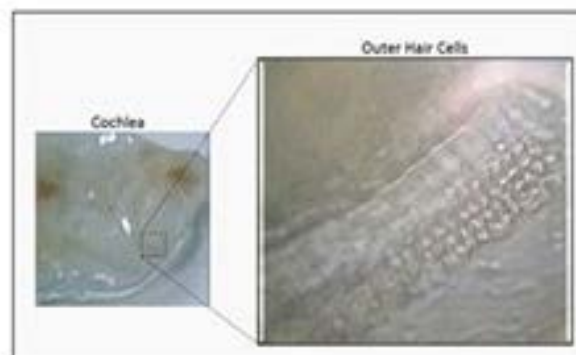
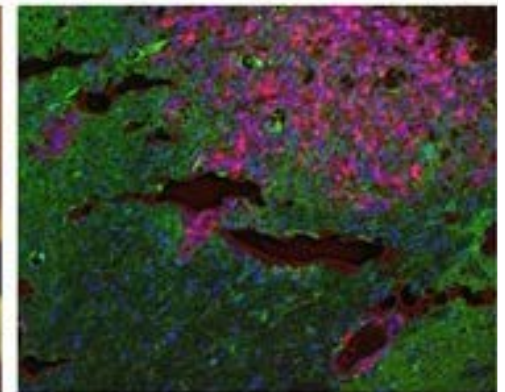
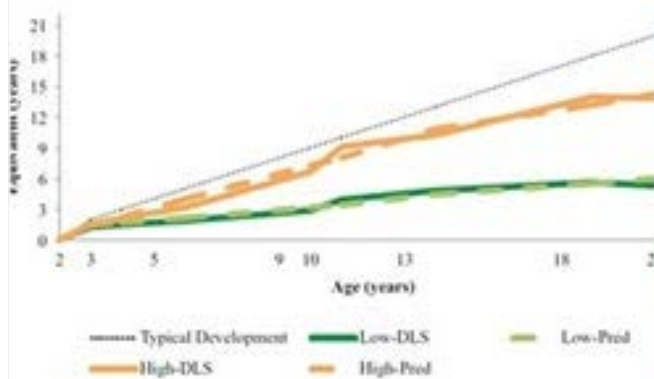
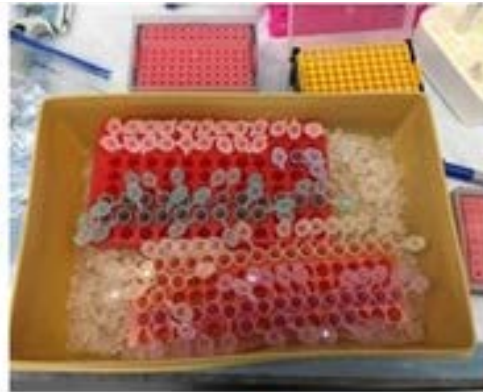
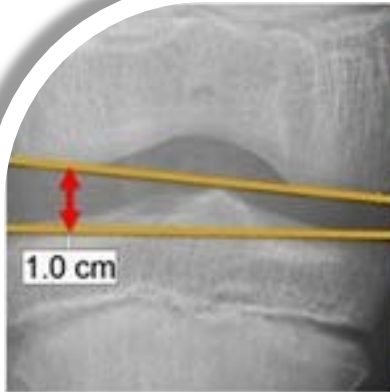


Medical and Dental STUDENT RESEARCH DAY

March 7, 2016



Support provided by the Irwin H. and Martha L. Lepow Visiting Professorship Fund and the Scholarship Linked to Discovery Fund

SCHEDULE OF EVENTS

March 7, 2016

POSTER SESSION

11AM-12:30PM | Keller Lobby

ORAL PRESENTATIONS

12:30-5PM | Keller Auditorium

KEYNOTE SPEAKER

5PM | Keller Auditorium

"Tuning Biomaterial Properties to Enhance Pluripotent Stem Cell Self Renewal"



Paul H. Krebsbach, D.D.S., Ph.D.

Roy H. Roberts Professor of Dentistry and Professor of
Biomedical Engineering, University of Michigan

ORAL PRESENTATIONS

Session 1 – School of Medicine

Introduction: Bruce T. Liang, M.D., F.A.C.C., Dean, School of Medicine

- 12:45 – 1:00 **Julia Koretski** (Mentor: Dr. Kevin Dieckhaus)
“Healthcare Workers’ Self-reported Knowledge, Attitudes, and Practice Implications Regarding Mental Health Care in Rural Uganda”
- 1:00 – 1:15 **Syed Alam** (Mentors: Drs. Dharamainder Choudhary and John Taylor)
“Potential Role of G1P3 in Development of Chemoresistance in High Grade Bladder Cancer”
- 1:15 – 1:30 **Cassandra Trammel** (Mentor: Dr. John Taylor)
“Enhanced Chemosensitivity of Urothelial Bladder Carcinoma Cells to a Combination of Cisplatin and Dichloroacetate (DCA), a PDK4 Inhibitor”
- 1:30 – 1:45 **Whitney Washburn** (Mentor: Dr. Cathy Wiley)
“Improving Vision Screening Rates of 3-year-olds in a Primary Care Clinic”
- 1:45 – 2:00 Poster Review and Break – Keller Lobby

Session 2 – School of Dental Medicine

- Introduction: Rajesh V. Lalla, D.D.S., Ph.D., C.C.R.P., D.A.B.O.M., Interim Associate Dean for Research, School of Dental Medicine
- 2:00 – 2:15 **Lauren Dulieu** (Mentor: Dr. Marion Frank and Dr. Thomas Hettinger)
“Discovering Component Qualities of Single Stimuli Mixtures Having Double Odors”
- 2:15 – 2:30 **Leila Fussell** (Mentor: Dr. Effie Ioannidou)
“A 10-year Bibliometric Analysis of Authorship Gender in Periodontal Literature”
- 2:30 – 2:45 **Owen Insel** (Mentor: Dr. Aditya Tadinada)
“CBCT Demonstrates Increased Bone Density in Osteoporotic Patients on Oral-Anti-Resorptives”
- 2:45 – 3:00 **Nicholas Camic** (Mentor: Dr. Aditya Tadinada)
“Using Motion-Sensing Technology as a Touchless Interface for Accessing Patient Records and Radiographs During Endodontic Procedures”
- 3:00 – 3:15 **Michelle Llinas** (Mentor: Dr. Caroline Dealy)
“Chondrocyte Progenitor Cells in Osteoarthritis”
- 3:15 – 3:30 **Steven Halepas** (Mentor: Dr. Frank Nichols) “PLA2 Hydrolysis of *P. gingivalis* Lipid 654 is Enantioselective”

3:30 – 3:45 Poster Review and Break – Keller Lobby

Session 3 – School of Medicine

- 3:45 -4:00 **Michael Lorinsky** (Mentor: Dr. Betty Eipper)
“Investigation of the Structural Interactions of the Spectrin and GEF Domains of Kalirin-7 via FRET Assay”
- 4:00 – 4:15 **Jelena MacLeod** (Mentor: Dr. Eli Lebowitz)
“Maternal Perception of Child Anxiety Symptoms: The Role of Prolactin”
- 4:15 – 4:30 **Benjamin Liba** (Mentor: Dr. Kourosh Parham)
“Serum Levels of Prestin in Response to Cisplatin Induced Ototoxicity as an Early Indicator of Acquired Sensorineural Hearing Loss”
- 4:30 – 4:45 **Andrew Duarte** (Mentor: Dr. Matthew Mileski)
“Do Weight Bearing Films Aid in Radiographic Analysis for the Presence of Discoid Lateral Meniscus in an Adolescent Knee”
- 5:00 **Introduction of Keynote Speaker**
R. Lamont MacNeil, D.D.S., M.Dent.Sc.
Dean, School of Dental Medicine
- 5:00-6:00 **Keynote Address**
“Tuning Biomaterial Properties to Enhance Pluripotent Stem Cell Self Renewal”
Paul H. Krebsbach, D.D.S., Ph.D.
Roy H. Roberts Professor of Dentistry and Professor of Biomedical Engineering
University of Michigan

POSTER PRESENTATIONS

Dental Student Poster Presentations

Student: Faith Adewusi
Title: Aquaporin-5-Cre-mediated targeted expression of TNF- α results in an Inflammatory Disorder of the Salivary glands
Mentor: Dr. Ashok Kulkarni, NIDCR

Student: Lena Cantone
Title: Salivary Urea and Periodontal Microbiome in End Stage Renal Disease
Mentor: Drs. Effie Ioannidou and Patricia Diaz

Student: Paul Dyrkacz
Title: Expression of BSP-GFPtpz Transgene during Dentinogenesis and Osteogenesis
Mentor: Dr. Mina Mina

Student: Andrew Emery
Title: Protein O-glycosylation in Secretory Granule Structure
Mentor: Dr. Kelly Ten Hagen, NIDCR

Student: Bradford Ganz
Title: Hamster Taste Preference for Salicin vs. Water or Saccharin
Mentor: Dr. Marion Frank

Student: Xiaoxiao Hong
Title: Identifying Anabolic and Catabolic Growth Factor Signals in Osteoarthritis
Mentor: Dr. Caroline Dealy

Student: Johnny Joseph
Title: Nuclear isoforms of fibroblast growth factor 2 and dentin mineralization
Mentors: Drs. Marja Hurley and Mina Mina

Student: Julia Karpman
Title: Effects of Peridex (Chlorhexidine) on Anterior-Tongue Salt Taste
Mentor: Dr. Marion Frank

Student: Daniel Lee
Title: The Effect of Varying Intensities of LIPUS (Low Intensity Pulsed Ultrasound) on the Rate of Orthodontic Tooth Movement and Osteoclastic Activity in Mice
Mentor: Dr. Sumit Yadav

Student: Jia Liu
Title: Secretome of Resolvin E1-activated Osteoblasts
Mentors: Drs. David Shafer (and Thomas Van Dyke, Forsyth Institute)

Student: Raquel Manley
 Title: Barriers to Oral Health Care in Select Federally Qualified Health Centers in Connecticut: A Comparison of Rural vs. Urban Locations
 Mentor: Geralynn McGee, Hartford Legal Aide and the Community Health Center Association of Connecticut

Student: Alana Marczak
 Title: Lower-Dose 180° CBCT Offers Comparable Information for Mini-Implant Placement when Contrasted to Conventional 360° Protocol
 Mentors: Drs. Aditya Tadinada and Sumit Yadav

Student: John Power
 Title: New enzymatic disruption protocol to quantify in vitro Candida albicans biofilm invasion
 Mentor: Dr. Anna Dongari-Batzoglou

Student: Emily Sachs
 Title: Gender variation in palatal bone thickness for mini-implant placement
 Mentor: Dr. Sumit Yadav

Student: Sydney Schneider
 Title: Evaluation of the Diagnostic Efficacy of Two CBCT Protocols in Reliably Detecting the Location of the Inferior Alveolar Nerve Canal
 Mentors: Drs. Aditya Tadinada and Sumit Yadav

Medical Student Poster Presentations

Student: Olajide Abiola
 Title: Sciatic Nerve Regeneration using a Biodegradable, Ionically Conducting Polymer
 Mentor: Dr. Sangamesh Kumbar

Student: James Aglio
 Title: Breast Patient Database
 Mentor: Dr. Susan Tannenbaum

Student: Kevin Braghirol
 Title: An Evaluation of Bleeding Events in Therapeutic Hypothermia Patients on Common Anticoagulant Therapies
 Mentor: Dr. Justin Lundbye

Student: Daniel Cheong
 Title: Daily Living Skills in Individuals with Autism Spectrum Disorder from 2 to 21 Years of Age
 Mentor: Dr. Catherine Lord

Student: Evins Clauther
 Title: Comparison of Blood Pressure and Cardiac Activity on Post Stroke Severity and Mortality between Young and Aged Mice
 Mentor: Dr. Louise McCullough

Student: Eileen Colliton
 Title: Relationship between Shoulder Pain and Non-Traumatic Multidirectional Instability in Competitive Swimmers
 Mentor: Dr. Carl Nissen

Student: Alexis Cordone
 Title: The Effectiveness of Therapeutic Hypothermia in Preventing Reperfusion Injury for Patients Who Were Resuscitated within Five Minutes of the Onset of Cardiac Arrest
 Mentor: Dr. Justin Lundbye

Student: Brooke Cunningham
 Title: Effect of Estrogen Replacement Therapy on Cognitive Function in Oligo-amenorrheic Athletes
 Mentor: Dr. Madhusmita Misra

Student: Matthew Eremita
 Title: Can We Identify Parents Who Will Not Voice Concerns For Their Child's Development?
 Mentor: Dr. Paul Dworkin

Student: Mario Felix
 Title: Maternal Exposure to Childhood Victimization and Prenatal Risk: Empirical Study and Systematic Review
 Mentor: Dr. Damion Grasso

Student: Nora Gibson
 Title: Osteopontin – A Potential Marker for Chemotherapy Resistance in Bladder Cancer
 Mentor: Drs. Dharamainder Choudhary, John Taylor

Student: Andrew Glick
 Title: Impact of A Decade of Advances in Pediatric Burns Care
 Mentor: Dr. Kevin Dieckhaus

Student: Sarah Grout
 Title: Knowledge, Attitudes, and Barriers towards Breast Cancer Screening Among Latinas and Health Care Providers in Hartford, CT
 Mentor: Dr. Amy Johnson

Student: Alexander Hoberman
 Title: Platelet-Rich-Plasma Enhances Mesenchymal Stem Cell Differentiation on Matrix Specific Constructs
 Mentor: Dr. Augustus Mazzocca

Student: Casey Jarvis
Title: Comparative Evaluation of Complication Rates Between Iliac and S2-alar Screw Fixation
Mentor: Drs. Matthew Solomito, Mark Lee

Student: Erin Kalla
Title: Antipsychotic Medication Use in Difficult-to-Place Patients before and after Transfer to a Specialized Skilled Nursing Facility
Mentor: Dr. Lisa Barry

Student: Christina Klecker
Title: Cell Adhesive Hydrogels for Bone Regeneration
Mentor: Dr. Lakshmi Nair

Student: Ling Lei
Title: Rapid and Effective Revitalization of Bone Allografts
Mentor: Dr. Syam P. Nukavarapu

Student: Jonathan Lis
Title: Assessing Factors Influencing Childhood Nutrition in Haiti
Mentor: Dr. Judy Lewis

Student: Robin Lo
Title: Albuminuria Leads to Proximal Tubule Damage through a CD13-dependent Mechanism
Mentor: Dr. Linda Shapiro

Student: Jessica Malcolm
Title: Chikungunya in Jamaica
Mentor: Dr. Kevin Dieckhaus

Student: Kaitlin Markoja
Title: Understanding Predictors of Home Birth in Kisoro, Uganda
Mentor: Dr. Kevin Dieckhaus

Student: Granger Marsden
Title: Predictive Modeling in Cancer Survivorship
Mentor: Dr. Cheryl Oncken

Student: Sarah Mattessich
Title: Design and Assessment of a Novel Database for Dermatological Images
Mentor: Dr. Justin Finch

Student: Michael Mei
Title: Characterizing the Differences in Inflammatory Processes between a Diabetic and Non-diabetic Rat Model of Posterior Glottic Stenosis
Mentor: Dr. Denis Lafreniere

