.90$  for all diameters). Using the lower 5<sup>th</sup> percentile threshold, the number of abnormal GCL-IPL inner macula (3.0mm) quadrants achieved the highest AUC (0.989) and was greater than the macula RNFL AUCs ( $P < 0.05$ ).

#### CONCLUSIONS:

Decreased GCL-IPL thickness ( $< 5^{\text{th}}$  percentile) can discriminate between children with and without vision loss from their OPG. GCL-IPL thickness could be used as a surrogate marker of vision in children with OPGs.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Pain Catastrophizing in Outpatient Chronic Pain Patients: A Preliminary Observation

#### BACKGROUND:

An individual's pain experience consists of many emotional determinants, one of which includes pain catastrophizing. Pain catastrophizing is an exaggerated, negative cognitive sentiment toward an actual or anticipated painful experience. Age, duration of pain, and knowledge of cause may play a role in pain catastrophizing since emotions toward pain may change throughout one's life.

#### OBJECTIVES:

The objectives of our study were one, to determine any relationship between the intensity of pain catastrophizing and factors such as age and duration of pain, two, to identify early risk factors for pain catastrophizing and three, consider the use of cognitive therapy as treatment for pain in this patient population.

#### METHODS:

Chronic pain patients are routinely asked questions about their pain and the impact of pain on daily life during their outpatient pain clinic visit. Their responses to these questions on chronic pain were gauged on a Pain Catastrophizing Scale (PCS) completed during the patient interview. The PCS total scores were compared with age, pain intensity, duration of pain, and knowledge of cause for pain.

#### RESULTS:

Of the 21 chronic pain patients interviewed, there were 15 females and 6 males. The PCS total score was found to be higher in younger adults than in older adults with a correlation coefficient of -0.43. Pain intensity and knowledge of causality was found to have correlation coefficient of 0.38 and -0.39, respectively when compared with the PCS total score. The PCS total score was found to have poor correlation (0.13) with duration of pain.

#### CONCLUSIONS:

In this survey completed by a small number of patients, increased age and knowledge of causality for pain appear to be associated with less pain catastrophizing. Longitudinal studies with a larger sample size may help further determine the impact of these factors on pain catastrophizing.

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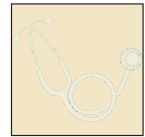
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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

The luteinizing hormone/chorionic gonadotropin receptor (LHCGR) rs4073366 polymorphism is associated with OHSS

### OBJECTIVE:

To determine the relationship between the *insLQ LHCGR* high function polymorphism and outcome to controlled ovarian hyperstimulation (COH).

### METHODS:

This was a prospective study of 172 patients undergoing COH at the Fertility and IVF Center at GWU. DNA was isolated from blood samples and a region encompassing the *insLQ* polymorphism was sequenced. The association of the *insLQ* and rs4073366 alleles and outcome to COH (number of mature follicles, estradiol level on day of hCG administration, the number of eggs retrieved and ovarian hyperstimulation syndrome (OHSS)) were determined.

### RESULTS:

Increasing age was significantly associated with a poorer response for all main outcomes and increasing day 3 (basal) FSH levels, a marker of ovarian reserve, were significantly associated with both a decreased number of follicles generated and eggs retrieved. For the *insLQ*, 107, 59 and 6 patients were no-*insLQ*/no-*insLQ*, no-*insLQ*/*insLQ*, *insLQ*/*insLQ*, respectively. We also investigated a polymorphism (rs4073366 G>C) that was 142 bp from *insLQ*. For rs4073366, 124, 43 and 5 patients had the GG, CG, CC genotypes, respectively. Both variants were in linkage disequilibrium (LD) and no patients were homozygous for both polymorphisms (*insLQ*/*insLQ*; C/C). The *insLQ* variant was not significantly associated with any of the main outcomes to COH. Carrier status for the rs4073366 C variant was associated ( $P = 0.033$ ) with an increased risk (OR 2.95, 95% CI = 1.09-7.96) of developing ovarian hyperstimulation syndrome (OHSS).

### CONCLUSIONS:

The *insLQ* polymorphism confers a high-function phenotype to the LHR *in vitro*. However, while age and day 3 FSH levels were predictive of outcome, we found no association between *insLQ* and patient response to COH. Interestingly, the rs4073366 C variant carrier status is potentially predictive of OHSS in patients undergoing COH.

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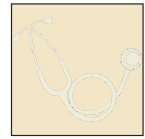
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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Obstructive Sleep Apnea and CPAP benefit on Atrial Fibrillation, Heart Failure and Stroke risk.

#### INTRODUCTION:

Obstructive Sleep Apnea (OSA) is associated with increased risk of Atrial Fibrillation (AF), Heart Failure (HF) and Cerebrovascular Accident/ Transient Ischemic Attacks (CVA/ TIA). Data about Continuous Positive Airway Pressure (CPAP) use in OSA and its effect on the risk of AF is controversial and its effect on the risk of CVA/ TIA and HF is lacking.

#### OBJECTIVES:

We aimed to examine the AF risk in OSA and check if CPAP use is associated with decreased risk of AF, HF and/or CVA/ TIA.

#### METHODS:

We conducted a retrospective analysis of patient's charts with Obstructive Sleep Apnea at the Veterans Affairs Hospital in Washington DC from January 2001 to December 2010 using the Electronic Health Records. We looked at patient demographics, comorbidities and CPAP use. Results were adjusted for baseline variables.

#### RESULTS:

A total of 4608 consecutive patients with OSA were identified. Among them, 243 patients found with AF (5.27%) and 122 patients found with CVA/TIA (2.65%).

We were able to evaluate CPAP use in 4087 patients; 3576 patients were using CPAP and 511 patients were not. CPAP use was defined as getting CPAP machine and having active follow up in the sleep clinic.

AF found in 5.84% (209 patients) of those using CPAP compared to 6.26% (32 patients) of those not using CPAP. The odds ratio for having AF was 0.93 (95% CI 0.63- 1.36) for those using CPAP, compared to those not using CPAP (p 0.7077).

CVA/TIA found in 2.49% (89 patients) of those using CPAP compared to 4.3% (22 patients) of those not using CPAP. The odds ratio for having CVA/TIA was 0.57 (95% C.I. 0.35 - 0.91) for those using CPAP, compared to those not using CPAP (p<0.018).

Among OSA patients who had echocardiograms (1107); EF<45 found in 229 patients (20.69%). In the echocardiogram group we were able to evaluate CPAP use in 1066 patients; Ejection Fraction (EF) < 45 found in 35 patients (30.43%) of those not using CPAP compared to 191 patients (20.10%) of those using CPAP. The odds ratio for having EF<45 was 0.60 (95% C.I. 0.39 - 0.92) for those using CPAP, compared to those not using CPAP (p 0.019).

#### CONCLUSION:

We confirmed a high prevalence of AF, CVA/TIA and HF in OSA. CPAP use in OSA patients was associated with statistically significant decreased risk of CVA/TIA and heart failure (EF<45), but with no significant statistical benefit on the AF risk.

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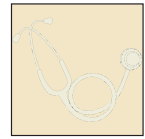
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# CLINICAL SPECIALTIES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Implementation and Clinical Outcome Analysis of a Pathway for Pediatric Septic Arthritis

#### BACKGROUND:

Septic arthritis most commonly occurs in young children by hematogenous spread of bacteria. With early diagnosis and appropriate treatment, excellent clinical outcomes can be expected. On April 1, 2008, a clinical pathway was implemented at Children's National Medical Center to standardize the management of septic arthritis.

#### OBJECTIVE:

1. To evaluate the septic arthritis pathway adherence and implementation
2. To compare the clinical outcomes between pre- and post-pathway cohorts

#### DESIGN/METHODS:

A retrospective chart review of patients with the discharge diagnosis of pyogenic arthritis was performed. Patients were divided into two cohorts, pre-pathway (July 23, 2003 to March 31, 2008) and post-pathway (April 1, 2008 to February 20, 2012). Exclusion criteria included underlying immunodeficiency, fracture, penetrating injury, post-surgical infection, implanted hardware, chronic osteomyelitis or a major co-existing disease processes associated with predisposition for septic arthritis, and transfer from an outside facility. Adherence factors included appropriate labs obtained, rates of blood and joint culture, and time to MRI. Clinical outcome measures included pathogen identification, length of stay, and rates of readmissions and complications.

#### RESULTS:

170 charts were reviewed and 56 met inclusion criteria, with 23 patients in the pre-pathway group and 51 patients in post-pathway group. For adherence factors, there was no significant difference in obtaining blood or joint cultures prior to antibiotics (91% vs 97%,  $p=.354$ ) and (93% vs 94%,  $p=.17$ ) respectively. There was no change in ESR usage (87% vs 97%,  $p=.152$ ), but CRP was obtained significantly more in the post-pathway group (61% vs 97%,  $p=.001$ ). Time to MRI decreased from 93 to 35 hours respectively ( $p=.044$ ). For clinical outcomes, pathogen identification was relatively unchanged (57% vs 55%,  $p=.884$ ) between cohorts. Although not statistically significant, the mean length of stay was reduced from 6.1 to 5 days ( $p=.183$ ). Readmissions and complications were significantly less in the post pathway group (35% vs 12%,  $p=.042$ ).

#### CONCLUSIONS:

The implementation of a septic arthritis management pathway has had a positive effect on clinical outcomes at our institution. A study with greater sample size is needed for further evaluation.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Whole Blood Platelet Aggregation and Release Reaction Testing in Uremic Patients

#### BACKGROUND:

Platelet dysfunction causes bleeding as well as thrombotic diathesis. Platelet function analysis utilizing platelet rich plasma and optical density based aggregometry fails to identify patients at risk for uremia associated complications.

#### METHODS:

We employed whole blood platelet aggregation analysis based on impedance as well as determination of ATP release from platelet granules detected by a chemiluminescence method. Ten CKD Stages 4 or 5 predialysis patients underwent platelet evaluation.

#### RESULTS:

Analysis revealed normal aggregation and ATP release to collagen, ADP, and high dose ristocetin. ATP release had a low response to arachidonic acid (0.37 +/- 0.26 nmoles, reference range: 0.6-1.4 nmoles). Platelet aggregation to low dose Ristocetin revealed an exaggerated response (20.9 +/- 18.7 ohms, reference range: 0-5 ohms). Diminished ATP release to arachidonic acid is similar to an aspirin-like defect. This finding in uremic patients may result in platelet associated bleeding. An increased aggregation response to low dose ristocetin appears to be identical to type IIb von Willebrand Disease, which is associated with thrombus formation. This platelet hyperreactivity may be associated with a thrombotic diathesis as seen in some uremic patients.

#### CONCLUSIONS:

Whole blood platelet analysis detected two separate mechanisms of platelet dysfunction which may be associated with bleeding and thrombotic risks in uremia.

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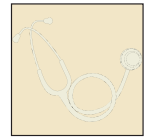
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Prospective, Multicenter Analysis of Peri-Operative Patency for Tibial Bypass: Comparison Among Different Conduit Configuration

#### BACKGROUND:

Despite advances in endovascular techniques, tibial bypass may still be required for revascularization to obtain healing and limb salvage. Perioperative (30 day) graft patency is an important outcome parameter reflecting technical considerations and acute graft thrombosis. Both are important prerequisites for long-term patency. In this analysis, we compare the 30-day patency of greater saphenous vein to alternative conduit configurations for tibial bypasses.

#### METHODS:

The study cohort consisted of all primary tibial bypasses entered in a prospective, multicenter database (ACS-NSQIP) from 2006-2010 with exclusion of re-operative cases. The bypasses were divided into six groups, 1) greater saphenous vein (GSV), 2) prosthetic conduit, 3) prosthetic conduit with a distal anastomotic venous adjunct such as a cuff or patch, 4) composite graft of ePTFE and a vein segment, 5) spliced autogenous vein, and 6) arm vein. Thirty-day graft failure, patient demographics and operative details were compared among groups. Univariate associations between patient factors and conduit were tested and those variables that had  $p < .20$  were used in a multivariate model to predict patency.

#### RESULTS:

5,375 tibial bypasses were analyzed by conduit; GSV 3,983 (74%), prosthetic 889 (17%), spliced vein 160 (3%), prosthetic with adjunct 112 (2%), arm vein 93(2%), composite 91 (2%). There was no difference among groups in terms of diabetes, renal failure, tobacco use, or rest pain as an indication for bypass. There was no difference in perioperative mortality based on conduit. After adjusting for gender, age, weight, race, and previous cardiac surgery (CABG), the bypass conduit had a significant independent association with 30 day graft patency ( $p = .006$ ). The GSV failure rate was 7.5%. Composite grafts had a significantly higher 30-day failure rate (15.4%,  $p = 0.006$ ). There was no significant difference in 30-day patency of spliced vein (5.6%,  $p = 0.37$ ) or arm vein (4.3%,  $p = 0.24$ ) conduits compared to GSV. However, spliced vein and arm vein involved longer OR time and spliced vein increased transfusion requirements. Prosthetic grafts had significantly lower 30-day patency compared to GSV (10.5%,  $p = 0.004$ ). The addition of adjuvant venous tissue at the distal anastomosis of prosthetic bypasses did not significantly improve their 30-day patency (Prosthetic/venous adjunct graft failure rate 9.8% vs. PROSTHETIC graft failure rate 10.5%).

#### CONCLUSIONS:

Venous conduits (GSV, spliced vein, arm vein) deliver the best perioperative patency for tibial bypass and GSV remains the most commonly used graft for tibial revascularization. Prosthetic grafts had a higher perioperative bypass failure rate. Composite grafts should be abandoned because their patency is not better than pure prosthetic conduits. The addition of a distal venous adjunct did not seem to improve acute prosthetic graft patency which may reflect lack of effect on thrombogenicity rather than the myointimal hyperplastic response that impacts long term failure of tibial bypass.

	GSV	SPLICED VEIN	ARM VEIN	PROSTHETIC	PROSTHETIC venous adjunct	COMPOSITE
n	3983	160	93	889	112	91
Female *	1,280 (32.2%)	49 (31.2%)	23 (24.7%)	315 (35.2%)	33 (29.7%)	39 (42.9%)
Age*	69.5±12.3	71.3±11.2	67.5±10.9	70.6±11.4	70.2±12.0	70.9±11.3
CABG*	874(21.9%)	55(34.4%)	43(46.2%)	311(34.6%)	41(36.6%)	22(24.2%)
Transfusion*	0.5±1.1	1.2±1.7	0.4±0.8	0.5±1.2	0.7±1.1	0.6±1.2
OR time (hrs)*	4.4±1.8	6.1±1.9	5.1±2.3	3.7±1.6	4.4±1.8	4.7±2.0
Mortality	127(3.2%)	4(2.5%)	2(2.2%)	40(4.5%)	1(0.9%)	4(4.4%)
30-day graft failure*	300 (7.5%)	9 (5.6%)	4 (4.3%)	94 (10.5%)	11 (9.8%)	14 (15.4%)
p value vs. GSV	--	0.37	0.24	0.004	0.37	0.006

\* $p < .05$

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Monitoring intracellular, intersitial and intravascular volume changes during dialysis

#### BACKGROUND:

Clinicians need to be able to measure the volume in the intravascular, interstitial, and intracellular compartments with a non-invasive real-time device.

#### OBJECTIVES:

The aim is to test the feasibility and validity of a novel electrical impedance spectroscopic (EIS) technique that permits on-line measurements of compartmental volume changes in human subjects.

#### METHODS:

EIS technique validation was performed during 3 consecutive hemodialysis (HD) treatments in 20 end stage renal disease patients by analyzing the timed profiles of fluid redistribution to mathematically derive post hoc hematocrit profiles. These profiles were then compared to the simultaneously measured hematocrit (HCT) values recorded independently using the CritLine® monitor. Regression and Bland Altman analyses were used to compare the EIS data and Critline® hematocrits at sequential times during 60 routine HD sessions.

#### RESULTS:

The statistical and graphical evidence confirms that the EIS system reliably monitors the continuous and real-time *rates of change* of the fluid volumes of the three compartments. An example of one profile is shown in Figures 1 and 2.

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# CLINICAL SPECIALTIES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Regenerative and Molecular-based Approaches to Treating Bladder Obstruction

#### OBJECTIVE:

Bladder outlet obstruction (BOO) is a common pathology in both women and men. Pathogenesis of BOO usually involves overstimulation of the neuromuscular activity of the bladder smooth muscle wall due to hypoxia or chronic mechanical stress. Consequently, the bladder smooth muscle cells (bSMC) switches to a hypertrophic phenotype, which actually contributes to the decompensation of the bladder due to reduced contractile efficiency, making urination difficult.

#### METHODS:

The goal of this project is to investigate the potential of using molecular and regenerative medicine in treating bladder obstruction. Current review of literature suggests that proliferation of smooth muscles is regulated by the mammalian target of rapamycin (mTOR) protein. Our primary goal is to inhibit the mTOR mediated growth of bSMCs. A second regenerative-based approach to treating BOO is to utilize stem cells. We used Skin-derived precursor cells (SKP)'s as our stem cell source. The goal of this project is to determine the optimum conditions for smooth muscle differentiation.

#### RESULTS:

By adding rapamycin, an mTOR inhibitor, we were able to prevent *in vivo* bladder smooth muscle hypertrophy that normally occurs in the presence of hypoxia, cellular injury or mechanical stress. When SKPs were cultured with FBS, we observed that there is a high degree of differentiation into smooth muscle cells. Interestingly, when SKPs were cultured with condition media exposed to normal bladder cells, they expressed high levels of smoothelin-A RNA, a specific marker for bladder smooth muscle expression. This suggests that SKPs can potentially be an alternative tissue source for use in tissue BOO replacement surgery.

#### CONCLUSIONS:

Both regenerative and molecular medicine has a major role in providing a less invasive treatment that specifically targets the pathological mechanism of BOO. However, many challenges lie ahead. Ultimately, more studies on human cells must be conducted before their potentials can truly be recognized.

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# CLINICAL SPECIALTIES

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## SCHOOL OF NURSING

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### Operating Room Teams and Turnover Time

Anesthesiologists and surgeons play a major role toward efficient operating room turnover while nursing and ancillary staff influence two significant entities of the turnover time: clean up and case set up. This study is a quasi-experimental design that looks at how implementation of a team concept in the operating room influences the turnover time efficiency including effects on team cohesiveness. Team concept is demonstrated through streamlining team members in the operating room according to their surgical specialties and preference. A team score inventory on cohesiveness is measured before and after the implementation of the team concept. The team concept foundation is based on Bruce Tuckman's theory on small groups development. The overall operating room turnover time improved by one and a half minutes after implementation of team concept. Team cohesiveness progressed to the next level of development towards the ultimate goal of "Performing" according to Bruce Tuckman's theory. Results from the study can be used to make changes in the operating room with the goal of positively influencing job satisfaction and work environment stress.

#### KEYWORDS:

turnover time, circulator, surgical technician, block time, case set-up, team concept, charge nurse, scrub

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#### STATUS

Graduate Student

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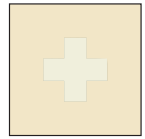
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## CHILDREN'S NATIONAL MEDICAL CENTER

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### Professional Identity Formation among Medical Students Who Volunteer at a Medical Specialty Camp

#### BACKGROUND:

The formation of a physician's professional identity involves deepening one's commitment to the values (humanism, altruism) and aspirations of the profession and is influenced more so by informal than formal teaching experiences. Identifying the impact of various experiences on the development of professional identity in the pre-clinical student remains challenging. While the notion of identity development is relatively unexplored in the medical literature, results from other fields (art therapy, teaching programs) suggest positive outcomes of service learning programs on professional identity. The purpose of our study was to examine how the professional identities of medical students may have been influenced by volunteering at a camp for children with chronic conditions.

#### METHODS:

Nine medical students between their 1st and 2nd year of school served as counselors for 1 week at a condition specific camp (epilepsy, heart disease, or diabetes) sponsored by Children's National Medical Center. Focus groups were held on the last day of camp for a total of 3 separate groups. Focus group data was audio taped, transcribed and assessed using standard qualitative techniques by two researchers trained in qualitative analysis to identify themes related to the students' experience at a medical specialty camp. The trustworthiness of the data analysis was enhanced through the use of 1) member checks, 2) triangulation of data coding and analysis by multiple researchers, 3) triangulation of data collection with the use of focus groups and interviews and 4) thick, rich, description and the use of quotes.

#### RESULTS:

Students described the experience as motivating and career reinforcing, and it helped them "move beyond the textbook." They strengthened their professional identity formation by deepening their commitment to serving future patients with empathy, by seeing and talking to patients as people and not just diseases, and by wanting to help patients' live healthier lives.

#### CONCLUSIONS:

A one-week service learning experience at a medical specialty camp may influence and strengthen the early formative professional identity of medical students as it may reinforce the importance of humanism and altruism in lecture dominated curriculums and provides an opportunity to connect formal knowledge with experiential learning. There is potential that other medical schools could utilize camps as experiential elective sites. Our plans include conducting individual more in-depth interviews with the students 6 months after their experience to explore the long-term effects of this program.

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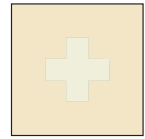
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## COLUMBIAN COLLEGE OF ARTS & SCIENCES

### Medical students' perceptions of ultrasound use for Gross Anatomy teaching by clinicians and anatomists

The utilization of bedside ultrasound by an increasing number of medical specialties has created the need for more ultrasound exposure and teaching at the medical student level. Although there is a widespread support for more vertical integration of ultrasound teaching throughout the curriculum, little is known about whether the quality of ultrasound teaching differs if performed by anatomists as opposed to clinicians. The purpose of this study is to evaluate medical students' perceptions of ultrasound anatomy teaching by clinicians and anatomists.

#### METHODS:

Study participants were the consenting first year medical students at The George Washington University Medical School enrolled in the fall semester Anatomy course. Three interactive ultrasound modules were taught by seven teachers (three anatomists and four clinicians). Students were divided into groups, rotated teachers between sessions, and voluntarily completed an anonymous survey after every module. The eight-question survey used a 5-point Likert scale, with a section for free response. Quantitative data from the survey are reported as means, standard deviations, and analyzed by two-tailed unpaired t-tests and a Univariate Analysis of Variance as appropriate. Qualitative data from the free response sections was analyzed for themes.

#### RESULTS:

For the clinician instructors, with the number of evaluations returned (n) equaling 277, the average mean and standard deviation per question on the 5-point Likert scale was  $4.84 \pm 0.42$ . For the anatomist instructors,  $n=159$ , the average mean and SD was  $4.72 \pm 0.58$ . The data demonstrated a slight, although non-statistically significant preference of the students to the clinicians' teaching. No major statistically significant differences were observed between the two groups of instructors with respect to preparation and knowledge. The two evaluation questions that resulted in a statistical significance were "Did the teacher present the information in an organized fashion?" and "Do you feel that ultrasound is helpful with understanding the anatomy?" with  $p \leq 0.001$  for both. Furthermore, the data show an increase in positive student responses to the anatomy faculty instruction as the sessions progressed, corresponding with the increased comfort level of the anatomists in teaching using ultrasound. This phenomenon is further reinforced by the qualitative data.

#### CONCLUSIONS:

The data suggest that even with minimal training, anatomists are as facile at teaching ultrasound anatomy as clinicians. Furthermore, with enough training and substantial teaching practice, the anatomists could easily use ultrasound as an effective teaching tool, based on the concept of a learning curve that was evident in the data.

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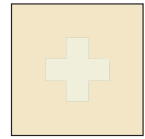
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## COLUMBIAN COLLEGE OF ARTS & SCIENCES

### Medical students' perceptions of ultrasound use for Gross Anatomy teaching by clinicians and anatomists

#### OBJECTIVE:

The utilization of bedside ultrasound by an increasing number of medical specialties has created the need for more ultrasound exposure and teaching at the medical student level. Although there is a widespread support for more vertical integration of ultrasound teaching throughout the undergraduate curriculum, little is known about whether the quality of ultrasound teaching differs if performed by anatomists as opposed to clinicians. The purpose of this study is to evaluate medical students' perceptions of ultrasound anatomy teaching by clinicians and anatomists.

#### METHODS:

Participants were first year medical students at The George Washington University Medical School enrolled in the fall semester Anatomy course. Three hands-on, interactive ultrasound modules were scheduled as part of the Gross Anatomy course following principles of adult learning and instructional design. Seven teachers (three anatomists and four clinicians) taught in each session. Prior to each session, anatomists were trained in ultrasound by the clinicians. Students were divided into groups, rotated teachers between sessions, and completed both quantitative and qualitative evaluations.

#### RESULTS:

Data demonstrated a slight, although non-statistically significant preference of the students to the clinicians' teaching. However, no major statistically significant differences are observed between the two groups of instructors with respect to preparation and knowledge. In addition, the data show an increase in positive student responses to the anatomy faculty instruction as the sessions progressed, corresponding with the increased comfort level of the anatomists in teaching using ultrasound.

#### CONCLUSIONS:

The data suggest that even with minimal training, anatomists are as facile at teaching ultrasound anatomy as clinicians. Furthermore, with enough training and substantial teaching practice, the anatomists could easily use ultrasound as an effective teaching tool, based on the concept of a learning curve that was evident in the data. This study will allow medical educators to assess ultrasound teaching by both anatomists and clinicians, and encourage the assimilation of hands-on ultrasound into human anatomy courses. This research will also have implications for medical school curricula, with emphasis on human resource utilization and allocation.

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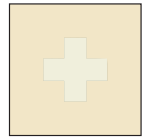
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Confidence, Knowledge, and Skills at the Beginning of Residency: A Survey of Pathology Residents

#### OBJECTIVES:

In medical school, pathology is not a core clinical clerkship. Elective experiences can be highly variable, which may lead new residents to feel underprepared for pathology residency. To assess this, we created a survey to document the pathology learning experiences residents had prior to starting pathology residency and to determine how confident they were with various skills and knowledge.

#### METHODS:

We designed an anonymous online survey utilizing SurveyMonkey software and e-mailed the link to all pathology residency program directors in the United States. We requested that interested program directors forward the survey link to their residents. Data was obtained on pathology electives, grossing experience, and frozen section experience. Likert scale questions assessed confidence level in knowledge and skills. For analysis, we considered an answer of very or extremely to be "confident" and an answer of slightly or not at all to be "not confident".

#### RESULTS:

201 pathology residents responded (31.9% first year, 23.9% second year, 21.8% third year, and 22.3% fourth year). Prior to starting residency, 15.4% were confident in their surgical pathology knowledge. 141 reported doing a surgical pathology elective in medical school. Of those who did a surgical pathology elective of at least four weeks (105), less than four weeks (34), or did not do a specific rotation (51), 21.9%, 6.0%, and 7.8% felt confident in their surgical pathology knowledge, and 63.8%, 38.3%, and 51.0% felt confident in their understanding of resident duties on surgical pathology. For grossing small cases, 6.4% of people who never grossed, 10.3% who only observed, 39.7% who only grossed small cases, and 85.2% who grossed both small and large cases felt confident, while 6.5%, 1.5%, 1.7%, and 48.1% felt confident grossing large cases. Of those with no experience, who only observed, and who actually cut frozen sections, 9.5%, 10.1%, and 58.4% felt confident they could cut frozen sections.

#### CONCLUSIONS:

Prior to beginning residency, most people are not confident in their surgical pathology knowledge and skill set, such as grossing and cutting frozen sections. The length of a surgical pathology elective appears to have a beneficial effect on confidence in surgical pathology knowledge when it is at least four weeks long. The effect of elective length on the understanding of resident duties on the surgical pathology service is less clear. For improving confidence in surgical pathology specific skills, hands-on experience is beneficial, but observation alone is similar to having no experience at all.

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#### STATUS

Staff

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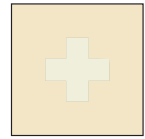
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Text-message Reminders Increase Patient Attendance at Outpatient Appointment Following ED Visits

#### BACKGROUND:

Timely and appropriate outpatient follow up to ED visits reduces healthcare costs, inefficiencies within the system and improves health outcomes. These appointments are often made or recommended in the ED, but attendance is low (less than 70% at LAC+USC). Patients most often report that they failed to attend scheduled appointments as a result of forgetfulness or confusion regarding dates, times, and locations of these appointment. A simple text-message reminder system may be the key to resolving this clinical problem.

#### OBJECTIVE:

To study the effect of a fully automated text-message reminder system on patient attendance to follow-up outpatient appointments.

#### METHODS:

Research Assistants (RAs) approached a consecutive sample of ED patients prior to discharge to screen for eligibility. Patients were included if they had an appointment scheduled between 3 days and 4 weeks of the ED visit. Patients were excluded if they were critically ill, admitted from the ED, had no subsequent outpatient appointments, did not speak English or Spanish, did not own a mobile phone or know how to receive a text-message or mobile phone carrier incompatible with the text message delivery system. The RAs provided a list of upcoming appointments to all patients. Patients were randomized to usual care versus the text reminder arm. Patients in the treatment arm received text message appointment reminders including date, time, and location at seven, three and one day prior to their appointment. Their attendance at these appointments was collected by RAs reviewing their outpatient records 30 days after enrollment, and the attendance rate of the intervention and control group were compared with a two sample t-test.

#### RESULTS:

2365 patients were approached. 1862 were excluded (254 for critical illness, 81 for language other than English or Spanish, 278 for not having a mobile phone, 76 for not knowing how to receive a text message, 72 for refusal of consent, 287 for admission and 794 for no outpatient appointments scheduled). Control and intervention group were similar in age, language and ethnicity. The intervention group attended 73.5% of outpatient appointments compared to 62.1% of the control group ( $p=0.027$ ).

#### CONCLUSIONS:

A simple text-message reminder system increased patient attendance at outpatient appointments following ED visits, potentially improving health outcomes and inefficiencies in the system.

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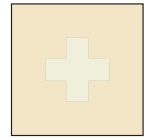
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Media Literacy and Homeless Teens

#### BACKGROUND:

Currently, there are almost 600 children living inside DC's main emergency shelter for families, located at DC General Hospital. Teen Night is a program of the Homeless Children's Playtime Project working directly with teenagers aged 11 to 17 at the shelter. The authors created a project attempting to develop an effective, sustainable curriculum exploring media literacy as a strategy for sex education and to provide homeless teens with the critical thinking skills necessary to make positive decisions about their sexual health. The study is a qualitative evaluation of the sex education sessions. Three sessions were developed to build awareness of how the media influences youth's view of sex and relationships and focused sequentially on the following topics: personal boundaries, respectful talk and the media's influence, and strategies to think critically about media messages regarding sex. The teens were randomly divided into 2-3 discussion groups.

#### METHODS:

A six question open answer survey designed to assess the teens' beliefs regarding personal boundaries, respectful talk, sex and relationships was administered prior to the first session and will be administered again after the final session on March 7th. Two investigators independently analyzed the survey answers by grouping like responses and identifying themes. They then met to review their theme analysis and reconcile any differences between identified themes. The post-test survey will be analyzed with the same method followed by a comparison of pre- and post-test responses.

#### RESULTS:

The pre-test survey analysis identified 4-6 different themes for each survey question. Some of these themes showed the teens believe boys are fundamentally different from girls. In terms of respectful talk, the teens said it would not include bad words or bad names, but would include a respectful manner. Some surprising comments included cyberbullying as a form of crossing boundaries and talking to a gang member when feeling they are in trouble. The post-test survey is pending and will be administered March 7th with results to follow.

#### CONCLUSIONS:

Many of these homeless adolescents have health beliefs that indicate they have a relatively good understanding of boundaries and respectful talk. However, based on some of the comments, not all of the teens exhibit healthy behaviors. Conclusions about the sexual education program will be determined after the final session. We hope to work with HCPP to continue to provide sex education focusing on media literacy in the future.

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#### STATUS

Graduate Student

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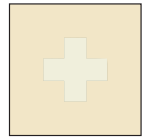
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Improving OB/GYN Anatomy Education through Nesting Interactive and Clinically Relevant Anatomical Sciences E-modules in the curriculum

#### BACKGROUND:

Deficits in retention of anatomy knowledge from the pre-clinical years to clinical application on the wards have been well documented in the medical education literature. Preliminary data from our research of third-year medical students entering the Obstetrics and Gynecology (OB/GYN) clerkship reveal weaknesses in knowledge of vascular anatomy, lymphatic anatomy, neuroanatomy, and embryology.

#### OBJECTIVES:

The goal of this study is to design, implement, and evaluate an interactive method of teaching clinically relevant anatomy to medical students on the OB/GYN clerkship through computer-based e-modules and related anatomy laboratory sessions.

#### METHODS:

Two educational models will be designed and their effectiveness evaluated by multiple choice testing and subjective surveys:

1) Adult learning-based e-modules were created by utilizing Camtasia, software that incorporates imported media and interactive content while recording on-screen activity. These modules highlight clinically relevant anatomical topics including perineal anatomy/laceration repair, abdominal wall anatomy/cesarean section, adnexal anatomy/ovarian cystectomy, and uterine anatomy/hysterectomy, among others. The e-modules include an assessment of baseline knowledge, an interactive learning session, and post-activity evaluations of comprehension and effectiveness.

2) Hands-on, interactive sessions for the anatomy laboratory have been developed to reflect the content of the e-modules, applying principles of adult learning and instructional design. These include model building and practicing clinical techniques.

#### PRELIMINARY RESULTS AND CONCLUSIONS:

Our integrated clinical teaching model builds on our unpublished study data, which indicates a need to close the anatomical knowledge gap found in medical students entering the third year clerkship. Our preliminary data so far predicts the success of nesting the anatomical sciences, when relevant, into the curriculum. Our multi-disciplinary team is currently designing interactive modules and will be assessing their effectiveness in the coming academic year. We hope to demonstrate that using this nesting technique improves clinically-relevant anatomical knowledge in adult learners.

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#### STATUS

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Graduate Student

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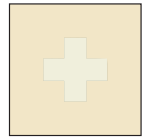
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Circumcision and your female patients: A review of the literature

#### BACKGROUND:

Female genital mutilation is a cultural tradition legally practiced in many countries throughout Africa, the Middle East and Asia. The World Health Organization defines female genital mutilation as “all procedures that involve partial or total removal of the external female genitalia” (World Health Organization, 2013). Procedures are mostly carried out on young girls between infant to age 15. It is estimated that up to 130 million women and girls have already been subjected to some form of FGM. A large number of such women reside in the Washington metro area, and show up as patients to local hospitals and clinics, presenting a need for health care practitioners to be aware of these practices and related complications of care.

#### PURPOSE:

The purpose of this review of the literature was to locate material that would help educate clinicians in North America about cultural practices that will help them better understand their circumcised female patients.

#### OBJECTIVES:

1. Describe the cultural practice and prevalence of female circumcision.
2. Elaborate healthcare complications related to circumcised female patients.
3. Make recommendations for clinicians to better serve the special needs of circumcised obstetric patients.

#### METHODS:

A review of the PubMed, Medline, CINAHL, and Google Scholar was conducted by one student researcher. The search included English language articles dating from 1990 through 2013. Key words used were as follows: female circumcision; female circumcision and western clinics; infibulation; sunna circumcision. Thematic analysis of the retrieved articles was conducted by the student researcher.

#### RESULTS:

Three themes emerged from the literature review, as follows: types of female circumcision; related healthcare complications; and the experiences of circumcised obstetric patients receiving healthcare in western countries.

#### CONCLUSION/RECOMMENDATIONS:

It is important for clinicians to be informed about the special needs of their circumcised female patients who present in local hospitals and clinics. Recommendations are made for ways in which clinicians may better serve these needs.

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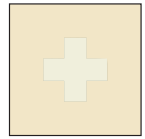
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(2002) Female “circumcision:” African women confront American medicine. *Journal of General Internal Medicine* 12 (8) 491-499.

World Health Organization (2013). Female genital mutilation. Online website retrieved from <http://www.who.int/mediacentre/factsheets/fs241/en/>

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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Understanding medical students' beliefs on abortion and sexual reproduction

#### BACKGROUND/OBJECTIVE:

As a controversial topic in American society, abortion occupies a precarious place in medical school curricula. Although medical students believe abortion is a valid and acceptable topic, fewer than 20% of U.S. medical schools offer formal abortion education in either the pre-clinical or clinical years. Only 40% provide abortion lectures during clerkships. According to Association of Professors of Gynecology and Obstetrics student learning objectives, abortion education should be included at a minimum in the third year core clerkship. In the absence of published curricula, health professional schools must develop their own methods to teach the medical aspects of the subject while respecting all points of view. This research presents a reproducible structure for addressing both medical and ethical considerations in educating pre-clinical students about abortion.

#### METHODS:

After being informed of the study, second year medical students enrolled in Practice of Medicine, Problem Oriented Case-Based Learning (PCL) attended a required Ethics Lecture, during which they used an audience response system to answer questions. Their answers were tabulated to measure the range of student opinions. Students were then invited to post questions to the library blog. Over the next three weeks, students in established small groups discussed a case that illustrated reproductive decision-making. They were invited to post reflections about abortion issues to a monitored Blackboard Discussion Board. Though allowed to post anonymously, ground rules required them to adhere to basic standards of professionalism. All identifiers were removed from the Blackboard postings. Content was coded to identify themes and subthemes. At the end of the case, 140 students completed a qualitative/quantitative survey and 112 agreed to participate in the study.

#### RESULTS:

Over 80% percent of students who responded to the survey found the case helpful in identifying physician's roles with respect to reproduction. Ninety six percent agreed that abortion was an appropriate topic to cover. The Blackboard postings identified major themes including physician responsibilities, unbiased information, and abortion laws. A constant theme that emerged was students' acknowledgement of the complications of abortion and the ethical dilemmas physicians face.

#### CONCLUSION:

Case based learning, a framing lecture, and a safe place to express and challenge opinions together constitute an effective strategy for introducing a controversial topic in medical education. In order to better assess the impact of the Case, we plan to follow up with the students and conduct a focus group of third-year medical students after completing their OBGYN rotation.

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#### STATUS

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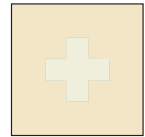
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Evaluating the Impact of a Multidisciplinary Approach to Teaching Mobile Healthcare in a Graduate Education Setting

#### PURPOSE:

Mobile healthcare is a rapidly evolving opportunity to leverage technology to improve access and quality of healthcare while reducing costs and increasing the mobility of patients and providers. Innovations are often created by technical experts without adequate knowledge of the interplay between various mobile health agencies (i.e. clinical, business, regulatory, etc.). In order to improve the communication and cross-silo collaboration between mobile health leaders in a variety of fields, a multidisciplinary approach to education is necessary. Integrative teaching has received relatively little recognition in the medical education literature. This study will evaluate the effectiveness of a multidisciplinary format to teach the topic of mobile healthcare to graduate students from various professional backgrounds.

#### METHODS:

During a one-week intensive course, 32 students received mobile healthcare training at GW. Lectures given by a variety of experts explained how business models, research design, and policy influence mobile healthcare and global health needs. Surveys were administered to evaluate the impact of each lecture on students' growth in knowledge and level of communication based on their current field of study or employment using a 6-point Likert scale, excellent (1) to poor (6).

#### RESULTS:

Students with knowledge of the lecture content gave an excellent rating of 1.61 in increased understanding of mobile healthcare. Students without content knowledge gave a very good rating of 2.38 in increased understanding of mobile healthcare. Ratings of increased ability to communicate in subject areas produced slightly lower results of 1.72 for those with content knowledge and 2.77 for those without. Analysis of ratings in specific subject areas was mostly consistent except for research design. This content area was given ratings closer to good in both increased understanding and communication by students with background knowledge (2.13, 2.24) and students without (2.96, 3.08).

#### CONCLUSIONS:

The multidisciplinary format to teaching mobile healthcare appears to have a positive increase in student understanding and ability to communicate in associated fields. The impact of growth in knowledge was apparent for students with and without background knowledge regardless of content area. These results support the use of multidisciplinary education in fields such as mobile healthcare that require collaboration from various professions. Future studies will consider the long-term benefit and alternative modalities of integrative teaching methods.

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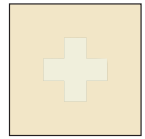
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### A Review of SPs in Medical Education

Standardized patients (SPs) are people who are trained to portray patients during interviews and physical examinations by medical students or doctors in training. They are used to depict realistic patient interactions and help students identify symptoms and signs of particular illnesses. After each encounter with a student, SPs are responsible for evaluating the performance to determine proficiency in both the interview and physical examination process. This is done by following a pre-determined checklist.<sup>1</sup> Thus, SPs provide the opportunity for students to learn and be evaluated on skills firsthand.<sup>2</sup>

One method of applying SPs in medical education is through OSCEs (objective structured clinical examinations), or case-based scenarios. The OSCE format can include teaching and learning opportunities, formative and cumulative assessment, or both. Students are assigned tasks in stations that utilize SPs and involve specific simulated cases. In this multiple-station setting, clinical skills can be taught and evaluated in a systemic and standardized manner.<sup>3</sup>

In the United States today, to become a licensed physician medical students are required to pass a clinical skills assessment with standardized patients as part of the medical licensing examination.<sup>4</sup> The clinical skills examination (CSE) has become a part of the United States Medical Licensing Examination (USMLE) by the National Board of Medical Examiners (NBME). Thus overall, the use of SPs and OSCEs in teaching and evaluating clinical skills is widely accepted as beneficial.

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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Does it take a village? Examining the role of social support in residency training.

#### OBJECTIVE:

The aim of this study was to describe the strength of social support networks of Obstetrics and Gynecology(ObGyn) residents and to determine if the strength of these networks impacts quantitative measures of residency success.

#### METHODS:

32 Obstetrics and Gynecology residents were surveyed at a large university program using the Norbeck Social Support Questionnaire (NSSQ). The NSSQ is a valid and reliable measure of social support networks. Resident's composite scores on were compared to the control group, ie. the "average person" from Norbeck's original study and then correlated with quantitative measures of residency success. Council on Resident Education in Obstetrics and Gynecology (CREOG) test scores and a compilation score of resident evaluations from faculty members were used as the basis for comparison of residency success.