Student:	Theresa Meotti
Title:	Barriers to Early Initiation of Breastfeeding in Rural India
Mentor:	Dr. Kevin Dieckhaus
Student:	Elise Mester
Title:	Determining the Effects of Silencing Prolyl Hydroxylase-1 (PHD-1) on Neovascularization and Ventricular Remodeling in the Infarcted Myocardium
Mentor:	Dr. Nilanjana Maulik
Student:	Alexandria Meyers
Title:	Gold Nanoparticle Distributions in Rat Brains/Tumors after IV and Direct Injections
Mentor:	Dr. Henry Smilowitz
Student:	Hetal Mistry
Title:	Orosomucoid-1 Protein Dynamics Following Ischemic Stroke in Humans and Mice
Mentor:	Dr. Louise McCullough
Student:	Emma Polidoro
Title:	The Effect of CPOE on CDI Guideline Treatment Adherence and Clinical Outcomes
Mentor:	Dr. Jeff Aeschlimann
Student:	Paul Sackstein
Title:	Peripheral and Central Nervous System Degeneration in Patients with Xeroderma Pigmentosum
Mentor:	Dr. Kenneth Kraemer
Student:	Veronica Schmidt
Title:	Predictors of Weight Status and Nutrition in Puerto Rican Children
Mentor:	Dr. Kevin Dieckhaus
Student:	Ayibatari Sikpi
Title:	Steps in Development of an Innovative Mouse Model for Cisplatin-Induced Chronic Kidney Disease
Mentor:	Dr. Gary Desir
Student:	Ye Sun
Title:	Systemic Inflammation Reverses Stroke-induced Changes in Astrocytic Aquaporin-4 Expression
Mentor:	Dr. Louise McCullough
Student:	Patrick Svrcek
Title:	Quantitative NMR for Evaluation of Metabolic Changes in EMT-induced Epithelial Breast Cancer Cell Lines
Mentor:	Dr. Jeffrey Hoch

Student: Franklin Sylvester
Title: The Relationship between Maternal and Child Psychosocial Stress and a Novel Biomarker of the Stress Response
Mentor: Dr. Jessica Hollenbach

Student: Michael Tassavor
Title: Primary Pectorals Major Repair Configurations: How to Optimize the Repair Biomechanics
Mentor: Dr. Augustus Mazzocca

Student: Ashley Wenger
Title: The Effect of Neuropeptide Substance P Interaction with Neurokinin-1 Receptor in Rhesus Monkeys following Pathogen Exposure
Mentor: Dr. Ian Marriott

Student: Meghan Wilson
Title: A Cross-sectional Study of Helmet Usage Behavior among Motorcyclists in Connecticut
Mentor: Dr. Garry Lapidus

Student: Karen Xiao
Title: Propensity Analysis of Mortality One Year after Acute Myocardial Infarction
Mentor: Dr. Garth Graham

Sciatic Nerve Regeneration using a Biodegradable, Ionically Conducting Polymer

Olajide Abiola¹, Matthew Anderson^{1,2,3}, Sangamesh G. Kumbar Ph.D.^{2,3}, Namdev Shelke Ph.D.^{2,3}

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Institute of Regenerative Engineering, UConn Health, Farmington, CT*

³*Department of Orthopedic Surgery, UConn Health, Farmington, CT*

Traumatic peripheral nerve injury affects twenty million Americans a year and costs the US health system \$150 billion dollars annually [1, 2]. When end-to-end anastomosis cannot adequately repair the injury, the gold standard surgical intervention of these defects utilizes autograft/allograft nerve graft transplantation therapy [3]. Clinically, these methods have their disadvantages, including neuroma formation [4], toxicity of immunosuppression for allograft acceptance [5], and donor site morbidity. Bioengineered nerve growth conduits have been developed to overcome these disadvantages; however, they have not provided the same results as autografts and allografts [4]. It is believed that these scaffolds failed because of the adverse biostability and biocompatibility changes that accompany many dopant oxidized electroconductive polymers upon graft and host assimilation [5]. Therefore, conjugated polymers with electrically conducting ionic side chains are a hopeful alternative [5].

The study focused on the creation of an electrically conductive, biodegradable nerve growth conduit using lignin sulfate. Thus, it was hypothesized that electrical stimulation of cells through a scaffold that incorporated lignin sulfate would facilitate better regeneration efforts compared to previously used electrically conductive polymers. Scaffolds were comprised of either Polycaprolactone (PCL) or Poly (D, L-lactide-co-glycolide) (PLGA) with Cellulose Acetate. Two thin film biodegradable polymers were synthesized using phase separation techniques at room temperature from a mixture containing 85% of either PCL or PLGA, 15% CA, with mass fractions of 0%, 20% or 40% lignin. The resulting scaffolds were characterized in vitro for biocompatibility with PC12 cells derived from proliferating rat pheochromocytoma cells which differentiate into neurons upon nerve growth factor stimulation. We hypothesized that both 40% lignin in PLGA and PCL would facilitate the greatest amounts of cellular growth because these scaffolds had the greatest electrical conductivity. Results indicated that the PCL with 40% lignin scaffolds showed greater durability and flexibility both before and after cell studies. PCL scaffolds promoted greater PC12 cell proliferation than PLGA when combined with 15% CA and 40% Lignin sulfate. In conclusion, the results demonstrated 85%PCL/15% CA scaffold has the potential to be an effective alternative to autograft for peripheral nerve damage. Further in vitro and in vivo studies need to be conducted to assess its nerve regeneration capabilities.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. G. Lundborg, Nerve injury and repair—a challenge to the plastic brain, *Journal of the Peripheral Nervous System* 2003; 8(4): 209–226.
2. C. A. Taylor, D. Braza, J. B. Rice, T. Dillingham, “The incidence of peripheral nerve injury in extremity trauma,” *The American Journal of Physical Medicine and Rehabilitation* 2008; 87(5): 381–385.
3. Scherman P, Kanje M, Dahlin LB. Bridging short nerve defects by direct repair under tension, nerve grafts or longitudinal sutures. *Restore Neurol Neurosci.* 2004; 22: 65–72.
4. Schmidt CE, Leach JB. Neural tissue engineering: strategies for repair and regeneration. *Annual review of biomedical engineering.* 2003; 5(1):293-347.
5. Kumbar, Sangamesh, et al. "Peripheral Nerve Regeneration Strategies: Electrically Stimulating Polymer Based Nerve Growth Conduits." *Critical Reviews™ in Biomedical Engineering.*

Faith Adewusi

Principal Investigator: Ashok Kulkarni, PhD.

Mentor: Advait Limaye

Project Title: **Aquaporin-5-Cre-mediated targeted expression of TNF- α results in an Inflammatory Disorder of the Salivary glands**

Lab: Functional Genomic Section and Gene Targeting Facility

Laboratory of Cell and Developmental Biology, NIDCR, NIH Bethesda, Maryland

Abstract

Objective: To study the mechanisms of salivary gland inflammation.

Background: In pathological salivary gland disorders such as the autoimmune disease Sjögren's syndrome and sialadenitis, inflammation is seen within the glandular epithelium, which affects the salivary gland acini and ducts. Tumor Necrosis Factor- α (TNF- α) is a major cytokine upregulated early during inflammation of the salivary glands. Acinar cells employ aquaporins, a family of protein water channels to transport water and small molecules to cross the apical membrane. Aquaporin-5 (AQP5), in particular, is responsible for water transport in the salivary gland and its localization to the apical membrane can be affected by inflammation.

Methods: To study the mechanisms of salivary gland inflammation, we created an AQP5 Cre transgenic line, where the AQP5 promoter is used to drive expression of Cre primarily within the salivary gland. The AQP5 Cre mice allow for conditional deletion or overexpression of genes involved in the inflammatory process in order to examine their effect on the salivary gland architecture. Although AQP5 is found in organs other than the salivary glands, our double fluorescent studies showed a robust Cre-driven expression in the secretory cells of lacrimal and salivary glands. The resulting AQP5 Cre mice were bred to another mouse line that requires Cre-mediated recombination of the transgene to promote conditional overexpression of TNF- α .

Results: The resulting double transgenic mice have overexpression of TNF- α localized to the salivary gland epithelium as seen by immunohistochemistry. In addition, increased amount of macrophages and inflammatory infiltrates were seen in the salivary gland epithelium as a result of the TNF- α expression. These results revealed that TNF- α is expressed in the salivary glands in the double transgenic mice, which, in turn causes recruitment of macrophages to the glandular epithelium.

Conclusion: The inflammation seen in these mice mimics the inflammatory process that occurs in Sjögren's syndrome and sialadenitis.

Future Directions: In continuing this project, immunohistochemistry staining for macrophage identification in the salivary gland will be performed, and an ELISA will be performed to detect other cytokines (in addition to TNF- α) that may be up-regulated during an inflammatory response. Furthermore, a peripheral blood smear and white blood cell differential for wild type mice will be compared to that of AQP5-Cre positive mice as well as saliva collection to investigate potential for dry mouth in wild type and affected mice.

Support: NIDCR Summer Dental Student Award and UConn School of Dental Medicine.

Breast Patient Database

James Aglio¹, Susan Tannenbaum, MD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Associate Professor, University of Connecticut School of Medicine, Neag Cancer Center, UConn Health, Farmington, CT*

Patient registries are created as a means to retrieve data that will aid in patient care. Additionally, they can be used for research purposes and possible quality improvement measures. Breast cancer patients are at risk of recurrent disease as well as new cancers. These patients are therefore followed for many years beyond their initial diagnosis. New data is constantly emerging on topics such as best therapy methods based on a patient's family genetic history or tumor phenotype. A database is necessary to both search for and identify patients of interest so that their treatment or survivorship care can be amended. Since there is currently no such registry available at John Dempsey Hospital, we have created one. There are approximately 125 new breast cancer cases at the Cancer Center at UCONN and we have begun to collect data on these patients both prospectively and retrospectively. This database is all encompassing and includes the following areas: demographic data, tumor characteristics, treatment details, disease status, clinical characteristics, bone health, family history, and genetics. There are more than 1700 fields for data collection under these categories, ensuring a comprehensive picture of the psychological, physical, and emotional characteristics of a patient's life that will be applicable now as well as 10 years in the future. In order to understand our practices and their outcomes, having this registry allows us to track all the clinical features of our patients that impact their breast health outcomes and quality of life. As we move forward into a new era of a more personalized medicine, using this registry to tailor specific aspects of healthcare needs in our patients will be an invaluable tool.

Supported by: The UConn School of Medicine Summer Research Fellowship

Potential Role of G1P3 in Development of Chemoresistance in High Grade Bladder Cancer

Syed Alam¹, Dharamainder Choudhary¹, Garrett M. Dancik², Carol Pilbeam¹, John Taylor III¹

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Eastern Connecticut State University, Mathematics and Computer Science Department, Willimantic, CT

Introduction: Cisplatin-based chemotherapy is the standard treatment for high-grade bladder cancer, but up to 50% of patients will not respond to this therapy. As such, identifying markers of tumor resistance would dramatically improve current treatment algorithms. G1P3 is a mitochondrial-membrane protein induced by Type I interferons. It has been shown to have anti-apoptotic properties in several cancers through suppression of cytochrome C release and inhibition of caspase function. G1P3 was found to be differentially overexpressed 15-fold in high grade cisplatin-resistant compared to cisplatin-sensitive patient tumors profiled by laser capture microdissection-coupled microarray. We sought to explore the role of G1P3 in bladder cancer cell lines and to determine its potential as a novel marker of cisplatin resistance.

Methods: Online microarray databases were used to assess expression levels in other bladder cancer datasets. Bladder cancer cell lines (HTB4, HTB5, HTB9, UMUC3) were cultured in defined media. Total RNA was extracted and RT-PCR performed. Transient transfections with G1P3 gene-specific siRNAs were performed. Cell cycle and apoptosis analyses were performed using flow cytometry, and cell viability assays were performed via an XTT assay. Clonogenic assays were performed using a crystal violet dye.

Results: The microarray datasets in the Oncomine database revealed a 3-8 fold increase in G1P3 expression in invasive vs. superficial bladder cancer. Prognostic analysis using BC-BET showed a hazard ratio of >2.80 for survival of patients in the top 50% of G1P3 expression versus the bottom 50%. G1P3 mRNA expression was detected in UMUC3, HTB4, and HTB9. G1P3 mRNA was measured following cisplatin exposure in HTB9 and UMUC3, and expression increased 1.7 and 1.6 fold, respectively. Knockdown of G1P3 expression by siRNA transfection in UMUC3 and HTB9 cells resulted in a 4.2% and 15% increase in total apoptotic cells following cisplatin (3 μ M) treatment for 48 h. Cell cycle analysis of cisplatin-treated UMUC3 and HTB9 cells revealed an increase in growth-arrested S-phase cells of 4.9% and 28.4%, respectively. However, G1P3 knockdown did not significantly alter cisplatin-induced cell cycle changes. Further, compared to mock transfected UMUC3 cells, G1P3 knockdown resulted in decreased cell viability, and it prevented HTB9 colony growth.

Conclusions: G1P3 may play a role in cisplatin-resistance and proliferation in bladder cancer cells through suppression of apoptotic pathways.

Supported by: The UConn School of Medicine Summer Research Fellowship, The Leo and Anne Albert Charitable Trust

References:

1. Sternberg CN, Yagoda A, Scher HI, et al. M-VAC for advanced transitional cell carcinoma of the urothelium: efficacy, and patterns of response and relapse. *Cancer* 1989. 64:2448-2458.
2. Cheriya V, Glaser K, Waring J. G1P3, an IFN-induced survival factor, antagonized TRAIL-induced apoptosis in human myeloma cells. *J Clin Invest* 2007. 117(10):3101-3117.
3. Tahara E, Tahara H, Kanno M, et al. G1P3, an interferon inducible gene 6-16, is expressed in gastric cancers and inhibits mitochondrial-mediated apoptosis in gastric cancer cell line TMK-1. *Cancer Immunol Immunother* 2005. 54:729-740.

An Evaluation of Bleeding Events in Therapeutic Hypothermia Patients on Common Anticoagulant Therapies

Kevin Braghirol, B.S.¹, Sanjeev Nair M.D.², Justin Lundbye M.D.²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Cardiology, The Hospital of Central Connecticut, New Britain, CT*

Therapeutic hypothermia is a treatment modality geared towards decreasing the neurological sequela of a cardiac arrest as a result of anoxic brain injury. This study aims to analyze the risk of bleeding events in patients who have undergone the therapeutic hypothermia protocol at Hartford Hospital and The Hospital of Central Connecticut from 2004-2015. Many protocols at various hospitals across the country exclude patients who are on common blood thinners such as warfarin and aspirin from their protocols due to a potential risk of increased bleeding events. We measured this by analyzing the difference in hemoglobin concentration from admission and day three of the patient's hospital stay. The control group, n=60, and the experimental group, n=354, had very similar rates of dyslipidemia, coronary artery disease, diabetes mellitus, hypertension, statin use, and warfarin usage. The primary difference between the two groups is that 15.3% more of the patients in the therapeutic hypothermia group were taking aspirin. The mean change in hemoglobin for the control group was 0.71 mg/dL, while the experimental group showed a change of 0.90 mg/dL. Overall, it was found that there was no significant difference between the two groups to a 95% confidence interval. The implication of this study is that the process of therapeutic hypothermia does not increase the risk of bleeding events in patients on these common pharmaceuticals and that these factors should not be considered when deciding if a patient should be initiated in the protocol. There are several other variables that need to be addressed in future studies, such as the use of the newer anticoagulants in patients who are undergoing the protocol. More work should be done within the experimental group to determine if individual drugs increase bleeding risk [1,2].)

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Holzer, M. (2002). Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest. *New England Journal of Medicine*, 549-556. Retrieved January 26, 2016.
2. Bernard, S., Gray, T., Buist, M., Jones, B., Silvester, W., Gutteridge, G., & Smith, K. (2002). Treatment of Comatose Survivors of Out-of-Hospital Cardiac Arrest with Induced Hypothermia. *New England Journal of Medicine*, 557-563. Retrieved January 26, 2016.

Using motion-sensing technology as a touchless interface for accessing patient records and radiographs during endodontic procedures

Nicholas Camic – University of Connecticut School of Dental Medicine

Alejandro Carrasco - Section of Endodontology

Fatima AlDashti - Section of Endodontology

Aniuska Tobin - Section of Endodontology

Aditya Tadinada – Section of Oral and Maxillofacial Radiology

Objective: The use of electronic health records (EHR) in dentistry has grown in recent years, with the complete switch to EHR an eventual mandate; as a result, the dental professional is becoming progressively reliant on integrating digital interfaces with procedures. Also, this reliance on technology is leveraged in the presence of aseptic fields, and has posed challenges with maintaining the aseptic field². The aim of this study was to prove the concept that a modified computer unit can be used to accommodate touchless control of EHR and radiographs during endodontic procedures via an infrared motion-sensing camera acting as a mouse (MSC). The use of a MSC in the dental operator will allow dental professionals to maintain an aseptic field with greater ease, as well as more efficiently control and view EHR and radiographs^{3,4}.

Methods: Computer control was achieved via a laptop, clinical software, the Leap Motion device©, and touchless mouse control software; the MSC was introduced to three endodontic clinicians in a non-surgical setting. After 1.5 hours of orientation, tasks were assigned to the clinicians to complete in a timed fashion on the EHR; the clinicians each did three trials per method of computer control: conventional mouse (CM) with two glove changes, CM without glove changes, and the MSC. Paired two sample t-tests were used to differentiate between the mean times of the three groups. After the time trials, the clinicians completed one endodontic procedure while using the MSC, and then took a Likert Scale survey valued 1-5; 1 correlated to 'Strongly Disagree', and 5 correlated to 'Strongly Agree'¹. Three question categories included: 'Good ability to maintain an aseptic environment', 'Realistic and short learning curve', and 'Good practicality'; confidence intervals were used to analyze the means of the survey.

Results: The CM without glove changes had a mean time of 18.7 seconds, while the CM with two additional glove changes and the MSC had mean times of 52.6 seconds and 42.2 seconds, respectively. The CM without glove changes was significantly faster than both the MSC ($p < 0.01$), and the CM with two glove changes ($p < 0.001$). Furthermore, there was no statistical difference between the MSC and the CM with glove changes ($p = 0.092$). The confidence intervals at 95% for the survey question categories 'Good ability to maintain an aseptic environment', 'Realistic and short learning curve' and 'Good practicality' were: $4.44 < \mu = 4.78 < 5.12$, $3.95 < \mu = 4.11 < 4.87$, and $3.86 < \mu = 4.17 < 4.48$, respectively.

Conclusions: The time trials demonstrated that the CM with glove changes is comparable to the MSC ($p = 0.092$); this indicates that highly simple hands-free technology may be used without time loss in the dental operator. Furthermore, the participating clinicians agreed that the MSC was able to effectively maintain an aseptic environment, had a realistic and short learning curve, and had good practicality. Also, the MSC may also be clinically significant due to a possible reduction in glove use. Lastly, it should be noted that due to a small sample size, the statistical power may have been too low to detect differences between groups in this study. However, it should be kept in mind that the aim of this study was to prove the concept that a modified computer unit can be used to accommodate touchless control of EHR and radiographs during endodontic procedures.

Future Directions: Forthcoming studies may include pairing voice recognition software with the hands-free mouse to introduce note dictation, as well as developing software for the infrared camera to create highly specific commands designed for clinical software. Larger sample sizes and more commands would also be added to increase the statistical power of future studies.

Support: We would like to thank the University of Connecticut School of Dental Medicine Alumni Fellowship Fund for providing funding for our project. We would also like to extend acknowledgements to the UConn Health Division of Endodontology.

References:

1. Allen, I. E., & Seaman, C. A. (2007, July). *Likert Scales and Data Analyses*. Retrieved May 12, 2015, from Quality Progress: <http://asq.org/quality-progress/2007/07/statistics/likert-scales-and-data-analyses.html>
2. Fukada, T., Iwakiri, H., & Ozaki, M. (2008). Anaesthetists' role in computer keyboard contamination in an operating room. *Journal of Hospital Infection*, 148-153.
3. Ogura, T., Sato, M., Ishida, Y., Hayashi, N., & Doi, K. (2014). Development of a novel method for manipulation of angiographic images by use of a motion sensor in operating rooms. *Radiological Physics and Technology*.
4. Rosa, G. M., & Elizondo, M. L. (2014). Use of a gesture user interface as a touchless image navigation system in dental surgery: Case series report. *Imaging Science in Dentistry*, 155-160.

Title: Salivary Urea and Periodontal Microbiome in End Stage Renal Disease

Authors: Lena Cantone, Michele Holzinger, Phillip Fava, Michel Araújo, Patricia Diaz, Effie Ioannidou.

Department/Institution: University of Connecticut School of Dental Medicine, Division of Periodontology

Objective: Chronic Kidney Disease (CKD) and Chronic Periodontitis are inflammatory diseases that are strongly correlated (Ioannidou & Swede 2011). Although in the general population severe periodontitis prevalence reaches approximately 8% (Eke et al., 2012), in CKD populations this prevalence is estimated up to 39% (Ioannidou and Swede, 2011) possibly due to uremic ecological effects on the oral environment, in combination with systemic comorbid factors, which alter host response and bone metabolism. As these uremic conditions become more pronounced in individuals with CKD, their salivary urea levels tend to rise significantly as well from 7.5 to 17-26 $\mu\text{mol/l}$ (Tomas et al., 2008). Uremia may explain the shift from microbial symbiosis to dysbiosis in the subgingival ecosystem. The aim of this study was to quantify salivary urea levels in CKD patients with periodontitis and test the association between urea, clinical periodontal parameters and microbial communities diversity.

Methods: A cross-sectional study of 14 CKD patients (ESRD) was conducted. Of the 14 participants, the average age was 60.1 $\pm$ 16.1, with 57.1% being male and 57.1% also being White. Medical, biochemical, periodontal and microbiological data were already collected and analyzed (Araújo et al. 2015). Salivary samples were collected and salivary supernatants were assayed using a colorimetric assay kit (Arbor Assay, DetectX) in the Clinical Research Center (CRC) Core Laboratory. Results were expressed as total urea amount/site (mg) and as local urea concentration (mg/dl). The sensitivity of this assay was well below the urea content in salivary samples of healthy individuals (Ciancio et al., 1977).

Results: The salivary urea ranged from 0.17-67.62 mg/dl, with a mean of 23.97 $\pm$ 20.70 mg/dl. This correlates with previous studies that found that there is an almost 5-8 fold increase in salivary urea when comparing CKD patients to healthy patients (Peterson et al, 1985). A trend towards significance was also found between BUN levels and salivary urea levels ($r^2=0.46$, $p=0.1$), which validated our hypothesis. In future studies with a higher sample size, this trend will likely reach significance. In our previous work, we identified two distinct microbial clusters in the CKD population. In a subgroup analysis, we found a negative correlation between urea levels and community diversity as measured by the non-parametric Shannon index ($r^2=-0.71$, $P=0.1$). Additionally, we found a positive correlation between urea levels and periodontal destruction measures (PD, and CAL), which did not reach significance. There was a significantly negative correlation of -.943 with a p value of .005 between dialysis vintage (time on dialysis) and salivary urea levels ($r^2=-0.66$, $p=0.037$).

Conclusions: This was a pilot investigation exploring the salivary concentration of urea in a group of CKD patients. The results suggested a possible relationship between urea concentration and microbial community diversity.

Future Directions: Further research is required in larger sample sizes to be able to investigate the above hypothesis and possibly expand the inclusion to CKD patients that are in Stage III or IV as opposed to end stage renal failure patients.

Support: Fellowship support from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving. This study was also supported by NIH/NIDCR grant K23DE018689.

References:

1. Araújo, MVF, Hong, B-Y, Fava, PL, et al. *BMC Nephrol BMC Nephrology*. 2015.
2. Ciancio SG, Golub LM, Mosovich L, Katz C, Kleinberg I (1977). *Journal of Dental Research* 56(10):1144.
3. Eke PI, Dye BA, Wei L, Thornton-Evans GO, Genco RJ. *J Dent Res*. 2012;91(10):914-20.
4. Ioannidou E, Swede H. *J Dent Res*. 2011;90(6):730-4.
5. Peterson, S, Woodhead, J, Crall, J. (1985). *Pediatr Res*.:796–799.
6. Tomas, I, Marinho, JS, Limeres, J, Santos, MJ, Araújo, L, Diz P (2008). *Arch Oral Biol* 53 (6):528-532.

Daily Living Skills in Individuals with Autism Spectrum Disorder from 2 to 21 Years of Age

Daniel Cheong¹, Vanessa Hus Bal², So Hyun Kim³, Catherine Lord⁴

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²University of California, San Francisco

³Yale University

⁴Weill Cornell Medical College

Daily living skills (DLS), such as personal hygiene, meal preparation, and money management, are important to independent living. Research suggests that many individuals with autism spectrum disorder exhibit impairments in daily living skills relative to their cognitive skills. This study examined predictors of daily living skills attainment and trajectories of daily living skills in a longitudinal sample referred for possible autism spectrum disorder and followed from 2 to 21 years of age. Consistent with previous studies, participants with autism spectrum disorder and nonspectrum diagnoses showed continual development of daily living skills throughout childhood and adolescence. Early childhood nonverbal mental age was the strongest predictor of daily living skills attainment for both diagnostic groups. Group-based modeling suggested two distinct trajectories of daily living skills development for participants with autism spectrum disorder. Skill levels for both groups of young adults with autism spectrum disorder remained considerably below age level expectations. Whereas the “High-DLS” group gained approximately 12 years in daily living skills from T2 to T21, the “Low-DLS” group’s daily living skills improved 3–4 years over the 16- to 19-year study period. Nonverbal mental age, receptive language, and social-communication impairment at 2 years predicted High- versus Low-DLS group membership. Receiving greater than 20h of parent-implemented intervention before age 3 was also associated with daily living skills trajectory. Results suggest that daily living skills should be a focus of treatment plans for individuals with autism spectrum disorder, particularly adolescents transitioning to young adulthood.

Supported by: This study was funded by National Institute of Mental Health (NIMH) 1 R01 MH81873-01A1 to C.L.

References:

Duncan AW and Bishop SL (2013) Understanding the gap between cognitive abilities and daily living skills in adolescents with autism spectrum disorders with average intelligence. *Autism*. Epub ahead of print 25 November. DOI: 10.1177/1362361313510068.

Farley MA, McMahon WM, Fombonne E, et al. (2009) Twenty-year outcome for individuals with autism and average or near-average cognitive abilities. *Autism Research* 2(2):109–118.

Comparison of Blood Pressure and Cardiac Activity on Post Stroke Severity and Mortality between Young and Aged Mice

Evins Clauther MS ², Venugopal Venna, Ph.D², Louise McCullough, M.D., Ph.D²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²University of Texas Medical School Neurology Department

Elderly stroke patients experience higher mortality and have slower and less complete delayed recovery after a stroke compared to younger individuals. Comparatively, mortality is also significantly higher in aged male mice after middle cerebral artery occlusion (MCAO) which is independent of infarct size. Clinical data suggests that physiological parameters such as blood pressure and cardiac rhythm stability play a critical role in stroke recovery and mortality. Few studies have attempted to understand the role of these physiological factors on post-stroke recovery in experimental models, and none have examined aged animals. It remains to be determined how these parameters vary between young and aged mice and whether or not they contribute to the higher mortality or incomplete recovery seen in aged mice. We hypothesize that there will be physiological abnormalities in both young and aged mice after experimental stroke, but that these are greater more prevalent and longer lasting in aged mice. We determined how physiological parameters vary between young and aged mice and examined their contribution to recovery and mortality. Young (3 months of age) and aged (18 months of age) mice were placed in randomized experimental groups/ control groups and were implanted with radio-telemetry transmitter prior to surgery (stroke inducing or sham). Once implanted continuous measurements of core body temperature, systolic BP (SBP), QT intervals (QTIN), PR intervals (PRIN), and locomotor activity was acquired. Analysis of all data was performed by an investigator blinded to surgical conditions. As a larger cohort of aged vs young: aged mice had a significant prolongation of the PRIN as well as a lower HR and core temp. Age was shown to naturally cause an increase in QRS duration, PRIN and P wave length. In post stroke comparisons mice had a more dramatic post stroke decrease in HR and increase in SBP. However only in post stroke young mice stroke significantly increased QRS and P wave length. In conclusion, we have determined that increased age can increase the risk of cardiac arrhythmias as shown by the prolonged duration of PRIN and QRS. In addition, a possible explanation to smaller infarcts in younger mice can be attributed to reduced elevation in SBP. The lower SBP decreases chances of aneurysm, rupture of aneurysm and subsequent vasospasm, ultimately decreasing the chances of a larger infarct.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Bushnell C, McCullough LD, Awad IA, Chireau MV, Fedder WN, Furie KL, Howard VJ, Lichtman JH, Lisabeth LD, Pina IL, Reeves MJ, Rexrode KM, Saposnik G, Singh V, Towfighi A, Vaccarino V, Walters MR.. Guidelines for the prevention of stroke in women a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014; 45(5), 1545-1588
2. Liu F, Benashski SE, Xu Y, Siegel M, McCullough LD Effects of chronic and acute oestrogen replacement therapy in aged animals after experimental stroke. *Journal of neuroendocrinology*. 2012; 24:319-330
3. Manwani B, Friedler B, Verma R, Venna VR, McCullough LD, Liu F Perfusion of ischemic brain in young and aged animals: a laser speckle flowmetry study. *Stroke*. 2014; 45:571-578.
4. Reith J, Jorgensen HS, Pedersen PM, Nakayama H, Raaschou HO, Jeppesen LL, Olsen TS. Body temperature in acute stroke: relation to stroke severity, infarct size, mortality, and outcome. *Lancet*. 1996;347(8999):422-5.

Relationship between Shoulder Pain and Non-Traumatic Multidirectional Instability in Competitive Swimmers

Eileen Colliton¹, Carl Nissen, MD², Matthew Solomito, PhD²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Connecticut Children's Elite Sports Medicine

Introduction: Competitive swimming places significant strain on the glenohumeral joint. Typically, swimmers start intensive training between 8 and 11 years old, and competitive swimmers perform approximately 1 million stroke revolutions per arm every year. 40% to 91% of swimmers will report shoulder pain at some point in their career. It is hypothesized that the repetitive stroke motion leads to microtrauma of the glenohumeral ligaments, resulting in laxity which can progress into multidirectional instability (MDI). MDI is defined as instability of the shoulder in two or more directions. In the literature, there have been discrepancies in the definition of MDI; therefore, the true prevalence of the condition is unknown; however, the incidence of MDI appears to be higher in overhead athletes. The purpose of this study was to determine the prevalence of non-traumatic MDI in competitive swimmers. It was hypothesized that swimmers with a history of shoulder pain will have a greater incidence of non-traumatic MDI.

Methods: 27 collegiate swimmers with more than 1 year of competitive swimming participated in this prospective study. The participants completed a survey and shoulder examination. The survey included questions regarding history of competitive swimming, shoulder pain, and the Western Ontario Shoulder Instability Index (WOSI). Based on the results of the survey, the study participant's shoulders were divided into two groups: shoulders with pain (group A), and shoulders with no history of pain (group B). Based on the physical exam, the percentage of shoulders with non-traumatic MDI was determined. Non-traumatic MDI of the shoulder was defined as having no history of shoulder trauma, and two of the following three findings on examination: 2+ sulcus sign, 2+ anterior load and shift, and/or 2+ posterior load and shift. A chi-square 2x2 contingency test was used to assess differences in the groups and $p < 0.05$ was considered significant.

Results: 27 collegiate swimmers, totaling 54 shoulders, were examined. 16 swimmers, totaling 25 shoulders, had a history of shoulder pain. Due to incomplete data, 3 of the shoulders could not be included in the MDI analysis. Of the 51 shoulders included in the analysis, 23 shoulders fell into group A and 28 shoulders fell into group B based on survey results. In group A, 21.7% of shoulders had non-traumatic MDI on physical examination, and in group B, 7.1% of shoulders had non-traumatic MDI on physical examination ($p = 0.1357$). The power for the study is 34%. 106 shoulders in each group will be needed to reach 80% power.

Conclusion: The results of this study, while not statistically significant, suggest that non-traumatic MDI of the shoulder may be associated with shoulder pain in competitive swimmers.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- Bak, K. (2010). The practical management of swimmer's painful shoulder: etiology, diagnosis, and treatment. Clin K Sport Med, 20(5), 386-390.
- Bak, K., Fauno, P. (1997). Clinical findings in competitive swimmers with shoulder pain. Am J Sports Med, 25(2), 254-260.
- Bahu, M.J., Trentacosta, N., Vorys, G.C., Covey, A.S., Ahmad, C.S. (2008). Multidirectional instability: evaluation and treatment options. Clin Sports Med, 27, 671-689.
- McFarland, E.G., Kim, T.K., Park, H.B., Neira, C.A., Gutierrez, M.I. (2003). The effect of variation in definition on the diagnosis of multidirectional instability of the shoulder. J Bone Joint Surg, 85(11), 2138-2144.
- Milewski, M.D., Nissen, C.W. (2013). Pediatric and adolescent shoulder instability. Clin Sports Med, 32, 761-779.