#### RESULTS:

32 of 39 residents participated in this IRB approved study. Mean age was 28-29 and 85% were female. Mean number of people in a resident's social network was 10.5.

The NSSQ results on average showed that ObGyn residents had statistically significant higher levels of emotional support than the "average" person (152.9 vs. 123.3, p value 0.02). ObGyn residents had total network support (99.0 vs. 96.0, p value 0.73 ), aid (60.0 vs. 62.3, p value 0.81), functional support (210.5 vs. 201.9, p value 0.61) and network size (10.5 vs. 10.9, p value 0.71) equivalent to the "average" person. Obgyn residents experienced an average higher loss score than the "average" person (4.3 vs. 2.3, p value 0.0001), although the percentage of residents whom experienced loss was equivalent to the "average" control group (40%).

Social support was not correlated with residency success in terms of CREOG scores or Evaluation scores. The subgroups with the most correlation were: men's social support correlated to CREOG score ( $r = 0.72$ ) and Asian's social support correlated to faculty evaluation score ( $r = -0.99$ ) and CREOG score ( $r = -0.76$ ). Age, female sex, white race, black race did not correlate with measures of residency success.

#### CONCLUSIONS:

The Norbeck Social Support Questionnaire is a valid and reliable measure of total network support, as well as emotional support, aid and total loss. ObGyn residents in this academic institution seem to have a high level of emotional support and a high level of total network, but may be lacking in terms of tangible support functions such as aid and network size. This may be related to living away from family and friends.

Interestingly, the selected measures of residency successes were not correlated to level of social support. This could reflect that the effect of a strong support system may be better examined by other measures than CREOG scores and faculty evaluations or that social support is not a factor in performance during residency training.

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#### STATUS

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Staff

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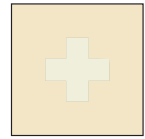
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# EDUCATION/HEALTH SERVICES



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Study on Residents Early in Training: Are They Observed, Do They Receive Quality Feedback and Does Time of Shift Matter

#### BACKGROUND:

Concerns exist about lack of faculty observation and the quality and frequency of feedback when PGY-1s perform procedures early in training. Lack of direct observation precludes the documentation of resident competency and reduces opportunities for feedback. Faculty availability nights and weekends could influence these factors.

#### OBJECTIVE:

Ob-Gyn PGY-1s completed a questionnaire when they performed procedures in order to: 1) document their experience being observed doing procedures 2) document their feedback experience and 3) determine the impact of the timing of their work shift on the observations and feedback they received.

#### DESIGN/METHODS:

Ob/Gyn PGY-1s at George Washington University were asked to log the following information on SurveyMonkey on 8 different 12 hour shifts in August, 2012: type of procedures they performed using a standardized checklist; who observed them performing the procedure; the frequency, timing and quality of feedback received; and time of their shift.

#### RESULTS:

Nine of the ten PGY-1s participated in the study. They recorded data from 33 of 72 possible shifts (46%), a mean of 4 shifts/resident. They reported that 71% of their total procedures (N=662) were observed. Senior residents observed them 43% of the time, nurses 15% and faculty 13%. PGY-1s reported receiving feedback 29% of the time--more likely on writing admission orders, hand-offs and performing a delivery. They reported feedback to be effective 96% of the time they received it and this did not differ regarding who provided the feedback ( $p=0.7384$ ). The shift had no statistically significant effect on the frequency of observation and feedback. Faculty, however, were more likely observers during the day ( $p<.0001$ ) and nurses during evening/weekend shifts ( $p<.0001$ ). Senior resident observations were split equally day and evenings/weekends.

#### CONCLUSIONS:

PGY1s reported being observed performing patient care activities 71% of the time. Senior residents and nurses were more likely than faculty to observe PGY-1s. Faculty were less likely to observe PGY-1s on nights and weekends. No matter who observed them, PGY1s reported receiving feedback on only a small percentage of these interactions. Program directors in all specialties will need to formulate plans for faculty to directly observe and provide feedback for PGY-1s early in their training to ensure competency as the milestones are implemented.

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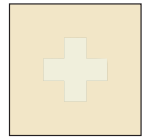
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Anatomical Knowledge Retention prior to Surgical Rotations

#### BACKGROUND:

Important surgical anatomy, such as vascular, abdominal, pelvic and neural anatomy, is taught early in medical school training. The literature shows that many physicians, especially surgical specialists, feel anatomical education of medical students is significantly inadequate and nesting of anatomical sciences in the curriculum is needed. This is of great concern for students entering their surgery rotation and quantitative data concerning this anatomical knowledge deficit is lacking.

#### OBJECTIVES:

The goal of this assessment is to identify areas of strength and weakness in surgical anatomy knowledge in medical students entering the surgical rotations, our first step in the nesting process.

#### METHODS:

One hundred thirty-two consenting third-year medical students at a large, urban medical school completed a 20-25-question evaluation prepared by anatomy faculty to assess retention of surgically relevant anatomical knowledge at the beginning of the general surgery and obstetrics and gynecology rotations. Examinations were scored, with questions divided into anatomic categories, based on the assumption that the knowledge in those areas should have been 100%.

#### RESULTS:

Over 87% of students were able to identify cross sections of structures on computed tomography scan. Students performed similarly well discussing breast anatomy with 92% of students answering questions correctly. Around 60% of students were able to answer questions about the abdomen and vertebral landmarks correctly. Retention of vasculature, inguinal and peripheral neural anatomy was poor, with only 45%, 44% and 32% of students answering respective questions correctly. Only 56% of students correctly answered questions concerning the anatomy of the uterus and fallopian tubes, and 51% had knowledge of pelvic vasculature. Students scored significantly lower in knowledge of lymphatic drainage of the pelvis (10.7%) and embryology (44.6%). Having had a prior surgical rotation, such as obstetrics and gynecology, did not improve students' anatomy knowledge at the beginning of the general surgery rotation as compared to having no prior surgical experience ( $p = 0.25$ ).

#### CONCLUSIONS:

Knowledge of surgical anatomy is varied for medical students entering clerkships in general surgery and surgical subspecialties. The data collected will be utilized to create interactive learning modules using principles of active learning and instructional design, aimed at improving clinically-relevant anatomical knowledge, a second step in the nesting process in our curriculum. These modules will be available to students prior to their inpatient surgical rotations with the goal of closing their anatomical knowledge gap, thus making them more successful on their surgical rotations.

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#### STATUS

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Graduate Student

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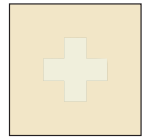
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Determining the Impact of External Stressors on Laparoscopic Skills and Performance

#### OBJECTIVE:

To evaluate the impact of external stressors on laparoscopic skills of Obstetrics and Gynecology Residents.

#### METHODS:

Residents completed two laparoscopic exercises divided into four modules each comprised of tasks that were novel to the residents. Module A tested the resident's dissection skills. Module B tested bi-manual dexterity and depth perception. Module C tested hand-to-hand coordination and Module D tested hand-eye coordination and bi-manual dexterity. In order to avoid repeat testing bias, the laparoscopic sessions were carried out six months remote from each other.

The first session served to establish performance baseline whereby tasks were carried out with no external stressors present. During the second session, the same modules were carried out in the setting of pre-determined stressors including unexpected camera movement and clearly defined and verbalized time constraints. Performance was assessed by the time required to complete each module was measured and the accuracy with which each module was completed was measured by a predetermined penalties for each module. Residents were also assessed for subjective measures of stress during both sessions by an administration of a Perceived Stress Survey (PSS) after modules were completed. A baseline PSS was established 2 weeks prior to session two. Data was analyzed using paired t tests and Wilcoxon signed-rank test with a p value of <0.05 considered as significant.

#### RESULTS:

The findings are summarized in table 1. Residents completed the modules quicker when stressed. Stress had an adverse effect on accuracy for 3 of the 4 modules (A, C and D). As compared to the baseline PSS of 14.5/36, no significant change was observed in the post session PSS (15.8/36).

n= 13	Module A Dissection Glove		Module B Ring of Fire		Module C Cobra		Module D Ring Transfer	
	1	2	1	2	1	2	1	2
Session #	1	2	1	2	1	2	1	2
Time (sec)	217.2	116.4	110.9	60.8	271.8	258.5	203.6	172.3
Penalties	1.2	1.8	6.4	5.2	1.3	3.2	1.2	4.1

#### CONCLUSIONS:

Stress appears to reduce the amount of time required for and the accuracy with which residents complete laparoscopic tasks. It is known that stress hinders learning. Our data indicate that stress hinders accuracy and, given the requirement for accuracy in laparoscopy, support the need to minimize stress in the training residents.

#### STATUS

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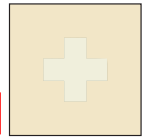
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### A Cost Effective Approach To Microbiological “Send Out” Test Requests: An Interdisciplinary Laboratory Utilization Management Program

The management of laboratory testing continues to be an ongoing challenge. We describe the design of a laboratory utilization and management program for the cost effective, clinically relevant use of microbiological “send out” tests, implemented in close collaboration with the Division of Infectious Diseases (ID), at an urban, medium sized academic hospital. The structure of this program defines the Clinical Pathology (CP) house staff member, as the “Gatekeeper” for approval of send out microbiological tests. Orders are received by “Client Services” staff members, who have been instructed to divert send out test requests to the CP house staff. Medical records are reviewed, and requests are either approved or held, pending interaction with clinical house staff. The interaction may be a phone call, or require direct contact and discussion. The interaction with clinical house staff is facilitated when ID has been consulted in the care of a patient. Pending patient test requests are discussed at interdisciplinary microbiology rounds, which are conducted three times a week in the Microbiology Laboratory. At these rounds, ID and CP house staff and the attending Microbiologist discuss ongoing patient care and present laboratory testing requests. We retrospectively analyzed send out test requisitions in order to evaluate the impact of this interdisciplinary program. A total of 403 requisitions were screened by CP house staff: 71% (287) were approved and 29% (116) were canceled. Canceled tests were further delineated into two categories that best described why the test was canceled, including pre-analytical problems (60%) and no clinical indication for the test (40%). In our experience, when ID was present at microbiology rounds, it was significantly easier to facilitate which send out tests were needed or relevant to patient care. Our goal, through this interdisciplinary approach, is to further the cost effective, clinically relevant usage of laboratory testing thereby allowing us to serve as a resource to both Hospital house staff and Laboratory management teams.

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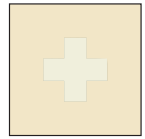
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Understanding the experience of mature-aged medical students compared to traditional medical students in the clinical setting

#### BACKGROUND:

Although the mean age of first year medical students is 24, an increasing number of "mature-aged" students, defined as over age 30, are entering medical school. These non-traditional students often report a different medical training experience compared to their younger counterparts. These students may be in their 30s or 40s, may already have families, and may have established themselves in another career before pursuing medicine. Most studies of mature-aged medical students have examined academic performance using quantitative research design. Few studies have employed qualitative methodology to determine the experience of mature-aged medical students, especially in the clinical setting. Therefore the purpose of our study is to understand the experience of mature-aged medical students on clinical rotations.

#### METHODS:

A recruitment e-mail was sent to all medical students enrolled in clinical rotations; first responders were interviewed until saturation in emerging themes was achieved. Interviews were conducted and recorded in a private office setting, then transcribed into a Word document. Five mature-aged students and four traditional students were interviewed. The investigators individually coded the transcripts to identify emerging themes. Coded themes underwent peer review, with triangulation of data collection, to determine main themes.

#### RESULTS:

Three main themes emerged from our study. First, abundant life experience influences students' perception of their role on clinical rotations. A mature student explained, "...having kids... being married and divorced... helps in connecting with patients." Previous work experience shapes expectations as a physician-in-training. While traditional students tend to be "intimidated," mature students desire to "take the initiative." Age plays a role in the students' ability to relate to senior team members, as well as medical student colleagues. Traditional students note that mature students are "more realistic" due to their "life experience in the workplace."

#### CONCLUSION:

Mature-aged students draw upon previous life experience, which shapes role expectations, as well as medical team dynamics. These differences may have implications in training the growing number of mature-aged medical students. A larger scale qualitative study including multiple medical school sites is being developed.

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#### STATUS

Graduate Student

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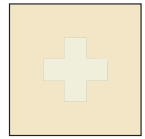
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### A just-in-time e-learning modified barium swallow program improves knowledge in pediatric radiologists

#### BACKGROUND:

Modified barium swallows are challenging studies to interpret and teach due to the complexity, subtlety, and rapidity of abnormal swallowing. Advancements in communication technology have popularized “e-learning” as an efficient learning tool with potential benefits ranging from reduction in costs, standardization of knowledge, and better delivery of educational materials. Just-in-time learning (JITL) is a structured, self-directed approach to online learning that targets a physician’s specific clinical needs. It was hypothesized that a JITL training module would enhance knowledge and improve interpretation skills. In particular, the value of dynamic embedded video to enhance understanding of normal and abnormal swallowing mechanisms was studied to evaluate the benefits of JITL in radiology education.

#### METHODS:

A learning website was created that provided easy access to educational and evaluation materials. A total of 32 video clips including multiple examples of normal and abnormal swallowing were transferred from the kayPENTAX swallowing station to .flv format and embedded in the pre-test, post-test, and training modules. The pre- and post- tests consisted of five basic knowledge questions and six video interpretations; the training module consisted of an anatomy, physiology, and pathology primer followed by annotated video with multiple examples of each abnormality.

#### RESULTS:

11 attending pediatric radiologists and 5 pediatric radiology fellows participated in the program. The participants’ mean pre-test correct values were 43.75% (n = 16) for basic swallowing knowledge and 73.33% (n = 15) for video interpretations. Mean post-test values were 90.00% (n = 16) (p < 0.0001) for basic knowledge and 91.11% (n = 15) (p = 0.06) for video interpretations.

#### CONCLUSION:

Just-in-time e-learning is an effective way to improve knowledge of normal and abnormal MBS studies. However, it was not statistically shown that the module increased interpretation performance. One possible explanation is that basic knowledge may not be reinforced by the day-to-day activities of the practicing radiologist whereas radiographic interpretive skills remain the same or are enhanced by daily experience. Nevertheless, a JITL model could be utilized for radiology education for both residency and continuing medical education, and affords many advantages such as being able to set an individual learning pace, high accessibility, and relatively short/concise educational segments. Further studies are needed to assess the efficacy and agreeability of a large scale roll-out of e-learning training

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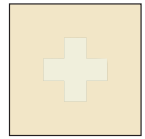
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Assessing the cultural beliefs of medical students: impact on the cadaveric dissection experience in the gross anatomy laboratory

It is well established that cadaver dissection offers a beneficial learning experience to medical students in gross anatomy courses. Although researchers have sought to identify different learning styles in the dissection lab among students of various nationalities, no study has addressed the specific question of how a student's cultural identity or beliefs play a role in the emotional aspect of cadaver dissection.

The purpose of this study is to examine the emotional impact of cadaver dissection across cultures and whether this impact affects the learners or learning experience. This is a quantitative/qualitative study targeting first year medical students of various cultural backgrounds partaking in cadaveric dissection. Students will be recruited via e-mail and will complete an online survey.

Based on preliminary oral responses, a relationship between students' cultural identities and unique experiences in the gross anatomy laboratory was reported. This study will help medical educators understand the student learning experience of cadaveric dissection as it relates to cultural identity and will facilitate the preparation of students for the dissecting room experience.

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#### STATUS

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Graduate Student

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A new E-Professionalism/Social Media course: student reflections and impact

#### BACKGROUND:

This poster provides a review of interim results from a qualitative study on first year medical students' attitudes and perceptions of their definition of medical professionalism in social media. Included in the study is an evaluation of changes in perspective since becoming a medical student and after participating in an E-Professionalism and Social Media instructional session.

#### METHODS:

In January 2012, the authors developed and led a session for first year medical students focusing on e-professionalism and social media. During the session, real-life examples of health care professionals and students posted content on social media (e.g. Facebook, blogs, Twitter) generated discussion about appropriate and inappropriate uses. A panel of GW physicians who use social media spoke about their own experiences and guiding principles, and answered questions from the students. After the session, students reflected in writing in response to brief prompts about their own experiences with social media both before and after entrance to medical school, and outlined their current behavior and expectations as a result of attending the educational session. Prompts included:

- Who are you representing online?
- How do you define e-professionalism online?
- How has your social media identity changed since you entered medical school?
- After participating in [the social media instructional] session, are you considering changing anything in your social media presence?
- If you were to draft a "social media guideline" for the incoming first-year class what would it look like?

A subset of students consented to participate in the study; their written reflections were de-identified, and then coded by two investigators to elicit common themes. All four investigators met to reconcile codes and ensure inter-rater reliability.

#### RESULTS:

Sixty-four students consented to participate in the study.

The analysis is only partially completed but so far multiple themes have emerged including:

- Online presence representing self, profession, family, and future career
- Changes in social media activity since entering medical school such as limiting access, changing content, increased awareness of possible repercussions, changes in amount of use
- Changes in social media presence after the workshop including increased awareness of positive uses of social media in medicine, and changes in content or access to personal sites

#### CONCLUSION:

Medical students are consumers and producers of social media. Including online professionalism in the curriculum in this way with a focus on implication and best practices can help them develop an awareness of their professional presence in this electronic era.

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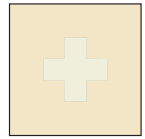
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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Assessing the USMLE Step 2 CS exam

#### BACKGROUND:

The USMLE Step 2 Clinical Skills examination was introduced to medical students in 2004 in order to assess students' clinical competence. The exam consists of 12 patient encounters in which students are evaluated on their clinical skills, interpersonal and communication skills, and English proficiency. Step 2 CS is currently offered in 5 cities and costs \$1200 to register. By 2011, a total of 118,333 US/Canadian students had taken their first attempt at this exam, and a total of \$122,254,700 had been paid in registration fees alone for first-time attempters.

#### OBJECTIVES:

To assess the value and impact of the USMLE Step 2CS in the educational process of US medical students, by doing an economic analysis, looking at the pass rates of the exam, and by speaking to medical school deans across the country.

#### METHODS:

A literature search was performed to research the exam. A financial analysis was performed by obtaining the number of students who had taken the exam and the registration fee for Step 2CS from the USMLE website. Next, using financial aid office estimates and the varying locations of medical schools, travel expenses were averaged at \$300. A list of 25 medical school Deans was made, and they were contacted by email. The 8 who agreed and were able to schedule an interview were interviewed via the phone.

#### RESULTS:

Our financial analysis showed Step 2CS cost medical students an estimated total of \$157,754,600 by 2011. Of the Student Affairs Deans that were interviewed, there were a variety of opinions. Some stated Step 2CS has helped medical schools improve clinical competency and helped drive curriculum. Another interviewee noted that this exam helped with funding for a comprehensive OSCE. Several Deans however feel that the exam is unnecessary; adding to students' debt, adding more stress to fourth year, being scheduling burden, and is redundant since a comprehensive OSCE is already in place. No Dean reported having a student that did not eventually pass, our current data shows a 99.7% passing rate. Additionally, almost all Deans agreed that they have a comprehensive OSCE in place for third/ fourth year medical students, and that they did not find the NBME score sheet helpful.

#### CONCLUSIONS:

Our research has shown that this is exam is a significant financial burden. With a possible pass rate of 99.7%, it is not identifying many clinically incompetent students. Over the past decade, most schools have implemented a comprehensive OSCE that could replace this exam.

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#### STATUS

Student

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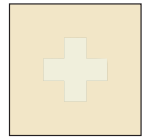
Dr. James Scott, MD



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# EDUCATION/HEALTH SERVICES

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## SCHOOL OF NURSING

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### Family Caregiver Training - Results from a literature review

#### BACKGROUND:

Family caregivers provide care to individuals who otherwise may be in a hospital, nursing home or assisted living facility. The role of the family caregiver is to be responsible for the care of an individual with a chronic condition by providing support and meeting their physical and emotional care needs. Training and education in the role of the family caregiver varies dramatically. Much of the currently training that is developed relates to a specific disease or type of patient, such as Alzheimer's disease or disabled veterans.

#### PURPOSE:

The American Red Cross (ARC) is considering becoming more involved in providing comprehensive family caregiver training. The results of this literature review will afford guidance to the ARC regarding the development of a comprehensive training program for family caregivers who are either currently in the role, or may need to assume the role in the future.

#### METHODS:

A comprehensive literature search utilizing multiple databases as well as the support of an expert librarian was performed. A thorough review of published evidence was performed and a table of evidence was created utilizing the Oncology Nursing Society's weight of evidence classification schema. The Prepared Family Caregiver model, developed by Houts, Nezu, Nezu and Bucher in 1994, utilizes four components of creativity, optimism, planning and expert information (COPE). This theoretical model will be utilized to guide the development of the training.

#### RESULTS:

Evidence from the literature review indicates that training that is individualized and incorporates a variety of media methods can be an effective method to provide didactic as well as hands-on skill building education to family caregivers.

#### CONCLUSION:

By utilizing evidence from the literature, the ARC will be able to develop a comprehensive training program that will promote resiliency and allow family caregivers to increase self-efficacy and self-mastery.

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#### STATUS

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Semi-Automated Scoring of Triple-Probe FISH in Human Sperm with Spectral Imaging and Linear Unmixing

Our experimental approach involves analysis of the frequency of X18, Y18, XX18, YY18, and XY18 from human sperm. Multi-probe fluorescence in situ hybridization (FISH) for chromosomes X, Y, and 18 was done to determine sex-chromosome disomy in sperm nuclei. Manual FISH scoring in sperm smear is labor intensive and introduces errors in variability due to investigator's fatigue; therefore, automated methods that rely on computer software to count fluorescence signals are needed.

Particularly challenging is the four labels span the entire visible spectrum while overlapping in both excitation and emission. Furthermore, the auto fluorescence overlaps with multiple probes, resulting in diminished signal to noise or false granularity that could be detected by the software as FISH signal.

In the initial studies, the emission peaks of Spectrum Aqua probe used to detect chromosome 18 (480 nm) and commonly used nuclear counterstain DAPI (470 nm), were too close. So we replaced DAPI with Topro-3 (661 nm). Although Topro-3 and Spectrum Orange (588 nm) emissions were spectrally too close to separate using conventional fluorescence microscopy, spectral imaging using online linear unmixing can be employed to separate these fluorescence emissions and to produce intensity modulated channels corresponding to the spatial contribution of each fluorophore. We adapted the linear unmixing procedure from commercially available software (Zeiss). Images were acquired with a Zeiss LSM 710 confocal microscope with Apochromat 63X/1.4 oil objectives in a high throughput manner. Z-stack were acquired from multiple positions preprogrammed on the system. Ten optical sections were acquired at each position and projected using maximum intensity. Image processing, segmentation, classification, and scoring were performed using custom image processing and analysis software developed in MATLAB® (Natick, MA). A Gaussian filter and adaptive histogram equalization were applied to all image channels [Topro-3 (nuclear), Spectrum Aqua (18), Spectrum Orange (Y), and Spectrum Green (X)] to reduce noise and to correct non-uniform field brightness. Image intensity threshold values were manually selected to partition images into background and foreground components. Threshold values were therefore visually adjusted for each image acquisition session to afford optimal segmentation of nuclei and signals.

With this approach, we are able to acquire data consistent with the previous literature. Among 12 men analyzed using the semi-automated method, median total sex chromosome disomy frequency was 1.62%, which is within range with previous reports. These results further validate that semi-automated methods can be used to score sperm disomy with results comparable to manual methods.

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# ENVIRONMENTAL SCIENCE

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Waste Diversion DC: A Clinton Global Initiative University 2011/12 Commitment

#### OBJECTIVES/BACKGROUND:

Recycling an empty drink container or a paper flyer at an outdoor event should be easy. Unfortunately, in Washington, DC, an event host can gain a Special Event Permit without providing any recycling or waste diversion infrastructure during their event. This lack of infrastructure places the responsibility of recycling at events solely on the attendees rather than being a joint effort between the host and the attendees. The outcome - most recyclable or compostable waste generated at these events lands in the trash. This burden negatively impacts the environment and places financial strain on the municipal government. In a time where climate change mitigation is a surmounting priority and government finances are strained, Waste Diversion DC (WDDC), set out to collect the data necessary to encourage the District of Columbia Council Members to change the special event permitting process, such that waste diversion is a mandatory component of all successful applications.

#### METHODS:

WDDC received \$10,000 in award money, and hundreds more with in-kind services. On October 7, 2012, WDDC ran a comparative study at 'Taste of DC' a 100,000 person-strong annual food event. The project employed and trained 31 low-income workers to assist in our project, 25 volunteers and enlisted the services of the DC Department of Public Works.

#### RESULTS TO DATE:

We were able to divert over 200 pounds of waste over a 3-hour period and our preliminary analysis shows that the staffed stations - stations that incorporated education from trained staff - had the most success; increasing recycling by 60% and increasing composting by nearly 50%, compared to the other stations.

#### CONCLUSIONS:

The outcome of this intervention was clear - when you offer waste diversion stations to event patrons, they will be used; when you staff these waste stations, the items collected are sorted more effectively than stations without support staff. These results have been presented to DC Council in the form of a policy recommendation, which also highlights existing event waste policies across the United States. This poster presentation will demonstrate the successes and challenges of Waste Diversion DC, along with a progress report for the policy change recommendation to DC Council.

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Graduate Student

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Is rushing a risk factor for laceration injury? It depends on how researchers ask the question.

#### BACKGROUND:

Little is known about the causes of laceration injury in meatpacking operation despite of its high prevalence.

#### METHODS:

Telephone-based interviews were conducted with workers who experienced laceration injuries at two pork processing plants within 14 days of the injury. In a narrative analysis, workers' responses to two open-ended questions about the causes of injury were analyzed and classified into 13 categories. In a case-crossover analysis, a Mantel-Haenszel estimator for person-time data was used to estimate association between risk of injury and each of seven transient risk factors.

#### RESULTS:

For knife-related injuries (N=96), results from narrative analysis identified rushing (33.0%) as the most common self-reported cause, followed by personal protective equipment (32.1%). Case-crossover analysis found that tool sharpening (RR: 8.26, 95% CI: 5.66, 12.06) and being tired (RR: 2.62, 95% CI: 1.43, 4.79) had significantly elevated risk ratios. For non-knife-related injuries (N=189), narrative analysis identified rushing (27.0%) and maintenance (22.2%) as the most common self-reported causes of laceration injuries. Case-crossover analysis found that equipment malfunction (RR: 7.97, 95% CI: 5.69, 11.17), using unusual work methods (RR: 4.87, 95% CI: 3.07, 3.93), and performing an unusual task (RR: 2.96, 95% CI: 2.23, 3.93) had significantly elevated risk ratios.

#### CONCLUSIONS:

Rushing was the most common self-reported cause of lacerations in narrative analysis, however it was not associated with elevated risk of laceration injury in case-crossover analysis. This paper found different hazards emerged as risk factors for laceration injuries based on the framework of questions and analysis methods used by researchers.

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# ENVIRONMENTAL SCIENCE

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Occupational Health in the Construction of the New GW Public Health Building: Evaluating Fall Safety among Skilled Trades in Construction

#### OBJECTIVE:

Falls are one of the leading causes of workplace death, lost work time, and costs to industry, particularly in construction. The public health burden of falls is significant, as approximately 25% of nonfatal injuries and 38% of fatalities in the general construction industry are due to falls. The goal of this study is to develop an assessment tool to evaluate fall safety in general construction and to evaluate fall safety among five skilled construction trades (i.e. electricians, painters, carpenters, welders, and roofers) throughout different stages of a new building construction project. The project is the new School of Public Health and Health Services building at The George Washington University at Washington Circle in Foggy Bottom, Washington, DC, being built by the general contractor The Whiting-Turner Contracting Company.

#### METHODS:

A comprehensive assessment instrument was developed through review of pre-existing assessment tools and modified according to Occupational Safety and Health Administration (OSHA) standards for general construction, validated through inter-rater reliability by a panel of experts (including the on-site safety superintendent), and tested for on-site usability through a two-week pilot study. Data were collected using the GW Audit of Fall Risk (GAFR) instrument by a master's-level researcher through routine observation of the construction site throughout the five construction phases (i.e. concrete pouring, skin, interior rough end, interior finishes, and roofing).

#### RESULTS:

Collected data are organized in the GAFR assessment instrument into eight domains: general safety, guardrails, personal fall arrest, safety net system, roof sheathing, scaffolding, aerial lifts, and ladders. Observations are scored dichotomously as to whether or not it was observed, and if observed, whether or not it meets the definition of best safety practice (as noted in OSHA regulations). Though the study is still ongoing, the current collected data presents statistics on the prevalence of fall hazards, and the frequency of fall safety compliances for each of the five trades by construction phase.

#### CONCLUSIONS:

Fall hazards in skilled trades have been understudied. This unique university-general contractor partnership capitalizes on the opportunity to ensure public health principles are being realized during construction. This presentation will include the application of the GAFR assessment instrument and the current preliminary results, highlighting the importance of observational assessment of worksites. Additionally, the lessons learned from the field assessments will also be discussed.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Environmental Pyrethroid Exposures and Sperm Chromosomal Abnormalities

#### BACKGROUND:

Reproductive problems are increasing among the US population, specifically human infertility due to male factors. Previous researchers have been trying to characterize environmental exposures and their impact on men's reproductive health. The role of environmental contaminants, such as pyrethroid pesticides, and their relationship to sperm abnormalities is still not well understood.

#### OBJECTIVES:

This research aims to understand contemporary environmental exposures to pyrethroid pesticides and their association with altered frequency of chromosomal abnormalities (e.g., disomy) among adult men.

#### METHODS:

A subset of 75 men from a larger study assessing the impact of environmental exposures on semen was used in this investigation. Men between 20-54 years of age, seeking an infertility evaluation from the Massachusetts General Hospital, were eligible for the parent study (N=341). Participants provided urine and semen samples. Study subjects completed a self-administered questionnaire which collected information about medical history, demographic and lifestyle factors. Pyrethroid metabolites urinary concentrations [3-phenoxybenzoic acid (3PBA), cis- and trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (CDCCA and TDCCA)] were analyzed using high-performance liquid chromatography. Multiprobe fluorescence in situ hybridization for chromosomes X, Y, and 18 was used to determine XX, YY, XY and total sex chromosome disomy in sperm nuclei. Descriptive statistics were summarized for subject characteristics and outcome variables. Poisson regressions were used to model the association between pyrethroid exposures and disomy measures.

#### RESULTS:

Most men were white (90%) and non-Hispanic (96%); only 4% were current smokers and 77% of men had never smoked. About 56% of the pyrethroid metabolites urinary samples were above the limit of detection (LOD). All urinary metabolites were highly correlated ( $r = 0.92-0.97$ ). All types of disomy rates were increased by 8- 32% for men with CDCCA and TDCCA exposure levels above the LOD when compared to men below the LOD. For 3PBA exposure levels, YY18 disomy adjusted IRR was 1.29 times higher (95% CI: 1.16, 1.43) when compared to men below the LOD. An inverse effect was observed for XY18 disomy adjusted IRR and no effect was observed for XX18 and total disomy.

#### CONCLUSIONS:

This is the first epidemiologic study to examine the relationship between environmental pyrethroid exposures and sperm chromosomal disomy outcomes. These findings suggest that increased rates of disomy were associated with CDCCA and TDCCA exposure levels above the LOD; 3PBA findings were not consistent. The results of this study will be used to inform upcoming analyses in larger samples.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Environmental exposures to non-persistent pesticides and sex chromosome disomy in human sperm

#### BACKGROUND:

Aneuploidy, or an incorrect number of chromosomes, is the most common form of chromosomal abnormality, and sex chromosome disomy is the most frequent aneuploidy found in human sperm. While most aneuploid conceptions are lethal, certain types will result in viable offspring with abnormal karyotypes. While the underlying mechanisms of chromosomal nondisjunction are not well understood, a limited number of studies have reported associations between occupational exposure to non-persistent pesticides and increases in the frequency of sex chromosome disomy in human sperm. Non-persistent pesticides are commonly used residentially and in agriculture as insecticides.

#### OBJECTIVES:

This study will seek to evaluate the potential associations between environmental exposures to two non-persistent pesticides, carbaryl and chlorpyrifos, and the frequency of sex chromosome disomy in human sperm.

#### METHODS:

Urine and semen samples were collected from 192 men seeking evaluation for infertility at the Massachusetts General Hospital (MGH) Fertility Center. Two pesticide metabolites, 1-naphthol (1N) for carbaryl and 3,5,6-trichloropyridinol (TCPy) for chlorpyrifos, were detected in urine via GC/MS-MS and LC/MS-MS, respectively. Semen analysis for concentration, motility and morphology was conducted by the MGH clinic prior the disomy analysis. Disomy was assessed using fluorescence in-situ hybridization (FISH) with probes for chromosomes X, Y and 18. After imaging each sample using a wide-field fluorescence microscope, samples were scored using custom Matlab software that identified nuclei meeting inclusion criteria and signals contained within those nuclei. The software used a co-localization analysis to assess the frequency of three disomic conditions: XX18, YY18 and XY18.

#### RESULTS TO DATE:

Preliminary assessment of the exposure data shows that a majority of the men in the study had levels of 1N (98.4%) and TCPy (91.1%) above the method limits of detection. Of the 192 semen samples, 43.75% (n=84) had at least one semen parameter below the WHO reference criteria (i.e., concentration >20million sperm/mL, >50% motile sperm or >4% normal forms). The mean (standard deviation) percent disomy for each disomic condition were: XX18: 0.41(0.40); YY18: 0.38(0.33); XY18: 1.11(0.83); and total disomy: 1.90(1.26). Statistical analyses for this presentation will use Poisson regression to assess associations between exposure to carbaryl (as 1N) and chlorpyrifos (as TCPy) and the frequency of sex chromosome disomy, and will include covariates such as age, smoking status and abstinence time.

#### CONCLUSIONS:

This study will be one of the first to assess whether exposures to two non-persistent pesticides at environmentally relevant levels are associated with sex chromosome disomy in human sperm.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Healthcare in Khon Kaen, Thailand: A Comparison of Culture and Clinical Medicine

**BACKGROUND:**

For my summer experience, I traveled to Thailand as George Washington's first international summer intern for a new clinical elective program at Khon Kaen University.

My main objectives were threefold: to discover the medical educational differences between Thailand and America; gain clinical knowledge of the diagnosis and care of patients in Thailand in the Orthopedic Surgery and Obstetrics and Gynecology department; and create a student manual and web-blog for future GWU classes traveling to KKU to learn about my experiences.

**METHODS:**

I spent six weeks working in Srinagarind Hospital in Khon Kaen, Thailand: four weeks in the orthopedic surgery department and two weeks in the Ob/Gyn department. For the remaining two weeks I created a manual for future GW students traveling to Thailand. While in Thailand, I assisted the staff both in out-patient and in the OR. In orthopedics, I assisted physicians by casting clubbed feet, suturing, and scrubbing in on surgeries. In Ob/Gyn I performed pelvic exams, annual exams, prenatal exams, and witnessed both cesarean and vaginal deliveries.

**RESULTS:**

As a foreigner, I first learned basic words and phrases and how to understand the Thai culture. Almost all professors and students can speak English. However, most patients, and general public don't speak any English. It is not traditional to hug or shake hands. The traditional Thai greeting is called a "whi", where you put your palms together in a prayer-like gesture and bow to the person. Students are very soft spoken and it is perfectly acceptable to laugh or giggle with the professor and in front of the patient.

I witnessed the Doctor-patient relationship in Thailand first hand. There is no patient confidentiality in Thailand, but it maximizes time and space. There are generally 2 people interviewed within one outpatient room, and all patients share one room when in-patient. For the most part, international students cannot communicate directly with the patients because of the language barrier. I could communicate with the physicians, but learned to speak slowly, and be patient when misunderstood.

Thailand medical practice greatly differs from the US. While medical school in America is 4 years, it is 6 years in Thailand, and therefore students go straight from high school. George Washington University gets about 10 cadavers donated a year, while KKU has around 50 donated for the orthopedic residents alone. Between all the departments 7,500 bodies are donated each year. The OR in Thailand is different from America in many ways. First, the scrubbing-in technique is different. In America the scrubbers you use are disposed after one use, but in Thailand they can be autoclaved and reused. In Thailand you wear communal sandals in the OR. Lastly, everything in America is disposable with a one-time use: gloves, gown, instruments etc. In Thailand, everything can be reused. The gloves used during surgery are opened for the first time, but once you are finished with them you put them in a re-use bucket where they are cleaned and used for non-sterile techniques.

**CONCLUSION:**

Through my experience, I learned about Thai people and their culture, Doctor-patient and Doctor-student Relationships, Communicating with Patients and Doctors as a foreigner, Thailand Medical Practices and How They Compare to the US.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Health Prevention and Prevention in the Janampet Community, Andhra Pradesh, India

#### BACKGROUND:

The provision of basic education on personal hygiene, typhoid and dengue fever endemic to a remote area such as Janampet, in Andhra Pradesh will create an awareness and in the long run can be beneficial in lowering the incidence of disease.

#### OBJECTIVES:

To educate the children in the Janampet community to effectively combat the incidence of Typhoid and Dengue fever through preventative techniques and maintenance of personal hygiene and learn effective ways to implement health promotion and prevention in the Janampet community. The current status on educating children on disease is limited to the disease concepts learned in their respective class level curriculum. The current prevalence of Typhoid and Dengue fever in this community went from almost 70 cases a month in 2005 to 1 to 2 cases a month in 2012.

#### METHODS:

Three-week period of didactic training in the topics of personal hygiene, typhoid and dengue fever. Knowledge based pre and post-surveys were conducted on 3rd, 8th and 10th grade classes of St. Lucy's Medium High School to assess understanding of the concepts taught.

#### RESULTS:

After the end of the three-week training period, the 3rd grade students whose average age was seven went from getting 9% -58.5% of the class getting all the questions correct in the personal hygiene lesson. There were similar results in the 8th and 10th grade classes. The 8th graders whose average age was 13 went from no more than 50% to over 80% of the class getting all the questions correct for both Dengue and Typhoid fever lesson. Similarly, the 10th graders whose average age was 16 went from 0%-25% of the class getting all questions correct in the Dengue fever session. The assessment on the level of improvement in the knowledge of Typhoid fever could not be made because a pre-survey was not carried out for the 10th graders.

#### CONCLUSION:

The results of the survey demonstrates that the 3rd, 8th and 10th grade students were better able to recognize the mode of transmission, signs and symptoms and treatment of both Dengue and Typhoid fever. A future assessment should be carried out to observe the statistical impact of child education in the incidence these diseases in the local community of Janampet.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Examining the Impact of International Volunteer Service and Village Health Teams on Community Health in Uganda's Mukono District

In many third world countries there is a dramatic shortage of doctors available for the countries growing population. Similarly, the countries infrastructure lacks adequate public transportation at an affordable cost. This is especially true throughout the continent of Africa. As a result, many people do not seek care until it is too late and do not receive basic medical education on how to keep their family and themselves healthy. To try to alleviate this issue many countries have begun training community health workers. In Uganda, they are called Village Health Teams (VHT). VHTs are people selected by their community to serve three functions: 1) instruct villagers in preventive medicine, 2) become local first responders and links to local health centers, and 3) to track health data for the Ministry of Health. To explore this idea VHTs are being trained within the Mukono district in Uganda to determine the effectiveness of incorporating a villager with basic health information on general health within the community. Omni Med is a program that has been in place since March 2008. In an effort to train VHTs in Uganda, members of this non-governmental organization partnered with the Ugandan Ministry of Health, the US Peace Corps, and St Elizabeth's Medical Center in Boston. The goal of this partnership is to revive a previously successful program led by the Ugandan Ministry of Health and empower local communities to improve their own health and create a sustainable and measurable health impact. Volunteers from the United States are employed to carry out this effort by assisting in the education of VHTs, but local Ugandans are essential to make this program successful. The VHTs live in rural communities and are trained to provide primary and preventative health care. The hope is that by empowering local communities to improve their own health care in Uganda's Mukono District, there will be measurable impact on life expectancy, infant, and child mortality. An initial randomized controlled trial carried out by this NGO and researchers from Washington University and Makerere University found that VHTs trained in the Mukono District were able to make a measureable improvement in the health behaviors of local villagers, as long as the behaviors did not rely on externalities (such as ITNs, ORS packets, antibiotics, anti-malarials, etc) that required villagers to spend scarce resources.

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#### STATUS

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Project Anoopam Sanjivani Health Awareness

#### BACKGROUND

Anoopam Sanjivani Health Awareness Project was founded by Anoopam Mission and is dedicated to the tribal populations of Narmada District, Gujarat, India. Anoopam Mission has adopted 132 villages of Narmada District and started working in the areas of health and hygiene improvement, education, self-employment, and integrated, sustainable development of the villages.

#### OBJECTIVES

- Identify common illnesses, disease motifs common to the underserved populations in the tribal villages of Narmada District
- Understand the contribution of biopsychosocial elements present for the manifestation of recurrent and continued disease within the region
- Understand the current problems faced by the villagers and Anoopam Mission healthcare providers in order to effectively apply medical interventional strategies to both remove and prevent the villagers from the sustained cycles of disease
- Observe the action of Anoopam Mission healthcare providers and local Indian Government on the wellbeing of the villagers and the effects on the incidence and prevalence of certain diseases in Narmada District

#### METHODS

4 weeks were spent in an observational study, rounding with a team of onsite medical officers. Both the villagers and healthcare providers were interviewed regarding the types of illnesses prevalent within the region and the biopsychosocial causes of these common diseases. A week was spent researching and interviewing the local government's forest conservation officers and their role in the development of the wellbeing of the villagers. 3 weeks were spent performing independent research on the socioeconomic and cultural demographics of Narmada District and reviewing literature on the prevalent diseases of the region to better understand the medical interventions that were employed by the healthcare providers.