The Effectiveness of Therapeutic Hypothermia in Preventing Reperfusion Injury for Patients Who Were Resuscitated within Five Minutes of the Onset of Cardiac Arrest

Alexis Cordone¹, Justin B. Lundbye, M.D. FACC²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*The Hospital of Central Connecticut*

One of the devastating complications of successful resuscitation following cardiac arrest is post-resuscitation syndrome, which is a series of metabolic changes that damage neurons in brain tissue after the brain experiences 2 to 4 minutes of anoxia. Consequently, post-resuscitation syndrome is responsible for decreased neurological performance in individuals who have experienced a cardiac arrest. Targeted therapeutic hypothermia (TTM) involves cooling a patient's core temperature in order to prevent metabolic damage to brain tissue during recovery after cardiac arrest, which slows the onset of post-resuscitation syndrome. Recent studies have demonstrated that applying TTM is helpful in preventing metabolic damage as measured by neurological outcome in patients who have experienced an out-of-hospital cardiac arrest due to ventricular fibrillation and initially non-shockable rhythms. However, these recent studies have only evaluated the outcome for cardiac arrest survivors for whom the first resuscitation attempt was estimated to occur within 5 to 15 minutes of the person's collapse. Therefore, this study examines whether TTM is effective in preventing reperfusion injury for patients who were successfully resuscitated within 5 minutes of their collapse, since the onset of the metabolic changes of post-resuscitation syndrome does not occur until after approximately 2 to 4 minutes following cardiac arrest. The study was performed using a database of retrospectively collected data to compare survival rates for patients at Hartford Hospital who received TTM after experiencing a cardiac arrest during the period from 01/01/2004 to 11/01/2010. Specifically, the aim of this study is to use the Pittsburgh cerebral performance category (CPC) scale to compare neurological outcome for patients who survived cardiac arrest after which successful resuscitation occurred within 5 minutes after collapse and were discharged from the hospital with and without the application of TTM. Statistical analyses were performed in order to establish significance. Upon univariate analysis, the results of this study strongly suggest an absence of any improvement in the CPC scores of patients who received TTM with a time to resuscitation less than 5 minutes. A multivariate analysis was also performed to determine the association of TTM to good and poor neurologic outcomes as two separate end-points, the results of which also supported the hypothesis by confirming the association seen in the univariate analysis.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- Hypothermia After Cardiac Arrest (HACA) Study Group. (2002). Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest. *NEJM*, 346(8): 549-556.
- Kupchik, N (2009). Development and implementation of a therapeutic hypothermia protocol. *Crit Care Med*: 37(7, suppl): S279-84.
- Lundbye, J. B., Rai, M., Ramu, B., Hosseini-Khalili, A., Li, D., Slim, H. B., Bhavnani, S. P., Nair, S. U., and Kluger, J (2012). Therapeutic hypothermia is associated with improved neurological outcome and survival in cardiac arrest survivors of non-shockable rhythms. *Resuscitation* 83: 202-207.
- Nielson, N. et al (2013). Targeted Temperature Management at 33oC versus 36oC after Cardiac Arrest. *NEJM*, 369(23): 2197-2206.

Effect of Estrogen Replacement Therapy on Cognitive Function in Oligo-amenorrheic Athletes

Brooke Cunningham BA¹, Charu Baskaran MD², Franziska Plessow PhD², Vibha Singhal MD², Ryan Woolley², Kathryn E. Ackerman MD², Kamryn Eddy PhD², Madhusmita Misra MD, MPH²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Neuroendocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

Background: Studies suggest that estrogen and exercise may play a role in improving cognitive function. While the effects of estrogen replacement therapy (ERT) in improving cognition in postmenopausal women are equivocal, ERT in girls with Turner Syndrome has resulted in improved nonverbal processing speed. Female athletes who develop amenorrhea secondary to an energy deficit state, as in the female athlete triad, are in a state of estrogen deficiency. However, effects of ERT on cognition in oligo-amenorrheic athletes (OA) have not been studied.

Objective: The objective of this study was to examine the impact of 6 months of ERT on the cognitive scores of 14-25 year old OA. We hypothesized that ERT would result in an improvement in cognitive scores.

Methods: Cognitive assessments were performed at baseline (BL) and 6 months in 48 OA. Subjects were randomized to either estrogen treatment (ERT+) (oral 30 mcg ethinyl estradiol pill (n=16) or transdermal 100 mcg 17-beta estradiol patch (n=13)) or no estrogen treatment (ERT-) (n=19) in an ongoing clinical trial. Neurocognitive tests were performed to assess different cognitive domains including crystallized and fluid intelligence (Wechsler abbreviated Scale of Intelligence (WASI)), verbal learning and memory (California Verbal Learning Test II (CVLT-II)), and executive function (Delis-Kaplan Executive Function System Color-Word Interference Test (DKEFS-CWIT)).

Results: The subjects (age 19.9 ± 3.1 years; BMI 20.6 ± 2.3 kg/m²) participated in an average of 10.3 ± 5.9 hours/week of lower limb weight bearing exercise. There was no difference between ERT+ and ERT- groups for general intelligence scores (WASI), as well as the BL CLVT-II and DKEFS-CWIT scores. After 6 months, the ERT+ group showed greater improvement than the ERT- group in the CLVT-II verbal memory immediate recall scores ($p < 0.05$, even after controlling for age and BL score). There was no difference between groups for changes in DKEFS-CWIT scores after 6 months; however, after controlling for age and BL scores, a greater improvement was seen in the ERT+ group compared to the ERT- group for inhibition switching completion time ($p = 0.01$). Subjects treated with transdermal estrogen performed better than the oral estrogen and ERT- groups on the CVLTII immediate recall test when adjusting for BL scores ($p < 0.05$), and exhibited greater improvements in the DKEFS inhibition switching completion after adjusting for age and BL scores ($p = 0.04$).

Conclusion: OA show improvement in both verbal memory and executive function with 6 months of ERT. The fact that these female athletes are in the prime of their neurocognitive development further emphasizes the importance of these findings and the need for future studies of the impact of OA on cognition.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Berchtold, N.C., Kesslak, J.P., Pike, C.J., et al., *Estrogen and Exercise Interact to Regulate Brain-Derived Neurotrophic Factor mRNA and Protein Expression in the Hippocampus*. European Journal of Neuroscience, 2001. 14(12): p. 1992-2002
2. Luine, V.N., *Sex Steroids and Cognitive Function*. Journal of Neuroendocrinology, 2008. 20: p. 866-872
3. Ross, J.L., Roeltgen, D., Feuillan, P., et al., *Use of Estrogen in Young Girls with Turner Syndrome: Effects on Memory*. Neurology, 2000. 54(1): p. 164-170

Do Weight Bearing Films Aid in Radiographic Analysis for the Presence of Discoid Lateral Meniscus in an Adolescent Knee

Andrew J. Duarte¹, Ryan Krochak, MD², Joseph Marchese, MD³, J. Lee Pace, MD⁴, Alexander Broom, BA⁴, Matthew Solomito, PhD⁵, Matthew D. Milewski, MD⁵

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Maimonides Medical Center, Department of Orthopaedics, Brooklyn, NY

³University of Connecticut Department of Orthopaedics, Farmington, CT

⁴Children's Hospital of Los Angeles, Los Angeles, CA

⁵Elite Sports Medicine, Connecticut Children's Medical Center, Farmington CT

The human knee contains two fibro-cartilagenous pads known as menisci that allow for painless articulation of the femur and tibia. This structure is usually semilunar in shape, but an anatomic variation known as a discoid lateral meniscus (DLM) is present in an estimated 5% of the population. Individuals with a DLM are prone to knee instability and recurrent injury¹. Several radiographic parameters have been associated with discoid lateral meniscus in adults and only one study has looked at the application of these measurements to children^{2,3}. We sought to determine the application of these measurements in an adolescent population and evaluate the effect of weight-bearing (WB) films in these measurements. The goal of this analysis is to provide evidence that plain film may be used as a means of identifying this anatomic variation in an office setting. Radiographs of patients with arthroscopically confirmed DLM were compared to age, side, sex matched individuals with confirmed normal menisci. The radiographs were measured by a pediatric orthopaedic sports medicine attending and two orthopaedic residents for the following parameters: lateral joint space width (LJSW), fibular head height (FHH), width of the distal femur (WDF), tibial spine height (TSH), cupping of the lateral tibial plateau (CLTP), and obliquity of the lateral tibial plateau (OLTP). 67 knees (15 WB films) with discoid lateral menisci with a mean age of 11.6 ± 3.2 years were compared to 68 control knees (15 WB films) with a mean age of 11.9 ± 3.2 years. Results indicated that there were significant differences between the discoid and control groups for the measurements: LJSW (8.7 ± 2.2 mm compared to 7.6 ± 2.1 mm in control, p-value 0.002), FHH (13.5 ± 4.5 mm compared to 18.6 ± 3.9 mm in control, p-value <0.001), WDF (79.4 ± 12.8 mm compared to 84.4 ± 12.7 mm in control, p-value 0.024), and CLTP (-0.6 ± 1.1 mm compared to 0.0 ± 1.6 mm in control, p-value 0.002). WB status showed stronger intraclass correlation (ICC) for the following measurements: LJSW (0.729), WDF (0.928), TSH (0.579), and OLTP (0.702); while non-WB films showed improved ICC for FHH (0.868). We corroborate findings that measurements on plain film can identify the presence of DLM as well as assert that the WB films provide stronger consensus among readers for LJSW measurement and non-WB films showed improved agreement for FHH. We assert that the usage of these radiographic parameters can guide differential diagnosis in adolescents with knee pain and that the usage of WB films is important in this method. Usage of plain films is cheaper and quicker than MRI or arthroscopy; though the latter remains the gold standard in assessing the presence of DLM.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Rohren EM, Kosarek FJ, Helms CA. Discoid lateral meniscus and the frequency of meniscal tears. *Skeletal Radiol.* 2001; 30:316-320.
2. Kim S, Moon S, Shin S. Radiographic knee dimensions in discoid lateral meniscus: Comparison with normal control. *Arthroscopy: The Journal of Arthroscopic & Related Surgery.* 2000; 16:511-516.
3. Choi SH, Ahn JH, Kim KI, et al. Do the radiographic findings of symptomatic discoid lateral meniscus in children differ from normal control subjects? *Knee Surgery, Sports Traumatology, Arthroscopy.* 2014; :1-7.

Discovering component qualities of single stimuli mixtures having double odors

Lauren Dulieu, Marion Frank, Thomas Hettinger

UConn Health, Dept. Periodontology

Objective: The aim of this study was to determine the phenotype of β -ionone (violet odor) perception by using vanillin (vanilla odor) as a reference odorant through recognition of β -ionone in the presence of vanillin. The β -ionone odor threshold distribution is bimodal indicating that non-smellers (40% of humans) require a concentration of about 100 times that of smellers for detection (McRae et al. 2013). Due to component dominance and mixture suppression, non-smellers of β -ionone would likely only perceive vanillin in a mixture consisting of both β -ionone and vanillin where the concentration of vanillin is 10 times detection threshold and β -ionone is 10 times the lowest common value between the bimodal threshold distributions. Contrastingly, smellers of β -ionone would likely perceive β -ionone.

Methods: Sixteen (consented male and female) subjects between the ages of 21-24 years underwent odor threshold testing to determine their thresholds for detecting vanillin and β -ionone as phase one of the study. Subjects returned for phase two and they were asked to identify vanillin and β -ionone in mixtures of the two compounds where the concentration of vanillin was held constant as the concentration of β -ionone varied. T-tests were performed on data sets including all subjects, subjects classified as “non-smellers” of β -ionone only, subjects classified as “smellers” of β -ionone only.

Results: Four subjects were identified as non-smellers (25%) and twelve subjects were identified as smellers based on β -ionone odor threshold detection. The observed to the expected proportions from the literature do not significantly differ (χ^2 p = 0.2206). Subjects identified as “non-smellers” and subjects identified as “smellers” were compared in their ability to identify vanillin and β -ionone in a series of mixtures. T-tests indicated a significant difference (p = 0.0095) between the ability of “smellers” and “non-smellers” to correctly identify a mixture of 10 ppm vanillin and 100 ppb β -ionone. Subjects labelled as “smellers” of β -ionone correctly identified this mixture as containing both vanilla and violet, while “non-smellers” all identified this mixture as only containing vanilla.

Conclusions: Subjects identified as “smellers” of β -ionone identified the mixture of 10 ppm vanillin and 100 ppb β -ionone as either violet or a combination of violet and vanilla while “non-smellers” of β -ionone only identified this mixture as vanilla. This result indicates that the presentation of an odor with a bimodal odor threshold against a reference odor can distinguish phenotypes of “smellers” and “non-smellers” of that particular odor. It has been suggested that odors with a bimodal distribution likely represent Mendelian traits (McRae et al. 2013) and the method employed in this study could more efficiently identify the phenotype of an individual for such odorant compounds. This may have implications for research based on genetics and inheritance patterns

Future Directions: Future experiments will develop a round robin binary odor wheel to study the cross adaptation of mixtures containing vanillin (vanilla), maltol (caramel), and hydroxyphenyl butanone (raspberry). A procedure to guide the future research has been established that could also be used to efficiently evaluate olfactory function in clinical settings.

Support: School of Dental Medicine Alumni Fellowship Fund, UConn Foundation; IRB # IE-01-262-1.

Reference:

McRae JF, Jaeger SR, et al. 2013. Identification of regions associated with variation in sensitivity to food-related odors in the human genome. *Current Biology*. 23:1596-1600.

Expression of BSP-GFPtpz Transgene During Dentinogenesis and Osteogenesis.

P. DYRKACZ, A. BANERJEE, I. VIDOVIC, P. MAYE, B. RODGERS, and M. MINA, School of Dental Medicine, University of Connecticut Health Center, Farmington, CT

Objectives: Bone Sialoprotein (BSP) is a non-collagenous protein (NCP) and a member of the SIBLING family with essential roles in skeletogenesis, including the initial formation of hydroxyapatite, mineralization, and turnover. In bone, BSP is expressed in abundance by osteoblasts, as well as by osteoclasts, osteocytes and chondrocytes. Although the expression and function of BSP in the formation of acellular cementum and periodontal attachment is well documented in developing teeth, there appears to be uncertainty regarding the expression and function of BSP by odontoblasts. Therefore, in this study we examined the expression of BSP and Bsp-GFPtpz transgene during odontoblast differentiation in vivo and in vitro.

Methods: Bsp-GFPtpz transgenic mice were generated using a bacterial recombination strategy with the mouse BAC clone RP23-395m11. Expression of the transgene in the developing teeth, calvarium and long bones were characterized in frozen serial sections (5-7 μ m) in P1, P6 and E20 by epifluorescence analysis in at least three different samples from each stage of development. The expression of transgene was also compared to the patterns of expression of BSP protein by immunohistochemistry (IHC) using Anti-BSP antibody and Bsp by in situ hybridization in three independent experiments. Expression of the transgene was also examined during the mineralization of primary pulp cultures from these animals and correlated with the expression of Bsp and areas of mineralization by qPCR and epifluorescence analyses.

Results: Epifluorescence, IHC and in situ hybridization analyses indicated that in developing mandibles and teeth (n $\geq$ 5), Bsp-GFPtpz transgene was expressed at high levels by cementoblasts, osteoblasts and osteocytes in the alveolar bones but not by cells in odontoblast lineage, similar to endogenous BSP and Bsp. In long bones and calvaria (n=3), expression of Bsp-GFPtpz was restricted to osteoblasts and osteocytes. Epifluorescence analysis of primary pulp cultures, showed that a few Bsp-GFPtpz expressing cells (Bsp-GFPtpz+) appeared at approximately day 10 within the mineralizing nodules (detected by XO staining) and increased with time in cultures. qPCR analysis showed a close correlation between the expression of Bsp-GFPtpz and endogenous Bsp.

Conclusions: Bsp-GFPtpz transgene, similar to endogenous BSP and Bsp, is expressed by cells in the osteogenic lineages but not in the dentinogenic lineage. The expression of transgene provides an experimental tool to distinguish cells in osteogenic and dentinogenic lineages and mechanisms that regulate the progression of progenitors into odontoblasts versus osteoblasts.

Future directions: This transgenic animal will be used to better understand the differential effects of various growth factors and reagents in dentinogenic vs. osteogenic differentiation of dental pulp stem cells.

Support: Supported by a fellowship from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving and NIH Grant R01-DE016689.

Title: Protein O-glycosylation in Secretory Granule Structure

Authors: Andrew R. Emery, Duy T. Tran and Kelly G. Ten Hagen

Department/Institution: Developmental Glycobiology Section, NIDCR, NIH

Objective: Protein O-glycosylation is a major form of post-translational modification that is conserved across most eukaryotic species. One form of O-glycosylation, known as mucin-type O-glycosylation, is initiated by a family of enzymes (PGANTs in *Drosophila*). This project aimed to investigate the effects of reduced O-glycosylation on the structure and cargo properties of secretory granules in *Drosophila* larval salivary glands.

Methods: By using transgenic flies expressing a GFP-tagged secretory protein (Sgs3-GFP), we were able to directly visualize secretory granules in living salivary glands using confocal microscopy. To determine the role of protein O-glycosylation on granule structure, we performed RNA interference (RNAi) to PGANTs specifically in salivary glands. Additionally, fluorescence recovery after photobleach (FRAP) experiments were performed to characterize the cargo properties of secretory granules for each larval strain in which a PGANT was knocked down. Finally, to determine if secretory cargo is O-glycosylated, we harvested glue plugs from salivary glands and subjected the secreted cargo to SDS-PAGE and lectin blotting to detect O-glycans.

Results: Our experiments found that knocking down PGANT5, PGANT6, and PGANT35a enzymes resulted in irregular granule morphology. Tran *et al.* showed a reciprocal relationship between the expression of PGANT5 and PGANT35a, with a decrease in expression of one causing an increase in the other by no more than 0.6-fold. They also found that a decrease in PGANT6 expression slightly reduced the expression of PGANT5 and PGANT35a, and that PGANT6 expression was reduced by about 0.3 fold when either PGANT5 or PGANT35a was knocked down. Also, our study found that knocking down PGANT5 and PGANT35a enzymes produced granules that demonstrated faster fluorescence recovery than wild type, while PGANT6 knockdown granules showed slower recovery time. The average cross-sectional areas of the secretory granules for control, PGANT5, and PGANT6 strains were about 29 square microns, while PGANT35a had a smaller area of about 21 square microns. The PGANT9 had granules that were too small to use for the photobleaching protocol and thus were not measured. Lastly, secretory glue produces a characteristic banding pattern at 90 kDa for wild type and PGANT mutants.

Conclusions: Our study showed that mucin-type O-glycosylation is required for proper secretory granule morphology, that secretory granule cargo properties are affected by O-glycosylation, and that secreted glue proteins contain mucin-type O-glycans. All together, our study utilized a novel *in vivo* approach for identifying the role of mucin-type sugars in secretory granule structure.

Future Directions: In the future, we would like to identify protein bands that are different between wild type and PGANT mutants and determine how the secretory granule cargo changes with PGANT mutations, and what effects that has on granule morphology.

Support: NIDCR Summer Dental Student Award and University of Connecticut School of Dental Medicine.

Reference: Tran, Duy T. et al. "Multiple Members of the UDP-GalNAc: Polypeptide *N*-Acetylgalactosaminyltransferase Family Are Essential for Viability in *Drosophila*." *The Journal of Biological Chemistry* 287.8 (2012): 5243-5252.

Can We Identify Parents Who Will Not Voice Concerns For Their Child's Development?

Matthew Eremita¹, Eileen Semancik¹, Paul Dworkin, M.D.²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Office for Community Child Health; Help Me Grow National Center; Department of Pediatrics, Connecticut Children's Medical Center, Hartford, CT

Developmental surveillance and screening is integral to pediatric clinical practice. Screening involves periodic administration of standardized developmental tests at set ages; surveillance is a longitudinal monitoring process that includes eliciting parent's concerns during all encounters. Although extensive research has examined physicians' developmental screening practices, few studies have examined parents' willingness to share their opinions and concerns for their child's development. We aimed to identify characteristics of parents who do NOT voice developmental concerns when prompted by their child's health care provider (HCP) despite reporting such concerns on formal developmental screening tests to identify implications for the practice of surveillance and screening. We reviewed 377 medical records of children seen at the Primary Care Center (PCC) between Sept. 2011 and Dec. 2012 for sociodemographic variables hypothesized to affect parents' sharing of developmental concerns including: the child's birth order and gender; parents' education level, employment and relationship statuses, and primary language; and family size and racial/ethnic background. The target population was parents who identified concerns on the Parents' Evaluation of Developmental Status (PEDS), a development screening tool routinely administered to parents at their infant's 9-month well-child visit. Parents who reported concerns on the PEDS (N=86) were subdivided based on whether developmental concerns were voiced when prompted by their child's HCP. Two-sided Fisher's Exact tests and logistic regression were used to evaluate the relationship between sociodemographic variables and parents' voicing of developmental concerns (or lack thereof). Parental education level was the most salient variable characterizing parents who did NOT voice concerns. Parents with less than a high school education (<HS) were more likely to NOT voice concerns for their child's development when prompted by their child's HCP than parents with at least a high school degree or equivalent (≥HS) (<HS=63.2%, ≥HS= 34.6%, P=0.056). While we were unable to demonstrate statistical significance at the 5% level for a difference of this magnitude, logistic regression analysis showed that parents with <HS were 3.238 (1.085-9.663, 95% CI, P=0.035) times more likely to NOT have raised developmental concerns than those with ≥HS. In conclusion, the process of developmental surveillance and screening may be strengthened by a greater emphasis on screening tools to monitor the development of children of under-educated parents, as they are more likely NOT to verbally share their concerns despite prompting by their child's HCP.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

Dworkin PH. British and American recommendations for developmental monitoring: The role of surveillance. *Pediatrics*. 1989; 84:1000-1010.
Schonwald A, Huntington N, Chain E, et al. Routine developmental screening implemented in urban primary care settings: More evidence of feasibility and effectiveness. *Pediatrics*. 2009; 123:660-668.

Maternal Exposure to Childhood Victimization and Prenatal Risk: Empirical Study and Systematic Review

Mario Felix¹, Damion Grasso¹

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

Maternal exposure to adversity and trauma during and prior to pregnancy has been shown to be associated with adverse pregnancy and birth outcomes. However, not much is known how maternal exposure to childhood trauma leads to increased prenatal risk, specifically prenatal behaviors.

Objective: A systematic review was undertaken to examine the statistical relationship between maternal exposure to childhood victimization outcomes in two domains: (1)maternal behaviors during pregnancy and (2) pregnancy and birth outcomes. Concurrently, a high risk sample of pregnant women (N=66) was analyzed for the relationship between a maternal history of interpersonal violence and pregnancy and birth outcomes.

Methods: We searched PsychINFO, PsychArticles, SCOPUS, and CINAHL databases for peer-reviewed articles showing the relationship between maternal childhood victimization and the 2 domains. For the empirical study, responses of mothers in their third trimester to psychometrically sound instruments and demographic questionnaires were examined in their relationship to pregnancy and birth outcome data that were extracted from their medical records.

Results: Of the total 2328 (maternal behavior) and 5371 (pregnancy outcomes) articles retrieved in the search process, 16 (maternal behavior) and 18 (pregnancy and outcomes) met inclusion criteria for full text review. Preliminary findings of the literature review suggest that (1)childhood victimization is associated with earlier use of prenatal care and more use of health care services throughout pregnancy, (2) childhood victimization is not associated with adverse pregnancy and birth outcomes but (3) is associated with more complaints and feelings of discomfort during pregnancy, and (4) maternal childhood victimization is associated with increased risky behaviors during pregnancy such as smoking The empirical study revealed that childhood victimization was (1) not significantly associated with pregnancy and birth outcomes (weight gained, gestational age, preterm status, infant weight) but (2) did correspond to greater adulthood adversity.

Conclusions: Together these findings suggest that maternal exposure to childhood victimization has a strong association with increased health care utilization, presumably due to increased complaints. It is unknown why exposure to childhood victimization leads to greater adulthood adversity, but treatment and prevention of childhood maltreatment may help mitigate the risk of adulthood trauma and its impact on pregnancy and birth outcomes.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- Alhusen, J., Bullock, L., Sharps, P., Schminkey, D., Comstock, E., & Campbell, J. (2014). Intimate Partner Violence During Pregnancy and Adverse Neonatal Outcomes in Low-Income Women. *Journal of Women's Health, 23*(11), 920–926. doi:10.1089/jwh.2014.486
- Alhusen, J., Lucea, M., Bullock, L., & Sharps, P. (2013). Intimate Partner Violence, Substance Use, and Adverse Neonatal Outcomes among Urban Women. *The Journal of Pediatrics, 163*(2), 471–476. doi:10.1016/j.jpeds.2013.01.036
- Alhusen, J., Ray, E., Sharps, P., & Bullock, L. (2014). Intimate Partner Violence During Pregnancy: Maternal and Neonatal Outcomes. *Journal of Women's Health. doi:10.1089/jwh.2014.4872*
- Urquia, M., Patricia, Maureen, Janssen, P., & Thiessen, K. (2011). Experiences of violence before and during pregnancy and adverse pregnancy outcomes: An analysis of the Canadian Maternity Experiences Survey. *BMC Pregnancy and Childbirth. doi:10.1186/1471-2393-11-42*

A 10-year bibliometric analysis of authorship gender in periodontal literature

L. Fussell, S. Kayeum, E. Ioannidou, School of Dental Medicine, University of Connecticut Health Center, Farmington, CT

Objectives: Although the proportion of women authorship in dental research has significantly increased in the United States over the past decades, women authors still maintain a minority status. The gender gap remains constant and expressed by lower frequency of women as first or senior authors and affecting scholarly productivity, grant funding, career development and tenure. More specifically, periodontology was found to be among the dental specialties with the lowest representation of women on journal editorial boards with women comprising only 22% of the periodontal faculty in the US. Therefore, the purpose of this bibliometric study was 2-fold: 1) to quantify the gender of first and last authors, and 2) to examine the predictors of first authorship in periodontal literature over the last ten years.

Methods: Gender of first and senior authors was recorded from publications in the *Journal of Periodontology* between 2004 and 2014. Gender designation was based on first name recognition. For each publication, the institution's geographic location and the financial support received by the authors were recorded using nominal variables. Statistical analysis was performed with the PASW Statistics, version 18.

Results: 2226 publications were reviewed. Women were significantly less likely to be first and senior authors and males were significantly more likely to be senior authors. Male-Male (MM) collaborations were significantly more frequent than Female-Female (FF) collaborations. Within mixed gender collaborations, female first authors were more likely to collaborate with male last authors. Men authored 87.5% of single author publications. Male authorship was consistently more prevalent in all geographical locations. In a multivariate regression model, senior author gender and geographic location significantly predicted first authorship gender. In rank order, South America had the greatest overall percentage of female first author publications followed by Asia, North America, and Europe. No significant correlations were found in funding between genders.

Conclusion: Over the last ten years, female first and senior authors remain underrepresented globally in *Journal of Periodontology*. These findings are important as they confirmed limited gender diversity in periodontal literature contributing to disparities in faculty retention, career development, and promotion.

Support: Supported by a fellowship from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving.

Limitations: Gender designation was based on name recognition. For cases when gender was uncertain, the Internet engine Google was used to determine the correct sex. Those that could not be identified after an Internet search were marked as unknowns and excluded from the data collection.

¹Hamster Taste Preference for Salicin vs. Water or Saccharin.
Bradford Ganz
UConn School of Dental Medicine Class of 2018
Advisor: Dr. Marion Frank, Department of Oral Health and Diagnostic Sciences

Objective:

Numerous studies show hamsters have a strong sensitivity to sweet taste but a weaker sensitivity to bitter taste. In the current study, 2-bottle taste preferences of the artificial sweetener sodium saccharin and the birch-bark product salicin, which taste primarily sweet and bitter, respectively to humans, were measured. Firstly, intake of a series of concentrations of salicin was compared to water intake. Secondly, intake of a series of concentrations of saccharin was compared to 10 mM salicin intake. Based on previous studies, intakes were hypothesized to decrease as bitterness appeared with increasing concentration.

Methods:

Between the two studies, 16 total hamsters (IACUC#100760) were tested with each study involving 8 hamsters. One preference study ‘salicin to water’ included two hamsters already diagnosed with diabetes and the other study ‘saccharin to salicin’ included one hamster with diabetes. The hamsters had continuous access to food, and were provided the choice between two samples of the chemicals: quinine, sucrose, saccharin, water and salicin presented in two separate tubes. One study tested varying concentrations of salicin (1mM to 100mM in half log steps) to constant water. The second study compared varying concentrations of saccharin (1mM to 100mM in half log steps) to constant 10mM salicin. To account for possible side preferences, the test tubes were switched between left side and right side every 24 hours. A new trial with two new substances was conducted after 48 hours. The total experiment ran for 36 days. Taste preference was calculated based on consumption as a preference ratio = ‘stimulus ingested (mL) ÷ total fluid ingested (mL).’ Scores of less than 0.50 indicate avoidance while scores greater than 0.50 indicate preference (Rehnberg et al., 1990). Average ingestion, standard deviation and standard error of mean for each trial was calculated.

Results:

Control ‘water vs. quinine’ resulted in a 73% preference for water, whereas the control ‘sucrose vs. water’ resulted in 75% preference for sucrose. Mean quinine intake was 3.02 mL while mean for water was 8.1 mL. Sucrose mean ingestion of 9.3 mL compared to a water mean of 3.1 mL.

Salicin vs. water showed preference for 1mM and 3mM salicin but aversion for 10mM salicin. At 10mM, preference switched to water (t-tests, $\leq 5\%$ significance level). The strong saccharin preference held at all concentrations vs. 10mM salicin for the majority of hamsters; with 100 mM saccharin preference greater than 1mM saccharin preference over 10 mM salicin (t-test, $p = 0.006$).

Conclusions:

Saccharin is well known as a sweet-bitter compound in humans and rodents, with bitterness emerging at higher concentrations. It is reported for the first time here that salicin may be a sweet-bitter compound in hamsters, a species with weak bitter taste compared to humans. Hamster saccharin taste preference over the aversive 10mM salicin is consistent with the strong hamster sweet taste, which is nevertheless reduced more at lower concentration than at high.

Future Directions:

The next step would be to determine if saccharin is also preferred to quinine and the concentration at which saccharin preference dissipates. Another important step is to determine how the diabetic hamsters may have skewed the data by doing further statistical analysis without the diabetic hamsters included.

Support: Funds for this project were made available by the University of Connecticut School of Dental Medicine Alumni Fellowship Fund and Department of Oral Health and Diagnostic Sciences.

Osteopontin – A Potential Marker for Chemotherapy Resistance in Bladder Cancer

Nora Gibson¹, Dharamainder Choudhary², Carol Pilbeam¹, John Taylor III²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Surgery, UConn Health, Farmington, CT*

Introduction and Objectives: Osteopontin (OPN) is a secreted extracellular matrix protein known to play a key role in tissue remodeling, inflammation and tumor development. In a laser capture microdissection-coupled microarray gene expression analysis of chemoresistant vs. non-chemoresistant bladder tumor samples, OPN was found be the most highly (24-fold) expressed gene. We sought to explore the role of OPN in bladder cancer chemoresistance.

Methods: Bladder cancer cell lines (HTB4, HTB5, HTB9, UMUC3) were cultured in ATCC defined media. Total RNA was extracted and qPCR was performed. OPN protein expression was analyzed in cell lysates by Western Blotting and in culture medium by ELISA. Transient transfections with OPN genespecific siRNAs were performed. Apoptosis and cell cycle analysis were evaluated by flow cytometry. Clonogenic survival and XTT-based cell viability assays were also performed.