#### RESULTS

The prevalent diseases of Narmada District include: general and protein-energy malnutrition, micronutrient deficiencies, parasitic worm infections, scabies, lice and nits, bacterial and fungal infections. All of these illnesses were found to be worsened due to poor geographical situation of many villages, lack of infrastructure, and major deficiencies in education, hygiene, health, and poverty.

#### CONCLUSIONS

The villagers' way of life intrinsically increases their susceptibility to disease which synergistically affects their economic productivity further sustaining the deeply-seated poverty and the related diseases of poverty—undernutrition and malnutrition (Khan & Bhutta, 2010). With this fact, the Anoopam Mission healthcare providers and local government officers are not only treating the individuals burdened with illnesses but are also educating them the importance of daily health and hygienic practices and providing their villages with proper infrastructure and self-sufficient sources of employment.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Diabetes among Arab immigrants living in northern Virginia

**BACKGROUND:**

There is a high prevalence of diabetes in the United States. Today, 18.8 million have been diagnosed, but roughly 7 million are living undiagnosed with this silent disease. In the Arabic population there is no consensus on the burden of the disease, but prevalence estimates range from 5-30% depending on geographical location and data sets.

**OBJECTIVE:**

The objective of this study is to statically calculate the prevalence of diabetes among low socioeconomic immigrants seeking healthcare from a faith based organization in Northern Virginia.

**METHODS:**

Data was extracted from electronic medical records (EMR) to identify patients who showed clinical signs of diabetes (type I and type II). Factors such as cholesterol levels, glucose levels, hemoglobin A1c levels, weight, height, BMI, and related diseases were recorded in Microsoft Excel. Screening of undiagnosed patients will commence in March.

**RESULTS:**

Data collection is currently under way. At the time of submission, 68 EMRs have been extracted to reveal preliminary results indicating that a majority of diabetic patients in Northern Virginia are of Arabic, Korean, and Hispanic descent.

**CONCLUSION:**

Preliminary evidence indicates that diabetes is a significant problem in this population. Factors such as poor screening, language, transportation, and monetary funds may be barriers for this population in receiving diagnosis and treatment.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Medical Training in Beirut Lebanon

#### BACKGROUND:

Lebanon is one of the most advanced countries in the Middle East, and the American University of Beirut Medical Center (AUBMC) is a top-ranked hospital and medical school in the region. Nevertheless, Lebanon's 16-year civil war and continuing national and regional political tensions and conflicts have challenged significant efforts to fully modernize its healthcare system. My objectives were to 1) learn about Lebanese health care and medical student training, 2) gain skills and knowledge in Emergency and Family Medicine, and 3) develop enhanced cultural awareness and understanding to guide future endeavors in the United States and abroad.

#### METHODS:

Eight weeks in Beirut were split between the AUBMC Emergency Department (ED), and Family Medicine Service. I also made several visits to the Lebanese American University (LAU) Volunteer Outreach Clinic (VOC) in a Palestinian refugee camp. In the ED, I worked alongside American University Beirut (AUB) third-year medical students, interviewing patients, performing physical exams, ordering tests, and presenting my findings to physicians. The Family Medicine rotation featured site visits to familiarize students with community resources. Together with my cohort of fourth-year AUB medical students, I visited a rehabilitation hospital, a residential drug rehabilitation facility, and a school and support facility for children with mental and physical disabilities.

#### RESULTS:

The AUBMC ED is similar to a U.S. university hospital ED; the most prominent difference is that patients must pay for any required laboratory test or medicine before it is administered. The AUB medical students, who effortlessly switched between Arabic, English, and French, seemed to have very similar training to GW medical students. The community resources we visited with the Family Medicine rotation were impressive; the children's school, for example, had computers operated by breath and laser gait analysis. The LAU VOC was a basic facility located in an extremely impoverished and neglected community. Still, I came away impressed by the dedication of the physicians who staff the clinic, as well as with the fact that these visits are required for LAU medical students.

#### CONCLUSION:

The high quality of the medical care and medical education in Beirut impressed me. Particularly notable was the emphasis by AUB and LAU on social medicine, evidenced by AUB's holistic Family Medicine rotation and LAU's commitment to staffing the refugee camp medical clinic and training their students to care to the underserved.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Postnatal confinement: A blind spot in Maternal and Neonatal Health Programming

#### BACKGROUND:

Globally, 25% of neonatal deaths occurring in India, with most occurring in resource limited settings at home against a backdrop of high risk practices and behaviors, poor care seeking, and limited access to care. Despite the existence of cost effective interventions, the early neonatal period has received very minimal impact in mortality reduction because of the inability of health workers to perform early home visitations. This study will be a sub-study of the Shivgarh trial, a RCT looking at behavior change in reducing neonatal mortality that reduced NMR by 50% by performing home visitations to the "saur". The Saur is a community innovation and intervention that was created to prevent neonatal and maternal mortality.

#### OBJECTIVE:

To explore the historical and cultural basis of postnatal confinement in a northern Indian context.

To examine the role of this cultural phenomenon in delivering critical newborn care intervention and improve care seeking.

To describe how one intervention, the Saksham intervention, worked with the community, and its practices, to deliver critical interventions at the right time.

#### DESIGN METHOD:

Researches, in 2003, facilitated 83 in-depth interviews, 8 focus groups and collected 2 direct observations of deliveries in the home. Follow up to the Shivgarh intervention was performed in 2010 to assess how practices had changed over time.

#### RESULTS:

The saur's origins are rooted in three concepts: vulnerability, pollution, and consideration, which are reinforced for by tradition. These concepts contribute to the strict rules for entrance and exit into the saur. Although the exit of the newborn from confinement and the entry of others into confinement are strictly regulated, neither is entirely prohibited. The Saur is actually porous. Families will only allow access to the newborn to members who they believe will help the child in the cultural paradigm of illness, which is evil spirits. Negotiation into Saur was the critical part of the Shivgarh intervention.

#### CONCLUSIONS:

For any intervention to successfully impact the neonatal period, navigation into the Saur is a critical component. The only way to enter the Saur is by understanding and respecting the cultural paradigm that shaped it. Only then can an intervention be designed to fit the espoused values. Recognizing and appreciating confinement and the associated practices will allow interventions to have tremendous success. There is a blind spot that exists in interventions is that this confinement's role in service delivery is not recognized and is under appreciated.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Understanding Adolescent Sexual Health in Yaruqui, Ecuador

#### OBJECTIVE:

Understand unique aspects and barriers in the sexual health of adolescents in the Yaruqui area of Ecuador and develop a survey that will be distributed and analyzed by local physicians and healthcare officials to guide future programs on adolescent sexual health and adolescent pregnancy.

#### BACKGROUND:

Yaruqui is a rural town located in the outskirts of Quito, the capital of Ecuador, which serves as a major community hospital for many smaller rural clinics in the surrounding region (Area de Salud 14). Yaruqui and the subcenters in Area 14 are public hospitals and clinics operated by Ecuador's Ministry of Public Health (Ministerio de Salud Pública or MSP). The MSP currently has public health programs for adolescents in place but it remains evident by physicians in the region that adolescent pregnancy continues to be a significant social issue and further work needs to be done to uncover details such as the frequency of adolescent pregnancy, risk and protective factors that contribute to early pregnancy, and the adolescent thought process and outlook toward sexuality.

#### METHODS:

The survey was developed through a combination of literature research, weekly discussion with local physicians, and working in clinics with adolescents performing well child check-ups and family planning. International and national studies in other parts of Ecuador served as a foundation for creating the survey for Yaruqui. Weekly discussions with local physicians were utilized to add additional questions that would be both culturally sensitive and community specific. The downside to these additional questions was that they were not verified in previous studies.

#### RESULTS:

The survey compiled contained 140 questions and addressed over 10 different aspects of adolescent sexual health. From familial environment, economic status, and sexual education to religion, psychosocial conditions, and knowledge of contraception, abstinence, and the act of sexual intercourse, the questionnaire tried to address the adolescent's outlook on sexual health. Ultimately, the survey was given to local physicians in order to initiate research in the community, with the discretion to modify the survey as needed to best serve the community and research.

#### CONCLUSION:

By working in clinics with adolescents, performing well child check-ups, doing family planning, and consulting doctors and psychologists, we were able to develop the aforementioned survey in order to aid the current research in greater addressing some of the problems and misconceptions behind the rising adolescent pregnancy rate in rural Ecuador. The goal is that this survey can be utilized as a tool by physicians and healthcare officials to guide future programs on adolescent sexual health and pregnancy.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Clinical Rotations and Frontiers in Translational Medicine in Madrid, Spain

**OBJECTIVES:**

My main goal for my translational research internship at University of San Pablo-CEU was to actively participate in an international laboratory research collaboration and have the opportunity to become involved in direct patient-based clinical care as it is practiced in a contrasting cultural setting. Spain was a natural choice as I was interested in observing and participating in practices and procedures comparable to the United States as well as improving my Spanish.

**METHODS:**

I spent 8 weeks at Hospital Madrid in Montepincipe, which is one of five in a system of hospitals in the greater Madrid area. I started on a clinical rotation in the GI department, after which I transitioned into surgery. My focus in the translational program was the molecular pathophysiology of surgical oncology with an emphasis on cancer metastasis scoring using clinical parameters from the gene expression profiling of liver tissue and primary tumors from patients with early stage colorectal tumors as well as a study of proteomics on the tumor interstitial fluid factors from primary tumors.

**RESULTS:**

When I arrived, the research was still in its preliminary stages, due to the ongoing development of a novel procedure. I was able to observe the process, however, the project was not far enough advanced for my involvement. Instead, I spent the bulk of my time in clinical rotations, mostly in the GI department and surgery. I was able to observe and assist in a wide range of surgeries and procedures. During the second month of my internship, I attended a translational research seminar course, which featured various researchers from around the world, who presented their work on the translational research frontier, on topics such as bone pathophysiology, cancer microenvironment, regenerative medicine, infectious diseases and cardiovascular diseases. This course was very fascinating and an exceptional way to gain exposure to the innovative, cutting edge research in the global research community.

**CONCLUSIONS:**

Although I was not able to participate in the research portion of this program, I was able to focus my time more heavily on the clinical, as well as cultural, aspect. It was a tremendous learning experience, which gave me invaluable insight and exploration in to the various specialties. In effect, it helped shape my future goals and gave me a very strong sense of what I desire in my clinical practice and what I hope to accomplish as a physician.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Infrastructure for Health: Empowering Village Health Teams in Uganda

#### BACKGROUND:

The Ugandan National Health System, primarily organized by the Ministry of Health, utilizes community health workers which are structured as Village Health Teams (VHTs). Omni Med, a Boston-based NGO, works with the Ministry of Health to train and mobilize VHTs in the Mukono District.

#### OBJECTIVES:

Understanding how VHTs are empowered to improve health in their communities, educating VHTs in health and medicine, mobilizing VHTs by providing motivation and oversight, and understanding VHT-member experiences through focus groups.

#### METHODS:

Omni Med works with community chairpersons to organize VHT elections. Subsequently, Omni Med holds a training course on health topics like hygiene and malaria prevention and on practical topics like record-keeping and coordination within the broader National Health System structure. Omni Med conducts focus groups, performance reviews, and continuing education programs to help sustain the VHT's impact.

#### RESULTS:

Many VHT members are dedicated and capable to apply their health knowledge and perform their responsibilities. They eagerly participate in continuing education and initiatives like community-wide vaccination days. They are accepted and valued by their communities. Members report barriers to effectiveness in limited transportation, time, and mobile communications.

#### CONCLUSIONS:

As millions suffer preventable morbidity and mortality, there is opportunity to thwart these human rights violations by building an infrastructure for health, that is, the systems necessary for hygienic lifestyles and access to healthcare in times of illness. Uganda's VHT model carried out by Omni Med's training and mobilization efforts is an effective starting point for building infrastructure for health in underdeveloped regions. Though stunted economic and infrastructural development remains the overarching barrier to healthcare access, VHTs are indispensable conduits for better health in communities that would be otherwise cut off. It cannot be ignored, however, that VHT programs cannot long exist without new measures for permanent incentive, management, and coordination.

#### STATUS

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#### SOURCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Clinical Apprenticeship in Orthopedic Surgery and OB/Gyn at Khon Kaen Univeristy in Khon Kaen, Thailand

During the summer of 2012, the Health Services Scholarship afforded me the opportunity to travel to Thailand and participate in an eight-week medical student exchange program at Khon Kaen University situated in Northeast Thailand. The hospital affiliated with KKU is government funded, and the largest in the region, serving millions of patients annually. Khon Kaen University Medical School is establishing itself as an educational hub and recently took a spot on the top 50 Medical Schools in Asia list. As such, they are relatively technologically advanced in many areas. However, given the largely impoverished population of the Khon Kaen province, stark differences between Thai and American medical practices still exist. The goal of my summer project in Thailand was to experience medicine in a drastically different cultural setting in order to expand my understanding of medical practices on a global scale. Without a doubt, I accomplished this mission. Additionally, myself and Elizabeth Brunn were the first two students from GW to travel to Thailand through the Global Health Track. Part of our mission was to establish (or veto) KKU as an appropriate site for medical training abroad and to explore possible options for future students from GW to participate in at KKU. The exchange program set up by KKU has much room for improvement, but on a whole I would consider the experience to be tremendously beneficial and hope GW students participate in future years. Lastly, I wanted to use the experience as a starting point for creating a manual for future students travelling abroad in medical settings. The current first-year curriculum is lacking sufficient training in basic skills that American medical students are often expected to know when travelling abroad. While working at KKU, I identified a core set of skills to include in my manual, but I would like to survey other students who travelled abroad to learn from their experiences as well. My experience in Thailand was the first step in establishing what I hope to be a "crash course" in technical skills, basic pharmacology and cultural sensitivity for first year students travelling abroad. This project will require research, surveying and faculty support, which I hope to continue working on throughout my third and fourth years in conjunction with my POM scholarly project.

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#### STATUS

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Development and Implementation of a Sustainable Obstetrics and Gynecology Residency Program in Eritrea: A Model for Other Programs

**OBJECTIVE:**

To describe the experience of planning, developing, and implementing a unique Obstetrics and Gynecology postgraduate medical education program set in Eritrea.

**DESIGN:**

This is a descriptive study which outlines the cooperative work between the George Washington University Medical Center (GWUMC), Physicians for Peace, and the Eritrean Ministry of Health in The Partnership for Eritrea. Project collaborators drafted a curriculum modeled after the OBGYN residency training curriculum used at GWUMC, and modified it according to the unique needs and circumstances of the country of Eritrea. No prior residency program in Obstetrics and Gynecology had existed in Eritrea. The OBGYN residency program follows successful implementation of Pediatrics and General Surgery residency programs in Eritrea, launched in 2008.

**SETTING:**

Asmara, the capital city of Eritrea.

**RESULTS:**

The OBGYN residency training program at the Orotta Maternity Hospital in Asmara started in August 2009. Five fully trained Obstetrician Gynecologists graduated in February 2012. The Program Director assisted in the selection and initial training of a new class of OBGYN residents in September 2011, ensuring the continuation of the program.

**CONCLUSIONS:**

The Partnership for Eritrea helped to establish a sustainable residency program in Obstetrics and Gynecology in an East African country.

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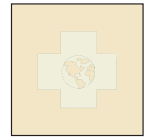
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Health Development Efforts in Communities along the Amazon River Basin

#### BACKGROUND:

The U.S. Naval Medical Research Unit - 6 Perú (NAMRU-6) is hosted by the Peruvian Navy at the Naval Hospitals in Lima and Iquitos. Together they conduct research and health surveillance on a wide range of infectious diseases of military or regional public health significance in the region. These endeavors have also expanded into the foreign aid realm. Each summer NAMRU-6 in Iquitos and the Navy collaborate on health interventions geared towards the communities located on the Momón River in the Amazon River Basin. To better gauge effectiveness of these interventions small teams conducted pre and post assessments with the goal of describing the health status and population needs at baseline and evaluating the impact on well-being outcomes.

#### METHODS:

This assessment had two main components: 1) a quantitative health survey identifying health burdens and 2) a qualitative environmental component focused on identifying attitudes to foreign aid. The study was conducted through convenience sampling of community members from three villages along the Momón River. Participants were selected based on age group: 0-5 and 15-49.

For both pre and post-assessments three procedures were applied: a questionnaire, anthropometric evaluations, and biological specimen sampling. Individuals were asked focused questions about health-related knowledge and behaviors and about immunizations received, perceived health status, recent illnesses, and health care usage. Biological specimens included stool and blood. Stool was analyzed for parasite burden, and blood for hemoglobin level and thin and thick malaria smears.

#### RESULTS:

In the pre-assessment 60 total patients enrolled (55 providing complete samples). Of these 18 children and 42 adults. The amount enrolled per community varied due to population differences. Four participants had positive malaria smears with three of these being asymptomatic for expected symptoms. In terms of parasite burden, nine children tested positive for an enteric parasite. Hemoglobin levels varied between communities, but had a mean of 12.90 +2.09. A T-Test stratifying for age and sex was done to analyze anemia by community. \*Post-assessment data is pending.

#### CONCLUSIONS:

Engaging communities based on their health indicators and assessing local response provided valuable information. Continuing these assessments will allow future interventions to better focus on the population's health needs. These assessments are also feasible at minimal cost.

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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## Social Handwashing Ladder: A practitioner's tool for initiating a handwashing intervention

**OBJECTIVE:**

A handwashing program is a cost-effective, life-saving public health intervention that can help decrease the incidence of various communicable diseases in developing nations. Unfortunately, handwashing interventions in impoverished communities are often hindered by the unilateral promotion of official handwashing guidelines, which are inappropriate for these communities since they assume soap, clean water and towels are readily available.

**METHODS:**

Current handwashing recommendations and their applicability to hygiene interventions in developing nations are discussed.

**RESULTS TO DATE:**

This paper presents a novel handwashing ladder which emphasizes that access to the physical resources of soap, water and towels should be addressed in hygiene interventions. Some examples of how to use this ladder to more sustainably move a population towards best known handwashing practices are also presented.

**CONCLUSIONS:**

This handwashing ladder allows for more sustainable progress in hygiene within a community than previous guidelines, since progress can be made incrementally, and, in many cases, on one individual aspect of the handwashing process at a time.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Children's knowledge and perceptions of Chagas disease through a drawing activity titled "The Pic and My House" in 4 rural villages of Yucatán, Mexico

#### BACKGROUND:

In accordance with the WHO classification of endemic countries, Mexico is placed in Group 2, which refers to those countries that do not have formal Chagas control programs, in spite of the presence of Chagas transmission. In fact, Chagas disease remains grossly underreported, as evidenced by an increasing number of serologic surveys indicating that about 1-2% of blood donors in the Mexican population are seropositive for Chagas *Trypanosoma cruzi*. This would correspond to at least 1-2 million persons exposed to the parasite in the country, with about 70,000 new cases annually. The southern states of Chiapas, Oaxaca, Puebla, Veracruz and Yucatan are among the highly endemic areas. Very limited intervention or education activities exist in these endemic regions, resulting in limited knowledge about Chagas disease.

#### OBJECTIVES:

The aim of the study was to evaluate children's knowledge, understanding and misconceptions about the insect vector and Chagas disease through a drawing exercise called "El Pic and My House." Specifically, the following information was collected from the drawings: Triatomine bug appearance, location and activity; Chagas hosts and vectors; control methods; house description, and written/implied messages. The second aim of the study was to evaluate to what extent previous Chagas prevention education interventions in the community have informed children about Chagas.

#### METHODS:

This study was conducted in 4 villages of Yucatan peninsula where previous Chagas activities have been carried out, but none of which targeted children specifically.

A total of 261 drawings were collected from 4 villages from primary school children, ages 6-12. The images and the messages on the drawings were scored qualitatively. The scoring tool included 6 major themes and 50 subthemes that were inductively and deductively defined. The findings were further examined to determine differences by village, age and gender.

#### RESULTS:

Preliminary data analysis reveals differences in the drawings by village but not by age or sex. The drawings from the villages with more intervention and education activities showed greater knowledge of a number of themes in comparison to villages with less Chagas intervention activities. By April of this year, data analysis and summary of findings will be complete.

#### CONCLUSIONS:

The results of this study demonstrate that drawings can provide valuable insight into children's knowledge and the findings will be very influential in the development of future Chagas education efforts with specific activities for children.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Lessons Learned from Organizations Implementing Income Generation and Health Education Among Indigenous Guatemalan Artisans

#### BACKGROUND:

Many non-governmental organizations (NGOs) in Guatemala strive to alleviate poverty among indigenous women through income generation. Select NGOs incorporate health education within their programs as a strategy to address health more directly. This qualitative study identifies factors essential to achieving success for two such NGOs.

#### OBJECTIVE:

To identify lessons learned and best practices from organizations working to improve the livelihood and wellbeing of indigenous Guatemalan women through income generation plus health education.

#### METHODS:

Researchers conducted semi-structured, in-depth interviews with 34 indigenous Guatemalan women artisans and 9 NGO staff. Interviews explored respondents' experiences with an NGO's income generation and health education activities. Researchers analyzed the data employing a Grounded Theory approach. Researchers later used results to develop a conceptual model illustrating the pathway through which income generation plus health education can improve the lives of indigenous women artisans.

#### RESULTS:

Organizational- as well as artisan-level factors surfaced as instrumental to successful income generation plus health education efforts. Artisans expressed maximizing earning potential by diversifying into non-artisan work. At the organizational level, staff expressed a genuine dedication to the organization's social good mission. NGOs also placed importance on group interactions, which diffused and reinforced health education content. As a result, although health education activities were secondary to income generation, respondents recalled specific health information covered.

#### CONCLUSION:

NGOs implementing income generation plus health education among indigenous Guatemalan artisans have the potential to improve the health and wellbeing of their participants. Future income generation projects may benefit from applying the current study's lessons learned and conceptual model.

#### LEARNING OBJECTIVES:

By the end of the session, the participant will be able to:

1. Identify at least three best practices and lessons learned from organizations working to improve the lives of indigenous Guatemalan women artisans through income generation plus health education
2. Explain the way in which a strategy of incorporating health education within income generation programs can enhance the potential of income generation to improve the health and wellbeing of disenfranchised communities
3. Describe a conceptual model illustrating the pathway to improving the lives of indigenous women artisans through income generation plus health education

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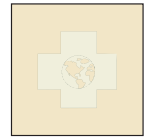
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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Trends and Justification of Intimate Partner Violence in Egypt

#### BACKGROUND:

Intimate Partner Violence (IPV) is an important public health problem in low- and middle-income countries and associated with poor reproductive health outcomes.

#### OBJECTIVES:

The study examined trends in justification of IPV in Egypt in the 2005 and 2008 Egypt Demographic Health Surveys (EDHS).

#### METHODS:

This exploratory study used data from the 2005 and 2008 Egypt Demographic Health Surveys (EDHS). EDHS is a nationally representative survey that uses multistage data sampling. Information on justification of IPV was drawn from 5,450 women in 2005 and 16,527 women in 2008. We conducted bivariate and multivariate analyses of variables related to justification of IPV and its association with reproductive health outcomes.

#### RESULTS:

At the time of this abstract submission only data for 2008 had been examined. Preliminary analysis indicated that 17.5% of women of reproductive age (15-49 years old) reported that IPV is justified if the wife argues with her husband, 32.5% that IPV is justified if the wife neglects her children, and 34.8% that IPV is justified if she goes out without telling her husband. All results will be available by Research Day.

#### CONCLUSIONS:

Egypt continues to have high rates of IPV and justification of it. Studies have demonstrated that prevalence of any justification of IPV is high. Those who justified violence were more likely to have greater negative health outcomes. Women were less likely to report IPV, know where to seek help, or be asked about injuries when IPV is suspected during health visits. Making support services available and educating women of how to access these resources are some of the steps that can be taken to reduce negative health outcomes. Training health professionals for diagnosing and referring injured women to these support services would also help reduce the prevalence of IPV in Egypt.

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#### SOURCES

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Waking up the Mind: Findings from a qualitative study on the empowerment of indigenous Guatemalan women artisans

#### BACKGROUND:

Since the conclusion of the Guatemalan civil war in 1996, many non-governmental organizations (NGOs) have seized the opportunity to engage indigenous women in income generation activities with the goal of improving their lives. Accompanying economic independence is a beginning shift in women's gender roles.

#### OBJECTIVE:

The current qualitative study explores the empowerment of indigenous Guatemalan women through their involvement with NGOs that have combined income generation with health education.

#### METHODS:

Semi-structured in-depth interviews, each lasting approximately 1 hour, were conducted with 34 indigenous Guatemalan artisan women. Interview topics included experience with an NGO that integrates health education with income generation, employment history as an artisan, recall of health education workshop content, and observed changes since involvement with the NGO. Data analysis applied a Grounded Theory approach.

#### RESULTS:

Respondents described newly gained confidence, stating that their minds "woke up" and that they no longer feared speaking up. This confidence resulted from the process of earning and managing their own money. Moreover, the use of group meetings by NGOs enabled women to interact with other women outside the home, creating further opportunities for sharing and learning. Women also discussed the importance of family, both in terms of the support required to ensure their continued participation with income generation as well as the motivation instilled to gain enough income and secure education for their children.

#### CONCLUSION:

NGOs combining income generation with health education can play a positive role in women's empowerment. The current study offers valuable recommendations for programs seeking to improve women's health through income generation.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Women's Autonomy and the Influence on Female Genital Cutting in Eritrea

#### BACKGROUND:

The prevalence of female genital cutting (FGC) in Eritrea is among the highest in the world, with 89 percent of women aged 15-49 in 2002 reporting some form of FGC. The Government of Eritrea announced a ban on FGC in 2007, and since then, numerous measures have been implemented at the community level to monitor and enforce the law. The advocacy and mobilization campaign following the ban focused on changing the attitudes among traditional birth attendants, circumcisers, community elders and religious leaders. Despite an almost universal awareness of FGC and the ban, the practice is still prevalent in Eritrea. It is important to understand women's autonomy in the household to get insight into women's control over their lives, domestic environment and gender roles, which are important in understanding demographic and health behavior, including behavior and attitudes towards FGC.

#### OBJECTIVES:

This study seeks to explore the impact of measures of women's autonomy on women's attitudes towards FGC and having a daughter circumcised.

#### METHODS:

The current study is a secondary data analysis of a sample of Eritrean women (n= 8, 754) surveyed in the 2002 Eritrea Demographic and Health Survey. Measures of women's autonomy and socio-demographic characteristic are included as independent variables. Two aspects of female genital cutting in Eritrea serve as dichotomous outcome variables: (1) at least one daughter circumcised (practice of FGC) and (2) support of the continuation of FGC (attitude). Bivariate logistic regression analysis will be used to assess preliminary associations between the outcome variables and independent variables. Multivariate logistic regression will be used to determine significant predictors, related to women's autonomy, of the practice of FGC and attitudes towards FGC. Data will be analyzed using Stata 12.0.

#### RESULTS TO DATE:

Data analysis is currently underway. Preliminary results show that 55.8 percent of women included in the survey support the continuation of FGC. Additionally, of women surveyed who have a daughter, 67.8 percent have at least one daughter circumcised.

#### CONCLUSIONS:

By examining the relationship between autonomy and FGC practice and beliefs we may identify factors that interventions can target to reduce the practice.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### A truly neglected tropical disease: A mixed methods study of prevalence, risk factors and health consequences of jiggers in a Kenyan village

#### BACKGROUND:

Tungiasis, commonly referred to as “jiggers” or by locals “the dirty peoples disease” is a neglected tropical disease caused by sand fly infestations. Jiggers has not yet become a public health priority in Sub-Saharan Africa despite a likely substantial but understudied disease burden in this region. Only few and very recent epidemiological studies have been published from Sub-Saharan Africa, none of which addressing the burden among children <5.

#### OBJECTIVE:

To quantify risk factors and prevalence of jiggers in rural Western Kenya, and to use qualitative methods to study associated stigma and perceptions of its health impact immediately after the dry season (May) when prevalence is highest.

#### METHODS:

A detailed questionnaire was administered to all persons at home in a random sample of village households immediately after the end of dry season, in May 2012. Each participant consented to have their feet examined for evidence of jiggers lesions (active or passive). If present, number of lesions and signs and symptoms of associated illness were recorded. Finally, 10 qualitative in-dept interviews were conducted with severely affected individuals .

#### RESULTS:

Of 128 village households, 39 (30%) were studied. Of 118 family members we approached, all consented to participate in the study including undergoing a clinical foot exam. Of all participants, 49 % had clinical evidence of active Tungiasis ( $\geq 1$  active lesion), males gender was a borderline risk factor (OR 1.3,  $p > 0.05$ ). Among the Jiggers patients, the most frequent complaints were itching (95%), pain (93.1%), trouble walking (32.8%). On exam 13.8% had signs of infection. We found that wearing shoes was highly protective (OR 0.1;  $p$ -value 0.0003) whereas low frequency of showering was not a risk factor. The in-dept interviews revealed that stigma was prevalent and described as feelings of embarrassment and social isolation and exclusion from school and work.

#### CONCLUSIONS:

Jiggers affected half of the village population of all ages, and with considerable evidence of associated morbidity, depression, secondary infection and stigma. The study was not powered to study rare severe outcomes including amputation and mortality. We demonstrated that “Jiggers” is not associated with poor personal hygiene but rather to time spent walking barefoot; insights that may combat the “dirty people’s” stigma. A broader study of villages in Sub-Saharan Africa is warranted. Jiggers was anecdotally suggested to be of recent origin in this setting and possibly linked to climate changes (droughts). Resources and awareness must be allocated to address and prevent this truly neglected tropical disease.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Taking action against gender-based violence: Bringing men and women together in Wentworth through the Prevention in Action movement

#### BACKGROUND:

Social norms about gender, power, and violence drive the gender-based violence (GBV) epidemic in South Africa. In response, the KwaZulu Natal Network on Violence against Women initiated the Prevention in Action (PIA) movement to achieve an end to GBV. Traditional interventions try to empower women to mobilize against GBV, but recent efforts work to engage men to take action. PIA now embraces this innovation by working with women *and* men against GBV.

#### OBJECTIVES:

This case study of Wentworth, South Africa aimed to: understand the potential of men to prevent GBV; evaluate how the Network tries to mobilize men and women to take action; and explore with community-organizers their goals, challenges, opportunities, and visions for the future of PIA.

#### METHODS:

The methodology used was “process use” in evaluation through informal and semi-structured interviews with experts and stakeholders. This method allowed participants to reflect upon their work with PIA, communicate concerns and recommendations, and ponder strategies to reenergize and improve their work.

#### RESULTS:

Initially, words articulated in PIA to involve the community alienated men as perpetrators of violence, and did not consider their potential as partners in prevention. This problem is slowly being addressed by changing rhetoric from “violence against women” to “GBV” and emphasizing men’s roles as partners, not perpetrators. Additionally, the process use in evaluation methodology seemed to encourage many of the participants during interviews to rethink their roles and responsibilities in PIA and re-energize their desire to end GBV through PIA. However, the Network has taken too much control over the intervention, with little consideration of the concerns and suggestions of community-organizers, which discourages them from working together to address challenges.

#### CONCLUSIONS:

Wentworth recognizes changes in attitudes toward GBV and accepts PIA as a long-term, prominent organization. Though there is great passion among stakeholders to end GBV, passion alone will not sustain PIA. As efforts to engage men are slowly succeeding, it is crucial for the Network to open lines of communication and transition responsibility and ownership to the community in order to have an inclusive and sustainable movement to end GBV.

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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## Fertility Reduction in Timor-Leste: The Role of Education and Family Planning Services

**BACKGROUND:**

Lowering fertility rates in developing countries could improve stability, increase economic productivity, and mitigate environmental degradation.

**METHODS:**

This study uses Demographic and Health Survey data to assess the effects of family planning and levels of education on fertility among women in Timor-Leste, a country with high maternal mortality and one of the fastest growing youth populations in the world. Four multivariate regression models were generated to test the impact of education and family planning knowledge and use on fertility levels.

**RESULTS:**

Among women reporting contraceptive knowledge and use, those with at least a secondary education have .280 and .223 fewer children respectively than those with no education. Those with a primary education have .101 and .152 fewer children respectively than those with no education. Furthermore, secondary or higher levels of education alone were determined to have a greater impact on reducing the total number of children born than primary education combined with contraceptive knowledge.

**CONCLUSIONS:**

These results highlight the significance of education in reducing fertility levels. Furthermore, this study finds education to be more important than contraceptive knowledge or use in lowering the total number of children born. The cyclical nature of the investment in secondary and higher levels of education could facilitate a demographic transition in Timor-Leste and provide policy makers the opportunity to improve the economic and social development of their nation.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Shifting Age Distribution of Dengue Infection: Analysis of Data Collected in Kamphaeng Phet Province, Thailand from 1994 to 2010

#### BACKGROUND:

Dengue is resurging as one of the most significant arbovirus diseases afflicting humans in the 21st century. Recent studies suggest the average age of dengue infection is increasing and may be due in part to a shift in dengue environmental and age distribution. Building upon initial reports, this study assessed the average age of symptomatic dengue infection in Kamphaeng Phet Province, Thailand from 1994 and 2010.

#### METHODS:

A pooled cross-sectional dataset developed by the Armed Forces Research Institute of Medical Sciences (AFRIMS) located in Bangkok, Thailand was used for the analysis. The dataset consisted of 6,240 serum samples collected from patients seen at the Kamphaeng Phet Province Hospital from 1994 to 2010. Using Student's t test and univariate regression, mean dengue incidence rates and their 95% confidence intervals were calculated by subgroup. Multivariate logistic regression was used to determine the association between age of infection by time (years) using dummy variables for each year.

#### RESULTS:

A dramatic shift in the average age of patients testing positive for dengue infection was documented from 8.6 to 17.0 years of age between years 1994 and 2010. Significant differences were also found between consecutive years and distinct year groups. Mean age of primary infection was 6.68 with a statistical difference between years 1994 and 2010. Mean age of secondary infection was 11.97 with a statistical difference between year 1994 and years 1999-2010.

#### CONCLUSIONS:

This is the first study to document an increase in dengue age incidence using lab confirmation over a 17 year period in Thailand. The large pooled cross sectional dataset provides high level of confidence in findings and the 17 year data facilitates trend analysis of infection during both endemic and epidemic years.

The shift in dengue incidence from 8.6 to 17 years of age from 1994 to 2010 is both significant and meaningful. This evidence has implications for the dengue vaccine development and implementation process and clinical practice guidelines for both diagnosis and treatment as the age of infection increases.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Utilizing a Five Point Intervention to Decrease Text Messaging Among Drivers

#### BACKGROUND:

Cell phone conversation has been shown to be a major distracter of drivers and has been linked strongly to an increased rate of car accidents and road fatalities. Drivers using cell phones are more likely to react slower to signals and are more likely to miss traffic signals. Text messaging is rapidly becoming another form of distraction for drivers and has been shown to be even more distracting than cell phone conversation. State-level legislation in 39 states including Washington, DC has limited the use of cell phones (calls, text messaging and/or both) but no state has completely banned the use of cell phones while driving. While this legislative action has been moderately successful, drivers continue to use their cell phones on the road despite the possible financial penalties. In response to this issue, the GW School of Medicine Emergency Department launched a pilot study in 2011 looking at whether a short, five point intervention would decrease patient intention to use cell phones while driving once they left the Emergency Department. Early data showed that the intervention changed driver intentions, but did not show whether or not there was actual behavior change. This follow-up study looks to track driver behavioral change after receiving the same five point intervention.

#### METHODS:

We enrolled 300 non-critically ill, English speaking patients from the GW School of Medicine Emergency Department between July 2012 and December 2012. Study subjects were randomly assigned into test group, which received a five point intervention regarding the dangers of text messaging while driving, or a control group, which received a pamphlet on the dangers of drinking and driving. Patients were left on their own to read the intervention which additionally included a pre-test to assess patient knowledge and driving behaviors. Follow up calls were made to study participants between 2-4 months after discharge from the Emergency Department. On follow-up, patients were asked the same exact questions assessing patient knowledge and driving behaviors as they were asked on pre-test. Analysis has not been carried out at this stage.

#### RESULTS:

Follow-up calls are still continuing and analysis has not been performed.

#### CONCLUSION:

As of today, no conclusions can be made.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Social Mission in Medical Education: A Literature Review of Three Modalities

#### BACKGROUND:

The Carnegie Foundation published *Medical Education in the United States and Canada* in 1910, by Abraham Flexner subsequently known as the Flexner Report. This report catalyzed important changes in medical education in the United States that continue to influence current methods of training. The resulting homogeneity of the surviving medical schools has produced unintended shortcomings to our current state of medical education, such as a lack of social mission. Broadly defined, the social mission of medical education is the contribution of a medical school to addressing the critical and unmet health problems of society. In this literature analysis, we explored methods by which select medical schools have developed a socially accountable medical education. The Beyond Flexner Study identified eight modalities which serve as a useful framework for social mission within medical education, three of which were the focus of this analysis: Structure of Curriculum, Mentorship and Residency Preparation.

#### METHODS:

The authors searched relevant literature pertaining to three modalities using the following databases: Pubmed, Medline and Google Scholar. Articles were considered relevant if they included keywords, fit into the modality scope, used data from US-based medical schools and contained outcomes data (e.g., associated with higher primary care graduates/physicians working in underserved communities).

#### RESULTS:

Although limited outcomes data exists, the most important characteristic in a medical school curriculum associated with an increase in primary care physician workforce is a required third year family medicine clerkship. The literature regarding the use of mentorship to influence students to enter primary care focused on the role of minority mentorship with underrepresented minority medical students. Primary care physician mentors do provide increased exposure for students. Outcomes-based literature on residency preparation was the most limited, however the hidden curriculum in medicine significantly impacts a student's perceptions of life as a physician and ultimately influences their behavior in their professional lives.

#### CONCLUSIONS:

The literature demonstrated a clear association between the role of required third year primary care clerkships of medical school and primary care mentors and the subsequent output of students entering a primary care career. The hidden curriculum plays a vital role in shaping the minds of medical students, exposing them to mixed messages regarding specialty selection from their teachers and peers. More outcomes-based research is needed to measure the success of some newer medical programs that promote primary care as part of their missions, hoping to answer the needs of the current state of healthcare in the United States.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Grasping at Straws – A Brief Introduction to Medicare Drug Reimbursement Policy

#### BACKGROUND:

Drug reimbursement policy in the United States is a complex and ever-evolving aspect of healthcare that affects millions of Americans, their healthcare providers, as well as the companies that manufacture and distribute these products. Reimbursement rates for drugs differ depending on factors such as individuals' insurance plan(s) coverage, nature of the biologic/drug and in what environment the product is administered. It is notable that there is no single national government price for any drug or biologic in the country.<sup>1</sup>

Policymakers have been working for decades to improve drug reimbursement policies so that physicians and drug manufacturers' incentives are aligned for the end consumer: the patient.<sup>2</sup> Each of these interested parties also has a vested interest in preserving their own bottom line. As a result, drug reimbursement reform continues to be an ongoing effort that requires the dedicated efforts of lawmakers, pharmaceutical companies and healthcare providers. Healthcare providers, in particular, should seek to understand and advocate on behalf of their patients for a more equitable and comprehensible drug reimbursement system.

#### OBJECTIVES:

- To develop a working knowledge of Medicare drug reimbursement policymaking and implementation processes
- To understand the major components of pharmaceutical companies' approach to meeting drug reimbursement rules and regulations

#### METHODS:

- Support Applied Policy's clients in their efforts to understand and navigate Medicare and Medicaid drug reimbursement policies
- Read articles and interview experts on prescription drug benefit plans and impact of proposed health reform
- Participation in health policy workshops on health policy reform

#### RESULTS AND CONCLUSIONS:

Navigating U.S. drug reimbursement policy for a pharmaceutical company or healthcare provider requires an open mind and willingness to embrace tried-and-true practices from previous legislative cycles. It also requires a guide: realizing the need for a consultant who is well-versed in the field is a key determinant of success at achieving end-goals, e.g. to land on the formularies of Medicare-approved plans and to be available for use in various sites of care. Healthcare providers would benefit from participating in and informing these policy conversations, insofar as their patients' ability to receive the best treatments at reasonable prices depends in large part on how these negotiations play out.<sup>3</sup> Spending eight weeks on the topic is barely enough time to grasp the ins-and-outs of drug reimbursement, but it is an important step toward gaining a better understanding of what kind of healthcare system medical students are going to graduate into.

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#### SOURCES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Hurricane preparedness and response in a geographically isolated hospital setting

#### BACKGROUND:

Hurricane disasters are common in the southeastern states of North America. In anticipation of hurricane disasters, hospitals develop emergency disaster plans detailing how to mitigate, prepare, manage, and recover from a hurricane impact. Often after a hurricane occurs, many hospitals re-evaluate their disaster plans, finding where problems occurred and recommending future changes. Common problems include insufficiency of generators, unanticipated damage from flooding and water surge, and difficulty returning the hospital to normal functionality.

#### METHODS:

A literature search was performed, and a survey was created based on the common difficulties that hospitals identified after a hurricane impact. The survey was sent to a healthcare facility located on a barrier island on the Atlantic Ocean.

#### RESULTS:

After phone and e-mail correspondence with the Director of Marketing and Development, the healthcare facility disclosed their Hurricane and Inclement Weather Plan but chose not to answer the questions in the survey. The Hurricane and Inclement Weather Plan provides a set of guidelines for operations during a hurricane. It provides a hierarchical command structure, where the Department Directors have full authority and flexibility over their department. Once a storm is predicted, it is assessed, and a Code Black is activated. Building structural components are enhanced, generators are assessed, supplies are inventoried, and the computer databases are converted into a paper system. Teams of employees are formed to determine who will work during the storm and recovery, and facility security is enhanced. The plan does not discuss how the facility will account for lost revenue or the financial burden of the storm. It also does not describe specifics about the generators.