Results: OPN transcript and protein expression in cell lysates and culture medium were observed only in HTB9 cell line. Treatment of HTB9 cells with cisplatin further increased the OPN gene expression by 29%. siRNA knockdown of OPN expression in HTB9 cells increased the cisplatin (3 μ M) treated apoptotic cells by 28% compared to mock-transfected cells at 24h. Similarly, a dose dependent decrease in cell viability was observed in HTB9 cells with cisplatin treatment (0.1 - 3 μ M) with OPN knockdown. Correspondingly, cell cycle analyses in OPN knockdown cells showed a 12% decrease in S-phase and a 39% increase in G0-G1 phase after 48h incubation with 3 μ M cisplatin. In a clonogenic assay, cisplatin treatment decreased the number of colonies in a dose dependent fashion and silencing of OPN expression completely inhibited the colony-forming ability. In silico analysis of OPN expression in the Oncomine database showed 3-9 fold upregulated expression in infiltrating bladder urothelial carcinoma vs. normal tissue.

Conclusions: These findings suggest that inhibiting OPN expression sensitizes bladder cancer cells to cisplatin by conferring a greater propensity for G1 arrest and inhibiting colony formation. Therefore, upregulated OPN expression may contribute to the development of chemoresistance in bladder cancer.

Supported by: The UConn School of Medicine Summer Research Fellowship, The Leo & Anne Albert Institute for Bladder Cancer Research

References:

Barretina, Blaveri, Dyrskjot, Garnett, Lee, Lindgren, Modlich, Ramaswamy, Rothenberg, Sanchez-Carbayo, Stransky, Wooster. Oncomine Bladder Cancer Datasets. Accessed June 2015.

Impact of A Decade of Advances in Pediatric Burns Care

Andrew Glick¹, Kevin Dieckhaus^{1,2}, Sharon Cox³, Roux Martinez³, Heinz Rode³

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Division of Infectious Disease, UConn Health, Farmington, CT*

³*University of Cape Town Faculty of Health Sciences, Division of Paediatric Surgery, Red Cross War Memorial Children's Hospital, Cape Town, South Africa*

Introduction: Pediatric burn injury in South Africa is the third commonest cause of external trauma under the age of 18 ^{1,2}. Burn care is expensive and lengthy ³. The management of pediatric burns has substantially improved over the last decade ⁴. Factors included early resuscitation, early excision and grafting, prevention and control of infection, management of inhalation injury and pain, early nutrition and early rehabilitation. This is a descriptive epidemiology study to audit the advances in various aspects of care.

Methodology: The retrospective administrative review was conducted for four years: 2004, 2007, 2011, and 2014. Data analysis includes: number of hospital admissions, number of outpatient visits, Western Cape Under-14 population, operative statistics (number, type, and duration of surgery), ICU admissions, and mortality, and topical therapy usage. Surgical data were collected from the burns surgery log books from the years 2004, 2007, 2011, and 2014. The remaining data were collected from the Information Management Unit at Red Cross Hospital. Official audited data from the hospital was used. Population data was collected from Statistics South Africa.

Results: From 2004 to 2014, the change in the number of inpatient admissions and surgeries was substantially smaller compared to change in number of outpatient visits: inpatient admissions declined by only 3.08% and the number of surgeries declined by 22.49%, whereas the number of outpatient visits increased by 178.10%. From 2004 to 2014 the amount of surgical cases increased and then declined. The number of surgeries from 2011 to 2014 declined by 30.46%. The number of change of dressing (only) surgeries declined over the decade (303 in 2004 to 97 in 2014), with the sharpest decline of 239 in 2011 to 97 in 2014 (a 59.41% decline).

Discussion: The decrease in total surgical volume from 2011 (856) to 2014 (596) is likely due to a number of factors—mainly the decrease in change of dressings (239 to 97). This change was most likely due to establishment of dressing changing room inside the burns ward, the hiring of a medical officer, and a decrease in Biobrane-only surgeries (87 to 18) due to the implementation of a substitute dressing, Suprathel, which does not require theatre time.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Van Niekerk A, Rode H, Laflamme L. Incidence and Patterns of Childhood Burn Injuries in the Western Cape, South Africa. *Burns*. 2004; 30(4):341-347
2. Rode H, Berg AM, Rogers A. Burn Care in South Africa. *Annals of Burns and Fire Disasters*. 2011; 24(1):7-8
3. Ahn C, Maitz PKM . The True Cost of Burn. *Burns*. 2012; 38(7):967-974
4. Allorto NI, Clarke DL, Thomson SR. A Cost Model Case Comparison of Current Versus Modern Management of Burns at a Regional Hospital in South Africa. *Burns*. 2011 37(6):1033-1037

Knowledge, Attitudes, and Barriers towards Breast Cancer Screening Among Latinas and Health Care Providers in Hartford, CT

Sarah Grout¹, Amy Johnson, MD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Hartford Hospital and University of Connecticut Health Center Department of Obstetrics and Gynecology, Hartford, CT*

Multiple studies have shown that Hispanic women have a lower overall risk of breast cancer than non-Hispanic women [5], but are more likely to be diagnosed at a later stage with lower survival rates [1,3]. Previous literature has indicated that there are logistical and psychosocial reasons for these differences [2,4]. About 45% of the total population in Hartford, CT identifies as Hispanic, making it an ideal setting to investigate breast cancer screening behaviors in this population. Few studies have examined provider perceptions as they relate to screening patterns in this patient population. The goal of this study is to establish community-specific knowledge gaps and barriers to explain low rates of breast cancer screening among Hispanic women in Hartford. A descriptive survey was given in an interview style format to Hispanic women seeking care at Hartford Hospital as well as providers in the Ob/Gyn specialties working at Hartford Hospital. 87 patients and 29 providers were surveyed. Data regarding demographics, family history of cancer, screening practices, and knowledge/beliefs was collected and analyzed. We observed an ethnic distribution of 71.9% Puerto Rican. 78% of patients used Medicare and 13.4% of patients had no insurance. Despite this, 67.8% of patients reported feeling financially secure. 67% of patients completed high school/GED or some college. There was a knowledge gap regarding screening, with 57.6% of patients believing mammograms should start before age 25, and only 3.4% of patients correctly identifying the age of 50 for the start of mammograms suggested by the USPTF. Providers identified cost/lack of insurance, lack of understanding of risks, and patient education level as the top 3 barriers to patient care. Interestingly, only 32.1% of patients reported their doctor discussing breast cancer with them, and only 1.1% reported their doctor discussing their individual risks for breast cancer. In contrast, 44.5% of providers reported that they discussed individual risk factors with 50% or more of patients. In conclusion, we found that basic knowledge surrounding breast cancer screening was lacking in Hispanic patients. Additionally, there was an obvious difference between the barriers reported by patients and those perceived by providers, indicating a significant communication barrier.

References:

1. Li CI, Malone KE, Daling JD. Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med* 2003;163:49–56.
2. Roman, L et al. Individual, provider, and system risk factors for breast and cervical cancer screening among underserved Black, Latina, and Arab women. *J Women's Health* 2014; 23(1):57-64.
3. Sassi F, Luft HS, Guadagnoli E. Reducing racial/ethnic disparities in female breast cancer: screening rates and stage at diagnosis. *Am J Public Health* 2006; 96(12):2165-72.
4. Shelton RC, et al. Sociocultural determinants of breast and cervical cancer screening adherence: an examination of variation among immigrant Latinas by country of origin. *J Health Care Poor Underserved* 2012; 23(4):1768-92.
5. Smigal C, et al. Trends in breast cancer by race and ethnicity: update 2006. *CA Cancer J Clin* 2006; 56:168–83.

PLA2 hydrolysis of *P. gingivalis* Lipid 654 is enantioselective
Authors: Steven Halepas and Frank Nichols
University of Connecticut School of Dental Medicine Department of Periodontics

Objective: Previous work has shown that *Porphyromonas gingivalis*, a periodontal pathogen, produces a serine dipeptide lipid class, called lipid 654, that is de-esterified by phospholipase A2 (PLA2) to form a very potent product lipid, termed lipid 430. Additional work demonstrated that only a portion of Lipid 654 is hydrolyzed by various types of PLA2. Since PLA2 is known to be enantioselective in hydrolyzing mammalian lipids, the present investigation sought to determine whether the phospholipase A₂ is enantioselective in hydrolyzing the either the R or S diastereomeric forms of Lipid 654.

Methods: Aliquots of synthetic R or S Lipid 654 (Prepared by Dr. Michael Smith and Mr. Chris Dietz, Dept of Chemistry, UConn, 250 ng) were sonicated in buffer (1 ml of 10 mM Tris, pH 7.5, 2.5 mM CaCl and 150 mM NaCl) for 20 sec and after adding 5ug of human recombinant secretory PLA2 (Cayman Chemical, >95% purity), samples were stirred at 37°C for up to 24 hours. Controls received no enzyme. Samples were then acidified with 25 ul of acetic acid and extracted three times with chloroform. The pooled extracts were dried and reconstituted in HPLC solvent. Lipid 654 and Lipid 430 were quantified using multiple reaction monitoring-mass spectrometry (MRM-MS) as previously reported (1). Samples were processed at 1, 2.5, 6, 12, and 24 hours after the addition of the enzyme and lipid ratios were plotted to obtain enzyme kinetics of the hydrolysis. In addition, we quantified free C_{15:0} released from Lipid 654 in the hydrolyzates by forming pentafluorobenzyl ester derivatives and quantifying free C_{15:0} using negative ion-GC-MS. Follow up experiments were performed with porcine pancreatic phospholipase A₂ as well as honey bee venom phospholipase A₂.

Results: Only R synthetic 654 was hydrolyzed by various PLA2 preparations. The ratio of 430/654 of the S isoform was unchanged from that observed in the control samples. C_{15:0} release paralleled the shifts in lipid ratios determined with increasing time of hydrolysis. Porcine pancreatic PLA2 also cleaved only the R synthetic Lipid 654. This evidence indicates that Lipid 654 from *P. gingivalis* is composed of two diastereomeric forms, one isoform is hydrolysable by PLA2, and another form of Lipid 654 that cannot undergo hydrolysis. The Lipid 430 produced is therefore enantioenriched for only one isoform.

Conclusions: In summary phospholipase A₂ is enantioselective in its hydrolysis of the lipid 654. The significance of this finding is important because isolated bacterial Lipid 654 has a variable ratio of R/S isoforms and the ratio of R to S isoforms determines the capacity of Lipid 654 to engage TLR2. Of note, Lipid 654 is not a phospholipid and does not contain a glycerol moiety, therefore, hydrolysis by PLA2 is a novel finding. This discovery suggests that PLA2 expression in chronically inflamed periodontal disease sites could impact the enzymatic hydrolysis of Lipid 654 to Lipid 430 thereby affecting bone loss and macrophage activation mediated through TLR2.

Future Directions: We will evaluate the levels of R and S lipid 654 and Lipid 430 in oral Bacteroidetes samples and dental samples.

Support: This research was supported by the School of Dental Medicine Alumni Fellowship Fund and NIH Grant DE 021055.

1. Farrokhi V, Nemati R, Nichols FC, Yao X, Anstadt E, Fujiwara M, Grady J, Wakefield D, Castro W, Donaldson J, Clark RB. Bacterial lipodipeptide, Lipid 654, is a microbiome-associated biomarker for multiple sclerosis. Clin Transl Immunology. 2013;2(11):e8. doi: 10.1038/cti.2013.11. PubMed PMID: 25505950; PMCID: PMC4232052.

Platelet-Rich-Plasma Enhances Mesenchymal Stem Cell Differentiation on Matrix Specific Constructs

Alexander Hoberman, B.A.¹, Mary Beth McCarthy B.S.², Mark P. Cote, PT, DPT, M.S.CTR², Carl Cirino B.A.¹, Leo Pauzenberger³, Felix Dyrna³, Knut Beitzel M.A., M.D.³, Augustus D Mazzocca M.S., M.D.²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Orthopaedic Surgery, University of Connecticut, Farmington, Connecticut

³Department of Orthopaedic Sports Medicine, Technical University, Munich, Germany

Introduction: Despite advances in surgical technique, the high failure rate and inconsistent results of rotator cuff repair (RCR) have prompted an exploration to improve the traditional procedure. The body's natural propensity to generate scar tissue creates a weaker union between the rotator cuff tendon and humeral head thereby increasing susceptibility to subsequent failure (1). Application of mesenchymal stem cells (MSCs) at the site of repair may improve healing by producing tissue reflective of the natural enthesis. Biological carriers (scaffolds) are a promising candidate for stem cell delivery as they have been shown to localize cells, serve as a suitable environment for cell proliferation and influence cell differentiation. In addition, optimizing stem cell proliferation and differentiation is important for maximizing the healing potential of MSCs in the setting of RCR. Platelet-rich-plasma (PRP) is a potential biologic tool in orthopedic surgery that has been shown to induce proliferation and differentiation in vitro. The purpose of this study was to assess the effect of PRP on bone marrow derived MSCs seeded in normal tendon, demineralized cancellous bone matrix and a fibrin clot. Our hypothesis was that PRP will enhance stem cell differentiation and proliferation and that the composition of tested matrices will significantly impact bMSC differentiation.

Methods: Bone marrow (BM) was aspirated from the proximal humerus of one 45 year-old-male patient during arthroscopic rotator cuff surgery (IRB #06577 2). Cells were seeded in 1) Freshly frozen rotator cuff tendon (RCT), 2) demineralized bone matrix and 3) a new fibrin clot scaffold. Cellular adhesion and proliferation assays were prepared for each scaffold. Established markers for tendon (decorin, tenascin c, type's I and III collagen), bone (osteocalcin, alkaline phosphatase cartilage (aggrecan, type II collagen) and fat (PPAR, FABP4) were chosen to quantify the differentiation capacity.

Results: Cells adhere to the Flexigraft and Fibrin Clot significantly better than the control rotator cuff tendon. Cells adherence was significantly improved with the addition of PRP. Additionally, cells with PRP adhered significantly better to the Flexigraft than to both the Clot and the RCT. MSC proliferation was enhanced on the Flexigraft and clot compared to the normal RC tendon. MSCs treated with PRP proliferated significantly more on the Flexigraft compared to the RC tendon. Significant differences were seen in MSC differentiation on the various scaffolds.

Conclusion: The results of this experiment demonstrate that the composition of biologic scaffolds and presence of PRP significantly influence MSC adhesion, proliferation and differentiation in vitro.

Supported by: The UConn School of Medicine Summer Research Fellowship, Department of Orthopaedic Surgery - University of Connecticut

References:

Duquin TR, Buyea C, Bisson LJ. Which method of rotator cuff repair leads to the highest rate of structural healing? A systematic review. Am J Sports Med 2010;38: 835-841

Identifying Anabolic and Catabolic Growth Factor Signals in Osteoarthritis

Xiaoxiao Hong, Melanie Fisher and Caroline N. Dealy
University of Connecticut School of Dental Medicine

Objective: Osteoarthritis (OA) is a painful, debilitating disease caused by deterioration of articular cartilage of the joints. It is well established that articular cartilage responds to injury that causes OA by initiating catabolic (degradative) responses, which over the long term lead to cartilage loss [1]. However, an emerging view is that there are also anabolic (growth-promoting) responses in articular cartilage, which occur transiently and shortly after injury [2]. Accordingly, we suggest that stimulating anabolic responses, while suppressing catabolic ones, may offer a new approach to OA treatment.

Catabolic responses in cartilage are mediated in part by signaling from the epidermal growth factor receptor (EGFR, also known as ErbB1) [1]. Intriguingly, it has also been shown that EGFR also plays a role in anabolic responses in articular cartilage [2]. Indeed, the articular cartilage is dramatically thickened in transgenic mice in which EGFR/ErbB family signaling is experimentally activated. Most signals transduced by EGFR/ErbB family members (i.e., ErbB1-4) are mediated by heterodimers. We hypothesize that the specific catabolic and anabolic activities of the ErbB family are mediated by formation of unique heterodimer pairs. Thus, the goal of this study is to identify potential ErbB family heterodimers which may mediate distinct catabolic vs. anabolic effects in OA.

Methods: The activation of ErbB family members in catabolic responses in OA was examined using knee joint tissues from a surgically induced OA mouse model (N=3, control N=2). On the other hand, articular cartilage of transgenic mice with genetic EGFR/ErbB activation (N=3, control N=3), in which anabolic responses are occurring, was used to determine EGFR/ErbB signaling in anabolic responses in OA [2]. Tissues for both experiments were sectioned and immunohistochemistry (IHC) analyses were performed to determine the presence of activated EGFR/ErbB receptors in the articular cartilage using antibodies specific for tyrosine phosphorylation (i.e., activation).

Results: In OA, ErbB2 and ErbB4 were co-localized in the superficial zone of the articular cartilage, where matrix degradation occurs. Additionally, activation of EGFR was observed in the deep zone, where abnormal cellular cloning and hypertrophy occurs. In articular cartilage in which anabolic responses are occurring, we observed co-localization of EGFR and ErbB2 in all zones.

Conclusions: Our results suggest that catabolic responses in articular cartilage are mediated by ErbB2/ErbB4 heterodimers and potentially EGFR homodimers, whereas anabolic responses are mediated by EGFR/ErbB2 heterodimers. The specific pattern of receptor co-localization within different articular cartilage zones - in which distinct cellular events occur - suggests dimer pairs that may mediate unique cellular behaviors. Our results support the potential of therapeutic modulation of catabolic or anabolic responses mediated by the EGFR/ErbB axis as a new interventional approach for OA.

Future Directions: Immunoprecipitation and Western blotting, and/or FRET (Förster Resonance Energy Transfer) are needed to confirm heterodimer formation in OA.

Support: 2015 AADR Student Research Fellowship (Hong X) and DOD W81XWH-15-1-0144 (Dealy CN)

References:

1. Yoon, Y.M., et al., *Epidermal growth factor negatively regulates chondrogenesis of mesenchymal cells by modulating the protein kinase C-alpha, Erk-1, and p38 MAPK signaling pathways*. J Biol Chem, 2000. **275**(16): p. 12353-9.
2. Shepard, J.B., et al., *Transient anabolic effects accompany epidermal growth factor receptor signal activation in articular cartilage in vivo*. Arthritis Res Ther, 2013. **15**(3): p. R60.

CBCT demonstrates increased bone density in osteoporotic patients on oral-anti-resorptives

Owen Insel, UConn School of Dental Medicine and Dr. Aditya Tadinada, UConn Div. of OMFR

Objectives:

To evaluate the reliability of Cone Beam CT (CBCT) in detecting changes in mandibular bone density using pixel intensity values (PIVs) in osteopenic/porotic patients on oral anti-resorptive drug therapy.

Experimental methods:

A subset of 50 patients, who were participants in a best-practice study of postmenopausal women on oral anti-resorptive drug therapy receiving dental implants was retrospectively analyzed for this study (UConn IRB approval number: 07-016). As a part of evaluating the survival of dental implants in osteopenic/porotic patients, which was the original intent of gathering this dataset, pre-operative CBCT (T-1), 12 month (T-2), and 24 months (T-3) follow-up scans were done. Using a combination of Klemetti's mandibular index and Taguchi's mandibular cortical index, bone density was measured. Pixel intensity values (PIVs) from CBCT images at specific regions of interest in the mandible representing cortical and trabecular bone were evaluated. Cortical bone density was measured on CBCT reconstructed cross sectional images at a standardized region marked by a line bisecting the mental foramen at the inferior cortical border. Trabecular bone density was measured 2 mm superior to the mental foramen on the cross sectional images along the same line bisecting the mental foramen. Thickness of the inferior cortical border at the specific cross-sectional images was also measured. Statistical analysis using one-way ANOVA with repeated measures and correlations were done using SPSS-18.

Essential results:

One way repeated ANOVA for cortical bone density showed that at time point one (T-1) the PIV was 987.92(St. dev-113.2), at T-2 it increased to 1067.42(St. dev-95.4) and at T-3 it further increased to 1168.62(St. dev-95.7) PIVs. The trabecular bone density at T-1 was 112(St. dev-80.9), at T-2 was 155(St. dev-69.6), and at T-3 was 200(St. dev-80.6). The cortical thickness at T-1 was approximately 3.8mm(St. dev-.75) and it was consistently maintained through all the progressive time points. For all data points $p < 0.001$

Conclusion:

There was a consistent increase in the CBCT derived pixel intensity values at all the progressive time points as a result of the anti-resorptive therapy. This shows that the oral anti-resorptives are working to increase the cortical and trabecular bone as predicted. More importantly it showed mandibular bone density can be reliably tested using PIV values from the CBCT images.

Future Directions:

A future study can be done to see if the dosage of bisphosphonates has an effect on bone density changes over time.

Limitations:

A limitation to this study is that there is no control group to compare the change of the cortical and trabecular bone to. This is because it is difficult to find patients with the same demographic to compare to the experimental group.

Support:

School of Dental Medicine Alumni Fellowship Fund.

g. References:

1. Agbaloo, T.L., Dry, S.M., Mallya, S. et al, Stage 0 Osteonecrosis of the jaw in a patient on Denosumab. J Oral Maxillofac Surg. 2014;72:4.
2. Devlin, H., Karayianni, K., Mitsea, A. et al, Diagnosing osteoporosis by using dental panoramic radiographs: The Osteodent project. Oral Surg, Oral Med, Oral Path, Oral Rad, Oral Endo. 2007;104:6.
3. Ruggiero, S.L., Dodson, T.B., Assael, L.A. et al, American Association of Oral and Maxillofacial Surgeons position paper on bisphosphonate-related osteonecrosis of the jaws—2009 Update. J Oral Maxillofac Surg. 2009;67:2.

Comparative Evaluation of Complication Rates Between Iliac and S2-alar Screw Fixation

Casey Jarvis¹, Mark Lee, MD², Matthew Solomito, PhD²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Connecticut Children's Medical Center, Hartford, CT

Study Design: Retrospective chart review

Objective: To compare the complication rates among iliac screws with crosslinks, iliac screws without crosslinks, and S2-alar screws in patients with neuromuscular scoliosis.

Summary of Background Data: The extension of spinal instrumentation to the pelvis is commonly indicated in patients with neuromuscular scoliosis. Despite the necessity to improve pelvic obliquity and sitting balance, this procedure is associated with high complication rates [1,2]. Although pelvic fixation has been extensively studied, there is little agreement as to which type of pelvic screw construct reduces the risk of complication.

Methods: Patients aged 8 to 25 years who underwent spinal instrumentation with pelvic fixation at a single institution from 2003 to 2014 were analyzed. Patient charts were reviewed for type of pelvic instrumentation, diagnosis, as well as hardware and medical complications. A Chi squared contingency test was used to determine differences between type of pelvic instrumentation and frequency of complication.

Results: A total of 52 patients were included in this study. Twenty-six complications were reported. Patients who received iliac screw fixation without crosslinks had the greatest frequency of hardware complications compared with those who received iliac screws with crosslinks or S2-alar screws. Iliac screws had a statistically higher rate of complication than iliac screws with crosslinks ($p < 0.05$) and bordered on significance when compared to S2-alar screws ($p = 0.051$). The complication rates between iliac screws with crosslinks and S2-alar screws were similar. There was no difference in medical complications or medical and hardware complication between the three instrumented groups.

Conclusion: Hardware complications occurred more often when patients received iliac screws without the supplementation of crosslinks. When utilizing iliac screws for pelvic fixation, a minimum of one crosslink should be placed to ensure extra stability in the construct and to help reduce hardware associated complications. The addition of crosslinks to iliac screw constructs has the potential to reduce the need for revision surgeries and additional medical care for patients with neuromuscular scoliosis

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Garg S, Holland C, LaGreca J, McNair B, Erickson M. Predicting Failure of Iliac Fixation in Neuromuscular Spine Deformity. *Spine Deformity*. 2014;2(3):214-8.
2. Myung KS, Lee C, Skaggs DL. Early pelvic fixation failure in neuromuscular scoliosis. *J Pediatr Orthop*. 2015;35(3):258-65.

Nuclear isoforms of fibroblast growth factor 2 and dentin mineralization

J. Joseph*, A. Banerjee, M. Mina, and M. Hurley, University of Connecticut Health Center, Farmington, USA

Our previous studies showed that the phenotype of transgenic mice with overexpression of high molecular weight FGF2 isoforms in osteoblasts (HMWTg mice) included dwarfism, decreased bone mineral density (BMD), osteomalacia, and decreased serum phosphate (phosphate wasting) due to increases in FGF23/FGFR/KLOTHO signaling and down-regulation of NPT2a in kidneys

Objectives: To examine the effects of phosphate wasting on teeth and supporting tissues in these transgenic animals.

Methods: HMWTg and control (Vector) age matched male mice were sacrificed at 30 and 60 days postcoital (dpc). Both mandibular and maxillary arches were isolated, examined by radiography and processed for histology.

Results: X-ray revealed smaller mandibles, and mineralization defects in alveolar bones and dentin in HMWTg mice as compared to controls at 30 dpc and 60 dpc. Histological analysis showed increased thickness of pre-dentin, decreased thickness of dentin, and decreased alveolar bone volume compared to the control mice. The phenotypic abnormalities were more severe at 30 dpc as compared to 60 dpc. There were also changes in vascularity of dental pulp.

Conclusion: The changes in the thickness of dentin and pre-dentin indicated that over-expression of FGF2 did not affect odontoblast differentiation but affected the conversion of unmineralized pre-dentin into mineralized dentin that is dependent on phosphate. These observations indicated the dentin abnormalities in HMWTg mice are due to hypophosphatemia and decreased serum phosphate.

Future Directions: Bone Sialoprotein (BSP) which is expressed in abundance by osteoblasts, will be used to examine the expression of BSP on HMWTg and control (Vector).

Support: School of Dental Medicine Alumni Fellowship Fund and NIH Grants R01-DE016689 and NIDDK 01DK098566

Antipsychotic Medication Use in Difficult-to-Place Patients before and after Transfer to a Specialized Skilled Nursing Facility

Erin Kalla¹, Julie Robison, PhD², Jennifer Glick, RN, MSW³, Lisa Barry, PhD, MPH²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²University of Connecticut Center on Aging

³CT Department of Mental Health and Addiction Services

Research Objective: Nationwide, the number of individuals residing in state-run psychiatric facilities or correctional facilities who need skilled nursing facility (SNF)-level care is increasing. The opening of a SNF for difficult-to-place patients in Connecticut provides an opportunity to better understand a growing and historically marginalized population. We evaluated antipsychotic drug use, a CMS quality-of-care indicator, among difficult-to-place patients before and after their transfer from state-r to this specialized SNF.

Study Design: We compared demographic characteristics, psychotropic drug use, and Minimum Data Set (MDS) data regarding depression, cognition, and behaviors of patients taking (n=33) and not taking (n=40) antipsychotic medications on admission. We also determined person-level changes in the number of antipsychotic medications taken between admission and 6-months.

Population Studied: Individuals (N=73) admitted from a state-affiliated inpatient psychiatric facility or state correctional facility to a specialized SNF between May 2013 and February 2015.

Principal Findings: Compared with those not taking antipsychotic medications at admission, the 33 (45.2%) patients taking at least 1 antipsychotic medication at admission were more likely to be age >60 (57.6% vs. 32.5%; p=0.03) and to show behavioral symptoms including hitting, kicking, and cursing (21.2% vs. 2.5%; p=0.01), but were not more likely to be taking another psychotropic medication such as an antidepressant, anti-anxiety drug, or mood stabilizer (72.2% vs. 60.0%; p=0.25). Those taking antipsychotics at admission were also less able to complete MDS cognition or depression screens (78.8% vs 97.5%; p=0.01), and had significantly lower/worse cognition scores (9.4 (+3.9) vs 12.6 (+3.0), p<0.001). Depression scores did not differ significantly between the two groups. At 6 months following admission, 16 (22.2%) had a change in the number of antipsychotic medications. Among the 40 patients who were not taking an antipsychotic at admission, 4 (10.0%) were taking an antipsychotic at 6-months. Of the 33 patients who were taking an antipsychotic at admission, 4 (12.1%) were taken off antipsychotics, 5 (15.2%) decreased from >2 antipsychotics to 1, and 3 (9.1%) increased from 1 antipsychotic to 2 at 6-months.

Conclusions: Antipsychotic prescriptions appear to be adjusted relatively often after transition to the SNF, with over 22% of residents increasing or decreasing the number of antipsychotics in the first six months. Findings suggest that residents with dementia, indicated by low cognition scores or inability to complete assessments, were frequently prescribed antipsychotics pre-transition to address behavioral symptoms.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

Ahalt C, Trestman R, Rich J, Greifinger R, Williams B. Paying the Price: The Pressing Need for Quality, Cost, and Outcomes Data to Improve Correctional Health Care for Older Prisoners. *Journal of the American Geriatrics Society*. 2013;61(11):2013-2019. doi:10.1111/jgs.12510.

Effects of Peridex (Chlorhexidine) on Anterior-Tongue Salt Taste

Julia Karpman, Dr. Marion Frank

U Conn Health, Department of Oral Health and Diagnostic Sciences

Objective: It is well documented that chlorhexidine affects salt taste mechanisms, causing salty tastes to be tasteless or slightly bitter, but does not affect sweet taste in human subjects. This study, which focused on the anterior tongue, determined whether (1) stimulation locus or the (2) NaCl concentration affected the dysguesia. Additionally, the prediction was made that chlorhexidine treatment would disrupt tastes of salts with monovalent cations, but not salts with divalent cations. For experimentation, solutions of NaCl and sucrose [0 M, 0.1 M, 0.3 M, 1.0 M], as well as the following salts were used: CaCl₂ [0.2 M], MgSO₄ [0.3 M], Na₂SO₄ [0.5 M], NaBenzoate [0.5 M], NaCitrate [0.5 M], NH₄Cl [0.5 M], and KCl [0.5 M]. Sucrose was used as a control.

Methods: 15 stock solutions were made for use in the experiment. Solutions were then applied to the anterior 2/3rds of each subject's tongue with a Q-tip. Each solution was tested on five distinct locations on the tongue in the following fashion. The experimenter would apply a solution to a specific spot. The subject would identify the taste qualities recognized in the solution by pointing to a sheet listing the taste qualities. Then the subject was instructed to rinse with water before the experimenter applied the next solution. Data were collected in a spreadsheet, in which identifications were given a value of 1 and non-identifications given a value of 0. Two sessions were performed per subject, one with a control water rinse and a second with a chlorhexidine rinse. The data, converted to proportions, were statistically analyzed using t-tests.

Results: There was no conclusive evidence that location of the stimulus had a significant impact on taste qualities perceived. As hypothesized, NaCl was most frequently "salty" prior to Peridex and, after Peridex treatment rinse, NaCl was more frequently "tasteless" ($p < 0.004$) regardless of how concentrated. The proportion of times when NaCl was detected as tasteless with/without Peridex was 2.03; meaning that it was twice as frequently identified as "tasteless" after the rinse. In contrast, the frequency at which "sweet" was used to describe sucrose was equal with or without Peridex; the proportion was 1.09. Sodium benzoate, a monovalent cationic salt, was most frequently labeled "sweet" compared to "bitter" prior to Peridex ($p < 0.04$); the "sweet/sweet+bitter" proportion equaled 0.92. However, sodium benzoate was most frequently identified as "bitter" compared to "sweet" after Peridex rinse ($p < 0.002$); when the "sweet/sweet+bitter" proportion equaled 0.12. Also, monovalent cation salt Na₂SO₄ was identified as salty fewer times after use of Peridex ($p < 0.04$), while the divalent cation salt CaCl₂ tasted the same throughout the study. This supports the hypothesis that monovalent cationic but not divalent cationic salt-taste is affected by Peridex rinse.

Conclusions and Future Directions: The study confirmed previously published results regarding ageusia to NaCl with chlorhexidine treatment, without effect on sucrose, or "sweet" taste. Neither variation in stimulation site nor variation in NaCl concentration from 0.1-1.0 M affected the salty-taste ageusia on the anterior portion of the tongue measured after treatment with Peridex (0.12% chlorhexidine gluconate). (1) Future testing of applications to more posterior lingual sites, weaker and stronger NaCl concentrations, as well as chlorhexidine rinses at lower concentrations than Peridex are required for development of additional hypotheses on mechanism of action. (2) Our experiments with salts other than NaCl, which include a variety of chemical compositions and ionic characteristics, also provide insight into the non-salty tastes that result from salt-taste transduction. Specifically, future studies are encouraged by the novel interaction observed between Peridex and sodium benzoate, which turned this salt's usual sweet taste into bitter.