#### CONCLUSIONS:

The plan is a comprehensive blueprint that each department can use for direction during a hurricane disaster. It is flexible, allowing Department Directors to have full authority over their department. Some weaknesses in the plan appear to be the lack of training exercises prior to a disaster and direction for the recovery phase. Without a description of the generators, it is also possible that the facility would be susceptible to generator failure. Finally, the financial hardship that storms produce has the potential to cause irremediable damage. The Hurricane and Inclement Weather Plan provides a summary of the events that are expected to occur during a hurricane disaster. The plan has areas of weakness, however these could be corrected through careful re-evaluation of the plan, disaster drills, and a study of the available literature.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Developing Standardized Language for Use in LGBT Health Research

#### BACKGROUND:

In the past two decades, the LGBT community in the United States has been more visible, active, and positively accepted by society. As acceptance progresses, research interests on the LGBT population have increased, driving the need for standard language for researchers to share for comparative and community-based participatory research. "What term is right?" is often the question researchers ask a very diverse LGBT community. In August 2012, the District of Columbia's Office of LGBT Affairs identified incongruent language in a number of published reports commissioned by the Mayor's Office. The Office realized the importance of standardized language for health services research in order for studies and findings to be generalized.

#### OBJECTIVE:

To create an executive document for the Mayor's Office of Gay, Lesbian, Bisexual and Transgender Affairs (GLBT) of standardized LGBT language that can be distributed and used by DC Government agencies in survey questions and other data collection tools in order to assess reliability and gain fidelity.

#### METHODS:

Three previous research reports were analyzed along with the Philadelphia LGBT Community Assessment Report (2006) that presents the results of data collection and analysis about LGBT populations in the City of Philadelphia. These report expanded upon a growing body of work being done nationally that examined the demographics and trends of LGBT communities and their cultures. The new ACA guidelines regarding HHS standards for data collection was also analyzed for this research. About 15 - 20 current studies, reports, and surveys on the LGBT community were also analyzed to gain knowledge of current language usage in LGBT research. Finally, a literature review was conducted to gather terms used in published works.

#### RESULTS:

A glossary of thirty new standardized terms were created defining words, including homophobia, sexual identity, intimate partner, among others. The glossary was provided to the Mayor's Office for utilization during data collection within the LGBT community and was distributed to DC Government agencies for drafting LGBT surveys, in-take forms, and other data collection tools.

#### CONCLUSIONS:

The current climate surrounding LGBT issues calls for both politically correct and culturally sensitive language. Minimal research has been conducted to strengthen LGBT terminology for health services research. Creating a standardized glossary of terms for the Office of LGBT affairs was necessary to bring clarity and consistency to research conducted in the LGBT community.

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## The Quality of Healthcare Provision Received by Lesbian Community

**BACKGROUND:**

Lesbian women face health issues that are distinct and require personalized preventative services in which to deal with them (Mayer et al., 2008). Generally speaking, gay women are a population that has a poorer health status than their heterosexual counterparts (Koh, 2000). The lack of preventative services sought by lesbians has the propensity to lead to poor health outcomes in this population (Koh, 2000).

**OBJECTIVE:**

Hence the purpose of this research is to explore the quality of healthcare provision that the lesbian community receives. Gay women's health concerns have only recently entered the forefront of medical literature and research agendas (Malterud, Bjorkman, Flatval, Ohnstad, Thesen & Rortevti, 2009). Lesbians are a habitually overlooked population that deserves to be a focus in order to improve their health outcomes.

**METHODS:**

The study used a semi-structured interview approach in which data was gathered on the experiences of four self-identified gay or lesbian women aged 19 to 32 while interacting with their healthcare providers. Each interview was recorded, transcribed, coded, and analyzed for themes found in the data.

**RESULTS TO DATE:**

Initial results reveal the importance of knowledge by the providers, the comfort of the women with providers, and the relationship of trust between patient and provider.

**CONCLUSIONS:**

From the results implications will further be discussed in order to make further suggestions to aid in the improvement of the quality of healthcare provision by providers to the lesbian community.

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Malterud K., Bjorkman, M., Flatval, M., Ohnstad, A., Thesen, J., Rortveit, G. (2009). Epidemiological research on marginalized groups implies major validity challenges: Lesbian health as an example. *Journal of Clinical Epidemiology*. 62(1), 703-710.



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Nutritional Prevention of IAPP Aggregation in Type II Diabetes

#### BACKGROUND:

The study of amyloid protein aggregation is critical to the pathological understanding of several diseases—Type II Diabetes, Alzheimer’s, Huntington’s—that can be fatal and continue to plague patients, as there is no known cure for these disorders.<sup>1,2</sup> Research in this field has been ongoing for the past few decades, yet a significant obstacle in conducting amyloid studies is defining the mechanism by which amyloid protein aggregation occurs.<sup>2</sup> One technique used to monitor aggregation activity is circular dichroism, which is the differential absorbance of left and right circularly polarized light. Circular dichroism (CD) detects differences in secondary and tertiary protein structure by quantitatively assigning values of circularly polarized light absorbance to proteins.<sup>3,4</sup> Though CD could be used to research most, if not all, amyloidogenic diseases, we used CD to study the protein folding of the Type II Diabetes-associated amyloid protein called Islet Amyloid Polypeptide (IAPP). IAPP’s characteristic rapid *in vitro* aggregation makes it a desirable protein for study.<sup>2</sup> Previous research has shown that certain foods, specifically fruits and vegetables, exhibit amyloid aggregation-inhibiting characteristics, though it has yet to be determined which components of these foods are responsible for this therapeutic effect.<sup>5</sup>

#### OBJECTIVES:

To study the protein folding of IAPP and the aggregation-inhibitory capabilities of various fruits using CD.

#### METHODS:

In these preliminary studies, the following fruits were tested: banana, grape, lemon, cherry, and pineapple. Samples of each fruit—both isolated and in combination with IAPP—were made at the concentration of our IAPP control and were run through the CD instrument. Results were confirmed using AFM.

#### RESULTS:

Proteins that are run through the CD instrument yield some combination of the three secondary structures—alpha-helix, beta-sheet, or random coil. IAPP is an a-helical protein, yet when given the time to aggregate, IAPP exhibits a random coil secondary structure due to its amyloidogenicity. Of the fruits tested, banana, grape, and lemon yielded structures similar to the alpha-helix seen in IAPP samples prior to aggregation.

#### CONCLUSIONS:

Because certain fruit samples combined with IAPP yielded alpha-helical structures, we believe that these fruits are capable of IAPP-aggregation inhibition *in vitro*. The therapeutic moieties within the samples have yet to be determined. Further studies must be done using other fruit and vegetable samples, followed by studies using mammalian cells.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Syndromic Approach to Emergency Department Surveillance for Skin and Soft Tissue Infections

#### OBJECTIVE:

We sought to describe the epidemiology of emergency department (ED) visits for skin and soft tissue infections (SSTI) in an urban area with diverse neighborhood populations using syndromic surveillance data.

#### METHODS:

We sought to achieve our objectives by using Boston Public Health Commission's Syndromic Surveillance System data from 2007-2011. Final diagnosis ICD-9 codes for SSTI related visits were identified, and the corresponding patient was mapped to one of sixteen Boston neighborhoods. Each neighborhood had a unique demographic profile with differences in race, socioeconomic status, age, and population density.<sup>1</sup> Trends within patient demographics and neighborhood clustering of SSTI related ED visits were examined.

#### RESULTS:

Unique SSTI visits represented 3.29% (n=45,252) of all visits to Boston EDs from 2007-2011. We observed a seasonal pattern with the peak incidence of SSTI visits occurring in the summer. The majority of SSTI visits (54%) were among patients 18-44 years old, which is consistent with the age distribution of the Boston population.<sup>4</sup> Males accounted for less than half of all ED visits for each year of the study but accounted for 52% of SSTI visits. Although just 24% of Boston's population,<sup>2</sup> Black patients accounted for a disproportionate 43% of SSTI visits. The five-year average rate of SSTI visits for Black patients was 2.8 times greater [CI 2.7-3.0] than the rate for White patients. The five-year average percent of neighborhood-specific ED visits for SSTIs had a geographic distribution ranging from a low of 2.69% to a high of 4.11%.

#### CONCLUSIONS:

Our study demonstrates the use of syndromic surveillance to track the epidemiology of community acquired SSTIs through the creation of a novel SSTI syndrome. Additionally, our syndromic surveillance methods can provide information regarding the local epidemiology of SSTIs, including the identification of neighborhood clustering. Local syndromic surveillance systems have the potential to provide public health and ED clinicians near real-time data on trends in demographic risk factors.

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1. Chen JT, Rehkopf DH, Waterman PD, Subramanian SV, Coull BA, Cohen B, Ostrem M, Krieger N. Mapping and measuring social disparities in premature mortality: the impact of census tract poverty within and across Boston neighborhoods, 1999-2001. *J Urban Health*. 2006;83(6):1063-84.
2. 2010 United States Census. Available from: <http://www.census.gov/2010census/data/>



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### What Can Health Care Learn from the Aviation Industry? A Systematic Review of Workflow Analysis in Health Care

#### BACKGROUND:

Human factors engineering utilizes methods from social science, engineering, and psychology to reveal how to improve the performance and reliability of systems that involve the interface of humans and technology. Unlike other high reliability systems where only very low rates of error are acceptable, healthcare has been slow to embrace the need to understand how work is performed. Rather than imagining how work should be performed, proper observation and analysis would enable the design of systems that support performance of real work, reduce error-producing conditions, and make good on the promise of increased efficiency.

#### OBJECTIVES:

We propose conducting a systematic review to identify existing application of human factors engineering in health care associated with the measurable impact to process improvement.

#### METHODS:

The authors, assisted by a reference librarian, searched PubMed as well as nursing, psychology and engineering databases using a search strategy based upon a Problem, Intervention, Comparison, Outcome (PICO) question. Problem: Shortcomings in workflow in the clinical team setting that potentially result in medical errors or inefficient use of resources. Intervention: Workflow analysis can better inform process improvement and efficiency. Comparison: A cohort of similar hospitals or comparing the impact against historical data at the same hospital. Outcome: Any statistical method that provides measures of improvement in clinical, health care process, workload, economic, or provider use outcomes.

#### RESULTS:

The search strategy returned a total of 2,328 unique hits (no additional studies were identified from the review of references). Following the PRISMA approach, the end result was 8 studies suitable for analysis. There were no identified prior systematic reviews or meta-analyses on this subject.

#### CONCLUSION:

Quality analysis of the existing studies and presentation of the results will demonstrate the current state of utilization of human factors methods in healthcare, and identify where future work should focus.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Management of labor pain in a parturient with complex regional pain syndrome, a case presentation

Complex regional pain syndrome is a chronic pain condition resulting from dysfunction of the nervous system. Although this condition affects women four times more than men, there is little literature regarding the management of complex regional pain syndrome (CRPS) in the parturient. This case presents the pain management of a nulliparous woman diagnosed with CRPS Type I for four years, presenting to labor and delivery at full term and literature review of CRPS in the gravid patient.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Analysis of Fiber Optic Device in Measuring Spinal Cord Blood Flow and Oxygenation

#### BACKGROUND:

Spinal cord integrity may be compromised after trauma or during surgery. Progress in the management of spinal cord injury has been slow, frustrated in part by the inability to measure the real-time impact of treatment upon spinal cord ischemia. Diffuse optical and correlation spectroscopy and Doppler flow has been shown to measure blood flow and oxygenation.

#### OBJECTIVE:

Continue to develop and test a fiber optic device (FOD) that will allow for the measurement of spinal cord blood flow and oxygenation.

#### METHODS:

Dahl sheep were placed under general anesthesia with controlled ventilation. Surface ECG and proximal and distal mean arterial blood pressure were measured and an intra-aortic balloon was placed to allow endo-aortic clamping. A multi-level mid-thoracic laminectomy was then performed. The FOD was placed, percutaneously, in the subdural space, facing the posterior spinal cord. The following conditions were created: pharmacologic hypertension and hypotension, proximal aortic occlusion, and hypoxia via ventilation reduction. The FOD measured flow and oxygenation using diffuse optical and diffuse correlation spectroscopic (DOS, DCS) principles and laser Doppler flow (LDF). Fiber optic DCS, DOS, LDF, and tissue pO<sub>2</sub> data were collected simultaneously and recorded digitally using ADI Powerlab interfaced with LabView Chart software. Both DOS and DCS data was analyzed off-line with homemade scripts written in MatLab.

#### RESULTS:

The FOD immediately detected changes in blood flow. Administration of pressors resulted in increased spinal cord blood flow, while nitroprusside resulted in decreased blood flow. Inflation of the endo-aortic balloon resulted in hypertension above and hypotension below the balloon. With the probe positioned over the mid-thoracic spinal cord, an increase in blood flow was initially detected. Epidural placement did not impair the ability to measure changes relative to subdural positioning. No change in tissue oxygenation was detected over the range of blood pressures tested.

#### CONCLUSIONS:

Results indicated that the thoracic spinal cord in sheep was generously supplied by the vertebral arteries superiorly. Lumbar positioning may better detect ischemia in sheep to correlate with humans as flow to the human lumbar spinal cord is more dependent upon vessels originating lower in the aorta. Return of blood flow toward baseline levels, even when hypertension persisted, may demonstrate robust spinal cord autoregulation. It is hypothesized that such a device will have wide applicability in the care of spinal injuries, potentially enhancing the efficacy of interventions for prevention of secondary ischemic injury, improving neurologic outcomes. However, more research is necessary to improve measurement of oxygenation via this device.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Social Participation in Children with Friedreich Ataxia

#### BACKGROUND:

Friedreich Ataxia (FA) is a genetic disease resulting in progressive impairments in the nervous, cardiac, endocrine, and musculoskeletal systems and leads to gait and limb ataxia. Research demonstrates psychosocial involvement and quality of life of children and family with degenerative conditions are negatively impacted by progressive impairments in mobility and motor control.

#### OBJECTIVES:

The purpose of this study was to explore psychosocial engagement, based on activity preferences in a group of children with FA as reported by their parents.

#### METHODS:

Following IRB approval and informed consent, telephone interviews were conducted with parents of 30 children with FA, including 18 males and 12 females, between the ages of 9 and 17 years old. All of the children were Caucasian and demonstrated a range of system involvement. In order to gain insight into the child's psychosocial network and quality of leisure activities, open and closed ended questions were posed about the child's top three preferred activities, and with whom they participated in those activities (alone, with family members, with peers/friends, or combined).

#### RESULTS:

For the most preferred or frequent activity, 35.7% reported solitary activity, 21.4% participated with family members, 17.8% with peers/friends, 17.8% fell into mixed categories, and 7.1% declined to respond. Similarly, for the second most preferred activity, more than a third of children described solitary activities over those that included family and friends. The most frequently reported solitary activity was reading, followed by playing video/computer games. Activities involving peers were more varied, and included participating in sports, swimming, going to school, and spending time with friends.

#### CONCLUSIONS:

More than one third of children with FA report solitary activities for their top two preferred activities, rather than activities performed with family or peers. Only a small percentage of the group engaged in activities with peers. Psychosocial involvement can have a significant impact on an individual's quality of life. Particularly in children with progressive diseases, social interaction can lead to enhanced participation in the community, symptom management, and maintenance of a positive outlook. Physical therapists and other health care professionals should be aware of the need to promote activities that include social engagement in the community when treating children with progressive conditions such as Friedreich Ataxia.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Communication With Families Before Hospital Discharge

#### BACKGROUND:

Parents need to know the discharge plan for their child in order to care for them as an outpatient. A family familiar with events that occurred will be better able to provide important information for future providers. In 2007, the functional literacy rate in the District of Columbia was reported as 36%. As discharge instructions are primarily in the written form, it is important to establish effective verbal communication with caregivers during the hospitalization.

#### OBJECTIVE:

To identify the parental knowledge of key events of the hospitalization and discharge plan prior to receipt of written discharge instructions.

#### DESIGN/METHODS:

A cross-sectional, prospective, descriptive study was conducted on the hospitalist service at Children's National Medical Center. Investigators interviewed a convenience sample of parents on the day of discharge to assess parental understanding of hospital course (diagnosis, therapies, testing, procedures) and discharge plan (medications, follow up instructions). Concordance with the medical record was assessed by two other investigators. Inter-rater reliability was established ( $k=0.8$ ).

#### RESULTS:

Of 113 participants, 96% stated that they felt completely or mostly prepared and 4% reported feeling unprepared to care for their child upon discharge. All felt completely or mostly prepared to explain the hospital course to their child's pediatrician. 69% stated that they were completely confident filling out medical forms by themselves, which was a surrogate for health literacy. Discordant information between the participant and the medical record for hospital events most often pertained to non-serum laboratory testing (37%). Discordant information between the participant and the documented discharge plan most often involved follow up appointments with subspecialists (13%) and the type of new medications to begin at discharge (16%). There were no significant differences in discordance between participants whose child was admitted to a team comprised of trainees or to an attending-only service.

#### CONCLUSIONS:

Prior to receiving their discharge paperwork, at our institution, parents of hospitalized patients may not be sufficiently informed about their child's laboratory testing. Greater effort to improve counseling about subspecialty follow up appointments and new medications is likely to be beneficial.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Curriculum Module Selection for Ultrasound Training in Gross Anatomy

#### BACKGROUND:

The portability and cost-effectiveness of ultrasound makes it an ideal learning tool to supplement traditional methods employed in Gross Anatomy curricula. The introduction of ultrasound anatomy modules into the first year of medical school facilitates the transition between the didactic anatomy course and clinical applications. Studies have shown that the basic operation and interpretation of ultrasound can be effectively taught to medical students, using short instructive sessions and hands-on training.

#### OBJECTIVES:

Currently, there is not a consensus on the content of Ultrasound-Applied Anatomy Training (USAAT) for medical students. We sought to identify the high-yield anatomical topics that are the most clinically relevant and feasible for ultrasound guided teaching in Gross Anatomy courses taught to first year medical students.

#### METHODS:

This study uses a modified Delphi Survey Method and a quantitative scoring system to prioritize the high yield training modules incorporated in Gross Anatomy curriculum. The Focus Group compiled a list of structures that had the capacity to be detected by ultrasound, given the physical properties of the ultrasound waves and the composition of the anatomical structures. These structures were selected from the Clinical Anatomy curriculum adapted from the Medical Sciences Division at the University of Oxford, in conjunction with the Clinical Anatomy Curriculum generated by the Educational Affairs Committee of the American Association of Clinical Anatomists. This qualitative data was used to inform the First Round of the Delphi survey, which was administered to GW ED physicians that incorporate ultrasound in their clinical practice. These participants were asked to "include" or "exclude" each structure from consideration for the curriculum based on whether or not it can be detected by ultrasound. The results informed the Second Round Survey, a national survey generated to develop a subcohort analysis, evaluating each structure on an ordinal scale (1-10) in 3 constructs: educational yield, technical feasibility, and clinical relevance. Second Round participants included faculty of the 2nd World Congress on Ultrasound in Medical Education, and academic educators identified on PubMed.

#### RESULTS:

The Focus Group generated a list of 1460 structures, which was narrowed down to 312 structures by the First Round Survey (Head and Neck-34, Eye-13, Thorax-39, Abdomen and Back-80, Pelvis and Perineum-24, Upper Extremities-81, Lower Extremities-41). Second Round Survey is pending in the data collection phase.

#### CONCLUSIONS:

The results of this study can be used to identify and implement the high-yield educational topics as ultrasound curriculum modules in Gross Anatomy training.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### It's a Beautiful Thing: Adolescents Beliefs Regarding Pregnancy

#### PURPOSE

For many adolescent pregnancies, both the desire and timing are often the result of either an active or passive plan on the part of the individual. This “pregnancy intention” is a complex concept that is difficult to describe and measure. Prior research has focused on the assessing adolescent pregnancy intention and accompanying contraceptive behaviors retrospectively, following the birth of a child. This study seeks to develop a more complete prospective understanding of the degree to which individual attitudes toward pregnancy are part of active or passive intention.

#### METHODS

Sexually active female adolescents’ ages 13 to 22 years were recruited from an urban academic adolescent health center in Washington, D.C. Participants answered a 17-item reproductive health survey followed by a semi-structured interview including views on pregnancy and contraceptive use. Interviews were performed by research assistants, audio taped, transcribed, and analyzed by research team to identify common themes. Descriptive statistics were performed on the survey data.

#### RESULTS

The median age of the 37 participants was 18.0 years (SD 1.57), almost all African American (n=36/37), with n=6 reporting prior history of pregnancy without giving birth, and 78.4% (n=29/37) reported being in steady or committed relationship at the time of study participation. The mean age of sexarche was 15.4 (SD 1.4), 86% (n=32/37) reported condom use and 29% (n=11/37) reported using Depo-Provera or oral contraceptive pills to prevent pregnancy at last intercourse. Three patterns of pregnancy intention emerged when asked about their views of pregnancy and how they would feel if they found out they were pregnant today. The majority (n=17/37) discussed only positive content regarding pregnancy. All participants reporting previous pregnancies were in this group. Thirty-five percent (n=13/37) discussed contradictory views about pregnancy. Nineteen percent (n=7/37) had negative or neutral views about pregnancy. Timing, preparation, financial support, and age were important factors in whether participants expressed positive or negative content in regards to pregnancy. Conversely participants described many concerns with hormonal contraception, with most common being including side effects including weight gain (n=18) and reducing future fertility (n=5). There were no statistical differences between the groups in regards to age, reported condom use, relationship status, and hormonal contraception use to prevent pregnancy at last intercourse.

#### CONCLUSION

Adolescents in this study had both positive and negative perceptions of pregnancy, often simultaneously. Assessing pregnancy decision making among adolescents should include acknowledging their ambivalence while interventions should address how their beliefs influence reproductive health behaviors. Further studies should focus on developing better methods to assess pregnancy intention and prospective pregnancy outcome measurement.

#### SOURCES OF SUPPORT:

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Complementary and Alternative Medicine Use, Effectiveness, Interest And Barriers To Use At A Tertiary-Care Pain Medicine Center

#### BACKGROUND:

The popularity of complementary and alternative medicine (CAM) increased significantly in the U.S. over the last decade, particularly in patients with chronic pain<sup>[1]</sup>. Despite this increase, chronic pain patients continue to experience barriers to CAM access while their physicians remain unaware of their use<sup>[2,3]</sup>. We attempted to quantify the extent of CAM use by patients with painful conditions and to characterize their interactions with pain physicians regarding CAM use.

#### METHODS:

Following Institutional Review Board approval, we performed an anonymous, prospective survey of patients at a tertiary-care spine & pain center. Data collected included patient demographics, pain characteristics, experiences with and perceived barriers to utilizing CAM, and communication with pain physicians regarding CAM.

#### RESULTS:

65% of respondents indicated prior CAM use. Pain physician were least likely to ask about CAM use to those in the 31-50 year age range (51.7%), of female gender (55.8%), of Asian/Indian ethnicity (25%), who completed some graduate school (45%), and with a yearly income between \$50-100,000 (52.5%). Of the 35.7% indicated perceived barriers to CAM use, the most common barriers were expense (28.7%), lack of providers (14%), and lack of insurance coverage (11.6%).

#### CONCLUSION:

Despite interest, barriers to CAM use remain. Disparities exist regarding patient-physician discussion of CAM use. This group utilized CAM at a higher rate than previous reports (65% vs. 38%), which might reflect an improvement in communication and access. There remain groups with whom discussion is limited. Improved access to and physician-patient discussion of CAM use are ongoing issues.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Health Impact Assessment For High Volume Hydraulic Fracturing Via Long Laterals In Livingston County, New York

**BACKGROUND:**

High volume hydraulic fracturing via long laterals is an unconventional process of natural gas extraction that utilizes the injection of hydraulic fluids into vertical and horizontal wells in order to retrieve gases from underlying shale formations. Reports have been made that such a technique may have health consequences for residents nearby. The purpose of this study was to do a health impact assessment for Livingston County, NY - one of many areas in western NY where fracking is predicted to begin.

**METHODS:**

Using GPS coordinate systems, all public water wells, schools, summer camps, lakes, and rivers were mapped out. Based on depth and thickness of the Marcellus Shale layer, proximity of these coordinates to potential drilling sites was determined. A literature review of previous studies on the health effects of hydraulic fracturing was performed and used in conjunction with the analysis of wind patterns, geography, and demographics in order to assess how the establishment of hydraulic fracturing may affect residents of Livingston County.

**RESULTS:**

From an economic perspective, hydraulic fracturing could bring more than \$5,000 additional income to landowners and farmers who may lease out their land. In the Southern portion of Livingston County, the Marcellus Shale and Utica Shale Formation are deeper and thicker than in the north, running 1,000 feet deep, 50 feet thick and 6,000 feet deep, 150 feet thick respectively, making it the most likely area for hydraulic fracturing to take place. In addition to the Genesee River, there are 3 major summer camps, 2 public schools, and 10 towns containing approximately 10,660 residences in the southern area of the county that are at increased risk of water, air, and soil contamination that can potentially result in an array of health manifestations including cancer, chronic lung diseases, and congenital abnormalities. Risk from air pollution is magnified in the eastern portion of the county because of prevailing wind patterns from the west. Its lower geographic elevation and surrounding contours also puts the county's major water shed, Conesus Lake, at particular risk from sedimentary and toxic runoff that may result from the construction of well pads at higher elevations. There seems to be a substantial increased risk of environmental health concerns that would be introduced following high volume hydraulic fracturing in Livingston County, NY.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Integrative Genomic Analysis Revealed Differential mRNA-microRNA Gene Regulatory Networks between Prostate Cancers from African American and Caucasian American Patients

#### OBJECTIVES/BACKGROUND:

Prostate cancer (PCa) is a disease conferred by multiple gene mutations, numerous alternations in gene expression and aberrant changes in genome composition/architecture. An area of research that continues to garner attention is PCa health disparities, wherein the African American (AA) population exhibits higher incidence and mortality rates compared to Caucasian Americans (CA). Although accumulating evidences have suggested that the widespread microRNA and mRNA deregulation may play crucial role in cancer development, the relationship between regulation of mRNA-microRNA genetic network and PCa disparities remains largely unknown.

#### METHODS:

To identify the genetic predispositions and oncogenic networks associated with the observed PCa disparities, we applied a systems biology approach by combining: 1) mRNA expression profiling, 2) microRNA profiling, 3) microRNA target searches, and 4) mRNA-microRNA genetic network analysis to elucidate the molecular mechanism underlying PCa disparities between AA and CA patients. Affymetrix human exon ST1.0 arrays and Agilent human miRNA V2 arrays were used to analyze the global mRNA and microRNA expression profiles in AA and CA prostate cancer specimens and the patient-matched normal counterparts.

#### RESULTS:

Our 4-way statistical analyses (AA cancer vs. CA cancer; AA cancer vs. AA normal, CA cancer vs. CA normal, AA normal vs. CA normal) of mRNA and microRNA gene profiles have identified hundred of mRNAs and dozens of microRNAs which were differentially expressed (FDR < 0.1, fold change > 1.5). mRNA-microRNA pairing and canonical pathway analysis suggested that differential regulation of oncogenic networks may be related to the PCa disparities between AAs and CAs. qRT-PCR, western blot and immunohistochemistry validations have further confirmed the up-regulations of PI3K/AKT and EGF pathways in AA cancers.

#### CONCLUSION:

In summary, this study demonstrated that differential mRNA-microRNA genetic networks may contribute to the differential oncogenic properties of PCa between AAs and CAs. This work was supported by NCI grant 5U01-CA-116937 and ACS-IRG-08-091-01.

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**SCHOOL OF NURSING**

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## The Patient-Centered Medical Home and Emergency Room Utilization

**BACKGROUND:**

Chronic disease care makes up a large portion of health care costs and poor management of these conditions leads to increased utilization of health care services in the emergency room (ER) setting. Many of the visits to the ER could be prevented with improved use of primary care medical services and better care coordination to prevent exacerbation of chronic diseases. The Patient-Centered Medical Home (PCMH) model of care is one method being used to improve chronic disease management, outcomes and to decrease non-emergent ER visits by those with ambulatory care sensitive conditions.

**OBJECTIVES:**

The primary objective of this study was to determine if the new model of health care being implemented across Navy Medicine demonstrated an impact on the use of the emergency room for care of conditions that could be treated within the outpatient setting. Another objective for this study was to examine whether the change to a PCMH model for primary care delivery across Navy medicine would reduce healthcare costs and improve efficiency of care delivery. Research question: What is the impact of the Patient-Centered Medical Home (PCMH) model on emergency room (ER) utilization for non-emergent, outpatient treatable diagnoses?

**METHODS:**

The study was conducted as quantitative observational research in the form of a retrospective data analysis. Data analyzed included PCMH enrollee ER utilization data for eight ambulatory care sensitive conditions seen within the ER at seven Navy military treatment commands and in their communities.

**RESULTS/FINDINGS:**

This study analyzed 233,527 ER visits for the eight included diagnoses. The total included 106,874 direct care visits at the seven military medical Commands and 126,653 purchased care visits at facilities within the local community ERs. Three of the diagnoses demonstrated P values of a statistically significant impact when comparing the pre and post implementation data for direct care visits. Upper respiratory infections had a P value of 0.01, otitis media had a P value of 0.05 and acute conjunctivitis had a P value of 0.03.

**CONCLUSION:**

ER visits remain high for primary care treatable medical conditions and additional practices need to be developed to maximize access to care within primary care settings in order to recapture patient overflow into the emergency setting.

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## SCHOOL OF NURSING

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### Kidney Transplant Essentials for Nursing Students

#### BACKGROUND:

Transplantation, once a rare operation performed only in large academic hospital settings, is becoming a more common surgery with patients being admitted to medical, surgical, and transplant floors within many hospital systems. The numbers of kidney transplant surgeries in the United States have grown tremendously over the years; there were 3,786 performed in 1980, 10,035 performed in 1990, and 14,629 performed in 2000 (NKUDIC, 2012). In 2010, the number of kidney transplants performed in the US reached an all time high of 16,899 (OPTN, 2012).

#### OBJECTIVES:

It is not uncommon for the nursing students of today to have clinical placements with pre or post transplant patients in the hospital setting. In order to better prepare these students to take care of this population, this study explored the potential to enhance student preparation by administering an educational intervention that focused on the dynamics of transplant care delivery.

#### METHODS:

A specific module on kidney and pancreas transplantation was developed along with a ten-question pre-test and post-test. After a study group to assess this testing tool, two groups of nursing students, a summer and fall semester, were invited to take part in the study to assess the impact of the specific transplant module that was presented as a 2-hour lecture.

#### RESULTS:

A pilot study was done to evaluate the pre-test/post-test tool developed prior to usage. Final analysis of the study revealed that there was a significant improvement in post-test as compared to pre-test scores among these two groups of nursing students.

#### CONCLUSIONS:

As transplantation is becoming more commonplace it may be beneficial for nursing schools to place specific modules such as this one on renal transplantation into nursing curriculum.

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## SCHOOL OF NURSING

### Evaluating Pressure Ulcer Risk in Cardiac Surgery Patients

#### BACKGROUND:

Pressure ulcers (PU) that develop during an acute hospitalization can cause undue patient pain and harm, require complicated treatments, and increase length of stay that can place a burden on healthcare resources. Research supports several surgical related risk factors associated with PU, and patients undergoing cardiac surgery have been recognized at increased PU risk. Tools are available to assess risk but may not adequately predict risk in this population.

#### OBJECTIVES:

To determine in cardiac surgery patients, if there was a relationship between extrinsic (procedures) and intrinsic risk factors (co-morbidities) and the development of PU.

#### METHODS:

This was a retrospective, chart review study using a representative sample of two randomly selected cohorts of cardiac surgical patients (106 patients without HAPU; 104 patients with HAPU) discharged from a large, urban, teaching hospital between January 1, 2009 and March 31, 2012. Patient records were evaluated for selected intrinsic and extrinsic risk factors identified in the literature to be associated with PU formation in critically ill cardiac surgery patients. The Statistical Package for the Social Sciences (SPSS) version 20.0 was used to code responses collected from the survey, compute composite scores, calculate descriptive statistics about variables of interest, and conduct inferential statistical analyses to draw conclusions about the population from the sample tested.

#### RESULTS:

An initial 9609 cardiac surgery patients were identified as discharged without PU and 219 were screened to meet inclusion and exclusion criteria. A total of 282 cardiac surgery patients were identified as discharged with PU, and 166 met enrollment criteria. Combined intrinsic variables of respiratory disease and diabetes were found to have a statistically significant relationship ( $p = .035$ ) to the development of PU. Extrinsic variables found to have a statistically significant relationship to PU development were related to vasoactive infusion ( $p = <.001$ ) and hospital-to-hospital transfer ( $p = .004$ ).

#### CONCLUSION:

This information further contributes to the body of knowledge for PU prevention. Combining these intrinsic and extrinsic factors with Braden assessment as indicators of risk for cardiac surgery patients will lead to development of an individualized prevention plan for each cardiac surgery patient. Having this individual plan will decrease PU in this population.

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## SCHOOL OF NURSING

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### Health Literacy Knowledge and Experience: Advanced Practice Registered Nurses in the Acute Care Setting

#### BACKGROUND:

Individuals who are deficient in health literacy (HL) abilities cross all boundaries of race, age, gender, education and socioeconomic status. It is proposed that a person's literacy level is the strongest correlate of health knowledge, and is a contributing factor in existing health care disparities. Increasing numbers of Advanced Practice Registered Nurses (APRNs) treating patients in the acute care setting have a responsibility to effectively communicate health information during each patient interaction. Patients require adequate HL skills in order to understand and act upon the information provided by APRNs. Deficient HL skills impact patient-provider communication and health outcomes. The APRNs treating patients with low HL may be ill-prepared to meet the learning needs of their patients.

#### OBJECTIVES:

The study's aim is to describe the general knowledge of HL concepts by APRNs as captured in the Health Literacy- Knowledge and Experience Survey (HL-KES) by Catherine Cormier. It describes five HL content areas, including basic facts on health literacy, consequences associated with low health literacy, knowledge about health literacy screening, evaluating the effectiveness of healthcare information, and guidelines for presenting written healthcare information. The study describes the experiences that APRNs have with HL activities like providing and evaluating educational materials. Demographic characteristics and relationships among the variables are explored.

#### METHODS:

This is a one sample, one time, descriptive, cross-sectional study of 106 APRNs working in acute care settings within a multi-hospital health system, who responded to Cormier's HL-KES through a mixed mode collection process. Data analyzed by SAS<sup>®</sup> was primarily descriptive in approach. The Communication Accommodation Theory provided a theoretical framework for the concept of the study.

#### RESULTS:

Statistical analysis revealed knowledge gaps among APRNs in all five HL content areas. There were no associations between APRN knowledge and years' experience in the APRN role, age of the APRN, or with most educational preparations. The APRNs enrolled in terminal degree programs had statistically significant higher scores regarding HL knowledge than study subjects not enrolled in these programs.

#### CONCLUSIONS:

Information from the study may provide a framework for addressing HL learning needs of APRNs. Educational enrichment may translate into improved patient-provider communication for all practitioners and improved patient health outcomes. Organizational policy and practice changes regarding the impact of activities to increase HL awareness are potential outcomes as a result of this study.

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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## The Effects of Smoking on Metabolic Control and Diabetes-Related Complications in Type 1 Diabetes

**OBJECTIVE:**

Several studies have demonstrated the significant effects of smoking on the risk of microvascular complications, however, few have also examined the mediating effects of HbA1c. Using publicly available data from the well-characterized cohort of 1,441 subjects with type 1 diabetes who participated in the Diabetes Control and Complications Trial (DCCT), we describe the acute and long-term risks of smoking on glycemic control and microvascular complications (nephropathy and retinopathy).

**METHODS:**

Over a mean of 6.5 years of follow-up, the DCCT recorded self-reported smoking behaviors, glycemic exposure based on HbA1c values, and complication status. Generalized linear mixed models were used to assess whether time-dependent measurements of smoking predict HbA1c levels. Cox proportional hazard models were used to assess time-dependent smoking exposures as predictors of nephropathy and retinopathy. All models were adjusted for potential baseline confounders.

**RESULTS:**

During the DCCT, current smokers had consistently higher HbA1c values compared with former and never smokers (0.35% mean difference vs. never smokers; 0.29% mean difference vs. former smokers). Additionally, current smokers had a 42% higher risk of retinopathy and 34% higher risk of nephropathy compared with never smokers. The significant associations between smoking and complications were fully attenuated after adjusting for HbA1c. Former smokers did not differ significantly from never smokers with respect to HbA1c and the risk of complications.

**CONCLUSIONS:**

Smoking is associated with poor glycemic control and an increased risk of microvascular complications in individuals with type 1 diabetes. Our data suggest that the negative effects of smoking on glycemic control may be a mechanism by which smoking leads to complications of type 1 diabetes. The harmful effects of smoking on HbA1c and the risk of complications may not persist after quitting smoking.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Opening up online: an observational study on the use of Facebook for disclosing personal health and wellness information

#### BACKGROUND:

Health professionals may need to shift their methods of practice among college students if they wish to effectively communicate and influence this population. With the development of social media networks, confiding is an immediate process. The 2012 Pew Report concluded that majority of social networking users are between the ages of 18-29 (1), with Facebook being the most popular social networking site among college students (80% of all college students are Facebook users (2). As of 2011, Facebook was the most frequently sought out website and had the most time spent on the website by visitors (4). Facebook pages are being developed as forums for those struggling with topics relevant to public health, such as the Weight Watchers Facebook page (3), a place where members can express feelings, share experiences, and ask for advice. However, the cyber world may not provide the diagnosis and treatment necessary for clinical conditions.

#### OBJECTIVE:

This study assesses the content in the newly created Facebook Page: GWU Secrets, a page moderated by student(s) allowing for "secrets" to be posted anonymously through survey monkey or Gmail.

#### METHODS:

All Facebook posts (n=474) as of 02/23/2013 were downloaded. Of the total number of posts, approximately 25% (n=123) were selected randomly and evaluated in terms of frequency and content. An initial coding revealed 6 public health related themes: 1=weight, eating disorder, and body image 2=sexuality and sex, 3=alcohol and drug, 4=relationship, 5= socioeconomic, and 6= loneliness/depression.

#### RESULTS:

Among all posts 47% were related to specific public health themes: socioeconomic status (3%), weight or body image dissatisfaction (3%), loneliness/ depression (3%), drugs or alcohol (7%), relationships (14%), sex or sexuality (17%). Other themes included life as a varsity athlete, grades, residence life, Greek life, and religious beliefs.

#### CONCLUSIONS:

The data provides a snapshot of the relevant public health issues discussed in an online medium amongst college students. The GWSecrets Facebook page has only been live for two weeks and has already generated 474 posts, some of which indicate students seeking help for health and mental health related topics. These data are important for emphasizing the cultural change occurring among our college students. Public health professionals must also adapt to these changing times in order to be maximally effective at reaching all populations with the right messages, in the right forums, at the right time.

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#### SOURCES

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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## Asymptomatic African Americans with high-risk APOL1 genotypes show signs of impaired angiogenesis

**OBJECTIVE:**

*African Americans having two high-risk Apolipoprotein L-1 (APOL1) alleles, termed G1 and G2, are about 7 times more likely to develop non-diabetic kidney diseases. We sought to identify potential urine biomarkers differentially excreted by young, asymptomatic African Americans having high-risk APOL1 genotypes when compared with WT participants.*

**METHODS:**

Thirty-seven previously genotyped participants (5 high-risk G1 homozygotes, 20 WT homozygotes, and 12 heterozygotes) donated mid-stream, first morning urine samples. Three label-free urine samples from each homozygote group were processed for SDS-PAGE, LC-MS/MS analysis and proteome profiling.

**RESULTS:**

About 315 proteins were identified in each urine sample. Proteins that were elevated in urine in those having high-risk APOL1 genotypes relative to control participants included: angiotensinogen, haptoglobin, pyruvate kinase isozymes M1/M2, alpha-enolase, lymphatic vessel endothelial hyaluronic acid receptor 1, alpha-1-antichymotrypsin, alpha-1-antitrypsin, vesicular integral-membrane protein VIP36. The following proteins were excreted less by high-risk participants: kallikrein-1, aminopeptidase N, syndecan-4, IST1 homolog, leukocyte-associated immunoglobulin-like receptor, mucin-20, leukocyte elastase inhibitor, glutathione peroxidase 3, protein HEG homolog 1, and small proline-rich protein 3. Many of these proteins are associated with angiogenesis and subsequent urinary cytokine analysis with Milliplex Human Cytokine/Chemokine Panel bead assay revealed that four angiogenesis-promoting cytokines are significantly reduced in the high-risk group: TGF- $\alpha$  (P=0.004), PDGF-AA (P=0.016), IL-1-alpha (P=0.032), VEGF (P=0.036).

**CONCLUSION:**

This pilot data indicates that young, asymptomatic African Americans with high-risk ApoL1 genotypes may have impaired angiogenesis. These results are consistent with prior evidence indicating that vascular disease may underlie ApoL1-associated kidney diseases. This study was funded by a CTSA pilot award.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### HIV Status, HAART, and Sperm Aneuploidy

#### BACKGROUND:

With the use of Highly Active Antiretroviral Therapy (HAART), HIV has transitioned to become a chronic disease rather than a life threatening illness. This allows HIV positive men to lead more normal lives and pursue opportunities to procreate. There have been a few studies that have evaluated the sperm health in HIV positive men undergoing ART, suggesting that standard sperm parameters are negatively affected by treatment.

#### OBJECTIVES:

This study examines the current knowledge of the effects that HAART may have on sperm health, particularly looking into potential chromosomal abnormalities and proposes a new study to evaluate the impacts of HIV, HAART, and sperm aneuploidy.

#### METHODS:

A systematic search of the literature was done using the key words "sperm health", "HIV", and "antiretrovirals". The resulting studies were divided between those that found negative associations between ART and semen health and those that found no association or a positive association (improvement in semen quality).

#### RESULTS:

The search resulted in eight studies that looked at the effects of ART on sperm parameters. Looking across the studies, there is suggestion that ART has a greater impact on sperm parameters than HIV. Of the eight studies, only one of those studies looked directly at chromosomal abnormalities, while the others focused on sperm parameters as defined by the World Health Organization. Only one found a positive association between ART and semen parameters. One study suggests that ART improves the outcome of IUI and sperm washing. One study suggests that HAART may improve semen parameters but states that the study was too short to see the potential detrimental effects. The remaining five studies saw negative relationships between ART and semen parameters, one of which suggests that ART is toxic to gametes and can cause mitochondrial damage.

#### CONCLUSION:

Studies previously conducted suggest that ART is more detrimental to semen health than HIV and may lead to mitochondrial damage. However, very few studies have looked into the possible chromosomal abnormalities that result from the use of HAART and the effects on male fertility. This literature review has resulted in the initiation of a study examining sperm chromosomal abnormalities among participants in the Men's AIDS Cohort Study (MACS). A comparison of sperm chromosomes will be made between HIV-positive men undergoing HAART and HIV-positive men not using HAART. It is hypothesized that men currently undergoing HAART will have a higher frequency of aneuploidy. Results to date will be presented.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Prevalence and Genotype Distribution of HPV in Atypical Glandular Cell-Grade Liquid-Based Cytology Specimens: Case-Control Study

#### INTRODUCTION:

Although the incidence of squamous cell cervical cancers in the U.S. has markedly declined over time with the introduction of the Papanicolaou (Pap) test, the incidence of glandular cell cancers has increased. The sensitivity of detecting lesions containing abnormal glandular cells is much lower than that for lesions containing abnormal squamous cells. While AGC-grade cytology results represent <1% of all Pap test results reported annually in the U.S., up to 40% of them represent a corresponding high-grade lesion on the follow-up biopsy. Guidelines for managing AGC-grade cytology released in 2006 by the American Society for Colposcopy and Cervical Pathology include HPV testing. The purpose of this study was to determine the prevalence and genotype distribution of HPV in AGC-grade liquid-based cytology (LBC) specimens compared to control specimens negative for intraepithelial lesion or malignancy (NILM).

#### METHODS:

Quest Diagnostics provided de-identified case and control LBC specimens. Cases were women with AGC-grade LBC specimens collected between 2007-2012. Controls were a sample of women with NILM-grade LBC specimens collected between 2011-2012. DNA was extracted from LBC specimens using the QIAamp MinElute Media Kit (Qiagen Inc.) and amplified by PCR using the Linear Array HPV Genotyping Kit (Roche Molecular Inc.). To compare HPV prevalence and genotype distribution between AGC-grade cases and NILM controls, we used multivariate logistic regression to generate age-adjusted odds ratios (ORadj) and 95% confidence intervals (CI).

#### RESULTS:

Fifty-three AGC-grade LBC specimens (mean age; 57 yrs, age range; 18-95 yrs) and 338 NILM LBC specimens (mean age; 45 yrs, age range; 20-91 yrs) were screened for 37 types of HPV DNA: 13 high-risk (HR) HPV types and 24 low-risk (LR) HPV types. Any HR-HPV was present in 34% of AGC-grade specimens and 7.4% of NILM specimens (ORadj=9.11; 95% CI: 4.08-20.33, p-value<0.001). When limited to HPV 16/18, at least one was present in 20.1% of AGC-grade specimens and 1.2% of NILM specimens (ORadj=40.10, 95% CI: 10.73-149.88, p-value<0.001). In contrast, prevalence of low-risk (LR) HPV was similar between the two groups: 15% of AGC-grade specimens and 17.2% of NILM specimens (ORadj=0.91; 95% CI: 0.35-2.31, p-value=0.834).

#### CONCLUSION:

AGC-grade specimens were found to contain a significantly higher rate of HR-HPV, especially HPV types 16 or 18 when compared to NILM specimens. These findings support the earlier recommendation that HPV testing should be performed on LBC specimens with AGC-grade diagnosis and suggests that genotyping may be a useful addition to the follow up testing being performed.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Non-invasive tests for liver fibrosis in patients with Human Immunodeficiency Virus and Hepatitis C Virus co-infection

#### BACKGROUND:

End-stage liver disease due to HCV is now emerging as a major cause of death in HIV+ patients treated with HAART. Liver biopsy is now the standard procedure to determine the extent of liver fibrosis in HIV+/HCV+ patients for decisions on HCV treatment and management. Repeated assessments of liver fibrosis are desirable, but liver biopsy is invasive with known errors in sampling. There is a need for non-invasive markers of liver fibrosis in this patient population.

#### OBJECTIVES:

The purpose of this study was to evaluate three non-invasive markers of liver fibrosis in HIV+/HCV+ patients using markers described as useful in previous studies: APRI (AST, platelets), FIB-4 (age, AST, ALT, platelets), and HGM-1 (platelets, AST, glucose).

#### METHODS:

Pathology reports 2003-2011 at GWU-Hospital were reviewed to identify liver biopsies from HIV+/HCV+ patients who had clinical data and lab tests available for calculation of APRI, Fib-4 and HGM-1 (within 2 months of biopsy on average). Liver biopsies were assigned a fibrosis score as determined by the METAVIR scoring system (scale of F0-4; F0 none to F4 cirrhosis). The positive predictive value (PPV) of each non-invasive marker was calculated according to cut-offs established by previous studies as most reliable in the prediction of significant fibrosis on liver biopsy, APRI ( $\geq F3$ ), Fib-4 ( $> F2$ ), and HGM-1 ( $\geq F2$ ).

#### RESULTS:

Forty-four HIV+/HCV+ patients had liver biopsy and requisite lab tests available for analysis. Mean age was 52, 64% male, 88% were black. HIV Mean CD4 count was 464.4 (n=33), HIV RNA 32,800 copies/ml (3 pts  $> 100,000$ ; n=34). HCV was genotype 1 in 97% (n=34), mean HCV RNA  $> 3$  million IU/ml (16 pts  $> 1$  million; n=35). METAVIR fibrosis scores on liver biopsy were F0 (n=2), F1 (n=16), F2 (n=9), F3 (n=7), F4 (n=10);  $F \geq 2$  in 26 patients (59%). In predicting the presence of significant fibrosis on liver biopsy, APRI had a PPV of 0.846 (AUC 0.834), Fib-4 PPV was 0.867 (AUC 0.836) and HGM-1 PPV was 0.929 (AUC 0.799). In predicting the absence of significant fibrosis, APRI, Fib-4 and HGM-1 all had a PPV of 0.75.

#### CONCLUSIONS:

Our findings suggest that APRI, Fib-4 and HGM-1 can be reliable surrogate markers to predict liver fibrosis in HIV+/HCV+ patients. The markers can be readily calculated from laboratory tests that are routinely done in these patients. The use of these non-invasive markers may reduce the need and frequency for invasive liver biopsy in this high-risk population.

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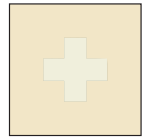
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# HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Bringing Community Awareness to Animal-Assisted Therapy: How AAT Can Be Implemented in Washington D.C. Service Facilities

#### BACKGROUND:

Over time, AAT has been implemented in a variety of healthcare settings due to its positive psychological, emotional, and physiological effects. Most of the research on AAT, however, does not include its effects on the community. For example, homeless shelters, abuse shelters, etc. are services for the community that primarily deal with individuals suffering from psychological, emotional, or physical distress. More research must be conducted in community settings to determine how effective AAT can be as a therapy.

#### OBJECTIVES:

The goals of the project included to incorporate a community service opportunity into a learning experience by creating an educational video on AAT; to learn the benefits of AAT in a healthcare setting; and to identify which service facilities for the homeless in Washington D.C. have an interest in implementing AAT.

#### METHODS:

A video was created to capture the benefits of AAT entitled The Healing Powers of Dog Therapy. Four D.C. service facilities viewed the video and completed surveys composed of twelve questions used to assess the effectiveness of The Healing Powers of Dog Therapy video as an educational tool on AAT and to assess the interest in implementing AAT as a service. The facilities that were surveyed included Community Council for the Homeless at Friendship Place, N Street Village, Bread for the City, and the GW Breast Care Center.

#### RESULTS:

36 surveys total were completed with 30 being current staff members at the previously listed facilities. Over 90% of those surveyed thought that The Healing Powers of Dog Therapy video was an effective educational tool on AAT. Only 47% of those surveyed, however, thought that AAT would be applicable at their facility. The greatest concern, which 20% of people that were surveyed conveyed, was that their residents/patients might have had a traumatic experience in the past, leading them to be resistant to AAT.

#### CONCLUSIONS:

Due to the survey results, it appears that there is a great interest in the beneficial effects of AAT but in terms of implementation, more research will need to be done for each facility individually. Further research should include an assessment of how the patients/residents feel about AAT in order to accurately gauge how beneficial it will be in a specific setting. Because facilities that serve the community are extremely versatile, it would be crucial to analyze the population in which the facility serves to best assess how AAT can be implemented in that facility.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Investigation of Factors Limiting Completion of Chlamydia Screening in Adolescents Age 12 Through 21 Years

#### BACKGROUND:

According to the Center of Disease Control and Prevention (CDC), chlamydia is the most commonly sexually transmitted disease with reports of 1,307,893 chlamydial infections in 2010<sup>1,2</sup>. The National Collaborative for Innovation in Quality Measurement (NCINQ) has defined three steps to address the issue of chlamydia in adolescents: documentation of sexual activity, screening all sexually active adolescents and treating all who tested positive<sup>3</sup>. However, an effective method of screening is necessary to find all those at risk of infection. The rate of chlamydia screening is currently untracked and unknown at the Adolescent Health Center (AHC) at Children's National Medical Center (CNMC). The following study was completed to pilot the documentation of female sexual activity at CNMC.

#### OBJECTIVES:

To determine the rate of sexual activity documentation among AHC females patients, ages 12 through 21 years seen in the AHC, reporting methods of screening results and the impact of pre-completed templates on documentation.

#### METHODS:

A retrospective chart review of adolescent females, ages 12-21, was conducted and analyzed for documentation of sexual activity. Patients were defined as sexually active if there was documentation of one of six criteria for sexual activity: self reported sexual activity, number of partners, contraceptive use, non pharmaceutical contraceptive use, previous STI or previous pregnancy. Patients were analyzed in two cohorts: Week1 (116 patients) and Week2 (159 patients). Results for documented sexual activity were obtained for Well Child Checks (WCC), and Not Well Child Checks (NWCC). AHC Burges Clinic and Eating Disorder patients were excluded from the study. Changes in electronic documentation style were made between Week1 and Week2.

#### RESULTS:

During Week 1, sexual activity in females was documented for 31 of 33 WCC cases (93.94%) and 77 of 83 NWCC cases (92.77%) with a total of 8 undocumented cases.

During Week 2, sexual activity in females was documented for 22 of 24 WCC cases (91.67%) and 78 of 89 NWCC cases (87.64%) with a total of 11 undocumented cases.

Sexual activity documentation was completed by all providers using electronic structured data.

#### CONCLUSIONS:

While there was near perfect documentation of sexual activity during Week1, there was a drop in documentation from 92.77% to 87.64% during Week2. This increase in improper documentation may be due to the use of pre-selected templates. Further studies are required to fully evaluate chlamydia-screening methods.

#### STATUS

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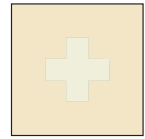
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2. Centers for Disease Control and Prevention. 2011. *Sexually Transmitted Diseases: Chlamydia - CDC Fact Sheet*. STF Facts - Chlamydia
3. Draft Document for NCINQ 2012 Public Comment. 2012. Chlamydia Identification and Follow-Up Measure Suite.

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# HEALTH SERVICES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Exploring Sexual Health Practice Patterns and the Need for a Center for Sexual Health at The George Washington University

#### BACKGROUND:

Healthy sexual function plays a fundamental role in a patient's overall health and wellbeing. Despite the pervasiveness of sexual problems within the general population, physicians often lack the knowledge and comfort level necessary for the adequate screening, management and referral of patients with sexual health and function concerns. These problems can be devastating, especially if they are not recognized and managed appropriately. This project seeks to explore the perceptions and practice patterns of MFA providers regarding the sexual health and function of their patients.

#### METHODS:

An online survey was developed to examine the following: primary and secondary sexual health/function issues among patients within different MFA specialties, screening and referral patterns in addressing sexual health and function issues among MFA providers, perceived barriers to these practices, current capacity and comfort level of MFA physicians in addressing sexual health issues experienced by their patients, and interest in the development of a Center for Sexual Health at GW. Upon completion of the survey, one-on-one interviews will be conducted with consenting physicians to explore the specific health needs of their specific patient populations. As this is an initial exploratory study, basic descriptive analyses will be performed to calculate means and percentages and examine the distribution characteristics of the survey data.

#### RESULTS TO DATE:

The survey has received IRB approval, but data collection has yet to be completed. Preliminary data from a small number of responses suggest that about 50% of MFA practitioners see patients with sexual health issues "often" or "very often". Responses suggest that the top barriers experienced by MFA practitioners to screening for and referring patients for sexual health issues include time constraints, lack of competence in treating sexual health issues, financial/insurance issues, and lack of available providers. Thus far, there has been overwhelmingly positive response among MFA practitioners in regards to the need for a Center for Sexual Health at GW as well as an eagerness to refer to such center were it to exist.

#### CONCLUSIONS:

Findings from the proposed survey and follow-up interviews will provide MFA practitioners interested in developing a Center for Sexual Health at GW with the information necessary to provide effective and comprehensive sexual health services for MFA patients. The project will also help inform providers of the need for such a clinic and the availability of sexual health specialty care within the MFA.

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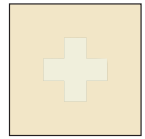
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## SCHOOL OF NURSING

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### Veterans Perception of Co-residents Death in the Community Living Centers of South Texas Veterans Health Care System

#### BACKGROUND AND SIGNIFICANCE:

Veterans share a unique history and camaraderie. The Veterans living in the Community Living Centers of the South Texas Veteran's Health Care System experience emotions and feelings that would indicate that they experience the death of their co-residents in a unique manner that is consistent with their military experience.

#### RESEARCH QUESTION:

The purpose of this study was to explore veteran's perception of the death of the co-residents whom they live amongst in the Community Living Centers of the South Texas Veteran's Health Care System.

#### METHODOLOGY:

This study used Husserl's phenomenology as a basis for this qualitative research study. Individual interviews were conducted in the Community Living Centers of the South Texas Veteran's Health Care System in the room of the veteran's choosing.

#### FINDINGS:

Veterans related their perceptions of the death of co-residents to the death of previous deaths experienced while serving in the military. Combat veterans linked the death of their co-resident to the death they experienced while serving in combat. Veterans experiencing the death of a fellow veteran regardless of period served experienced these memories of combat and previous death

#### CONCLUSION:

This study was designed to identify the perceptions veterans have on the loss of their fellow military veterans. The results of this study will assist healthcare professionals with the knowledge needed to understand how veterans perceive the loss of their comrades. The results indicated that health care providers may need to provide additional support for veterans and especially combat veterans in adjusting to the death of fellow veterans.

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#### STATUS

Graduate Student

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#### AUTHORS

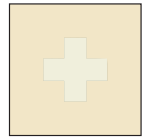
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## SCHOOL OF NURSING

### Nurse Practitioner Safety Net Clinic: Health Care Access and Chronic Disease Management

#### BACKGROUND:

The population without health insurance in America is continuously increasing. Safety net clinics provide access to care for the uninsured, and nurse practitioners (NPs) are often the primary care providers. The NP Timely Access to Care (TAC) clinic provides primary care to low income, uninsured adults eligible for services from the Arlington Free Clinic (AFC). Chronic disease management depends on the ability of the population to access health care. Wagner's Chronic Care Model (CCM) framework is used to evaluate disease management and access to care in this study.

#### OBJECTIVE:

The study purpose is to better understand chronic disease management in the uninsured population accessing health care through the NP TAC clinic. The primary aim is to evaluate the effectiveness of the TAC clinic in achieving high blood pressure (BP) reduction. The study aims to identify clinic resources affecting disease management to improve health care outcomes.

#### METHODS:

A convenience sample of 27 subjects was selected. Retrospective medical record review evaluated new NP TAC clinic patients for chronic disease management as evidenced by high BP control. Study data collection focused on the first and last NP TAC clinic visit within twelve months with an indication of high BP according to *Seventh Report of the Joint National Committee on Evaluation and Treatment of High Blood Pressure (JNC7)*. JNC7 guidelines were used to develop an audit tool for data collection from care access to the last TAC encounter, Time 1 to Time 2. CCM intervening variables were counted from Time 1 to Time 2. Study data for BP were analyzed by paired t-test for before and after change. CCM variables were analyzed using descriptive statistics for mean and correlation with BP control.

#### RESULTS:

Findings included a statistically significant reduction in average systolic BP ( $p = 0.012$ , 95% CI [-21.05, -2.80]), and reduction in diastolic BP ( $p = 0.057$ , 95% CI [-12.78, 0.191]). Average number of NP TAC clinic encounters was 3.89. Subjects with BP above goal had an increased average use of CCM elements including TAC and medical clinic, diet education, nurse case management, and medication treatment at AFC.

#### CONCLUSION:

NP TAC clinic's management of hypertension reduced average BP. Access to free clinic resources was augmented to improve chronic disease management in subjects with poorly controlled BP. Study results can be used to describe the role of the NP TAC clinic in chronic disease management and access to care to improve patient outcomes.

#### STATUS

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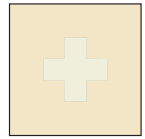
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**SCHOOL OF NURSING**

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## A Descriptive Study Investigating Medical Evacuations of Foreign Service Personnel from Overseas

**BACKGROUND:**

Living and working abroad can conjure up images of a captivating lifestyle, however the realities of life overseas often fall far short of these idealistic expectations especially in the context of foreign healthcare systems. The Department of State Office of Medical Services (MED) provides medical care in most of its Embassies and Consulates around the world and managed approximately 1500 medical evacuations in 2010. Foreign Service personnel requiring medical evacuation (medevac) from overseas is increasing at a rate of approximately 10% every year. Other than numbers there is little other information known regarding these patients.

**METHODS:**

Utilizing a retrospective chart review of medevac's from six overseas posts in the Balkans, the researcher reviewed the causes of the evacuations and sought to answer the following research questions: What are the characteristics of patients who are medically evacuated from an overseas post? What are the common characteristics among medevac patients that could be used to develop and improve care system processes?

**RESULTS:**

The average population of the six posts evaluated was 1056 persons, with a yearly medevac rate of 4%. The top four causes of evacuation (excluding OB and prenatal screening were, Orthopedic (31%), Gastrointestinal (16%), Cardiac (9%), and Urologic (9%). Males and females were evacuated in equal proportions (51% and 48%), employees at a higher rate than eligible family members (56% and 44%), and married persons at a greater frequency than single people (48% and 31%). Only 31% of all medevac cases were classified as true emergencies, and only 15% were hospitalized before evacuation. Almost 46% of patients did not receive treatment before evacuation, and a U.S. licensed provider did not evaluate 21% of patients prior to medevac.

**CONCLUSIONS:**

This study was small and its results should be viewed with caution. Nevertheless based on this small sample the results show that meaningful data can be obtained by looking at medical evacuations. Additional studies encompassing more posts in different regions would serve to elicit data that is generalizable to our population as a whole with the eventual goal of improving our care processes to better serve our patients.

**STATUS**

Postdoctoral Student

**AUTHOR**

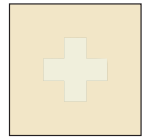
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## SCHOOL OF NURSING

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### One Week Follow-up Visits Post-Hospitalization and its Effect on Reducing One Month Readmissions

#### BACKGROUND

Prevention of 30 day re-admissions of Medicare patients is at the forefront of health care reform and a provision of quality care. Since this population faces many uncertainties during the transition period from hospital to home, addressing and understanding causes and factors for re-hospitalization is imperative in reducing Medicare spending and improving quality outcomes.

#### OBJECTIVES

The research question that steered this study: In the Medicare population with chronic illness, will a 7 day post hospital visit with a primary care provider reduce readmission within 30 days? This study strived to determine if data shows reduction in 30 hospital readmissions in the Medicare population with chronic illness after implementation of a 7 day follow up hospital appointment by a primary care provider.

#### METHOD

A retrospective study was used to collect data via chart reviews from a non-random sample of two independent groups of Medicare age patients with one or more chronic illnesses. One group received a 7 day post hospitalization follow up visit with a primary care provider and the other did not receive the intervention. A discharge check list was discussed with the patient at the 7 day appointment to ensure completion and uniformity among providers.

#### RESULTS

Multiple logistic regression analysis determined that a significant association occurred with the odds of not being readmitted after a 7 day follow up appointment was 20 times greater than a patient without 7 day appointment. Age was found to be a significant factor for readmission. For every age a patient was older the odds of being readmitted was increased by a factor of 1.175. Furthermore, patients with social support were 38 times not to be readmitted within 30 days and heart failure was shown to predict readmission by a factor of 62.82.

#### CONCLUSIONS

The data reveals 7 day follow-up appointments are beneficial for Medicare patients in the prevention of hospital readmissions. Data results also demonstrated that having social support, not having heart failure as a diagnosis, and being in a younger Medicare age bracket was significantly predictable in preventing readmissions. The association of a 7 day follow up appointment post hospitalization in the prevention of readmission may warrant changes in preventative guidelines to decrease readmissions and improve quality of care.

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#### STATUS

Graduate Student

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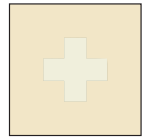
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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Formative Evaluation of the New Mexico Quitline's Quit for Life Program, a Text Messaging Pilot Study

#### BACKGROUND:

Despite widespread awareness about the health risks associated with smoking, about 43.8 million Americans still smoke cigarettes—about 1 in 5 adults. As a result tobacco use remains the leading cause of disease and premature death in the US. Therefore, innovative strategies and programs that encourage Americans to quit—and remain quitters—are sorely needed. Text messaging combined with phone counseling offers one prospective method that has not yet been investigated.

#### OBJECTIVE:

To evaluate callers to a Quitline in New Mexico for their satisfaction with an integrated text messaging program offered in conjunction with Quitline services.

#### METHODS:

Forty (n=40) 10-15 minute semi-structured interviews were conducted, consisting of questions related to participants' use of mobile phones; their feelings about quitting; their experiences using Text2Quit; and the potential for combining Quitline counseling with text messaging services. Adult smokers 18 years of age and older were recruited from a database of callers to the New Mexico state Quitline. Participants were surveyed after at least two weeks from their self-selected "quit date." There was no follow up conducted.

#### RESULTS:

As of the study midpoint, roughly two-thirds (64%) of participants reported using a smartphone, while 36% admitted to using a feature phone. Those who had quit versus not quit smoking on their scheduled quit date was almost evenly split, with 47% not quitting and 53% quitting. Despite the fact that the majority of participants admitted to quitting on their quit date, 59% still smoke either "everyday" or "somedays," while 41% say they don't smoke at all.

Overall, the participants rated the text messaging program a 3.8 out of 5. The majority would "highly recommend" the text messages and phone counseling separately to a friend, 68% and 77%, respectively, a figure that increased to 100% when the two services were combined. The website did not appear to be a useful service for the participants.

While each of the services individually and collectively was well-received, participants did note that they would have preferred fewer texts and texts with more variety, but they didn't specify at what point in time. Only two participants, however, remarked that they had stopped the texts altogether.

#### CONCLUSION:

The results support the notion that text messaging combined with phone counseling offers a promising strategy for tobacco cessation. Future studies are recommended that examine how best to integrate these two services so as to optimize quit rates and minimize relapses.

#### STATUS

Graduate Student

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#### SOURCES

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# HIV/AIDS

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### World Health Organization, Department of HIV/AIDS Investigation of Proposed Indicator: Annual Infection Rate

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#### BACKGROUND:

The Annual Infection Rate (AIR) has recently been proposed as a new indicator at a consultation to discuss the Framework for Metrics to Support Treatment as Prevention in order to assess the progression of HIV in countries annually and quantitatively measure its prevention. AIR is defined under the following equation:

$$\text{AIR} = \text{Pi} * (0.1 * (1 - \text{Pts}) + .004 * \text{Pts})$$

AIR: Annual Infection Rate

Pi: HIV Prevalence %

Pts: % ART Coverage with Viral Suppression

It should be noted that such data is not always concretely found and has to be estimated based on the number of people who are in need of ART and have also received treatment.

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#### METHODS:

In this study, AIR was calculated for 6 countries based on the 6 WHO Regions - Afghanistan, Mali, the Russian Federation, Thailand, Viet Nam, and the United States - and was analyzed based on data from the year 2009, 2010, and 2011 and projected to represent the infection rate in 2020. We used the prevalence data and % ART coverage from various sources, including the 2010 UNAIDS Report on The Global AIDS Epidemic and WHO/HIV data, and for the United States, we used the Centers for Disease Control and Prevention (CDC) database.

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#### RESULTS:

The results have shown that as the % ART coverage with viral suppression increases the AIR decreases, as long as it is not superseded by the increase in HIV prevalence. If the rate of HIV prevalence increases at a higher rate than the suppression of viral load, then there will be an increase in the AIR and incidence. However, there are cases where there is already a large percentage of the population with ART coverage and viral suppression, that the country is continuously inflicted with the high prevalence burden of HIV, and other preventive measures must be taken to reduce the Annual Infection Rate and incidence of HIV.

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#### CONCLUSION:

The project has revealed the potential of a new WHO indicator, as there are many benefits to using the Annual Infection Rate (AIR) as a possible tool to measure the success of Treatment as Prevention (TasP) of HIV. Though there are many factors that conflict with the AIR equation as being a flawless indicator to demonstrate the risk of transmission, further development would allow monitoring through the Annual Infection Rate as a means towards eliminating the infection and curbing the global epidemic of HIV.

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#### STATUS

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Mg-supplementation protects against ritonavir-mediated endothelial oxidative stress and eNOS downregulation and dysfunction

**BACKGROUND:**

Ritonavir (RTV), a prototypical protease inhibitor currently used as a key component for anti-HIV therapy, is well known for its endothelial toxicity.

**OBJECTIVE:**

The effects of high Mg on RTV-mediated endothelial oxidative stress and nitric oxide synthase (NOS) down-regulation were investigated.

**METHODS AND RESULTS:**

When bovine aortic endothelial cells (ECs) in normal Mg (0.8 mM) were incubated with RTV for 48 hrs, cell viability, determined by the MTT assay, was reduced dose-dependently by RTV in clinical relevant levels (5-20 uM). High Mg (2 mM) significantly and substantially reversed the lost cell viability up to 100%; N-acetylcysteine (1 mM) was also found partially effective. ECs incubated with 15 uM RTV for 6 and 24 hrs resulted in 2.5- and 3.8-fold elevation of GSSG levels and a 25% decrease (24 hrs) of GSH. At 24 hrs, elevated EC intracellular superoxide production due to RTV treatment was detected by dihydroethidium (DHE) staining, and was increased 41% when quantified by flow cytometry; both decreased GSH and increased superoxide levels caused by RTV were completely suppressed by 2 mM Mg. Concomitantly, the NO product, nitrite level, determined by the DAN fluorescence assay, was reduced 20-40% 24-48 hrs later; such decreases were substantially prevented by high Mg. eNOS expression was determined by real time quantitative PCR; RTV diminished the eNOS mRNA by 25% ( $p < 0.01$ ) which was reversed back to 107% of control by 2 mM Mg. Western blot analysis revealed that RTV treatment did not decrease the total eNOS protein, but resulted in substantial eNOS protein monomerization which was significantly attenuated by Mg-supplementation.

**CONCLUSION:**

It is suggested that RTV-mediated eNOS monomerization and uncoupling may also contribute to elevated superoxide production and GSH oxidation and depletion. The protective mechanisms of high Mg may be related to its direct anti-peroxidative and calcium blocking properties. (Supported by NIH-R21NR012649)

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Progress Realized: Trends in Community HIV-1 Viral Load and CD4 Cell Count in a VA Medical Center between 1999-2011

**BACKGROUND:**

HIV care has changed dramatically in the last thirteen years due to advancements in antiretroviral therapies, which have allowed improvements in HIV-1 RNA or viral loads (VL) and CD4 cell counts (CD4). Our Infectious Diseases Clinic at the Veterans Administration Medical Center (VAMC) has provided HIV and primary care in a comprehensive model with a multidisciplinary team of nurses, physicians, social workers, pharmacists, and medical subspecialists on-site. We describe VL and concurrent CD4 during 1999-2011 for patients in this clinic within the District of Columbia, which has the highest US HIV prevalence.

**OBJECTIVES:**

To describe VL and concurrent CD4 over a thirteen year period in the VAMC in DC.

**METHODS:**

For this evaluation, a person had one or more, paired VL and CD4 performed from 1999 through 2011. Log<sub>10</sub>-transformed averages of VL and geometric means of CD4 were determined by month, as were the distributions of the final test values by calendar year. Two-limit Tobit (censored regression) models were used to estimate the true mean log VL.

**RESULTS:**

Ranging from 575 persons in 1999 to 854 in 2011, a total of 1,814 individuals had one or more paired tests (~ 25,000 total). Final VL decreased by 86 copies/ml annually and final CD4 increased by 16 cells/ $\mu$ L (Fig. 1A) with correlations ( $R^2$ ) from second-order polynomial regressions of 0.94 (Fig. 1B) and 0.84 (Fig. 1C), respectively, for the monthly means. The percentage of veterans with viral loads below the lower limit of quantitation rose from 29% to 72%, while the percentage of veterans with CD4 <200 cells/ $\mu$ L dropped from 31% to 11%.

**CONCLUSIONS:**

Community trends in both VL and CD4 for our patients have shown marked improvement over this 13-year period. This is likely due to many factors including better antiretroviral therapies and the coordination of care for HIV and patient co-morbidities within our clinic. These community trends have significance for patient care and HIV transmission in the District of Columbia.

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## Immunologic and Virologic Outcomes of Interruption of Combination Antiretroviral Therapy in Pediatric HIV-Infected Patients

### BACKGROUND:

The success of combination antiretroviral therapy (cART) has led to a significant decrease in morbidity and mortality in pediatric HIV-infected patients. However, the reality of continuing cART throughout a child's development transitioning through multiple preparations is challenging. As a result, pediatric HIV providers face the feasibility of temporarily discontinuing cART in children at different stages of their lives. As there are limited data on treatment interruption (TI) effects in pediatric HIV-infected patients, a better understanding is needed.

### OBJECTIVE:

To conduct a retrospective cohort study to determine if pediatric HIV-infected patients who experience TI have similar outcomes to children on continuous uninterrupted cART.

### METHODS:

HIV-infected pediatric patients treated at the Special Immunology Services Program at Children's National Medical Center and enrolled in the city-wide DC Cohort of HIV Infected Persons in Care in the District of Columbia were enrolled in this study. Data were collected through a retrospective review of medical records. The two study groups consist of treatment-experienced participants on continuous uninterrupted cART compared to treatment-experienced participants with ongoing TI and those who underwent TI and were restarted on cART.

### RESULTS:

In the non-TI group, 85 children (median age 12 years; age range 1-19; male: female ratio 0.8) were enrolled. The majority of patients were Black (n=55; 65%), born in the US (n=66; 79%), and a large number were African (n=15; 18%). The median age of starting cART was >16 months of age. The median ever achieved maximum CD4 T-cell count was 1516 cells/mm<sup>3</sup> (38%).

The TI group enrolled 33 children (median age 15 years; age range 4-18; male: female ratio 1.2). The majority of patients were Black (n=27; 82%) and were born in the US (n=28; 85%). The median age of starting cART was >10 months of age. The median ever achieved maximum CD4 T-cell count was 1490 cells/mm<sup>3</sup> (38%). The median length of treatment before TI was >7 years (range 1 month-16 years). The most common reason for TI was poor adherence to medications (n=16; 44%). The median duration of TI was 16 months (1-53 months). At the cART restart date, the median CD4 T-cell count was 380 cells/mm<sup>3</sup> (20%). The median time to achieve maximum CD4 count after TI was 1 year with an increase to a median of 632 cells/mm<sup>3</sup> (25%). More data and analyses are needed to fully evaluate the impact of TI on immunologic outcomes in pediatric HIV-infected patients.

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# HIV/AIDS



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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### CD4 as a tool to monitor HIV treatment; Evaluation of Latent Tuberculosis Treatment After a Positive PPD Post- BCG Immunization

#### BACKGROUND:

The long standing recommendation for treating patients with positive PPD post- BCG immunization continues to be the subject of controversy. For many years, clinicians recommended 9-12 months treatment for a positive PPD post- BCG immunization. Many immigrants from Africa, Asia, and Europe received the BCG vaccine as children to prevent tuberculosis. Most of these immigrants test positive for PPD. These patients are always labeled as having latent tuberculosis and given nine months of tuberculosis medication called isoniazid (INH)

#### OBJECTIVES:

To evaluate the recommendation on the use of nine months of treatment for suspected latent tuberculosis after a positive PPD post- BCG immunization.

#### METHODS:

This is a stratify retrospective case control study. People has been randomly selected. The study will be conducted among immigrants from Africa, Asia, and Europe leaving in the United States. The target is to have a sample of about 1,000 peoples by the end of the year. As of now, this is a preliminary result based on a sample of 200 people (120 males and 80 females). All patients in the study have received BCG vaccine in their countries before immigrating to the USA and showing a positive PPD test in the USA. One group received the treatment and another group did not. Two criteria have been taken into consideration when selecting people: their stay in USA and whether they received treatment for tuberculosis or not.

Duration in the USA: Five categories were established from five years to 20+ years living in the USA.

Stay in USA/ years	%	Treatment in %	No treatment in %
Less than 5	20	10	10
5- 9	20	10	10
10-14	20	10	10
15- 19	20	10	10
20, or more	20	10	10

#### RESULTS:

One percent of people who did not receive treatment after a + PPD become infected with tuberculosis infections compare to .9 % of people who received nine-month treatment with tuberculosis medication called INH.

#### CONCLUSION:

At this point, the study does not show a health benefit from receiving nine months of treatment of tuberculosis medications after a positive PPD compared to these one who did not receive the medication. Our recommendation will be to stop the practice. There are more disadvantages from putting these people on nine months treatment than advantages.

Disadvantages include: discomfort, side effects of the medications, direct and indirect cost related to the treatment, clinician's wasted time; and the cost of the treatment for the government.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Separating Optimism and Pessimism in a Population of People Living with HIV/AIDS on Antiretroviral Therapy

#### BACKGROUND:

Adequate adherence to antiretroviral therapy (ART) reduces morbidity and mortality and preserves immune function for HIV-infected persons; in addition, it has the potential to slow HIV-transmission on the population level. For both individual- and population-level impact, adherence is critical. Understanding the relationship between optimism and adherence may provide opportunities for intervention. The purpose of this study was to characterize the relationship between optimism and pessimism and medication adherence, and to determine whether these are best expressed as polar opposites on a unidimensional continuum or as two independent constructs.

#### METHODS:

Data were obtained from a randomized controlled trial conducted by the University of California San Francisco School of Nursing examining the efficacy of a symptom management manual. In this secondary analysis, we examined the structure of optimism-pessimism and its relation to three variables: depression, quality of life (QoL), and self-efficacy. The measure of optimism was based on the eight-item Life Orientation Test consisting of four ordinal-scaled items reflecting optimism and pessimism, respectively. Bivariate associations among the variables were obtained with simple correlations. Dimensionality was assessed with principal component analysis and reliability with Cronbach's alpha. To determine independent associations, each potential confounder was regressed against bipolar optimism-pessimism and the disaggregated measures, respectively, controlling for age and the other two confounders.

#### RESULTS:

Our sample (n=353) was 62% male, 35% African American/Black, and mean age was 44 years. The principal component analysis yielded two factors capturing 65% of the variance with the four optimism items clustering together and the four pessimism items clustering together. Reliability was 0.81 for optimism, 0.72 for pessimism, and 0.68 for optimism-pessimism. In the multiple regression analyses, optimism had an independent, positive association with QoL (p=0.002) while controlling for pessimism (p=0.51), depression, and self-efficacy. Pessimism was positively associated with depression (p<0.001) while controlling for optimism (p=0.14), QoL, and self-efficacy. Both optimism and pessimism were independently associated (p<0.05) with self-efficacy while adjusting for depression and QoL.

#### CONCLUSIONS:

Our data suggested that optimism and pessimism represent independent constructs. This study will inform development of future interventions to improve adherence interventions among HIV-infected persons.

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# HIV/AIDS

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### A Comparison of the Portrayal of HIV/AIDS in Mainstream versus African American Magazines

#### BACKGROUND:

Given the disproportionate rate of HIV infection among African American women, compared to their non-Black counterparts, there may be a difference in media messaging which may lead to a different decision making process among the two populations. Women's magazines may be an important indicator of the type of public health messages women are exposed to, and thus may be associated with perceived vulnerability, sexual decisions, and ultimately HIV incidence and prevalence. It is therefore critical to examine the key differences in media messages related to HIV targeting African-Americans, and their non-Black counterparts.

#### OBJECTIVE:

The objectives of this content analysis are to examine to what extent HIV/AIDS is discussed in Black versus mainstream women's magazines, and to identify which themes are most predominant in the portrayal of HIV/AIDS, in both Black and mainstream women's magazines.

#### METHODS:

The sampling frame for this conceptual content analysis is every 2012 issue of four selected magazines (two African American and their two counterpart mainstream women's magazines) to yield a total of 48 issues. The magazines will be manually coded for the mention of HIV, related concepts (health, global health, empowerment, stigma, violence), frequency, and the type of message (advertisement, feature, editorial, etc.).

#### RESULTS:

Preliminary results indicate there are more mentions of HIV/AIDS in African American women's magazines than in mainstream magazines. HIV/AIDS is usually mentioned in the context of global health in mainstream magazine's. Data collection and analysis are currently underway and will be completed by the presentation date. This research is being completed in partial fulfillment of Ms. Davis' MPH requirements.

#### CONCLUSION:

This expectation of this content analysis is that it will lead to the identification of themes around the portrayal of HIV/AIDS in both sample sets of US magazines. Once themes have been identified, the analysis is expected to shed light on why African American and mainstream women's magazines portray this topic differently.

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**SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES**

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## Disparities in Length of Stay for Pediatric HIV Hospitalization, 2003-2009

**BACKGROUND:**

Improvements in health outcomes have been made in HIV positive youth though disparities still exist, particularly among African-Americans and females. Little literature exists on social and demographic disparities on length of stay of HIV related pediatric hospitalizations in a nationally representative survey.

**METHODS:**

The effect of race and gender on length of stay (LOS) in HIV related pediatric (< 20 years old) hospitalizations were examined in 2003, 2006 and 2009 using Kid Inpatient Databases (KIDs). Descriptive statistics on demographics, potential confounders and covariates were reported as well as bivariate analysis of variables and length of stay. Multivariate Linear regression examined the combination of all variables effect on LOS. All analyses of KID data will be conducted in SAS 9.2 utilizing survey procedures to account for design effects, including hospital characteristics.

**RESULTS:**

Of the HIV related hospitalizations in the study years (weighted n=13,266), 58.90% of the sample was female and 61.93% was black. Those two demographic categories accounted for the most hospitalizations, on bivariate and multivariate analysis, neither factors were significantly associated with LOS. Multivariate analysis indicated that controlling for all other covariates, depression comorbidity increased LOS by 4.72 days(  $p=.01$  ), Hispanic ethnicity decreased LOS by 1.36 days ( $p=0.02$ ) as did elective admissions by .98 days.

**CONCLUSIONS:**

Among HIV related hospitalizations in the study period, gender and race/ethnicity did not significantly predict length of hospitalization. Though this lack of association may be due to small sample size, this study indicates that depression comorbidity may be a significant factor in HIV health outcomes among adolescents.

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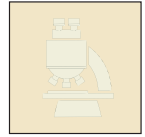
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## CHILDREN'S NATIONAL MEDICAL CENTER

### An Alternative Replication Pathway Induced by Apoptosis in Cell Lines Latently Infected with Human Herpesviruses

#### BACKGROUND:

Human herpesviruses (HHV) are characterized by their unique ability to productively infect or remain latent in the host cell. In addition to external and internal stimuli, chemical agents such as tetradecanoylphorbol-13-acetate (TPA), that stimulate cell signal transduction pathways can induce viral replication.<sup>1</sup> A recent study showed that inducing apoptosis can trigger viral replication in the absence of replication and transcription activator protein (RTA) in cells latently infected with Kaposi's Sarcoma-associated Herpesvirus (KSHV or HHV-8).<sup>2</sup> This suggests that an alternative replication program induced by host cell apoptosis can initiate KSHV replication.<sup>2</sup>

#### OBJECTIVES:

Our goal was to determine whether this alternative replication program is unique to KSHV or if it is a common feature of all herpesviruses. We focused our efforts on HHV-4 (also known as Epstein Barr Virus or EBV), HHV-6B, HHV-6A and HHV-7.

#### METHODS:

Viral infected lymphoma cell lines were used. A subset of each cell line was left untreated as a negative control. Cell lines latently infected with KSHV were used as a positive control. A subset of each cell line was induced with either tetradecanoylphorbol-13-acetate (TPA) or 2[[3-(2,3-dichlorophenoxy)propyl]amino] ethanol (DCPE) to induce normal viral replication and apoptosis, respectively. Cells were then centrifuged and protected viral DNA was isolated from the supernatant for each treatment condition and quantified using RT-PCR. Cell were then re-suspended and stained with Annexin V-APC to visualize apoptosis using a fluorescent microscope. Virus-specific proteins were targeted with primary and secondary antibodies and visualized by confocal microscopy.

#### RESULTS:

We successfully demonstrated that DCPE induces apoptosis in cell lines latently infected with EBV, HHV-7, HHV-6B and -6A. We further showed that DCPE induces viral replication in EBV and HHV-7 latently infected cells lines as evident by a significant increase in the amount of viral DNA present in the supernatant as compared to the negative control. Lastly, we demonstrated viral protein expression induced by apoptosis occurs for KSHV, HHV-4, HHV-6B, and HHV-7 latently infected cell lines.

#### CONCLUSIONS:

Overall, our data suggests that an alternative apoptosis-triggered replication program appears to be a general feature of the herpesvirus. Cytotoxic therapy is often required to treat neoplasms caused by these viruses including Kaposi's sarcoma and Burkitt's lymphoma caused by KSHV and EBV, respectively. Since cytotoxic therapy is often used to treat herpesvirus-associated cancers, and since cytotoxic agents apparently activate herpesvirus replication, it may prove advantageous to treat patients with antiherpesvirus agents in addition to cytotoxic agents.

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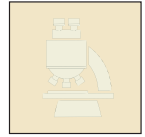
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2. Prasad, A., M. Lu, et al. An alternative Kaposi's sarcoma-associated herpesvirus replication program triggered by host cell apoptosis. *J Virol* 2012; 86(8): 4404-19.



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Recent Trends in *Streptococcus pneumoniae* Antibiotic Susceptibility

#### OBJECTIVES:

Decreasing susceptibility of *S. pneumoniae* isolates to commonly used antibiotics has been an ongoing healthcare concern. The study objectives were to investigate trends in antimicrobial susceptibility over a 12 year period at the George Washington University Hospital (GWUH), and to compare our results to national data from the SENTRY Antimicrobial Surveillance Program 2008.

#### METHODS:

Antibacterial minimum inhibitory concentrations were determined using the E-test® procedure, according to the Clinical and Laboratory Standards Institute (CLSI) 2011 Performance Standards for Antimicrobial Susceptibility Testing. CLSI interpretive standards for non-meningitis and meningitis breakpoints were used as applicable. Susceptibility patterns to nine antibiotics were analyzed in blocks spanning 2000 through 2003 (block A), 2004 through 2007 (block B), and 2008 through 2011 (block C).

#### RESULTS:

486 *S. pneumoniae* isolates were collected over the 12 year study period from non-sterile and sterile sites, including cerebrospinal fluid. 81% of isolates were susceptible to cefuroxime, 79% were susceptible to trimethoprim/sulfamethoxazole, 78% were susceptible to penicillin G, 100% were susceptible to vancomycin, and 99.6% of isolates were susceptible to both levofloxacin and moxifloxacin, with no statistically significant trend to decreasing susceptibility. Erythromycin susceptibility decreased from 79% in block A to 69% in block C ( $P=0.018$ ), ceftriaxone decreased from 99% to 93% ( $P=0.001$ ), clindamycin decreased from 92% to 78% ( $P=0.001$ ). The proportion of isolates exhibiting multi-drug resistance increased from 10.6% in block A to 19.3% in block B, and 21.2% during block C.

#### CONCLUSION:

There has been a statistically significant decrease in susceptibility among *S. pneumoniae* isolates to erythromycin, ceftriaxone and clindamycin over the last 12 years at our institution. Compared to national surveillance data, overall *S. pneumoniae* susceptibility at GWUH was better for ceftriaxone, cefuroxime and erythromycin but worse for penicillin G. All isolates have remained susceptible to vancomycin, and nearly all isolates to respiratory quinolones. However there has also been an alarming increase in multi-drug resistant isolates.

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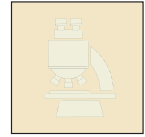
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Novel neutralizing antibody assays for recombinant human hookworm Na-GST-1 vaccine

#### BACKGROUND:

*Necator Americanus*, a human hookworm causes approximately 85% of the global hookworm infections. Hookworm ingest hemoglobin containing erythrocytes. Hemoglobin is further digested to Heme and Globin by hookworm's gut enzymes. Iron-containing Heme is a potent enzyme inhibitor and generates toxic reactive oxygen species which is toxic to hookworms. Hookworm's gut enzyme Na-GST-1 (*Necator Americanus* Glutathione S-Transferase-1) has been hypothesized to detoxify Heme. Na-GST-1 adjuvanted with Alhydrogel® is a new vaccine which is currently under clinical development. Na-GST-1 has two active sites, the ligand binding or Heme detoxification site (H-site) and the catalytic active glutathione binding site (G-site). We have developed in-vitro assays to assess the neutralizing capacity of antibodies against the functional activity of these two active sites. The antibodies used in this assay were purified from serum of BALB/c mice vaccinated with Na-GST-1 vaccine. Here, we report the development and results of these two novel in-vitro assays.

#### METHODS:

Heme detoxification function (H-site) of Na-GST-1 was evaluated by oxidizing and degrading hematin to release iron using a potent oxidizer, hydrogen peroxide. Free iron released from hematin was measured by iron detection reagent called ferrozine. BALB/c mice were vaccinated with Na-GST-1 vaccine and polyclonal IgG from the mice sera was purified using immuno-precipitation. The neutralizing capacity of IgG against the catalytic activity (G-site) of Na-GST-1 was assessed using the CDNB assay. Similarly, the neutralizing capacity of IgG against the H-site was assessed by the ferrozine iron releasing assay after incubating Na-GST-1 with Hematin and polyclonal IgG.

#### RESULTS:

Na-GST-1 significantly inhibited free-iron release from hematin when incubated with hydrogen peroxide. No statistically significant reduction in iron release was found when other iron containing molecules like cytochrome C, ferredoxin or myoglobin were incubated with Na-GST-1 and H<sub>2</sub>O<sub>2</sub>. Four microgram of polyclonal IgG reversed 56.9% of the free-iron release from Hematin. Moreover, 4µg monoclonal Sj-GST IgG completely reversed the inhibition of the release of free-iron caused by Na-GST-1. The neutralizing antibody assay against G-site of Na-GST-1 generated a dose response (%Inhibition vs Negative-IgG) when 20µg (25.87%), 15µg (19.61%), 10µg (13.78%) and 5µg (6.32%) of the purified IgG was incubated with 500ng of Na-GST-1.

#### CONCLUSIONS:

In-vitro assay showed that Na-GST-1 could prevent release of free-iron from hematin. Antibodies purified from Na-GST-1 vaccinated mice neutralized both the heme-detoxification activity (H-site) and catalytic activity (G-site) of Na-GST-1. These neutralizing antibody assay results of Na-GST-1 vaccine lay the foundation for a Phase 2 Clinical Trial in Brazil.

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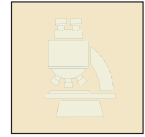
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Puromycin activity against *Schistosoma mansoni* for development of an antibiotic selection system mediated by retroviral transgen

We developed a method to derive transgenic schistosomes employing the murine leukemia virus (MLV) to transfect schistosome eggs. After infecting snails with miracidia from eggs transduced by MLV, genomic DNA from cercariae released from the snails revealed the presence of transgenes, demonstrating that retroviral transgenes had been transmitted through the asexual developmental cycle, and thereby confirming germline transgenesis. Cryopreserved transgenic cercariae retained infectivity for mice, and were transmitted through the sexual developmental cycle to produce F1 and subsequent generations of transgenic schistosomes. These findings provided the first description in schistosomes of germline transmission of transgenes integrated in the parasite genome. Drug selection is widely used in transgene studies of microbial pathogens, mammalian cell and plant cell lines to facilitate the elimination of wild type organisms or transgenic organisms not expressing drug resistance. Recently we have demonstrated that MLV-transduced schistosomules expressing a neomycin resistance marker could be rescued using the aminoglycoside antibiotic, geneticin (G418). However, given that the aminonucleoside antibiotic puromycin was proven to be faster than G418 in selecting transgenic vertebrate cells (i.e. within 48 h) we decided to employ puromycin selection to derive transgenic lines of schistosomes by transducing eggs with MLV carrying puromycin resistance marker. *S. mansoni* schistosomules and eggs were cultured in the presence of increasing concentrations of puromycin for 10 days; media and antibiotic were replaced every second day. Schistosomules were scored, every other day, as live or dead via dual-fluorescence bioassay. Egg viability was evaluated by hatching assay on days 5 and 10. Schistosomules were sensitive to puromycin at levels similar to those known for mammalian cells, e.g. on day 8; ~70% of schistosomules cultured in 1.25 µg/ml puromycin were dead. Although no phenotypic changes were evident in the eggs, a marked inhibition of hatching was seen at 250 µg/ml puromycin by day 5. Whereas G418 did not kill eggs even at concentrations as high as 10 mg/ml in previous experiments puromycin was toxic to both eggs and schistosomules. Therefore puromycin would allow for the selection of MLV-transduced eggs expressing antibiotic resistance marker facilitating the generation of transgenic lines. In addition, given that G418 was successfully employed to select transgenic schistosomules, 'dual selection' with both antibiotics could be employed in future assays. Antibiotic selection systems to enrich transgenic populations of parasites will advance functional genomics for schistosomes and indeed other platyhelminth parasites.

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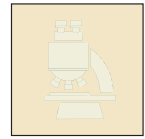
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Aging Is Sufficient To Induce Progenitor Cell Mitotic Dyssynchrony

#### OBJECTIVE:

Aging is associated with a pro-inflammatory state in serum and many tissues. Indeed, nearly all risk factors linked to most age-associated chronic diseases that are leading causes of disability and death worldwide are associated with a pro-inflammatory state. However, it has been challenging to determine cause and effect - do the age-associated pathologies increase inflammation, or does an increased pro-inflammatory state induce the age-associated pathologies, or both? Recently, we identified the cause/effect relationship between tissue repair and inflammation by demonstrating that normal tissue repair is mitotically synchronous and non-inflammatory, whereas chronic inflammatory states are intrinsically mitotically dyssynchronous and release pro-inflammatory cytokines. Given this, we hypothesized that aging alone is sufficient to induce progenitor cell mitotic dyssynchrony.

#### METHODS:

Tracheal epithelial cells from healthy C57BL6 mice in two age groups of both genders were isolated. Young mice were between 8 and 12 weeks of age. Aged mice were acquired from the NIA aged rodent colonies and were 34 months of age. Tracheal epithelial progenitor cells (i.e. basal cells) were cultured on collagen-coated membranes for 6 days. Cultures were exposed continuously to bromodeoxyuridine (BrdU). Cell proliferation was analyzed by flow cytometry for 7-AAD DNA staining in BrdU<sup>+</sup> cells.

#### RESULTS:

More than 50% of the cultured cells were BrdU<sup>+</sup> in the young mice while less than 30% were positive in the aged mice. Additionally, the tracheal epithelia progenitors from male and female aged mice were dyssynchronously distributed along the cell cycle (G1, S, G2/M: 40, 15, 45% and 40, 33, 26%, respectively) compared to those from male and female young mice (62, 16, 22% and 61, 11, and 28%, respectively).

#### CONCLUSIONS:

Our data support the concept that aging is sufficient to induce progenitor cell mitotic dyssynchrony. It is possible that this epithelial mitotic dyssynchrony would then contribute to the pro-inflammatory state associated with aging, as we have seen in other chronic inflammatory states.

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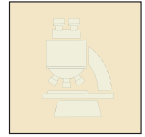
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### VBP15 ( $\Delta$ 9,11 Glucocorticoid) Induced Glucocorticoid Receptor Dependent Repression of MUC5AC Gene Expression in Human Lung Epith

#### RATIONALE:

Overproduction of secretory mucins contributes to morbidity and mortality in lung diseases. Few reagents directly repress mucin gene expression. Our lab has shown that the glucocorticoid Dexamethasone (Dex), transcriptionally represses *MUC5AC* gene expression in lung epithelial cells and that Dex-activated GR binds to two GRE cis-sites in the promoter. Glucocorticoids are commonly used to treat inflammatory diseases but result in adverse side effects with long-term treatment due to GRE-mediated regulation.  $\Delta$  9, 11 glucocorticoid analogues, also known as VBP compounds, do not induce GRE-mediated transcriptional upregulation, but rather inhibit inflammatory mediator-induced NF $\kappa$ B signaling. Thus, they have the potential to maintain the therapeutic effects and minimize the harmful side effects of long-term steroid therapy. Therefore, we investigated the mechanism of VBP15 on *MUC5AC* gene repression in lung epithelial cells.

#### METHODS:

Expression levels of *MUC5AC* and  $\beta$ -actin mRNA were determined by qRT-PCR in A549 or primary differentiated normal Human Bronchial Epithelial (NHBE) cells. Cells were pre-exposed to RU486 (GR antagonist), U0126 (CREB inhibitor), or IMG-2000 (NF $\kappa$ B inhibitor) and then to VBP15. Immunofluorescence and chromatin immunoprecipitation (ChIP) were used to demonstrate cellular movement of GR and GR binding to the *MUC5AC* promoter, respectively.

#### RESULTS:

VBP15 reduced *MUC5AC* mRNA abundance in a dose- and time-dependent manner in A549 and NHBE cells. Repression occurred optimally between 6-18 hours of exposure with 1 $\mu$ M VBP15. VBP15-induced repression of *MUC5AC* was abrogated in the presence of 1 $\mu$ M RU486. In contrast to RU486, U0126, and the NEMO inhibitor reduced baseline levels of *MUC5AC* mRNA abundance but did not affect VBP15-induced repression of *MUC5AC*. VBP15 induced nuclear translocation of GR within 0.5 hours in A549 cells, but VBP15 activated GR did not bind to the GRE3 site of the *MUC5AC* promoter, in contrast to Dex activated GR.

#### CONCLUSIONS:

Data demonstrated that VBP15 repressed *MUC5AC* gene expression. This process required nuclear translocation of GR; however, in contrast to Dex, VBP15/GR does not bind to the GRE3 site in the *MUC5AC* promoter. We hypothesize VBP15 represses *MUC5AC* gene expression via GR interactions with inflammatory transcription factors, such as NF $\kappa$ B and/or CREB. This hypothesis is supported by preliminary results with inhibitors against CREB and NF $\kappa$ B reducing baseline levels of *MUC5AC* mRNA abundance similar to VBP15 suggesting a similar mechanism. VBP15 may be a useful drug if its potential to reduce mucin overproduction in the lungs of patients with airway diseases without the harmful side effects observed in long-term glucocorticoid treatment is fulfilled.

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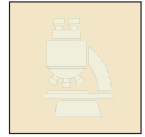
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Directing a Complement Inhibitor to the Neuromuscular Junction

#### BACKGROUND:

Myasthenia gravis (MG) is a debilitating autoimmune disease, in which anti-acetylcholine receptor (AChR) antibodies induce membrane attack complex (MAC) and damage neuromuscular transmission via a complement mediated mechanism.

#### OBJECTIVES:

The aim of this study is to verify the targeting of a complement inhibitor, rEV576, to the neuromuscular junction (NMJ) utilizing two reagents, a single chain fragment (scFv) and a peptide (laminin). The inhibitor will function to curtail the activation and complement deposition at the endplate that is seen in MG.

#### METHODS:

C57B1/6J black mice were injected with scFv-rEV576 (400 µg) or Laminin-rEV576 (200 µg).

Twenty-four hours following the injection animals were sacrificed and tissue was taken for the analysis.

Diaphragms from each animal were cryosectioned. Immunohistochemical staining was performed using an antibody to rEV576 to detect the complement inhibitor recombinant protein and bungarotoxin to identify NMJs. Hematoxylin & Eosin stain was performed to look at infiltrates to the NMJ region. To verify the inhibitory activity of rEV576 *in vitro* analysis by hemolytic assay on sensitized sheep erythrocytes was conducted. In addition, *In vivo* studies utilizing anti-C5b-9 implemented to confirm the lack of MAC deposition at the NMJs.

#### RESULTS:

Administering scFv-rEV576 and Laminin-rEV576 to an animal model does target the NMJ through colocalization. Targeting the scFv- to the NMJ does not induce complement activation in the animal model. The serum complement hemolytic assay demonstrates that rEV576 retains the complement inhibitory function in the recombinant protein by a decreased quantity of erythrocyte lysis.

#### CONCLUSIONS:

Complement inhibitor, rEV576, can be targeted to the NMJ and retain activity. With therapeutic potential, rEV576 will bind specifically to the damaged exterior of the NMJ and restrict the toxicity associated to complement inhibition. Thus, treatment would consist of decreased dosages and reduce complications that current treatment cannot provide for patients with MG. Future experimentation will be fulfilled on complement inhibition in the experimentally acquired MG model.

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#### STATUS

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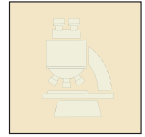
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Biomarker Profiles in Hospitalized Patients with Centra Venous Catheters

**BACKGROUND:**

Transcutaneous central venous catheters are required in many patients in internal medicine wards and ICU settings. CVCs breach the body's natural barriers allowing for normal skin flora to enter the bloodstream inducing catheter associated bloodstream infection (CABSI). CVC related infection is difficult to diagnose. Symptomology can be limited and certain parameters (fever, leukocytosis) are neither sensitive nor specific in the setting of a complex hospitalized patient. Clinically, there needs to be a better way to characterize the natural course of CABSI, as well as identify patients in the early stages of CABSI. In this study we attempt to analyze the role of certain biomarkers, specifically pro-calcitonin, to help elucidate the presence of an occult infection. Procalcitonin has been shown to be ubiquitously and uniformly expressed in multiple tissues throughout the body in response to a bacterial infection and sepsis. We propose to assess the utility of biomarkers in the circulation as a novel and non-invasive technique for the early identification of hospital-acquired bacterial infection of transcutaneous CVCs.

**OBJECTIVES:**

1. Characterize levels of circulating biomarkers in all hospitalized patients with central venous catheters.
2. To determine if biomarkers can predict CVC-related infection through the comparison of circulating level of the inflammatory biomarker drawn at the time of clinical signs/symptoms
3. Temporal responses in circulating biomarkers will be correlated to clinical outcomes including mortality, source of infection and signs of infection

**METHODS:**

This protocol will be based on the usual practices of clinicians employed during admission and evaluation for patients entering the intensive care setting/ internal medicine ward, when treating physicians deem that an indwelling intravascular device is required for their clinical care.

We will prospectively collect samples on consenting adults who have had a CVC placed after admission or transfer to the medical intensive care setting. With prospective observation, we expect that a small percentage of those patients will go on to develop a CVC-related infection or suspected CVC-related infection. Serial blood samples from the catheters and from the peripheral blood will be drawn from these patients in order to characterize the presence, type and temporal response to treatment of circulating inflammatory biomarkers.

**RESULTS/CONCLUSIONS:**

At this time there are no significant results/conclusions because the study is still ongoing.

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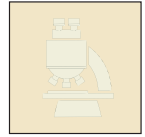
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# IMMUNOLOGY/INFECTIOUS DISEASES

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Vaccination Rates Among Immigrants in Spain

Emergency room patients were surveyed for immigrant status and vaccination rates of at Ramon y Cajal Hospital in Madrid, Spain. The patients were selected by their immigrant status and their low level priority in the emergency room. Any patient with life-threatening illness was not asked to participate in the study and all patients were informed of their right to choose not to participate. Patients were given an information sheet on the study as well as an anonymous questionnaire asking for their vaccination history including: *Hepatitis A, Hepatitis B, Tuberculosis, Meningitis, Tetanus/diphtheria/ polio, Measles/mumps/rubella, Influenza*. Demographic information collected included the patient's age, sex, immigrant status, country of origin, number of years living in Spain, and the reason for the hospital visit. I saw 99 patients, ranging in age from 18-91 years-old. While a majority of patients were foreign-born Spanish citizens, 10% were undocumented immigrants. The most common birth country of the patients seen was Ecuador (24% of patients seen) followed by the Dominican Republic (8%) and Bolivia (7%). Patients were most commonly unvaccinated for the yearly flu. Conversely, the majority of patients were vaccinated against Tetnus/dipteria/polio. It was largely unknown by patients if they were vaccinated for meningitis, Hepatitis A or Hepatitis B (in that respective order of uncertainty).

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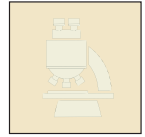
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Rapid 13C Urea Breath Test to Identify Helicobacter Pylori Infection in Emergency Department Patients with Upper Abdominal Pain

#### INTRODUCTION:

In emergency department (ED) patients with upper abdominal pain, management includes ruling out serious diseases and providing symptomatic relief. One of the major causes of upper abdominal pain is an ulcer caused by *Helicobacter pylori* (*H. pylori*), which can be treated and cured with antibiotics.

#### OBJECTIVES:

We sought to estimate the prevalence of *H. pylori* infection in symptomatic patients using a convenience sample at a single urban academic ED and demonstrate the feasibility of ED-based testing.

#### METHODS:

We prospectively enrolled patients with a chief complaint of pain or discomfort in the upper abdomen for 1 year from February 2011 until February 2012 at a single academic urban ED. Enrolled subjects were tested for *H. pylori* using a rapid point of care 13C Urea Breath Test (UBT) [Exalenz Bioscience]. We compared patient characteristics between those who tested positive versus negative for the disease.

#### RESULTS:

A total of 205 patients with upper abdominal pain were tested over 12 months, and 24% (95% confidence interval: 19% to 30%) tested positive for *H. pylori*. Black subjects were more likely to test positive than white subjects (28% v. 6%,  $P < 0.001$ ). Other factors, such as age and sex, were not different between the 2 groups.

#### CONCLUSION:

In our ED, *H. pylori* infection was present in 1 in 4 patients with epigastric pain, and testing with a UBT was feasible. Further study is needed to determine the risk factors associated with infection, the prevalence of *H. pylori* in other EDs, the effect of the test on ED length of stay and the cost-effectiveness of an ED-based test-and-treat strategy.

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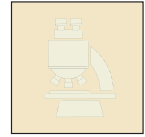
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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Vaccination of BALB/c mice with the Na-APR-1 M74 hookworm vaccine generates neutralizing antibodies and a potent immune response

#### BACKGROUND:

Human Hookworm Infection, a neglected tropical disease infects more than 600 million people around the world. Hookworms ingest hemoglobin containing erythrocytes and *Necator americanus* Aspartic Protease-1 wild type (Na-APR-1wt) a hemoglobinase cleaves hemoglobin to form Heme and Globin. Globin is further digested by other gut enzymes and the nutritional products are absorbed by the hookworm's gut wall. Also, Heme which is toxic to hookworm is detoxified by the *Necator americanus* Glutathione Transferase-1 (Na-GST-1); a detoxification enzyme secreted by the gut of the hookworm. *Necator americanus* Aspartic Protease-1 M74 (Na-APR-1 M74) is a new vaccine which is currently under pre-clinical development. This vaccine is an Alhydrogel® adjuvanted vaccine containing the mutant form of the Na-APR-1wt. Potent antibodies (IgG) will neutralizing Na-APR-1wt and will block the initiation of the hemoglobin digestion cascade and starve the hookworms from essential nutrition, leading to their death. Here, we report the results of the neutralizing capacity of antibodies and potency (immunogenicity) of Na-APR-1 M74 vaccine in BALB/c mice.

#### METHODS:

Serum for IgG was generated by vaccinating BALB/c mice twice subcutaneously with Na-APR-1 M74 an enzymatically inactive mutant form of Na-APR-1wt formulated with Alhydrogel®. Assessment of neutralizing capacity of IgG was performed using the in-vitro Cathepsin-D protease assay. Intra-Operator Precision and Ruggedness (inter-operator precision) of the assay were assessed by calculating the percent coefficient of variation (%CV). Dose response (% Inhibition vs Dose) was assessed using linear regression analysis. Potency testing of the Na-APR-1M74 clinical drug product was performed by standard bioassay. Median Effective Dose 50 (ED50) with the 95% fiducial limits (95%FL) was estimated using Probit Analysis (SAS® 9.3). Also, Relative Potency (RP) was estimated by the methods described in European Pharmacopeia's Chapter 5.3.

#### RESULTS:

Five microgram of purified IgG neutralized 51.06% of the enzymatic activity of 250ng of Na-APR-1wt. This assay generated an excellent inter- and intra-operator precision with the %CVs < 20. An excellent dose response was also observed. ED50 of 14.15µg (95%FL = 10.47µg -- 18.93µg) and 11.46µg (95%FL = 4.86µg --27.42µg) was estimated for time 1 and 7 month post manufacture respectively. RP at 7 months was found to be 1.23 (95%FL = 0.792--1.917).

#### CONCLUSIONS:

These neutralizing antibody and potency assay results of Na-APR-1 M74 vaccine lay the foundation for a Phase 1 Clinical Trial in USA and Brazil. Subsequently, this vaccine will be combined with *Necator americanus* Glutathione transferase-1 (Na-GST-1) vaccine to form a multivalent human hookworm vaccine.

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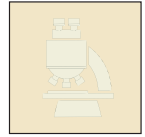
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# IMMUNOLOGY/INFECTIOUS DISEASES



## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Immunological risk factors for HIV acquisition and transmission in post-menopausal women

#### PROBLEM:

Heterosexual transmission still accounts for the majority of new HIV infections with women being more likely than men to be infected during vaginal intercourse. The female reproductive tract (FRT) offers the first line of defense against sexual transmission of HIV in women through the barriers of the mucosal and epithelial cell lining, the presence of immune cells, antibodies and endogenous antimicrobials. Many of these antimicrobials are regulated by sex hormones and little is known as to whether loss of estradiol in postmenopausal women results in a less robust innate immune system in the FRT and makes them more susceptible to acquiring and transmitting HIV. Furthermore, it is unknown whether postmenopausal women on hormone replacement therapy (HRT) might recover these antimicrobials reducing their risk to the sexual acquisition and transmission of HIV. In this study, we specifically investigated the changes in levels of Interleukin-8 (IL-8), Elafin, Macrophage Inflammatory Protein3- $\alpha$  (MIP3 $\alpha$ ) and Human Beta Defensin-2 (HBD-2), all potentially protective in HIV pathogenesis, in genital tract secretions of HIV positive and HIV negative postmenopausal women and compared them to premenopausal and postmenopausal women on HRT.

#### METHODS:

Cervical-vaginal lavage (CVL) samples of HIV positive and HIV negative premenopausal, postmenopausal and post-menopausal women on HRT were obtained from the Washington DC Women's Interagency HIV Study (WIHS) repository and analyzed for IL-8, Elafin, MIP3 $\alpha$  and HBD-2. Cytokine and antimicrobial concentrations were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits. Statistical analyses were performed using the Kruskal-Wallis test (Graphpad Prism).

#### RESULTS:

In the HIV positive group, IL-8 was significantly reduced in the CVL of postmenopausal women on HRT (n=7) compared to CVL from premenopausal (n=11) and postmenopausal women (n=11). In the HIV negative group, both MIP3 $\alpha$  and HBD-2 were significantly reduced in postmenopausal women (n=11) compared to premenopausal women (n=11). However, no significant alterations in Elafin levels were observed in any of the groups.

#### CONCLUSION:

These findings indicate that the levels of immune mediators in the FRT such as IL-8, MIP3 $\alpha$  and HBD-2 are altered based on hormonal status in both HIV negative and HIV positive women. In addition, our data suggests HRT might have an effect in genital tract mucosal immune responses against sexually transmitted infections such as HIV. Future experiments are necessary to correlate these levels of endogenous factors in the CVL samples to anti-HIV activity in vitro and develop therapeutic interventions to boost genital tract immunity against HIV in older women.

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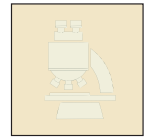
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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Evaluation of Latent Tuberculosis Treatment After a Positive PPD Post BCG Immunization

#### BACKGROUND:

The long stand recommendations of treating patients with positive PPD post BCG immunization has been subjected to a big debate nowadays. For many years, clinicians recommend 9-12 months treatment for a positive PPD post BCG immunization. Many immigrants from Africa, Asia and Europe received BCG vaccine when kids as a preventive measure against tuberculosis infection. Most of these immigrants always test positive to PPD. These patients are always labeled with latent tuberculosis and treat with nine months treatment of tuberculosis medication.

#### OBJECTIVES:

To evaluate the recommendation on the use of 9 months treatment for latent tuberculosis after a positive PPD post BCG immunization.

#### METHODS:

A study is being conducted among immigrants from Africa, Asia and Europe. The studies will recruit about 1000 peoples by the end of the years. For now, the conclusion of this study will be based on a sample of 200 peoples (120 males+80 females). All patients in the study received BCG vaccine in their countries before immigrating to USA and a Positive PPD tested in USA. One group received the treatment and another group did not. Two criteria has been taken in consideration when recruiting people: their stay in USA and either they received a treatment or not for tuberculosis.

Duration in USA: Five categories have been established from 5 years of leaving in USA to over 20 years.

Stay in USA/ years	%	Treatment in %	No treatment in %
Less than 5	20	10	10
5- 10	20	10	10
10-15	20	10	10
15- 20	20	10	10
Over 20	20	10	10

#### RESULTS:

One percent of people who did not receive treatment after a + PPD become infected with tuberculosis infections compare to .9 % of people who received nine month treatment with tuberculosis medication.

#### CONCLUSION:

At this point, study does not show any health benefit of receiving 9 months treatment of Tuberculosis medications after a positive PPD compare to these one who did not receive the treatment. Our recommendation will be to stop the practice. There are more disadvantages of put these people on 9 months treatment than the advantages. Some of these disadvantages are: discomfort, the side effect of medications, direct and indirect cost related to the treatment, clinician's wasting time.; the cost of the treatment for the government.

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## SCHOOL OF ENGINEERING AND APPLIED SCIENCE

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### Analysis of the network signature of normal and impaired cortical development

#### RESEARCH BACKGROUND:

Currently individuals with Fragile X Syndrome (FXS), the largest single gene cause of autism, are diagnosed based on behavioral symptoms and genetic testing, but these diagnoses occur too late to prevent the initial FXS-based disruptions of brain function. It is possible to detect abnormal cortical activity, including seizures, using electroencephalography (EEG). Previous studies have determined some of the EEG characteristics of Fragile X children and have also examined cortical function in mouse models of the disease. However, when cortical activity defects arise in FXS and what form they take are unknown. An understanding of the early network impairments in FXS will guide treatment options and provide novel diagnostics to monitor treatment efficacy.

#### RESEARCH OBJECTIVE(S):

The objectives of the proposed research are to compare EEG development in wild type and Fragile X model *Fmr1* knock out rats throughout three age groups equivalent to the third trimester, first post-natal months, and the first six to twelve months of age in human development.

#### RESEARCH METHODS:

Using 32 channel linear multi-site probe electrode arrays, both single unit and depth EEG are collected from all cortical layers. Selected EEGs traces are pre-processed to remove motion artifacts and to determine periods of normal EEG activity. Multiunit spikes are extracted from high-pass filtered traces and clustered. Both continuous and discrete analysis methods are applied including cross-correlation, Welch, Thomson Multitaper, and wavelet methods.

#### RESEARCH RESULTS:

Based on the preliminary results we selected the following EEG properties to detect early cortical malfunction in the Fragile X model: (1) the power spectral densities differences at equivalents to pre-symptomatic ages in low frequency EEG range (1-10 Hz) between control and Fragile X groups; and (2) cross-correlation measures and their change across development.

#### RESEARCH CONCLUSION:

Our results suggest several measures for early detection of cortical abnormalities in Fragile X model. Similar techniques can be used during the pre-symptomatic ages in humans. Future studies of these cortical properties will facilitate finding novel EEG diagnostics for pre-term and term infants at risk for autism.

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#### FACULTY ADVISOR

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#### SOURCES

This project was supported by Award Number UL1TR000075 from the NIH National Center for Advancing Translational Sciences.





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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Role of Oxytocin Neurons in Obstructive Sleep Apnea Mediated Cardiovascular Disease

#### INTRODUCTION:

Daytime tachycardia and hypertension are associated with Obstructive Sleep Apnea (OSA) one primary, yet poorly understood disease that causes stress to the cardiovascular system. Oxytocin (OXT), a conserved neuropeptide secreted from the paraventricular nucleus of the hypothalamus (PVN), modulates the cardiovascular responses to stress. When an organism is stressed, OXT projections from the PVN to areas in the brainstem modulate the baroreceptor reflex and increase vagal outflow to the heart resulting in decreased blood pressure (BP) and heart rate (HR). This work will utilize Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) to test if selective activation of PVN OXT neurons:

- 1.) decreases resting HR and BP and
- 2.) mitigates the observed hypertension and tachycardia caused by chronic intermittent hypoxia/hypercapnia (CIH/H), our animal model of OSA.

#### METHODS:

Male rats were injected into the PVN with two viral vectors: one expresses Cre recombinase under an OXT promoter and the second expresses the excitatory hM3Dq DREADDs and implanted with a wireless telemetry device to monitor arterial BP and EKG activity. Animals received daily injections of clozapine-N-oxide to activate PVN OXT neurons expressing DREADDs, and the effects on resting HR and BP and after an 8 hour exposure CIH/H were analyzed.

#### RESULTS:

Our animal model of OSA is sufficient to induce hypertension and tachycardia in animals implanted with a telemetry device. Furthermore, selective activation of PVN OXT neurons in telemetry equipped animals decreases resting BP and HR.

#### CONCLUSIONS:

We found that selective activation of OXT neurons in the PVN decreases resting BP and HR in animals implanted with a telemetry device. Ongoing experiments will examine the effects PVN OXT neuron activation has on the observed hypertension and tachycardia after 28 days CIH/H exposure.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Specific cognitive symptoms that best discriminate clinically normal elderly from those with mild cognitive impairment

#### BACKGROUND:

Earlier diagnosis of Alzheimer's disease (AD) is critically needed. Activities of daily living (ADL) impairment is a hallmark of AD dementia, but milder impairment in instrumental ADL has been reported at the stage of mild cognitive impairment (MCI). The Structured Interview and Scoring Tool-MADRC Informant Report (SIST-M-IR) is designed to rate individual items of the Clinical Dementia Rating Scale and has been shown to be a reliable and sensitive tool for assessing daily functioning and cognitive changes across the spectrum of impairment, including MCI. Of the 60 SIST-M-IR items, 41 target instrumental ADL, and the present study was designed to determine which of these items are most likely to differentiate individuals with MCI from clinically normal (CN) elderly.

#### METHODS:

We investigated which ADL-related SIST-M-IR items best discriminate between CN and MCI subjects in 447 subjects participating in the Massachusetts Alzheimer's Disease Research Center (MADRC) longitudinal cohort (289 CN, 158 MCI). We first performed data reduction analyses to reduce the 41 items to 10 items which appeared to best discriminate CN from MCI. We then performed backward elimination ( $p < 0.05$  cutoff) logistic regression analyses predicting the probability of CN vs. MCI diagnosis using the 10 selected items. Analyses were adjusted for age, sex, education, and estimated premorbid intelligence (AMNART Verbal IQ).

#### RESULTS:

We found that "participating in games that involve retrieving words" ( $p = 0.0001$ ), "navigating to unfamiliar areas" ( $p = 0.001$ ), "performing mental tasks involved in a former primary job" ( $p = 0.002$ ), and "fixing things or finishing projects" ( $p = 0.002$ ) best discriminated between CN and MCI subjects with MCI subjects performing worse than CN.

#### CONCLUSIONS:

These results identify which ADL-related SIST-M-IR items are most informative in differentiating CN elderly from MCI, thus helping identify the earliest functional changes in elderly at risk for AD. Overall, refining the sensitivity in clinical assessment tools will help clinicians differentiate those individuals with normal aging from those who are developing cognitive impairment. By distinguishing individuals at early stages of cognitive decline, efforts towards prevention and ultimately treatment of AD will be more effective.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Optogenetic stimulation of the locus coeruleus noradrenergic neurons increase inhibitory neurotransmission to cardiac vagal neurons in the nucleus ambiguus

Locus coeruleus (LC) neurons play an essential role in wakefulness, analgesia and autonomic regulation, but the descending projections to caudal medulla that alter autonomic function remains unclear. Cardiac vagal neurons (CVNs) located in nucleus ambiguus control heart rate. Since heart rate changes in awake-sleep cycle and anesthesia status we hypothesized that these changes may be mediated by LC modulation of CVNs. Mice that express Cre recombinase selectively in tyrosine hydroxylase neurons were crossbred with a channelrhodopsin-2/EYFP Cre-dependent mouse strain. CVNs were identified by the retrograde tracer rhodamine. Photostimulation evoked depolarization and induced an average inward current of 150pA in ChR2 LC expressing neurons. Laser stimulation of LC neurons did not alter excitatory neurotransmission to CVNs but evoked a significant increase in postsynaptic inhibitory neurotransmission. The IPSCs frequency in CVNs was facilitated by  $73.7 \pm 21.8\%$  ( $p < 0.01$ ) upon LC photoexcitation. This increase was blocked by  $\alpha$ -1 receptor inverse agonist, prazosin ( $3 \mu\text{m}$ ),  $\alpha$ -2 receptor antagonist, Yohimbine ( $5 \mu\text{m}$ ), and  $\beta$ -1 receptor antagonist, atenolol ( $100 \mu\text{m}$ ). This LC induced modulation is likely a mechanism for heart rate changes that occur in awake/sleep cycles and during anesthesia mediated by LC induced inhibition of CVNs.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Correlation between Gamma-Glutamyl Cysteine and Glutathione in Neonate Mice Brains

#### BACKGROUND:

As surgical techniques improve, more children are surviving corrective surgery for congenital heart defects. It has been hypothesized that surgery utilizing cardiopulmonary bypass (CPB) can result in neurologic damage due to oxidative stress caused by ischemia-reperfusion and reoxygenation injury of CPB.<sup>1,2</sup> Injection of gamma-glutamylcysteine (GGC), a precursor of glutathione which crosses the blood brain barrier, has been demonstrated to increase levels of glutathione in mice.<sup>3,4</sup> Glutathione (GSH) is known to protect cells from free radical damage.

#### OBJECTIVE:

We set out to determine the tissue concentrations of glutathione achieved in murine brain following injection of GGC intraperitoneally. This was done to determine if GGC could be used therapeutically to protect against neurologic damage from CPB-induced oxidative stress.

#### METHODS:

Reconstituted GGC at doses of 250, 400, 550 and 700 mg/kg or saline as a control was injected intraperitoneally into 20 newborn mice, which were sacrificed at 60, 120, 180, or 240 minutes. The brains were then harvested and homogenized and brain glutathione levels were measured as compared to standard glutathione solution, using a Microplate Reader spectrophotometer.

#### RESULTS:

With 400 mg/kg injections of GGC and sacrifice at 2 hours post-dose, the recorded values for GSH were 160, 186, 190 and 262, with a control of 223. With sacrifice at 3 hours post-dose, values were 138, 218, 219 and 250, with a control of 169. With 400mg/kg of GGC and sacrifice at hours 1, 2, 3 and 4, GSH was measured at 230, 252, 276 and 269, respectively, with 1 and 4 hour controls of 243 and 222, respectively. A group of mice were then injected with increasing GGC doses of 250, 400, 550 and 700 mg/kg and sacrificed 3 hours post-dose. The values for GSH were 196, 186, 200 and 204, with the control at 200. This was repeated a second time with values of 155, 164, 165 and 123, and the control at 182.

#### CONCLUSION:

Our data demonstrate inconsistent levels of GSH, lacking correlation to the dose of GGC injected or the time between dose administration and sacrifice. As past experiments in adult mice have shown a direct correlation between increasing doses of GGC and GSH levels, we hypothesize that immature molecular machinery of newborn mice may interfere with the linear conversion of GGC to GSH. Further work must investigate increased doses of GGC and the maturation of the glutathione conversion pathway and its effects in mice as they age.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## TxnRd2 imbalance during critical stages in development results in changes in mitochondrial distribution and neurite outgrowth

**BACKGROUND:**

The structural and functional changes observed in brains of 22q11DS patients, which may contribute to the patient's increased vulnerability to psychiatric disorders, are thought to result from aberrant cortical development. Neuropsychiatric abnormalities, such as schizophrenia, which has a higher incidence among 22q11DS individuals, have been linked to mitochondrial dysfunction. A subset of genes in the 22q11-deleted region is targeted to mitochondria. One of the six 22q11 mitochondria-targeted genes, TxnRd2, is a known mitochondrial H<sub>2</sub>O<sub>2</sub> scavenger that reaches maximum expression late during gestation and early postnatal life. The purpose of this study was to determine TxnRd2 role in neuronal development. We hypothesized that TxnRd2 imbalance during periods of maximal expression would result in aberrant neurite outgrowth due to mitochondrial dysfunction.

**METHODS:**

Primary cortical neuronal cultures from E16.5 mouse embryos were electroporated with farnesylated-GFP and mitochondrial-flagged TxnRd2 knock-down and overexpression plasmids. A set of TxnRd2 depleted neurons was treated with H<sub>2</sub>O<sub>2</sub> scavengers to reestablish intracellular redox balance and link TxnRd2 scavenging activity to neuronal morphology. Changes in neurite outgrowth and mitochondrial distribution were evaluated after 96 hrs in culture.

**RESULTS:**

Sholl analysis of neurons transfected with SiRNA-TxnRd2 reveals an increase in small processes and a decrease in large processes, while no changes in neurite outgrowth are observed in neurons transfected with overexpression constructs. TxnRd2 depleted neurons treated with H<sub>2</sub>O<sub>2</sub> scavengers showed normal neurite outgrowth. Mitochondrial distribution to peripheral neurites was increased in neurons transfected with knock-down and overexpression plasmids when compared to neurons transfected with control plasmids.

**CONCLUSION:**

The changes in neuronal morphology observed due to TxnRd2 imbalance during neurite outgrowth suggest that neuronal development depends on TxnRd2 dosage. Reestablishment of neuronal morphology in TxnRd2 depleted neurons cultured with H<sub>2</sub>O<sub>2</sub> scavengers implies an inverse correlation between ROS accumulation and TxnRd2 activity. The aberrant neuronal morphology, resulting from TxnRd2 imbalance, could contribute to the changes in neuronal circuitry in 22q11DS patients.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Relationship between preoperative cerebral perfusion and brain development in newborns diagnosed with congenital heart disease

#### BACKGROUND:

Infants with congenital heart disease (CHD) are at risk for neurologic and developmental deficits. The high prevalence of abnormal brain development prior to open-heart surgery is thought to result from antenatal cerebrovascular hemodynamic disturbances due to the cardiac defects. However, the relationship between postnatal brain perfusion and preoperative brain micro-organization in CHD newborns has not been inquired.

#### OBJECTIVES:

The aim of this study was to assess the relationship between preoperative cerebral perfusion and cerebral microarchitecture in newborns diagnosed with complex CHD using quantitative magnetic resonance imaging (MRI) measurements.

#### METHODS:

In this prospective observational study, 24 term newborns with complex CHD underwent 3T brain MRI before cardiac surgery. We excluded babies with congenital infection, known genetic or dysgenetic brain lesions, and perinatal insults. Conventional MRI results by expert pediatric neuro-radiologists were used to separate CHD newborns with presence (cases) and absence (controls) of brain injury based on the conventional MRI: 9 babies exhibited brain injury whereas 15 babies had a normal MRI. We used arterial spin labeling (ASL) to quantify regional and total cerebral blood flow (CBF) and diffusion tensor imaging (DTI) to assess brain microstructure. Post-processing and quantification were performed using FSL (Oxford, UK) and AFNI (Bethesda, MD) software. Regions of interest were placed over the thalamus and basal ganglia and over the frontal, parietal and occipital white matter. Differences between groups were assessed using Student's t-test and Fischer's exact test and correlations between regional CBF and DTI measurements using Pearson's coefficient.

#### RESULTS:

Mean birthweight, gestational age at birth, and age at MRI for cases/controls were 3.10/3.07 kg, 38.34/38.74 weeks, and 4.13/4.27 days, respectively ( $p > 0.05$ ). Clinical characteristics of the cohort including Apgar score and diagnosis were similar in newborns with/without brain injury. Mean preoperative whole brain perfusion was significantly lower in babies exhibiting brain insults (15.2 versus 19.2 mL/100g/min;  $p = 0.016$ ). Newborns with brain injury exhibited lower regional CBF measurements, however none of the differences was statistically significant. Regional microarchitecture assessed with DTI metrics was similar in these two populations. There were no significant associations between regional CBF measures and DTI metrics calculated within the same region of interest.

#### CONCLUSION:

These preliminary data suggest that preoperative brain impairments in newborns with critical CHD may be associated with decreased total cerebral blood flow before surgical correction. Quantification of whole brain perfusion by ASL is a promising non-invasive biomarker for investigating neuronal insult in babies diagnosed with CHD.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Exploration of the Functional Connectivity Differences Between Short and Long Pain Stimulations

#### INTRODUCTION:

Functional magnetic resonance imaging (fMRI) investigations has emerged as a useful diagnostic and scientific tool to elucidate meaningful insights into the mechanisms of the human brain. Data from the fMRI is manipulated (FSL Software, [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl)) and different regions of the brain are analyzed. In functional connectivity studies, results are predicated on how a certain region of the “pain matrix” will co-vary with another region when different tasks are performed. This information acts a proxy for neuronal interconnections between these related regions. Functional connectivity has shown patterns of connectivity between the anterior cingulate cortex (ACC) and the insula in a variety of disease states. Current investigations use longer painful stimulations in an attempt to understand how the brain processes “real-life” pain instead of the artificial on-off pattern that is typically used in experiments. Direct comparisons of functional connectivity during these different patterns of pain processing in non-pathological volunteers have not been explored.

#### MATERIALS AND METHODS:

In an IRB approved study, transcutaneous electrical nerve stimulation at the lateral aspect of the PIP joint of the right index finger was performed in two different pain patterns on 15 healthy volunteers. “Pain 1” was designed as a repeated (4 times) 30 seconds of painful stimulation alternating with 30 seconds of rest. “Pain 2” was designed as a constant 2 minute stimulation. Each task was preceded by 4 minutes of rest. A 3-T scanner was used to collect whole brain fMRI images. Using the contralateral insula as a seed region, FSL Software was used to process the data and create functional connectivity maps and compare and contrast results between the two pain tasks.

#### RESULTS:

Functional Connectivity maps were generated for each task and showed covariance between the contralateral insula and the known areas of the “pain matrix”. A visual/qualitative increase in connectivity is seen in the “Pain 1” map in comparison to “Pain 2”. Quantitatively, some subjects show a numerical difference in connectivity, but statistical analysis did not show any difference between the two at an aggregate level.

#### DISCUSSION:

Every year, the amount of money that is spent on pain management trends upwards at an exponential pace. Researchers hope that functional connectivity studies will help us understand the specific brain regions that contribute to the pathological manifestation of chronic pain. This nascent technique is still being reconfigured to facilitate meaningful understanding and our study is critical to devising a protocol that codifies outcomes with a high level of utility and statistical relevance. We are currently optimizing our analysis technique to further validate the qualitative differences between Pain 1 and Pain 2 as an adequately powered study.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Neuroimaging of Hippocampal Function during an Auditory Word Definition Decision Task

#### OBJECTIVES:

We examined if a language task would reliably elicit hippocampal activation (HA) in an epilepsy population. We compared lateralization of HA between patients and typically developing (TD) controls and the lateralization of HA between atypical and typical language dominant participants.

#### METHODS:

Patients with left hemisphere focal epilepsy and normal MRI ( $n=38$ ; mean age=27.3;  $SD=9.27$ ) and TD controls ( $n=59$ ; mean age=26.5,  $SD=7.75$ ) underwent a 3T EPI BOLD fMRI to measure HA during an ability-level adjusted auditory description decision task (reverse speech control). We determined language dominance within Wernicke's area (WA) and inferior frontal gyrus (IFG) region of interests (ROI). Data was analyzed in SPM8. The ROI analysis for bilateral hippocampi was based on the Anatomical Atlas Library in the Wake Forest PickAtlas and laterality index (LI) for the hippocampal ROI was calculated using the LI Toolbox.

#### RESULTS:

Thirty-five out of 59 controls completed HA processing. Individually, 24 of the 59 controls (41%) demonstrated HA at a threshold of  $p=0.05$ , uncorrected. Nineteen of 38 patients completed HA processing. Individually, 15 of the 38 patients (39%) demonstrated HA at a threshold of  $p=0.05$ , uncorrected.

Regarding hippocampal LI, there was a trend for the controls to demonstrate more left-lateralized HA than the patients, but this did not reach statistical significance ( $p=0.081$ , patients mean LI: 0.24, controls mean LI: 0.47). Categorically, for controls HA was left-lateralized in 26, bilateral in 5, and right in 4, while for patients HA was left-lateralized in 13, bilateral in 4, and right in 2.

Mean hippocampal LI for participants with typical language was left-lateralized (both groups combined=0.4) and atypically-lateralized for participants with atypical language (both groups combined=-0.43). Categorically, the consistent lateralization patterns were as follows: 39 left-lateralized language and left HA, 1 bilateral language and bilateral HA, and 0 right-lateralized language and right HA.

#### CONCLUSION:

Results demonstrated that approximately 40% of participants displayed HA during an auditory description decision task, indicating that this task does not robustly activate the hippocampus. However, the participants that did show HA were predominantly left-lateralized, regardless of diagnosis (patient vs. control). Furthermore, lateralization of language function was aligned with lateralization of activation of memory structures, such that individuals with typical language patterns (left) showed left-lateralized HA, while subjects with atypical language showed atypical activation. This left-lateralized HA in adults may be related to the material-specific lateralization of memory function in adults.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Myeloperoxidase inhibition decreases inflammation and improves recovery in a murine model of stroke

Stroke is the second leading cause of death in the world. Cerebral hypoxia and ischemia increase microglia/macrophage activation, which can generate damaging pro-inflammatory cytokines and enzymes, glutamate excitotoxicity and reactive oxygen radicals. Myeloperoxidase (MPO) is a key pro-inflammatory enzyme in inflammation and brain injury. MPO is mainly secreted by activated myeloid cells, including neutrophils, monocytes/macrophages, and microglia. We had previously found that MPO is significantly up-regulated following middle cerebral artery occlusion (MCAO) in mice. We hypothesized that blocking MPO activity in ischemic stroke could have beneficial effects. We performed transient middle cerebral artery occlusion (tMCAO) in mice using 30 min reperfusion model. 4-amino benzoic-hydrazide (ABAH), an irreversible highly specific MPO inhibitor, was administered intraperitoneally twice daily to the stroke mice for up to 21 days after stroke induction. Stroke mice given saline and sham mice (mice that underwent surgery but without actually inducing stroke) were used as controls. We found that MPO inhibition substantially decreased the number of myeloid inflammatory cells and neuronal cell death in the ischemic brain on day 7 after stroke. Post-insult ABAH treatment also markedly increased 5-bromo-2'-deoxyuridine (BrdU)-positive cells compared with saline-treated control mice in the ischemic subventricular zone (SVZ). We evaluated behavioral changes on day -1, 1, 3, 7, 10, 14 and 21 after ischemia. We found that ABAH-treated mice demonstrated significantly improved neurological functions compared to saline-treated mice, to nearly the same level of functions as that of the sham mice. Therefore, our study suggests that MPO inhibition could be a potential novel therapy for ischemic stroke.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Early cellular effects of sphingosine-1-phosphate on astrocytes

#### BACKGROUND:

Multiple sclerosis (MS) is considered to be an autoimmune degenerative disease characterized by death of oligodendrocytes, the myelinating cells of the central nervous system (CNS) and subsequently leading to neurologic decline. Immune system modulation has proven most effective in the treatment of MS. The oral drug Fingolimod (FTY720) works primarily by preventing lymphocyte egress from lymph nodes due to its functional antagonism of the sphingosine-1-phosphate receptor (S1P) on those cells [1]. Experiments conducted with autoimmune encephalomyelitis mice, the animal model for MS, suggest that the therapeutic effects of FTY720 are due not only to immune modulation but may also be due to astrocytic involvement in the CNS [2]. The goal of this project was to develop methods helpful in elucidating the role of astrocytes in the pathophysiology of multiple sclerosis and to further explore the mechanism of action of FTY720. We set out to determine the usefulness of a novel reporter gene expressing GFP and to determine the level of astrocytic activation in S1P treated astrocytes.

#### METHODS:

Cortical brain tissue was harvested from two day old mouse pups born of a reporter gene lineage. Primary cells were cultured in Dulbecco's modified Eagle's medium which included 0.0001% doxycycline to inhibit the reporter gene sequences from immediate expression and other components to promote astrocytic growth. Genotyping of pup tails via PCR was performed to confirm the existence of the astrocytic reporter genes in our cultures. Following culture, cells were split and treated in a variety of conditions which included treatments with S1P as well FTY720. Duration of time it took for GFP to be expressed following removal of the doxycycline inhibitor was observed. Early activation of genes was determined via quantitative PCR.

#### RESULTS & CONCLUSION:

We found that GFP is expressed in astrocytes 6 hours following the removal of doxycycline, though expression was low and non-ubiquitous. This result provides a time frame by which we may be able to use the novel mouse reporter gene to determine astrocytic activation in future experiments. In regards to early gene activation, quantitative PCR on S1P1 receptor knockouts showed no differences in early activation in comparison to astrocytes cultured from non-knockout mice. This result suggests that S1P does not immediately cause functional changes in astrocytes. Future research should examine the action of S1P on the morphological and functional changes of astrocytes over time as well as how the drug FTY720 modulates its effect.

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# NEUROSCIENCE

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Obstructive Sleep Apnea Model Utilizing Chronic Intermittent Hypoxia/Hypercapnia Evokes Hypertension and Tachycardia

Patients with Obstructive Sleep Apnea (OSA) have an increased risk of developing many cardiovascular diseases such as sudden death, hypertension, arrhythmias, myocardial ischemia, and stroke. While chronic intermittent hypoxia (CIH) has been a very useful model for studying alterations in blood pressure, baroreceptor and chemoreceptor sensory processing, and enhanced generation sympathetic activity, the diminished parasympathetic activity that occurs with OSA may be better modeled by chronic intermittent hypoxia/hypercapnia (CIH/H). I developed a CIH/H paradigm that mimics apneic episodes in OSA by cycling between room air and 6% oxygen, 5 % carbon dioxide, and 89% nitrogen. When exposed to a single CIH/H episode, telemetry-implanted male rats demonstrated an increase in arterial pressure and a biphasic tachycardia followed by bradycardia. Prolonged CIH/H exposure resulted in an increase in basal blood pressure to hypertensive levels and progressive increases in heart rate.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Endothelin-1 is an astrocyte-derived signal which inhibits remyelination

#### BACKGROUND:

Multiple sclerosis (MS) results in demyelinated lesions throughout the central nervous system. In response to demyelination, oligodendrocyte progenitor cells (OPCs) repopulate the lesion and begin to differentiate into mature myelinating oligodendrocytes (OLs). Some lesions, however, fail to remyelinate for unknown reasons. Reactive astrogliosis has been shown to inhibit OPC differentiation during remyelination, but the role of reactive astrocytes in regulating OPC differentiation is still controversial. We have previously identified an endogenous signal, endothelin-1 (ET-1), which promotes reactive astrogliosis, but its effects on remyelination have not been explored.

#### OBJECTIVES:

In this study we aimed to determine the role of ET-1 in the regulation of OPC differentiation using *in vitro* culture systems and experimentally induced demyelination in mice. We examined the role of ET-1 in inducing expression of downstream inhibitory molecules in astrocytes in an effort to identify signaling pathways which are detrimental to remyelination.

#### METHODS:

*In vitro* primary cultured astrocytes and astrocyte-OPC co-cultures were used to examine how astrocytes respond to ET-1, and the resulting effect on OPCs. Focal demyelinated lesions were created using lysolecithin in adult mice. Mini-osmotic pumps were used to deliver pharmacological agents into demyelinated lesions *in vivo*. Transgenic Notch Reporter (TNR) mice were used to visualize canonical Notch activation *in vivo*. GFAP<sup>CreERT</sup> and ET-1<sup>flox/flox</sup> mice were bred to selectively delete ET-1 expression in astrocytes. Western blot, immunohistochemistry, and immunocytochemistry were employed for both *in vivo* and *in vitro* experiments.

#### RESULTS:

ET-1 was highly expressed in reactive astrocytes of human MS lesions and lysolecithin-induced lesions in mice. Infusion of ET-1 into remyelinating lesions prevented OPC differentiation and limited remyelination. Conversely, selective ET-1 ablation in astrocytes (GFAP<sup>CreERT</sup>;ET-1<sup>flox/flox</sup> mouse) promoted remyelination. In co-cultures, astrocytes pre-treated with ET-1 inhibited OPC differentiation through Notch signaling. Infusion of the ET-receptor pan-antagonist PD142,893 into demyelinated lesions drastically reduced Notch activation in OPCs, accelerated their rate of differentiation, and promoted remyelination.

#### CONCLUSIONS:

Our findings indicate that ET-1 promotes astrocyte reactivity and induces activation of Notch signaling in OPCs during remyelination. This leads to inhibition of OPC differentiation, which ultimately slows the rate of remyelination, as confirmed at the cellular and ultrastructural (electron microscopy) levels. Blocking ET-1 activity could constitute a novel therapy for repair in demyelinating disease.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Review of Neural Biomarkers for Auxiliary Characterization of Mild Traumatic Brain Injury

#### BACKGROUND:

Mild traumatic brain injuries (mTBIs) also known as concussions, are caused by blunt force trauma to the head with one or more of the following conditions: a period of altered mental status, impaired cognitive ability, or loss of consciousness lasting less than 30 minutes and observed signs of neurological and neuropsychological dysfunction. In the United States, more than 1.5 million people experience traumatic brain injury each year, of which approximately 75 percent sustain an mTBI. The increasing incidence of these injuries through a variety of etiologies including motor vehicle accidents, sports, and combat injuries has encouraged efforts to better characterize this injury. However, heterogeneity of injuries and study designs have made evaluation of mTBI inconsistent; thus, there is a need to identify effective neural markers in brain injury in order to allow for standardization in diagnostic criteria and qualities of prognosis.

#### OBJECTIVES:

This review aims to consolidate and examine existing candidate neural biochemical markers that have been considered for mTBI characterization.

#### METHODS:

Literature search was performed through PubMed and MEDLINE databases, limited to the past ten years. Further searches utilized MeSH databases using keywords: mTBI, serum biomarkers, traumatic brain injury. Manual reviews of articles collected were made, examining candidate markers for mTBI with regards to their nature, effectiveness, and timing.

#### RESULTS:

Upon review of the literature, glial fibrillary acidic protein-breakdown products (GFAP-BDP) showed the most promising results as a biological marker for mTBI. GFAP-BDP was detected within one hour post-mTBI, and was associated with measures of injury severity as well as focal mass lesions. Ubiquitin carboxy-terminal hydrolase (UCH-L1) and alpha-II spectrin signature breakdown products (all spectrin SBDP) require further evaluation as viable markers for mTBI; however, are more promising than older researched markers such as S100 protein beta-beta homodimer isoform (S100 $\beta$ ), cleaved tau protein (CTP) and neuron specific enolase (NSE), which all show conflicting results and inconsistencies in published data.

#### CONCLUSIONS:

This brief review demonstrates the deficiency in research of candidate neural biomarkers for the evaluation of mTBI. Although GFAP-BDP shows the most promising results as a neural marker, additional research is required to validate these findings and there are ongoing studies to pursue consistency in the data. The availability of neural biomarkers to accurately characterize traumatic brain injury has multiple benefits besides advantages to diagnosis and prognosis, including healthcare cost reductions, identification in brain injury pathophysiology, and as an additional modality to treatment protocols.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Perinatal SO<sub>2</sub> exposure alters brainstem neurons that mediate autonomic control of heart rate

Exposure to outdoor air pollution in 2010 resulted in 3.2 million premature deaths, compared to the 800,000 deaths in 1990, making air pollution exposure a larger public health threat than high cholesterol. Sulfur dioxide (SO<sub>2</sub>), an air pollutant released upon the burning of coal for electricity generation, is strongly associated with cardiovascular disease. Epidemiological studies have shown SO<sub>2</sub> exposure leads to an increase in resting heart rate, which has been hypothesized to be caused by altered autonomic control of cardiovascular function, but the mechanism(s) responsible for these outcomes are unknown. Additionally, while these studies have focused on adult exposures, the Environmental Protection Agency (EPA) has stated that there is a lack of research addressing the health effects of prenatal and neonatal SO<sub>2</sub> exposure. To address this question, a chamber was designed to expose pregnant Sprague Dawley rats to 5 parts per million SO<sub>2</sub> for 1 hour daily throughout gestation and 6 days postnatal. Electrocardiograms were recorded from pups at 5 days postnatal to examine changes in resting heart rate elicited by perinatal SO<sub>2</sub> exposure. In vitro studies employed whole-cell patch-clamp electrophysiology to examine changes in neurotransmission to cardiac vagal neurons within the nucleus ambiguus upon SO<sub>2</sub> exposure using a preparation maintaining fictive inspiratory activity recorded from the hypoglossal rootlet. Perinatal SO<sub>2</sub> exposure increased heart rate, indicative of a loss of cardioprotective parasympathetic activity. Neither spontaneous nor inspiratory-related inhibitory GABAergic or glycinergic neurotransmission to cardiac vagal neurons was altered by SO<sub>2</sub> exposure. However excitatory glutamatergic neurotransmission was decreased by 50.0 percent upon SO<sub>2</sub> exposure. This diminished excitatory neurotransmission was tetrodotoxin-sensitive, indicating SO<sub>2</sub> exposure impairs the activity of preceding glutamatergic neurons that synapse upon cardiac vagal neurons. Additional studies examining SO<sub>2</sub> exposure in the prenatal versus postnatal time periods have shown that postnatal exposure through postnatal day 5 alone elicits the elevated heart rate and loss of glutamatergic neurotransmission to CVNs. These findings demonstrate that a cellular target of SO<sub>2</sub> exposure is a decreased excitatory neurotransmission to CVNs, causing decreased parasympathetic control of resting heart rate, tachycardia, and autonomic imbalance to the heart. They also suggest susceptibility to these health risks are highest during the postnatal time period, indicating there is a need for reducing exposure limits to protect the neonatal population.

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#### STATUS

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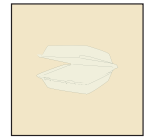
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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Metformin and Weight Loss in Patients with Prediabetes

**BACKGROUND:**

Prediabetes is a state of high risk of developing diabetes mellitus. It is strongly associated with obesity. Metformin is used in patients with prediabetes to prevent progression to disease and to aid in weight loss. However, the mechanism by which metformin aids in weight loss has not been completely understood. This study examines if its effect on weight is related to Hemoglobin A1c level (Hb A1c).

**OBJECTIVE:**

To determine if the effect of receiving metformin with lifestyle modification counseling on weight in obese prediabetic patients is related to their Hb A1c level.

**METHODS:**

This is a retrospective study. Charts of patients seen in the weight loss clinic at GW Medical Faculty Associates during the period from January 2009 to December 2011 were reviewed. All patients with prediabetes (defined in this study as Hb A1c in the range between 5.7 and 6.4) at the first visit that were receiving metformin during follow up were selected. Patients who didn't return for a second visit, followed up for less than 8 weeks, or were diagnosed with diabetes mellitus were excluded. Data was collected for up to 18 months of follow up. Patients were divided into 2 groups according to their HbA1c level on the first visit. High Hb A1c group was composed of patients with 6.0 to 6.4 Hb A1c level, and low Hb A1c group had those with 5.7 to 5.9 Hb A1c level.

**RESULTS:**

A total of 70 patients met the criteria, 35 in each group. They started with a mean BMI of 41.03 in the high Hb A1c group, and 43.41 in the low Hb A1c group. Follow-up period in the study ranged from 8 weeks to 18 months and the number of visits ranged from 2 to 11 visits. Both groups lost weight with a mean reduction of BMI of 1.40 in the High Hb A1c group, and 1.45 in the low Hb A1c group.

**CONCLUSION:**

In obese prediabetic patients that received metformin during following up in the weight loss clinic, there was no significant difference in weight loss at different levels of Hb A1c. Further prospective studies should be done.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### BMI Handout: A Helpful First Step?

#### OBJECTIVE:

More than two-thirds of Americans are overweight or obese, but most are unaware of their Body Mass Index (BMI). Further, less than two-thirds of overweight or obese patients are counseled on weight loss by their physicians. In this cross-sectional analysis, we investigated if providing a handout with patient's BMI and tips for healthy eating and exercise would help initiate a conversation between patient and physician regarding BMI and encourage patients to consider lifestyle changes.

#### METHODS:

Participants were recruited from a general medicine clinic in Washington DC. At the beginning of appointments, assistants measured height and weight, then provided the BMI handout and an anonymous survey about patient understanding of BMI, whether patients discussed weight with their physician and if they intended to make lifestyle changes after reviewing the BMI handout. Physicians were later e-mailed an anonymous survey, asking how often and who initiates discussions about patient weight and the usefulness of the BMI handout.

#### RESULTS:

A total of 411 adult participants completed the patient survey; 11% were morbidly obese, 31% obese, 30% overweight, 24% normal weight and 3% underweight. Fifty-nine percent reported BMI understanding as *not at all, not well or unsure*, whereas 41% reported well or very well, with no difference among BMI classes ( $p=0.66$ ). Twenty percent of patients were unaware of their BMI prior to receiving the handout. Thirty-five percent of patients who were aware of BMI intended to speak to their physician about weight, compared to 21% who were unaware ( $p=0.012$ ). Nearly 30% were *somewhat surprised or very surprised*, whereas 70% were *not surprised or not very surprised* about BMI results. By visit end, 57% of participants discussed BMI with their physician; those with above-normal BMI were significantly more likely to do so ( $p=0.0114$ ). Two-thirds of patients planned to modify diet and/or exercise based on the BMI information. Regarding the physician survey, there were 70 responders, of whom 52% reported discussing BMI with half or more of their patients. Forty percent of physicians reported that the patient initiated the discussion half or more of the time. More than 60% stated that the BMI handout was *very helpful or somewhat helpful*.

#### CONCLUSION:

Among a diverse, urban patient population with a high prevalence of obesity, a BMI handout can be a valuable tool for raising patient awareness about BMI. Additionally, physicians may find the handout to be a helpful first step in discussing weight management and lifestyle interventions.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Community Clinic-Based Obesity Intervention Program in the District's Ward 1 Hispanic Population

#### BACKGROUND:

Obesity is associated with an increased prevalence of many chronic health conditions, including diabetes, coronary artery disease, cerebrovascular disease, certain malignancies and depression. According to The Office of Minority Health, in 2010, Hispanic Americans were 1.2 times as likely to be obese than Non-Hispanic Whites, demonstrating that Hispanic Americans are disproportionately obese and overweight compared to the general population. Additionally, childhood overweight and obesity rates show sharply increasing trends among the Hispanic population, suggesting that preventative measures and nutritional care must start an early stage to mitigate weight-related health problems.

The patients at Columbia Road Health Services comprise a low-income segment of the District's population that is often culturally or linguistically isolated. CRHS is located in a census tract designated as a Medically Underserved Area in Ward 1, which contains the highest number of Hispanic residents in the District. Furthermore, in accordance with the national trend, the clinic's Hispanic patients are disproportionately affected by obesity, with 34% of Hispanic patients with a body mass index (BMI) in the obese range, and an additional 44% in the overweight range in a 2011 chart audit sample.

#### METHODS:

Over eight weeks, I worked on the program development and implementation of two preventative health programs aiming to provide overweight and obese patients with an avenue for physical activity as well as education on nutrition, stress and healthy lifestyle. The two parallel programs, The Adult Wellness Program and the *WE CAN!* (Ways to Enhance Children's Activity & Nutrition), serve the adult and pediatric patient populations respectively. Both programs include 45-60 minutes of physical activity and 15-30 minutes of patient education and discussion on a variety of health topics, including nutrition, alternative sources of exercise and stress reduction techniques.

#### RESULTS:

My summer efforts were very fruitful, as I was able to recruit new patients through phone calls and in-clinic consultations, lead bilingual and culturally sensitive educational sessions and discussions on topics such as "The Dangers of Sodium" and "Reading a Nutritional Label" and lead physical activity sessions, including a family field trip to a local community garden. I also compiled a binder of lesson and activity plans for future sessions. Additionally, I developed a spreadsheet to record and track attendance as well as changes in weight, blood pressure, eating behavior and screen time for the Adult Wellness Program and evaluated the data from quarterly program satisfaction surveys. Lastly, I was also able to gain valuable clinical experience by shadowing Dr. Rona Schwartz once a week.

#### CONCLUSIONS:

By working with the patients at Columbia Road Health Services, not only did I gain the opportunity to practice my patient education and Spanish language skills, I was able to witness firsthand the challenges faced by a low-income, immigrant population in maintaining their health. I plan to return to the programs to volunteer in the spring.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### A Majority of Weight Loss Clinic Patients Are Unaware of the Relationship Between Obesity and Cancer

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#### INTRODUCTION

Obesity has been increasing in prevalence in the United States. Obesity increases the risk of developing many medical conditions including certain cancers, especially endometrial, renal, colon, pancreatic, and esophageal. The purpose of this study was to assess if patients at a university weight loss clinic were aware of the relationship between obesity and cancer, and to determine if knowledge of this relationship affected their motivation to lose weight.

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#### METHODS

Patients at a university weight loss clinic were asked to complete a survey assessing their knowledge about the relationship between obesity and cancer. The survey asked for specific demographic information, including gender, age, level of education, and history of cancer diagnosis. The survey asked about awareness between obesity and cancer, to list cancers linked to obesity, and how knowledge of a link between obesity and cancer might affect his or her motivation to lose weight (greatly increase, somewhat increase, no impact, somewhat decrease, or greatly decrease motivation). Surveys were anonymously collected, and data were entered and stored in Microsoft Excel.

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#### RESULTS

Forty-eight weight loss clinic patients (36 female, 11 male, 1 unknown) completed the survey. The mean age of participants surveyed was 47.5 years old. Of the 48 patients, 27 were unaware of a relationship between obesity and cancer. Of these patients, 18 reported that knowledge of a relationship between obesity and cancer would increase their motivation to lose weight (15 greatly increase, 3 somewhat increase). There was a significant difference in degree of increased motivation (greatly increase vs. somewhat increase) to lose weight in unaware patients compared to those who were already aware of the link ( $p=0.02$ ). Patient gender ( $p=1.00$ ), age ( $p=0.73$ ), and previous cancer diagnosis ( $p=0.35$ ) did not influence awareness. In terms of listing cancers associated with obesity, 25% (12) of patients correctly noted breast cancer, 17% (8) correctly noted colon cancer, and 13% (6) correctly noted ovarian cancer.

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#### CONCLUSION

This study demonstrates that a majority of patients surveyed at the weight loss clinic were unaware of a relationship between obesity and cancer. It also reveals that if previously unaware patients learned about the link between obesity and cancer, there would be a significant difference in the degree of motivation to lose weight compared to those already aware of the relationship. These results imply that improved health education focusing on obesity is necessary to increase the public's knowledge about its multiple health effects.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### “Should I lose weight?” Examination of the relationship between social networks, social norms and body weight in a college sample

#### BACKGROUND:

Social networks and social norms have an influence on health behaviors. In adult populations, obesogenic behaviors/norms and social networks influence an individual's weight status. Despite these findings, there is limited empirical research replicating them in college populations, which may have a unique set of social norms and networks that influence weight loss.

#### OBJECTIVE:

This descriptive study examined the relationship between reported social norms and networks and participants Body Mass Index (BMI) in a college sample.

#### METHODS:

We conducted an online survey of GW undergraduate students (N=46; Mean age=19.8 ± 1.3 years). Participants were recruited via flyers and email announcements. Measures assessed social norms for weight loss (e.g., “How socially acceptable is it to eat unhealthy foods?”), overweight social contacts (e.g., “Is your best friend overweight?”), and self-reported height and weight. Weight status was categorized with normal/under-weight (NW): BMI < 24.9) and overweight/obese (OW/OB): BMI ≥ 25).

#### RESULTS:

15% of the sample (N=7) were OW/OB and 85% (N=39) were NW. Among OW/OB the mean BMI=30.03 ± 3.7; among NW, the mean BMI = 21.93 ± 2.06. 33% percent of OW/OB participants reported OW/OB best friends, compared to 12.8% of NW participants. However, OW/OB and NW reported similar percentages of casual contacts trying to lose weight (OW/OB=85.7%; NW=87.2%). Among NW participants 87.1% endorsed that it was socially acceptable to eat unhealthy foods, compared with 57.1% of OW/OB participants ( $p=.054$ ). NW participants (33.3%) also endorsed that it was socially acceptable to be physically inactive compared with 71.4% of OW/OB ( $p=.057$ ). Both NW and OW/OB participants endorsed similar norms for weight loss: 57.8% of NW and 66.7% of OW/OB participants reported their closest social contacts would approve them losing weight.

#### CONCLUSIONS:

Although OW/OB participants reported a higher percentage of overweight friends, more than half of the NW sample reported their friends would approve of them losing weight. These findings emphasize the need to address perceptions of weight and weight status among both NW and OW/OB college students. The perceptions of weight and weight behaviors on campus may be a precursor for identifying more severe eating pathologies. Limitations of this analysis included a primarily female sample (N=45), a small OW/OB sample (N=7) and self-reported weight data. However, the results of this formative research may lead to the development of a more informed eating pathology screening and obesity treatment programs on college campuses.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Clinician Compliance with Children's National Medical Center's Quality Improvement Guidelines for Pediatric Weight Management

#### BACKGROUND:

Since the release of the 2007 Expert Committee report on pediatric weight management, consistent adherence to approved weight management techniques is often under-achieved. Providers continually request standardized tools and counseling strategies to properly advise patients and families. The Children's National Medical Center (CNMC) performed a Quality Improvement (QI) assessment, and released 12 measures for clinicians to implement when managing obese and overweight issues with their patients. The present study sought to determine compliance with CNMC QI guidelines for pediatric weight management, and identify the barriers that CNMC providers faced in complying with treatment guidelines.

#### OBJECTIVES:

The specific aims were to: determine baseline and post-QI measurement for clinic-wide compliance with the recommended weight management practices and procedures; determine the common barriers with which providers are faced when attempting to follow QI guidelines.

#### METHODS:

Objectives were achieved through electronic medical record chart review (N=483), and a physician survey (N=7). Using SPSS, the researcher conducted analysis on charts to determine rate of compliance before and after the intervention was introduced. Crosstabs were used to determine the effects of patient age and gender on providers' compliance. Physician surveys were analyzed using frequencies to determine common barriers to compliance.

#### RESULTS TO DATE:

At six months post-QI, clinicians more closely adhered to the pediatric weight management guidelines than prior to the QI initiative. Clinicians showed bigger increases in compliance with measures specific to obese and overweight patients, particularly in setting self-management goals, and scheduling follow-up appointments. There were smaller increases in compliance with general preventative measures applicable to every patient- assessing family history, nutrition and physical activity. A major gap in the study was low response rates for the provider survey, though the responses received did indicate that clinicians are in need of more appealing handouts to give to families, and are highly in favor of an in-house nutritionist or health educator, and more access to a specialized weight management clinic.

#### CONCLUSIONS:

As providers continue to improve their implementation of the QI guidelines, the measures outlined in the Quality Improvement initiative will establish community-wide improvement in nutrition and wellness. The immediate next steps of the present study will be placement of a provider toolkit in the clinic. The toolkit will be developed based on the answers provided in the provider survey, to address some of the barriers they face in complying with the guidelines.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Associations Between School Nutrition Policies and Student Obesity-Related Behavior

#### BACKGROUND:

In the District of Columbia, 20 percent of adolescents are obese, and most do not consume the recommended amounts of fruits and vegetables. Several individual, social, and environmental factors have been found to impact adolescents' dietary habits. As adolescents spend much of their days in school, the school environment may have an effect on the nutritional habits and overall health of the students.

#### OBJECTIVE:

The objective of this study was to assess the impact of school-level nutrition policies on the obesity-related behaviors and BMI among public high school students in Washington, DC.

#### METHODS:

Data from the Centers for Disease Control and Prevention Youth Risk Behavior Survey (YRBS) were linked to information from School Health Profiles survey. A total of 1,154 students in 14 public high schools were included in the analysis. The dependent variables included a healthy eating index, frequency of soda consumption, and BMI percentile. The independent variables included in the analysis were the following school policies: 1) healthy and unhealthy food availability, 2) reduced price nutritious foods, 3) student-conducted taste tests of healthy foods, 4) collection of healthy eating suggestions from students, staff, and parents, and 5) provision of nutrition information to parents and families. Simple and multiple linear regression models were conducted to assess associations between school policies and student behaviors.

#### RESULTS:

After controlling for potential school and student-level confounding variables, the only statistically significant association that existed was between student soda consumption and school-conducted taste tests.

#### CONCLUSIONS:

These results do not agree with past studies that found significant associations between school policies and student behaviors. The only significant association does not appear to have a logical correlation and may be the results of a type I error. Limitations to this project include the use of a single school-level policy in analysis as opposed to the interaction or combination of multiple policies, and the self-report nature of the YRBS and possibility of over or underreporting in student behaviors.

While the current study did not find any significant and plausible associations between school-level policies and student dietary behaviors, past studies have determined that the school nutrition environment does impact students' behavior. Future research should examine the effects of the interactions of multiple policies on student behavior.

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#### SOURCES

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Story M, Neumark-Sztainer, French S. Individual and environmental influences on adolescent eating behaviors. *Journal of the American Dietetic Association*. 2002; 201(3): S40-S51. Accessed May 30, 2012.

Story M, Kaphingst KM, Robinson-O'Brien, Glanz K. Creating Healthy Food and Eating Environments: Policy and Environmental Approaches. *Annual Review of Public Health*. 2008; 29: 253-272.

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# OBESITY

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### The Association of Caregivers' Educational Level and their Knowledge of Children's Nutrition and Exercise Behavior

#### BACKGROUND:

Parents play an instrumental role in modeling their children's health behaviors and exposing them to new foods, and engaging them in physical activities.

#### OBJECTIVE:

To assess the association of parents' educational level on their nutritional and physical activity knowledge.

#### METHODS:

This is a prospective study of 72 participants from a nutrition and wellness program targeting parents of African American preschoolers. Socio-demographic, child's nutritional and physical exercise habit survey and anthropometric data were collected from all participants at baseline.

#### RESULTS:

77% of the participants were grandmothers or mothers; the mean age was 44.8 and 13% of participants were college graduates. 66% were obese. The mean scores for nutrition and physical activity knowledge were 41 % and 58%, respectively. 89% of the participants reported that their children exercised at least once a week. 51% of the participants' children drink soda or sweetened beverages. Mothers' educational level was significantly associated with nutrition knowledge ( $p = .01$ ).

#### CONCLUSIONS:

Larger sample size and longer time evaluation are needed to assess the association and impact of maternal education on between parents' knowledge of physical activity and nutrition and their children's behavior.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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#### RESULTS:

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#### CONCLUSIONS:

Larger sample size and longer time evaluation are needed to assess the association and impact of maternal education on between parents' knowledge of physical activity and nutrition and their children's behavior.

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## COLUMBIAN COLLEGE OF ARTS AND SCIENCES

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### Diagnostic Criteria for Autism Reflected in Graphic Features of Artwork

A team of investigators at GW has been collaborating on a study sponsored by the Medical Faculty Associates, to determine medication responsiveness of people with Autism Spectrum Disorders (ASDs). Results derived from parent and clinician surveys distributed in this study are inconclusive, as the range of medications prescribed to the participants with ASD ( $n=170$ ) is proving to be vast and varied. However, other interesting data have emerged. In addition to the survey-based data, a sub-group of the study participants with ASD ( $n=60$ ) completed an art therapy measure, the Face Stimulus Assessment (FSA; Betts, 2003). The FSA was developed for clients with developmental disabilities and ASD, as a drawing-based art therapy evaluation to help determine client strengths, aid in treatment planning, develop goals and objectives, and augment the diagnostic process. Its use is supported by the idea that by gaining a deeper understanding of artwork in the context of diagnostic evaluation, clinicians can better identify problems that may not be identifiable through other evaluative methods. The FSA is a departure from traditional psychological projective tests, and the resulting drawings are not analyzed for their symbolic content. Rather, the standardized format of the FSA and its corresponding objective scoring system enables examination of the graphic features identified in participant drawings, which may correspond to diagnostic criteria for ASDs.

The 60 participants in the present study present a range of ASD criteria: impairment in social interactions; impairment in language/communication; repetitive or stereotyped actions; restricted interests/activities, and obsessive thoughts. The graphic features of their FSA drawings were rated on the following nine scales: Prominence of Color, Color Fit, Implied Energy, Logic, Realism, Developmental Level, Details of Objects and Environment, Line Quality, Perseveration. This approach is conducive to applying the rigor of the scientific method to the important questions about common characteristics within groups. As such, results of a comparison of the graphic features scores to determine whether particular scales correspond to diagnostic criteria for ASDs will be reported. Outcomes of this study may contribute to further validation of the FSA as a measurement tool. Future research will seek to determine the construct validity of the FSA with ASD criteria by comparing FSA scale scores with scores on established ASD inventories such as the Autism Diagnostic Observation Schedule (ADOS) and the Childhood Autism Rating Scales (CARS).

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**COLUMBIAN COLLEGE OF ARTS AND SCIENCES**

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## Group Photo Therapy for At-risk Adolescent Girls

The 2011 DC Children and Youth Investment Trust Corporation Report called for a higher demand for mentorship and youth-specific programs that support interaction with peers. Multi-dimensional approaches to improving the well-being of youth that incorporate the art therapies have emerged to meet this need. Research in this area indicates that using photography as a therapeutic tool for adolescents may help teens increase self-worth, safely experience their emotions, and receive social support. While there is extensive literature narrating the benefits of photography in therapy through case examples, within the scope of current empirical research on the use of creative therapies with adolescent issues, photography is rarely considered. Therefore, the present study is investigating the effects of group photo therapy in a program for at-risk adolescent females. This program was developed through collaboration with a local non-profit organization that provides services for at-risk youth. Such factors that contribute to at-risk status for these participants include poverty, low self-esteem, poor self-efficacy, depression, self-destructive behaviors, and poor school performance. As such, the present study is examining whether the at-risk adolescent females' participation in the group photo therapy sessions has an effect on their mood, sense of self-efficacy, and social connectedness. Data being collected reflect the process and outcomes of participation in weekly photo therapy sessions for a duration of 10 weeks. Data sources include participants' journals, photographs, self-reflection questionnaires, transcriptions and field notes from photo therapy sessions. In addition, three instruments are being administered pre- and post-intervention: the CES Depression Inventory, General Self-Efficacy Scale, and The Hemingway Measure of Adolescent Connectedness. Preliminary data will be presented, reflecting any changes in participants' self-reported levels of depression, self-efficacy and social connectedness. Pertinent themes that emerge within the sessions will be reported, and the efficacy of photography as a tool to express identity, experience, and underlying conflicts and emotions will be discussed. Results of this study may demonstrate the benefits of photo therapy with at-risk female adolescents. Furthermore, the study results may provide an opportunity to gain awareness of the value of photography as a therapeutic tool in exploring topics relevant to adolescent development, and contribute to the continued exploration of effective interventions for improving adolescent transition to adulthood.

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# PSYCHIATRY/MENTAL HEALTH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Measuring trauma and stressful events in childhood and adolescence among patients with first-episode psychosis: Initial factor structure, reliability, and validity of the Trauma Experiences Checklist (TEC)

#### BACKGROUND:

A history of trauma and stressful events, especially in childhood and adolescence, is common among individuals with serious mental illnesses, including schizophrenia and other psychotic disorders. Traumatic experiences are thought to be a socio-environmental risk factor not only for poorer outcomes, but also potentially for the onset of these disorders, perhaps mediated by perturbations in dopaminergic neurotransmission in the mesocorticolimbic system. To further advance understandings of the association between childhood/adolescent traumatic experiences and serious mental illnesses like the psychotic disorders, improved measurement tools are needed.

#### OBJECTIVE:

To develop and validate a measurement tool to assess trauma and stressful events in childhood and adolescence among 205 patients with first-episode psychosis.

#### METHODS:

We developed the Trauma Experiences Checklist (TEC), which is a 41-item instrument, to thoroughly measure traumatic and stressful events across a range of social, familial, and environmental contexts specifically during childhood and adolescence. Participants were recruited from five inpatient settings and were asked to endorse the frequency of a broad range of traumatic and stressful experiences that may have happened before the age of 18 years. An analogous version of the TEC was developed (TEC-Informant Version) for use with close relatives, friends, or others. Exploratory factor analysis of the TEC was done and resulted in two internally consistent subscales, labeled *interpersonal abuse and family stress and violence, death, and legal involvement*. Validity of these subscales was assessed by comparing derived subscale scores to Childhood Trauma Questionnaire-Short Form, Parental Harsh Discipline, Violence Exposure, and TEC-informant scores.

#### RESULTS:

In this study, we describe the development, factor structure, internal consistency reliability, and initial validity of the TEC in measuring trauma and stressful events during childhood/adolescence. We uncovered two subscales that appear to have acceptable internal consistency reliability and concurrent validity.

#### CONCLUSIONS:

The TEC is a potentially useful tool in assessing traumatic life events across various social contexts during childhood and adolescence, and may help to advance measurement in this burgeoning area of research.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Understanding sexual identity: An arts-based narrative inquiry

The dominant American culture understands sexuality on a polarized system. This simplification labels people as heterosexual or non-heterosexual. And, the system relies on labeling individuals based on sexual behaviors, which limits the complexity of sexual minorities and categorizes people as abnormal, or differing from social norms. Many seek justification by searching for determinants of sexuality to reduce marginalization. Research has shown marginalization produces higher stress, which contributes to the prevalence of mental health disorders and substance abuse among sexual minorities (King et al., 2008; Meyer et al., 2008; Hatzenbuehler, 2009). The aim of this narrative inquiry is to explore the lives of adult sexual minorities in the District of Columbia to examine how marginalization affects the understanding and development of sexual identity over time. Art can contribute to this understanding by engaging participants in a nonverbal, visual language to explore meaning beyond the social constructed labels of sexuality. The labels for sexual orientation may not feel appropriate for some and may limit the understanding of sexual identity, but many adopt a label to help understand themselves in society and to identify with a community. The researcher's intention is to recruit 4 participants from different sexual identities, ethnicities, sexes, and ages. Data collected from the interviews, participant artwork, and journal entries will be reviewed by the participants and interpreted from the researcher's perspective, as well as Pamphilon's (1999) Zoom Model framework. Analyzing personal narratives through many lenses captures the richness and complexity of the stories by providing perspectives on a broad, small, and interactional level with the researcher

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

What demographic, socio-environmental, and substance use-related factors predict duration of untreated psychosis (DUP), and is DUP associated with neurocognition in first-episode psychosis?

### BACKGROUND:

Early intervention and prevention for psychotic disorders is of increasing importance to the mental health community. One way to advance early intervention is to better understand factors driving the duration of untreated psychosis (DUP), which has been linked to significantly poorer outcomes across multiple domains, including poorer prognosis and more severe symptoms. Research has shown that there are multiple risk factors that contribute to longer DUP: single marital status (Pek et al., 2006), living in poverty (Compton et al., 2011), a greater severity of negative symptoms (Boonstra et al., 2012), and most importantly, a gradual mode of onset of psychosis.

### OBJECTIVES:

This study aimed to reinforce previously studied predictors of DUP, examine never-yet-studied predictors, and assess the relationship between DUP and neurocognition. Neurocognition is important because it could be a link between psychosis and neurotoxicity explaining the established association between DUP and poorer outcomes (Perkins et al., 2005). Furthering the understanding of risk factors, such as premorbid adversity or gradual onset, could inform interventions focused on those at greatest risk for long periods of treatment delay. Examining novel factors, such as incarceration or childhood maltreatment, allow for a fuller understanding of DUP and a more directed approach to future research.

### METHODS:

We assessed 180 predominately African American, low-income, and socially disadvantaged first-episode psychosis individuals using a rigorous battery of measures of symptoms, substance use, family history, social history, and cognitive functioning. Symptom onset, and thus DUP, was carefully assessed using a standardized process.

### RESULTS:

After controlling for the effect of mode of onset of psychosis, previous incarceration, the level of childhood and adolescent maltreatment, and past history of substance use were significant predictors of DUP. Neurocognition, across all seven domains measured, was not associated with DUP.

### CONCLUSIONS:

Early intervention efforts should focus on those at highest risk for longer DUP. The social determinants, such as neighborhood disorder, demonstrate a need for more community-based prevention measures that will affect not only those at risk for psychosis but all children living in the geographical area. Better capacity to identify those with early psychosis will allow for earlier intervention, thereby promoting recovery.

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Boonstra N, Klaassen R, Sytema S, Marshall M, De Haan L, Wunderink L, Wiersma D (in press) Duration of untreated psychosis and negative symptoms - A systematic review and meta-analysis of individual patient data. *Schizophrenia Research*.

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Pek E, Mythily S, Chong SA (2006) Clinical and social determinants of duration of untreated psychosis in first-episode psychosis patients. *Ann Acad Med Singapore* 35:24-26.

Perkins DO, Gu H, Boteva K, Lieberman JA (2005) Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: A critical review and meta-analysis. *American Journal of Psychiatry*, 162:1785-1804.



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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Researcher-Rated and Patient-Reported Insight in First-Episode Psychosis: Their Association with Depression

Relatively little research has explored insight in first-episode psychosis patients. We collected data on researcher-rated (lack of judgment and insight item of the Positive and Negative Syndrome Scale) and patient-reported insight (Birchwood Insight Scale) among 267 hospitalized first-episode patients. Researcher-rated PANSS lack of judgment and insight was substantially correlated with the patient-reported BIS score  $r = .65$  ( $p < .0005$ ); however, agreement between the two measures of insight was low ( $\kappa = 0.23$ ), indicating considerable discrepancy between patient and clinician-rated insight. For both patient-reported insight and researcher-rated insight, depression was the most strongly associated predictor, and remained independent after controlling for all other patient-related characteristics. The only other remaining significant predictor of researcher-rated insight was positive symptoms, indicating patients who were more symptomatic exhibited lower insight. In contrast, the other remaining independent predictors of patient-reported insight included a small gender difference, with females reporting higher insight, and an association with premorbid academic functioning. Discordance between researcher-rated and patient-reported insight was predicted only by greater depressive symptoms. In contrast to previous reports, there was little evidence of an association between insight and neurocognitive functioning. A greater emphasis on patients' self-reported insight in conjunction with researcher/clinician-assessed insight might inform intervention development. Further research is needed on psychosocial interventions that enhance insight while addressing depressive symptomatology.

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#### KEY WORDS:

first-episode psychosis; insight; psychosis; schizophrenia

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Emergency Department Physicians' Comfort Levels With Diagnosing and Treating Depression

#### BACKGROUND:

The Emergency Department (ED) is often the first and only treatment for many people. ED physicians increasingly come into contact with patients suffering from issues such as major depressive disorder (MDD). This study sought to examine resident ED physicians' comfort levels in working with this population.

#### METHODS:

We examined levels of comfort in diagnosing MDD in comparison to hypertension and diabetes with a 5-point Likert Scale. We also examined comfort levels with prescribing medications for MDD compared to hypertension and diabetes in three scenarios: (A) without follow-up (no primary care provider/PCP), (B) with a PCP available for follow-up (but without speaking to him/her) and (C) with an available PCP that is reachable by phone. We examined perceived barriers to initiating treatment for MDD.

#### RESULTS:

Residents exhibited significantly lower levels of comfort in making an initial diagnosis of MDD 2.45 (95% CI 2.03, 2.87) when compared to either hypertension 3.90 (95% CI 3.28, 4.52) or diabetes 4.00 (95% CI 3.52, 4.48). Residents were less comfortable prescribing medication for depression as compared to hypertension or diabetes across all scenarios. The most common barrier to treatment was lack of comfort with treating patients without follow-up.

#### DISCUSSION:

Residents have a low level of comfort in treating MDD as compared to conditions such as hypertension and diabetes. Further research is needed to examine residents' attitudes toward diagnosing and treating depression, and its' perceived barriers. Resident curriculums should incorporate diagnosis and treatment of MDD given the high number of patients with MDD that utilize ED services.

This abstract has not been previously presented or published.

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Depressive Symptoms and Sexual Behavior Among Adolescent Girls in Ghana

#### BACKGROUND:

The high rates of risky sexual behaviors and subsequent sexual health problems among adolescent girls in Ghana make it imperative to identify and understand factors that may predict these risky sexual behaviors. Previous research has identified multiple psychosocial and social ecological factors that contribute and enable risk-taking sexual behaviors in adolescents. Factors regarding mental health problems such as depressive or anxious symptoms, however, have been neglected in the research exploring what potentially makes adolescent girls in the Sub-Saharan region more likely to engage in risky behaviors. A critical need exists to better understand how depressive and anxious symptoms affect sexual behavior in order to prevent further reproductive health issues among this population of young girls.

#### OBJECTIVES:

This study aimed to determine whether a predictive relationship exists between the prevalence of depressive or anxious symptoms and risky sexual behaviors among young girls living in Ghana. Moreover, we looked primarily at whether depressive and anxious symptoms predict risky sexual behavior eighteen months later with the assumption that depressed girls are more vulnerable to sexual and reproductive health problems such as contracting HIV/AIDS or unintended pregnancies.

#### METHODS:

As part of a 2-wave longitudinal cohort study conducted in Ghana, over 1,200 interviews were collected and a total of 697 adolescent girls were included in this analysis. Items from the Child Behavioral Check List (CBCL) measuring depressive symptoms were used to calculate an overall depressive/anxious score for each girl. Based on previous findings identifying specific sexual behaviors that increase STI exposure, three dependent variables were chosen to identify and analyze whether depressive/anxious scores predicted risky sexual behavior. These variables included: condom-use during most recent sexual encounter; number of sexual partners; and whether younger girls (13-15 years of age) transitioned from never having sex to having sex within 18 months.

#### RESULTS:

Multiple logistic regressions were conducted and determined depressive symptoms at Wave 1 significantly predicted an increased odds of having multiple sexual partners at Wave 2 ( $p=.046$ ). The relationship was not significant when confounding variables were placed in the model. Depressive symptoms did not significantly predict the other two outcome variables.

#### CONCLUSION:

Although the results were not entirely significant, this study provides insight into the individual, psychological factors affecting adolescent girls' behaviors. Future research should explore the differences between internalizing and externalizing psychological factors in order to more clearly identify traits that lead to risky sexual behaviors among this population of adolescent girls in Ghana.

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# REHABILITATION AND RECOVERY



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Intensive Goal-Directed Treatments in Enriched Environments Augments Patient Outcomes

#### OBJECTIVE:

Previous research indicates that patients post-stroke, average 400-800 steps within physical therapy sessions and demonstrate heart rate values of 24-35% of HR Max. This dosage and intensity is inadequate to promote neuroplastic changes and maximize recovery. The goal of this study was to quantify and examine the amount of high-intensity stepping practice that was delivered within an Acute Inpatient Rehabilitation (AIR) setting for individuals with sub-acute stroke.

#### METHODS:

14 patients with a diagnosis of sub-acute stroke were admitted to AIR. Standardized outcomes included the 6-Minute Walk Test (6MWT), 10-Meter Walk Test (10MWT), the Berg Balance Scale (BBS) and the Postural Assessment Scale for Stroke Patients (PASS). A step activity monitor with an internal accelerometer was applied on the non-paretic extremity from the hours of 7 am to 5 pm. During therapy sessions, subjects were exposed to a plan of care that involved high-intensity, high-frequency stepping practice through Body Weight Supported Treadmill Training (BWSTT), over-ground stepping, stair climbing, obstacle navigation, dynamic standing balance activities and error augmentation tasks. All individuals were continuously monitored with heart rate monitors, and perceived intensity was recorded within 5-minute intervals and after modification of activity with the Borg Rate of Perceived Exertion (RPE) Scale. Target intensity was defined with heart rate values of 70-85% of HR Max and RPE values of 14-20 (hard to maximal exertion). Time spent in target intensity ranges was collected. Each subject was scheduled for 1-2 hours of physical therapy per day.

#### RESULTS:

During the 2-month collection period, subjects demonstrated ability to tolerate a high-intensity, high-frequency stepping gait training program within the intensities defined. Stepping data indicated that subjects received an average daily stepping dosage of 2000-8000 steps per day, well above previously reported values.

#### CONCLUSION:

It is possible to implement a high-intensity, high-frequency stepping gait training program within an acute inpatient rehabilitation setting for the stroke population. However, future research concerning therapy intensity and frequency of stepping should be designed with a larger sample size.

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# REHABILITATION AND RECOVERY

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Rehabilitation of Proximal Hamstring Tendinopathy: A Case Series

#### BACKGROUND:

Proximal hamstring tendinopathy is a relatively uncommon overuse injury typically seen in middle to long distance running athletes. Despite a significant amount of literature addressing acute hamstring strain and ruptures, there is a lack of evidence regarding proximal hamstring tendinopathy. Specifically, the physical therapy management of proximal hamstring tendinopathy has yet to be well described in the literature beyond general recommendations to improve hamstring strength and flexibility, trunk stability, and correcting muscle imbalances. The purpose of this case series is to describe the successful physical rehabilitation of three active individuals with proximal hamstring tendinopathy utilizing eccentric training, trigger point dry needling, and trunk stability exercises.

#### CASE DESCRIPTION:

Three patients presented to a university outpatient physical therapy clinic with complaints of proximal buttock pain lasting several months with insidious onset, worsened with prolonged sitting and running. Each patient reported a gradual increase in symptoms combined with an increase in exercise. Following a comprehensive examination to exclude other potential pain generating tissues, a clinical diagnosis of proximal hamstring tendinopathy was made. The patients were treated with an individualized and progressive rehabilitation program including eccentric loading of the hamstrings, trigger point dry needling of the hamstrings, and trunk stability.

#### OUTCOMES:

The patients were seen for physical therapy treatment for an average of 9 visits over 9 weeks. Significant improvements were seen in pain and LEFS scores, sitting tolerance, proximal hamstring tendon point tenderness, and gluteal strength and control. Each patient was also able to return to his or her individual level of pain free running.

#### DISCUSSION:

Proximal hamstring tendinopathy can be a frustrating diagnosis to treat in physical therapy, and aside from general recommendations specific physical therapy management has not been well described. In the three patients included in this case series, significant improvements were noted in terms of pain and function following eccentric training, trigger point dry needling, and trunk stabilization exercises. Given the lack of available research and successful outcomes in these cases, the rehabilitation program described may be an appropriate guide for the treatment of patients with proximal hamstring tendinopathy. Clinicians are urged to utilize clinical reasoning, best evidence, and patient values when individually evaluating and determining an appropriate rehabilitation program.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Depo Medroxyprogesterone: Effect on Weight in the Postpartum Period

#### OBJECTIVES/BACKGROUND:

Depot- medroxyprogesterone acetate is an effective hormonal contraceptive that may be administered during the postpartum hospital stay to ensure women have access to reliable contraception. Weight gain is known side effect of depot- medroxyprogesterone. Weight loss is particularly important in the postpartum period and there are no previous studies looking at the relationship of depot- medroxyprogesterone to weight during this time period.

#### METHODS:

A retrospective cohort study was performed at The George Washington University Hospital. All women who delivered between 2008 and 2010 and received depot-medroxyprogesterone prior to discharge were identified. An age, race and BMI matched control was identified for each patient. Chart review was performed to obtain information about pregnancy, delivery and weight at any clinic or hospital visit in the next 18 months.

#### RESULTS:

Charts were reviewed and data available for 156 patients (78 who received depo-medroxyprogesterone and 78 who did not). No statistically significant baseline differences between groups were observed. The mean age was 26 and the mean pre-pregnancy BMI was 27. Patients gained an average of 29 lbs during their pregnancy. We compared pre-pregnancy, delivery and 6 week postpartum BMI and found no differences between the group who received depot-medroxyprogesterone and those who did not.

#### CONCLUSIONS:

Depot-medroxyprogesterone remains an important option for postpartum contraception. This small retrospective study does not show a significant difference in BMI between those women who received depot-medroxyprogesterone immediately postpartum and those who did not use this as a contraceptive method.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Recognizing Factors Associated With Doubling in Creatinine from Baseline in Children Through Automated Adverse Event Detection

#### INTRODUCTION:

Automated adverse-event (AE) detection using triggers derived from the electronic health record (EHR) is an effective method of identifying adverse events, including rise in serum creatinine (Cr). However, the occurrence of adverse events related to increasing Cr in hospitalized children and the harm that results remain largely unknown.

#### HYPOTHESIS:

To describe the use of a trigger based detection system to identify a doubling of Cr, categorize adverse events associated with Cr doubling and describe factors associated with these events in hospitalized children.

#### METHODS:

A retrospective observational study of 100 consecutive Cr triggers to assess the incidence of adverse events at a large urban children's hospital. Trigger was defined as a Cr value of at least twice from inpatient admission baseline and  $\geq 0.6$  mg/dL. Patients on dialysis and having been on cardiopulmonary bypass within 72 hours were excluded. Clinical and demographic variables were analyzed to identify subpopulations at risk for rise in Cr. Each trigger was reviewed to determine if there was an AE, its preventability and the harm associated if there was an AE.

#### RESULTS:

73 triggers were categorized as AEs (positive predictive value 73%), which represented 2.61 AE/1000 patient days and 1.61 AE/100 admissions. No AEs were categorized as preventable. 39 events (53%) occurred in either the pediatric or cardiac intensive care units. 36 events (49%) occurred in patients receiving vancomycin, which was associated with an increased absolute Cr elevation from baseline as compared to patients not receiving vancomycin (1.1 mg/dL vs. 0.7 mg/dL,  $p=0.025$ ). No other differences in Cr elevation were observed based on patient factors (e.g. gender, history of kidney disease) or clinical factors (e.g. receipt of diuretics, non-steroidal anti-inflammatory agents).

#### CONCLUSIONS:

Rise in Cr is common in hospitalized children, especially critically ill children. An automated EHR derived trigger system was effective in identifying rise in Cr associated with vancomycin in this patient population. Cr doubling was not associated with preventable AEs in this limited sample.

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**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

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## Determinants of Breastfeeding in High-Risk Infants

**BACKGROUND:**

Breastfeeding is well established as the optimal nutrition for infants and is known to provide numerous health benefits for both the infant and mother. Breastfeeding is also highly recommended for high-risk infants. This population includes premature, low birth weight (LBW) or very low birth weight (VLBW) infants who are typically admitted to the neonatal intensive care unit (NICU) shortly after birth. The benefits of breast milk for NICU infants include a reduced risk of short and long-term morbidities in premature infants, including enteral feed intolerance, nosocomial infection, necrotizing enterocolitis, chronic lung disease, retinopathy of prematurity, developmental and neurocognitive delay and rehospitalization. Despite the short and long term benefits, the rates of breastfeeding are fairly low and even lower among high-risk infants. The Women, Infants and Children Program (WIC) is a program that serves low-income families and offers checks for healthy supplemental foods, nutrition and breastfeeding education and support and referrals to community resources. Since WIC sees over half of all infants born in the United States they can play a vital role in supporting breastfeeding among high-risk infants.

**OBJECTIVES:**

The objectives of this literature review are to identify factors that support breastfeeding from birth until after hospital discharge in high-risk infants. This paper examines four time points: initiation of breast milk expression, maintenance of breast milk supply, transition to breastfeeding directly and post discharge follow-up and support. The paper also discusses what WIC is doing and what they can improve to prevent poor pregnancy outcomes and support breastfeeding in high-risk infants and their mothers.

**METHODS:**

Articles were selected based on their relatedness to the topic of breastfeeding in high-risk infants. Priority was given to randomized control trials and research conducted among WIC participants.

**CONCLUSIONS:**

Multiple factors contribute to successful breastfeeding in high-risk infants. Breastfeeding promotion programs and lactation counseling influence both initiation and duration of breastfeeding in NICU infants. Peer counseling also has a significant influence on duration of breast milk expression. Furthermore, Kangaroo Mother Care was found to have a significant impact on both breastfeeding duration and successful transition from gavage to direct breastfeeding. Since WIC is primarily a prevention program, it can play a vital role in preventing high-risk infants by targeting women who are at risk of delivering a premature infant. NICUs should consider establishing a breastfeeding promotion program that includes factors positively associated with breastfeeding in high-risk infants.

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### Systematic Review of Umbilical Cord Clamping Practices Worldwide

#### BACKGROUND:

The third stage of labor refers to the period between delivery of the baby and complete expulsion of the placenta. Although there is no standard definition of early versus delayed umbilical cord clamping, recent randomized controlled trials demonstrate benefits for both term and preterm infants from delayed cord clamping. Even a brief delay in cord clamping results in placental transfusion, giving the term neonate approximately 30% more blood volume and the preterm as much as 50%, thereby substantially increasing iron stores within the first few months of life.

#### OBJECTIVES:

With regard to umbilical cord clamping, what are the known practices of maternity care providers? Our working definition of delayed cord clamping referred to waiting any amount of time to cut the umbilical cord, in that, it not being immediate.

#### METHODS:

A search was conducted to identify studies that included information on umbilical cord clamping practices among maternity care providers worldwide. The databases MEDLINE, Scopus and CINAHL were searched for English publications from 1990 to the present. Articles were included if they contained information on the timing of umbilical cord clamping. The search included data on both term and preterm infants and all types of maternity care providers (physicians, midwives, nurse-practitioners). Surveys and observational studies were acceptable; topical articles and professional guidelines were excluded. Data from the selected articles was extracted by one author using a standardized data extraction form and checked for accuracy by the senior author.

#### RESULTS:

Five of the 13 articles were focused on the topic of cord clamping whereas the remaining eight articles investigated cord clamping in the context of the management of the third stage of labor. The demographics of the studies varied greatly depending on the location and the nature of the research design. Collectively, our review reports on the practices of 1457 obstetricians, 2124 midwives and 181 other maternity care providers. One study reported on 1175 maternity units in 14 distinct European countries. Some studies also used direct observation of practice resulting in a total of 884 observed births.

#### CONCLUSIONS:

Delayed cord clamping is rarely practiced despite substantial current evidence in its favor. Many professional organizations even recommend delaying cord clamping as part of their guidelines for the active management of the third stage of labor. Therefore, a change in practice is called for.

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# WOMEN'S/CHILD HEALTH

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

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### Training in the Provision of Care to Survivors of Sexual Assault and Childhood Sexual Abuse: A Needs Assessment

#### BACKGROUND:

An estimated one in six women experience some form of sexual assault in their lifetime, while significant under-reporting suggests that this number may in fact be much higher. In conducting small focus groups with survivors of sexual assault, themes arose suggesting strained physician-patient relationships and dissatisfaction with their reproductive care, at times leading to delayed care or avoidance entirely. Despite the impact of sexual assault on the lives and health care of survivors, little research exists regarding the role of the obstetrics and gynecology (OB/GYN) physician in the survivor's recovery process. While the care of patients immediately following a sexual assault has been studied and discussed, there is dearth of data or guidelines on the long-term role of the provider in these women's ongoing reproductive health visits. We hypothesized that the negative experiences reported may be due to a deficit in the OB/GYN residency curriculum. Through a survey of all domestic OB/GYN residency directors, we hope to better understand the current state of OB/GYN training regarding reproductive care of survivors of sexual assault and childhood sexual abuse .

#### METHODS:

A master list of domestic OB/GYN residency programs was obtained from the website of the American College of Obstetricians and Gynecologists (ACOG). Individual program websites were used to obtain public email contact information OB/GYN Program Directors. If unavailable, residency or department coordinator email addresses were obtained. An online survey was emailed to 183 programs, along with two follow up emails over the course of one month. All results were recorded anonymously. Results are pending, but will be analyzed using online analytics along with SPSS.

#### RESULTS:

At the time of writing, the study is still in the data collection phase. The study participants included 183 U.S. OB/GYN program directors. At this time, 16 program directors have responded, of which 80% (n=12) are university-based programs and 20% (n=4) are community programs. Seventy-three percent (n=11) of responding programs train their residents to ask patients about their sexual assault history, while 26% (n=4) stated that they do not. In addition, 60% (n=9) of programs do not have a formal didactic focusing on reproductive care for survivors of sexual assault. Further analysis and discussion are anticipated once data collection is complete.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### A Comparative Study of the Standard Prenatal Care in Nicaragua to Standard United States Prenatal Care

#### ABSTRACT OBJECTIVE:

To determine the efficacy and cost effectiveness of the standard prenatal care offered in Nicaragua and the United States.

#### METHODS:

In a comparative study of standard prenatal care in Nicaragua with the prenatal care in the U.S., the number of appointments, the types of tests/screenings, the frequency of tests/screenings, and the maternal and neonatal mortality rates were compared. Data concerning prenatal care was collected from a U.S. obstetric gynecologist and a Nicaraguan government nurse and doctor in the respective countries. The mortality rates used were provided by The World Bank<sup>1,2</sup>.

#### RESULTS TO DATE:

Standard prenatal care in Nicaragua recommended fewer appointments for pregnant mothers than U.S. standard care. In March 2012, the Nicaraguan government implemented a reduction of the recommended appointments from nine to six, whereas in the U.S., standard care provides mothers with at least 11 visits. Additionally, due to the different living conditions, there are some differences in tests/screenings performed in each country, and overall, the U.S. performs more screenings on mothers. For example, in Nicaragua, it is standard to screen expectant mothers for *Toxoplasmosis* due to general inadequate sanitation. Furthermore, in the U.S., screenings for the mother and fetus for genetic diseases are available; however these resources are limited in Nicaragua, and not even available in Las Salinas.

#### CONCLUSIONS:

Many unaccounted factors have interfered with the ability to make concrete conclusions about the efficacy and cost effectiveness of standard prenatal care in Nicaragua and the U.S. relative to one another. For example, the data collection in Nicaragua was completed primarily in Las Salinas, a very small and rural town not representative of all of Nicaragua. The differences in access to healthcare were another important factor. First, unlike the United States, the healthcare provided at the Nicaraguan government health posts are covered by government subsidies. Theoretically, this allows all pregnant mothers prenatal care, regardless of family income. However, transportation to these government clinics is another issue. While there is a public transportation system in the bigger cities, many patients are hindered by the limited transportation options. Therefore, though the standard of care recommends 6 appointments, the significant inconvenience of getting to the clinic reduced the actual number of visits for many women. Furthermore, the clinic did not have a phone and many patients also did not have phones. If the patient needed to contact the doctor or the nurse, they needed to find them in person or have their personal cell phone numbers.

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## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Outcomes of embryo transfers following cryopreservation at the blastocyst stage using slow freeze or vitrification protocols

#### BACKGROUND:

When patients undergo in vitro fertilization (IVF), it is common to obtain more high quality embryos than are transferred in the fresh treatment cycle. Surplus embryos are typically "cryopreserved" (frozen) and stored for later use. Ensuring the most effective method of cryopreservation of surplus embryos in IVF has important consequences for patients, including the minimization of time investment, discomfort, risk, and expense of undergoing a new cycle of ovarian stimulation for fresh IVF. Shady Grove Fertility Center, a large fertility practice, transitioned from slow freeze cryopreservation to vitrification protocols to cryopreserve surplus embryos.

#### OBJECTIVES:

Given the suggestive but inconsistent evidence of the superiority of embryo vitrification over slow freezing in the medical literature, this study was designed to retrospectively compare the clinical outcomes before and after transitioning to the new protocols at Shady Grove Fertility Center.

#### METHODS:

Frozen embryo transfer (FET) cycles among patients who underwent IVF using their own eggs performed from January 2003 through April 2012 were retrospectively reviewed. The embryos were obtained beginning in January 2002 and were cryopreserved by slow freeze protocols until December 2008 and by vitrification beginning in January 2009 at the blastocyst stage. Primary outcomes included clinical pregnancy and live birth rates. Secondary outcomes included the proportion of embryos that survived the freezing and thawing procedures, the percentage of intact cells in surviving embryos, biochemical pregnancy and implantation rates. Comparisons were done using  $X^2$  or t-test as appropriate.

#### RESULTS:

A total of 4,596 FET cycles, in which 7,599 embryos were transferred, was available for analysis. Of these 2841 used embryos frozen using slow freeze cryopreservation protocols and 1755 by vitrification. Vitrification yielded superior outcomes including embryo survival rates (92% vs. 96%,  $P < .0001$ ), intact cells (89% vs. 95%,  $P < .0001$ ), clinical pregnancy (35% vs. 58%,  $P < .0001$ ), implantation rate per embryo transferred (25% vs. 47%,  $P < .0001$ ), and live birth rate (25% vs. 44%,  $P < .0001$ ), as well as lower rates of biochemical pregnancies (24% vs. 16%,  $P < .0001$ ).

#### CONCLUSIONS:

Given that this is the largest study worldwide comparing vitrification to slow freeze cryopreservation embryos, there is substantial evidence to support the superiority of vitrification over slow freeze technology. All treatment outcomes were consistently and substantially better for vitrification compared to slow freeze embryos. The transition in protocols implemented at Shady Grove Fertility Center and other fertility centers around the world thus has important beneficial clinical consequences for patients in terms of treatment outcomes, risk factors, time investment, and cost.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Nutrition intake in youths with type I diabetes

#### BACKGROUND:

For youth with type 1 diabetes (T1D), adolescence is characterized by a period of poor adherence. One reason for poor adherence may be because during this time, youth are establishing their independence, including their nutritional choices<sup>1</sup>. High quality nutrition is strongly recommended to improve health (e.g., lower LDL plasma levels), and offset risk factors for cardiovascular (CV) disease in individuals with diabetes<sup>2</sup>.

#### OBJECTIVE:

To evaluate the rates of adherence to nutritional guidelines in young adolescents with T1D and the association of nutritional quality with HbA1c.

#### METHOD:

Baseline data from a randomized controlled trial (RCT) of an intervention designed to prevent deterioration of glycemic control in young adolescents with T1D were evaluated. Adolescent-parent dyads (n=257, youth mean age = 12 years, SD = 1.2 years, 49.4% female, mean HbA1c = 8.8, SD = 1.6) reported dietary intake via two 24-hour recall interviews as a component of their diabetes self-care. Dietary intake was scored using the The Food Processor® Nutrition Analysis Software (ESHA Research, Salem, OR, USA). Demographic variables and hemoglobin A1c were abstracted from questionnaires and medical charts.

#### RESULTS:

When compared to recommendations (ADA and ISPAD), many youths were not meeting nutritional guidelines. This included percent daily intake of protein, carbohydrates, fat, saturated fat, cholesterol and dietary fiber<sup>3</sup>. Further, 50.2% of youth reported LDL cholesterol levels greater than recommended guidelines for primary prevention of CV disease in youths with T1D. Significant positive correlations were found between HbA1c and percent of total calories from fat ( $r = .24, p < 0.01$ ), polyunsaturated fat ( $r = .16, p < 0.05$ ), dietary cholesterol ( $r = .20, p < 0.01$ ), and LDL ( $r = .24, p < .01$ ). Significant negative correlations were identified between HbA1c and percent of total calories from carbohydrates ( $r = -.23, p < 0.01$ ) and dietary fiber ( $r = -.13, p < 0.05$ ).

#### CONCLUSION:

The majority of early adolescents with T1D did not meet nutrition guidelines. This may place them at increased risk for CV diabetes-related complications. Further, their reported nutrition was associated with HbA1c, suggesting an immediate relationship with glycemic control. Diabetes education efforts regarding healthy eating and dietary management may need to be enhanced to achieve recommendations.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF MEDICINE AND HEALTH SCIENCES

### Survey of Knowledge, Attitudes and Practices of DC ACOG Members Related to Breastfeeding

#### BACKGROUND:

Although the American Academy of Pediatrics and the American Congress of Obstetricians and Gynecologists (ACOG) strongly recommend exclusive breastfeeding for the first 6 months, only 17.1% of babies born in the District of Columbia reached this goal. Physician counseling can increase breastfeeding initiation and duration rates. However, research shows obstetric practices are often inconsistent with promoting breastfeeding.

One method shown to increase exclusive breastfeeding is to improve prenatal and intrapartum breastfeeding education and support. Accordingly, in 2010 The Joint Commission introduced an evidence-based Perinatal Care (PC) measure set that includes rates of exclusive breast milk feeding during the birth hospital stay. It is unclear if obstetricians are aware about this core measure or aware if their primary hospital has adopted it.

#### PURPOSE:

- 1: Describe the attitudes and knowledge about breastfeeding among DC ACOG members.
- 2: Determine the proportion of DC ACOG members who include breastfeeding in routine prenatal discussions.
- 3: Determine the proportion of DC ACOG members who know if their hospital adopted the Perinatal Care Core Measure set.

#### METHODS:

After obtaining IRB approval from Children's National Medical Center, a survey modified from *Attitudes and Knowledge of Pediatricians in Training* was sent electronically to the members of the DC Section of ACOG. The voluntary survey assessed participants' knowledge, attitudes and practices related to breastfeeding. It also evaluated participants' barriers to breastfeeding counseling, management of breastfeeding challenges and awareness of their hospitals adoption of the PC measure set.

#### RESULTS:

Twenty-nine of eighty-six (34%) of practicing obstetricians participated. All felt that breastfeeding was better for infants than formula. Forty-eight percent of respondents correctly identified that frequent breastfeeding can help reduce newborn jaundice.

All participants indicated that physicians should strongly encourage breastfeeding with 96% stating that obstetricians should provide breastfeeding counseling. However, only 75% reported counseling most of their patients regarding breastfeeding and 27% reported that most of their patients were breastfeeding at the 6 week postpartum visit.

Perceived barriers to breastfeeding counseling include lack of time (66%), lack of reimbursement (10%), and lack of competence in managing breastfeeding problems (7%).

Fifty-two percent were unsure if their hospital had adopted the PC measure set and 55% were unsure if their hospital was collecting data about exclusive breastfeeding.

#### CONCLUSION:

While participating obstetricians were aware that breastfeeding is the best infant nutrition, they had knowledge gaps and identified barriers to their counseling the breastfeeding dyad. There was limited awareness of hospital data collection about exclusive breast milk feeding among participants. These results indicate that there is a need for more breastfeeding education among DC obstetricians and better outreach to staff obstetricians about the PC measure set.

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# WOMEN'S/CHILD HEALTH



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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Factors associated with early sexual debut among Ghanaian women from the Manya - Krobo district, - Ghana, 2011

#### BACKGROUND:

The dipo, a Krobo puberty initiation rite practiced annually among an estimated 2,000 Ghanaian females ages 2 - 20, is a cultural rite of passage into womanhood that is intended to promote abstinence from sexual activity until marriage.

#### OBJECTIVES:

This study examined the risk of early sexual debut among dipo-initiated Krobo females versus uninitiated Krobo females. This study also assessed Manya - Krobo societal opinions regarding the sexual health outcomes of initiates and existing modifications of the rite.

#### METHODS:

**MIXED-METHODS.** Utilizing a retrospective cohort study design, we surveyed 306 unwed Krobo females from Agormanya ages 13 - 20. We employed Cox proportional hazard regressions assessing the effects of model covariates upon sexual debut and age at sexual debut. Qualitative analysis included nine interviews conducted among Manya-Krobo district community members who either supported or opposed the dipo. Responses were analyzed using Dedoose QDA software to determine patterns in attitudes and opinions regarding initiates' sexual behaviors and to identify current ceremonial changes.

#### RESULTS:

Dipo initiated participants had a 1.8 increased hazard rate of early sexual debut as compared to uninitiated participants after adjusting for covariates, however, results were not statistically significant (aHR: 1.8, 95% C.I: 0.8 - 4.0). Qualitative data indicated that some dipo opponents stated participation promotes promiscuity and teen pregnancy while select supporters asserted the rite protects participants from these outcomes. Key ceremonial changes included a reduction in age eligibility and length of dipo preparatory period.

#### CONCLUSIONS:

These study findings do not offer conclusive evidence that participation in the dipo increases the risk of early sexual debut among initiated versus uninitiated Krobo females. Study findings suggest the reduction in age of dipo eligibility may increase the likelihood of sexual debut following the ceremony. Participants who received the rite as toddlers had a greater length of time between the dipo and adulthood to become sexually active post-initiation than females who were initiated during their late teens/early twenties.

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# WOMEN'S/CHILD HEALTH

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## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

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### Utilization of Online Resources for Sexual Health: A Comparison of Men and Women

#### BACKGROUND:

In order for the efforts of the public health community to be successful, it is critical for the public to improve their understanding of their health and make informed health decisions. It is imperative to increase the utilization of reputable online resources for sexual health information among adults age 22 to 35 years of age. The Internet is a widely used venue for accessing sexual health information, yet we do not know how this population uses the Internet to access sexual health resources.

#### OBJECTIVES:

The objective of the project is to determine how adults ages 22-35 perceive and use internet based resources for health in general and sexual health specifically.

#### METHODS:

Four focus groups, a web site usability tool, and data from a Wordpress hosted blog acted as a means of data collection for this study. Two focus groups consisted of females (n = 14) and two focus groups consisted of males (n = 12) between the ages of 22 and 35. For the website usability exercise, participants (n = 33) were asked to respond to sexual health scenarios using specific websites. Results from the usability surveys were compared by participant demographics (age, race, gender, and educational level) using IBM® SPSS® Statistics Version 20.

#### RESULTS:

Both men and women indicated they are likely to turn to the Internet for health related concerns. Men indicated using the Internet for nutrition and fitness information, while women did not specify any health topic in particular. Men were considerably more likely to read blogs compared to female participants; women were concerned with derogatory or untrue comments, lack of confidentiality and lack of credentialed information on blogs.

#### CONCLUSIONS:

As a result of the popularity of mobile devices, health information websites need to ensure their websites are easily accessible on mobile devices. Government domains (.gov) need an online presence that contains scientific data presented at a lower reading level. Incorporating symptom checkers specific to sexual health, or online games related to sexual health, will encourage men to engage in online health media. Finally, in order to address women's concerns with their fertility, websites must tailor their message towards reproductive choice and preventing pregnancy *right now*.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### Is the Length of Hospital Stay in Late Preterm Infants Predictable? A Study of the Nationwide Inpatient Sample (NIS) Database

#### BACKGROUND:

Late preterm infants are the fastest growing segment of the premature infant population in the U.S. However, it is not known if demographic and clinical factors can impact the length of hospital stay (LOS) in this population.

#### OBJECTIVE:

To determine a) factors associated with a LOS >3 days among late preterm infants and b) whether there is any difference in risks between infants born at 33-34 vs. 35-36 weeks.

#### METHODS:

Utilizing the HCUP NIS Database, a retrospective analysis of 81,913 infants born at 33-36 weeks from 2007-2008 was conducted. LOS outcome was defined as  $\leq 3$  and  $> 3$  days. Bivariable and multivariable logistic regression was used to evaluate predictors of LOS among this population.

#### RESULTS:

Only 42.7% of infants were discharged home within 3 days. Factors associated with a LOS >3 days included gestational age of <35 weeks (RR=1.63; CI 1.58-1.68), birth weight of <2,500g (RR=1.36; CI 1.33-1.39), male sex (RR=1.06; CI 1.05-1.07), delivery via C-section (RR=1.46; CI 1.41-1.51), and multiple gestation (RR=1.08; 95% CI 1.06-1.09). Other significant factors included race, birth region, primary insurance payer, and clinical complications. In the adjusted interaction model, infants born at 35-36 weeks had a higher risk of a longer LOS for birth weight and clinical factors ( $p < .0001$ ).

#### CONCLUSION:

Several demographic and clinical factors were associated with longer LOS. The older infant age group may be at increased risk of a longer LOS compared to the younger age group. This study brings to attention the associated factors of increased LOS in this population.

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# WOMEN'S/CHILD HEALTH



## SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

### The Characteristics of Women Seeking Funding from The DC Abortion Fund

#### BACKGROUND:

At least half of American women will experience an unintended pregnancy by age 45, and, at current rates, one in 10 women will have an abortion by age 20, one in four by age 30 and three in 10 by age 45.<sup>5i</sup> The DC Abortion Fund (DCAF) is an all-volunteer, non-profit organization that makes grants to women and girls in DC, Maryland and Virginia who cannot afford the full cost of an abortion. Studies have illustrated that children born as the result of an unplanned pregnancy are at greater risk of low birth weight and pre-term birth, both of which increase the likelihood of infant mortality; mothers and fathers are at greater risk to suffer from depression and relationship conflict; and children have lower cognitive scores in early childhood.<sup>5</sup> There is research available regarding abortion providers, but very little about abortion patients. Therefore the aim of this study is to add to the limited body of knowledge regarding this population and better inform DCAF's leadership in how to improve program outreach and programs.

#### METHODS:

An adapted version of The Guttmacher Institute's National Patient Survey will be used to collect data from women who contact DCAF for financial assistance for their abortion (n=120). The data will be collected for one month and then analyzed in SPSS.

#### RESULTS:

As of date, no results are found because data collection will be on-going until end of February 2013.

#### CONCLUSIONS:

If DCAF could rely on research already conducted regarding the population and specifically, the mid-Atlantic region, they could utilize that information as a justification for program expansion, but there is a gap in abortion research and inconsistency in DCAF client data collection by case managers.

#### KEYWORDS:

Induced abortion; Pregnancy termination; Second-trimester abortions; United States; Abortion Funding

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