Support: University of Connecticut School of Dental Medicine Alumni Fellowship Fund.

References:

- Cunha, J. Side effects of Peridex (chlorhexidine gluconate 0.12% oral rinse)." *RxList*. RxList Inc. Web. 9 Mar. 2015. <<http://www.rxlist.com/peridex-side-effects-drug-center.htm>>.
- Frank, ME, Gent, JF, and Hettinger TP. Effects of chlorhexidine on human taste perception." *Physiology & Behavior* 74 (2001): 85-99. Print.

Cell Adhesive Hydrogels for Bone Regeneration

Christina Klecker¹, Shalini V. Gohil², Lakshmi S. Nair^{1,2,3}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Orthopaedic Surgery, Institute for Regenerative Engineering, University of Connecticut Health, Farmington

³Department of Materials Engineering, Department of Biomedical Engineering, Institute of Material Science, University of Connecticut, Storrs

Injectable hydrogels are raising significant interest as optimal biomaterials for the delivery of cells and bioactive molecules to support tissue regeneration [1]. Chitosan has emerged as an ideal biomaterial for this purpose due to its natural abundance, in vivo degradation, biocompatibility, aqueous solubility, antibacterial nature, and exceptional wound healing properties [2]. Previous studies have demonstrated the excellent bioactivity of chitosan derivatives for chondrocyte delivery [3], supporting its efficacy as a synthetic extracellular matrix (ECM). However, the lack of cellular spreading in injectable chitosan based hydrogels raises challenges in using them as a delivery system for adherent cells, such as osteoblasts, to support bone regeneration. Therefore, the goal of this study was to develop a novel approach to increase the cell adhesiveness of injectable chitosan hydrogel by incorporating peptide binding sequences in the gel that may facilitate attachment and spreading of the encapsulated cells.

Injectable chitosan gel was prepared by the chemical modification of glycol chitosan (GC) polymer with 3-(4-hydroxyphenyl) propionic acid (HPP), as reported by this lab previously [1]. The quantification of available primary amine groups remaining after the modification was determined using Trinitrobenzene sulfonic acid (TNBSA) assay and NMR analysis. Subsequently, different concentrations of Arginine-Glycine-Aspartic Acid (RGD) peptides were incorporated into the polymer structure using carbodiimide chemistry. The enzymatically cross-linked injectable gels were prepared by mixing the RGD modified polymers with hydrogen peroxide (HP) and horse radish peroxidase (HRP). Lastly, 7F2 mouse osteoblast cells were encapsulated in the RGD modified and unmodified chitosan hydrogels and cultured for various time periods. Cell viability and morphology was followed as a function of time using LIVE/DEAD fluorescent staining assay.

The study demonstrated for the first time the feasibility of developing a range of RGD modified glycol chitosan injectable hydrogels with different physical properties by varying the concentrations of HP and HRP. We also identified a concentration-dependent increase in cellular spreading in RGD modified chitosan gels, indicating that a critical local concentration of RGD within the gel is required to facilitate cellular spreading. The promising results provide strong evidence for continued exploration of injectable glycol chitosan hydrogel as a cell delivery vehicle for bone regeneration. Current studies are focused on combining RGDs with other bioactive peptide entities to further enhance the biological activity of the delivery system, as well as in vivo studies to evaluate the potential therapeutic efficacy of the injectable.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Gohil, S. V. et al. Evaluation of enzymatically crosslinked injectable glycol chitosan hydrogel. J. Mater. Chem. B 3, 5511–5522 (2015).
2. Brittain, S. B. Development and Characterization of a Bioactive Injectable Chitosan Hydrogel for Bone Repair. Masters Theses, Paper 418, (2013).
3. Jin, R. et al. Injectable chitosan-based hydrogels for cartilage tissue engineering. Biomaterials 30, 2544–2551 (2009).

Healthcare Workers' Self-reported Knowledge, Attitudes, and Practice Implications Regarding Mental Health Care in Rural Uganda

Julia A. Koretski¹, Kevin D. Dieckhaus MD^{1,2}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Division of Infectious Diseases, UConn Health, Farmington, CT

Introduction: There are fewer than 0.1 psychiatrists per 100,000 population in Uganda, and they are distributed disproportionately between urban and rural areas.¹ The country is challenged by limited resources for managing the increasing recognition of mental health disorders.² Mentally ill patients are frequently provided with inappropriate and incorrect treatments.³ Lack of community mental health support in Uganda is seen as a cause of stigma associated with mental illness.⁴ Facilitation of early detection and intervention for mental health problems may be achieved through development of training programs for generalist healthcare workers (HCWs). The current study aimed to assess knowledge, attitudes, and implications for practice regarding mental health care among HCWs at the primary care level in a rural setting in Uganda.

Methods: Structured interviews with 65 HCWs were conducted at six healthcare facilities in the Kisoro district of Southwestern Uganda. The IRB-approved survey instrument was adapted from previously validated questionnaires.^{5,6} Independent variables included the participants' background and self-reported knowledge on diagnosis/treatment of mental illness. Primary outcome variables included perceived self-competency of mental health clinical management, therapeutic commitment, and stigma against mentally ill patients. Responses were scored on a 7-point Likert-type rating scale.

Results: Higher degrees of self-reported knowledge were associated with higher levels of perceived self-competency ($p < 0.01$) and higher therapeutic commitment ($p < 0.01$). HCWs who had received some form of mental health training were found to have higher levels of perceived self-competency than HCWs with no such training ($p < 0.05$). HCWs with higher levels of training (i.e., physicians and clinical officers) had lower levels of stigma than nurses ($p < 0.05$). The length of post-secondary education was also inversely associated with stigma levels ($p < 0.05$). HCWs at the local private hospital with no mental health specialist on staff self-reported a lower degree of knowledge on mental illness management than did their colleagues in the public sector with access to a psychiatric referral system ($p < 0.05$), despite having, on average, higher levels of post-secondary education ($p < 0.01$).

Conclusions: Educational programs for HCWs should focus on stigma reduction and improvement of knowledge on diagnosis and treatment of mental health disorders. Special focus should be on nurses, who are often the primary provider. Access to a psychiatry specialist is shown to be associated with higher self-reported knowledge on mental illness management, and thus higher perceived self-competency and therapeutic commitment – elements that lead to more effective practices.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. WHO-AIMS Report on Mental Health System in Uganda, WHO and Ministry of Health, Kampala, Uganda, 2006.
2. Ndyabangi S, Basangwa D, Lutakome J, Mubiru C. Uganda mental health country profile. *Int Rev Psychiatry*. 2004; 16(1-2):54–62.
3. Cooper S, Ssebunnya J, Kigozi F, Lund C, Flisher A, MhaPP Research Programme Consortium. Viewing Uganda's mental health system through a human rights lens. *Int Rev Psychiatry*. 2010; 22(6):578–588.
4. Quinn N, Knifton L. Beliefs, stigma and discrimination associated with mental health problems in Uganda: implications for theory and practice. *Int J Soc Psychiatry*. 2014; 60(6):554–561.
5. Lauder W, Reynolds W, Reilly V, Angus N. The development and testing of the Mental Health Problems Perception Questionnaire. *J Psychiatr Ment Health Nurs*. 2000; 7(3):221–226.
6. Uçok A, Soygür H, Atakli C, Kuşcu K, Sartorius N, Duman ZC, Polat A, Erkoç S. The impact of antistigma education on the attitudes of general practitioners regarding schizophrenia. *Psychiatry Clin Neurosci*. 2006; 60(4):439–443.

The Effect of Varying Intensities of LIPUS (Low Intensity Pulsed Ultrasound) on the Rate of Orthodontic Tooth Movement and Osteoclastic Activity in Mice

Authors: Lee, Daniel; Rangiani, Afsaneh; Yadav, Sumit

Department: University of Connecticut School of Dental Medicine; University of Connecticut School of Dental Medicine Department of Orthodontics; University of Connecticut Health Center

Objective: Low Intensity Pulsed Ultrasound (LIPUS) delivers acoustic pressure waves as a mechanical energy for therapeutic purposes. Previous studies have demonstrated contradictory results about the effects of LIPUS on OTM (orthodontic tooth movement) and osteoclastic activity. The present study was designed to investigate the role of LIPUS and different intensities on osteoclastic activity and the rate of OTM by comparing the amount of OTM and osteoclast number by using 15, 30 and 50 mW/cm² intensity.

Methods: The orthodontic appliances were placed between the first molars and upper central incisors in mice under general anesthesia. The WT male BALB mice were divided randomly into 4 groups with 6 animals and were subjected to 20 minutes of LIPUS treatment every 3 days at intensities of 15, 30 and 50 mW/cm², with the last group being control. Animals were sacrificed after 2 weeks and samples were used for Micro CT analysis and paraffin embedding for TRAP staining. Statistical analyses were conducted by Mann Whitney-testing.

Results: The amount of tooth movement was reduced in both the 15 and 50 mW/cm² intensity groups, but this reduction was marginal and not significant. There was a trend of increased movement in the 30 mW/cm² group compared to control ($P=0.08$), but it was only significant when compared to the 50 mW/cm² group ($P<0.01$). The osteoclast count also showed increased number and activity in the 30 mW/cm² group compared to the 15 and 50 mW/cm² groups.

Conclusion: Different intensities of LIPUS may have an effect on the amount of tooth movement and osteoclastic activity. Using 30 mW/cm² increases the bone turnover while 50 mW/cm² seems to have an inhibitory effect. Therefore for orthodontics purposes 30 mW/cm² can be used for increasing the rate of tooth movement while 50 mW/cm² might have a clinical use to reduce the amount of relapse after OTM is finished. However, further preclinical and clinical research is needed before final delineation of optimal LIPUS administration.

Future: The results of this study can be used for future investigations in clinical trials in humans to measure the amount of relapse and acceleration of tooth movement in different LIPUS intensities.

Support: Fellowship support from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving

Rapid and Effective Revitalization of Bone Allografts

Ling Lei¹, Anslip A N², Barbu R², Joshi S², Nukavarapu SP³

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Materials Science & Engineering, University of Connecticut, Storrs, CT

³Institute for Regenerative Engineering, UConn Health, Farmington, CT

Repairing large segmental bone defects has been a significant challenge in the field of orthopedic surgery. Allografts as a natural substitute have become the most commonly used bone-grafting technique. They provide mechanical strength needed for bone defects and they are histocompatible. Moreover, they have unlimited supply and are much less costly in comparison to autografts. However allografts are associated with a small risk for disease transmissions. And during the sterilization process the cellular contents and biological factors are greatly reduced. The aim of this study was to revitalize allografts by forming an “allograft-gel” hybrid graft using bone-forming cells and a patient-derived hydrogel.

In order to harvest fibrinogen-rich plasma, platelet-poor plasma (PPP) was separated from human peripheral blood using the MAGELLAN® technology. Calcium chloride was then added to activate the gelation between fibrinogen and thrombin to create the fibrin gel. For our preliminary study, we studied the cell retention of the patient-derived hydrogel using poly(lactic-co-glycolic acid), PLGA, scaffolds and mouse pre-osteoblastic cells, MC3T3s. We then studied the cell retention of hybrid allograft-gel system using hydrogel, canine bone allografts and MC3T3s. The MTS assay was performed to quantify viable cells. To assess cell spreading and cell density, the hybrid grafts were cultured for 1, 7 and 14 days and stained for live-dead cells. The stained cells were visualized via confocal imaging. Allograft with no hydrogel but loaded with MC3T3s served as the control group. All quantitative data was expressed as mean and standard deviation. One-way analysis of variance was used to compare differences between cell loading efficiencies of the “allograft-gel” hybrid graft and control groups (n=3) in vitro.

Our results indicated that as a completely automated and close-looped system magellan system was able to separate platelet-poor-plasma from patient's peripheral blood. Derived plasma gelation with CaCl₂ showed that it is possible to form hydrogel intra-operatively without using the animal derived Thrombin. Cell retention data of the scaffold and the plasma-derived hydrogel group showed significantly higher cell retention of the MC3T3s, compared to the scaffolds without the hydrogel. Similar result was observed in the hybrid allograft-gel system.

Through this study, for the first time, we have shown the feasibility of developing a patient-derived hydrogel by combining plasma with calcium chloride. Cell retention studies have shown that it is possible to efficiently seed scaffolds/allografts with bone-forming cells. The long-term objective of this study is to effectively revitalizing allograft at the bedside during orthopedic surgery.

Supported by: The work was supported by the UConn School of Medicine Summer Research and a junior investigator award from the Musculoskeletal Transplant Foundation (MTF)

References:

1. Finkemeier CG. Bone-grafting and bone-graft substitutes. J Bone Joint Surg Am. 2002;84-A(3):454-64.
2. Delloye C, Cornu O, Druez V, Barbier O. Bone allografts: What they can offer and what they cannot. J Bone Joint Surg Br. 2007;89(5):574-9
3. Igwe JC, Mikael PE, Nukavarapu SP. Design, fabrication and in vitro evaluation of a novel polymer-hydrogel hybrid scaffold for bone tissue engineering. J Tissue Eng Regen Med. 2014;8(2):131-42.

Serum Levels of Prestin in Response to Cisplatin Induced Ototoxicity as an Early Indicator of Acquired Sensorineural Hearing Loss

Benjamin Liba¹, Kourosh Parham, M.D., Ph.D.²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Surgery, Division of Otolaryngology - Head & Neck Surgery*

Hearing loss affects approximately 5% of the world's population. In the United States alone almost 50 million people are affected, with 60% of the veterans returning from war complaining of hearing loss or tinnitus (1,2). The process of permanent sensorineural hearing loss initially involves the death of outer hair cells (OHCs) following exposure to either acoustic trauma or ototoxic agents. The higher frequency basal regions of the cochlea are damaged initially with apical progression towards lower frequencies (3). Clinically these losses are detected with such tools as auditory brainstem response (ABR) threshold measurements. However, these methods are insufficient in terms of early detection that would allow for interventions that may slow or even halt the irreversible progression of hearing loss. Biomarkers are commonly used for detection of disease processes and provide an easy and affordable method of early diagnosis. Here we show that measurement of prestin, an inner ear protein found specifically in the basolateral membrane of OHCs, can serve as a sensitive biomarker of OHC injury, and is detectable prior to any significant changes in a functional measure, auditory brainstem response (ABR) thresholds. Following injection with cisplatin, hearing thresholds of mice were measured using click evoked ABR. These measurements revealed no significant changes in hearing thresholds. However, subsequent serum analysis revealed that prestin levels were in fact increased. Since prestin is uniquely expressed in outer hair cells, the current results suggest prestin expression in the cisplatin-exposed outer hair cells is upregulated. This provides insight into some of the pathophysiological mechanisms related to tinnitus as well as identifying a possible biomarker for early detection of hearing loss. There is major translational significance for such a biomarker as it could be used for monitoring of toxicity when treating patients with antibiotics and chemotherapeutic agents with ototoxic potential. In addition, it may provide a means by which we can diagnose and treat the many members of our population suffering from hearing loss that are currently unavailable.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Organization WH. Deafness and Hearing Loss: Fact sheet. 2014; www.who.int/mediacenter/factsheets/fs300/en. Accessed December 26, 2014.
2. Foundation HH. Hearing Loss & Tinnitus Statistics. 2014; hearinghealthfoundation.org/statistics.
3. Schacht J, Talaska AE, Rybak LP. Cisplatin and aminoglycoside antibiotics: hearing loss and its prevention. *Anatomical record* 2012; 295:1837-1850.

Assessing Factors Influencing Childhood Nutrition in Haiti

Jonathan B. Lis¹, Judy M. Lewis²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*University of Connecticut Department of Community Medicine and Health Care, Farmington, CT*

Introduction: Malnutrition is a major problem for children under 5 years in the North Department of Haiti: 25% are stunted and 10% are wasted. Malnourished children are at high risk of permanent physical and cognitive deficits.

Methods: 53 caregivers of Haitian children ages 6 months to 5 years interviewed at three health clinics (2 rural, 1 urban) in northern Haiti. Nutritional status was based on enrollment in the Medika Mamba malnutrition program. A 110-item questionnaire was used to assess caregiver demographics, socioeconomic status, food portion and variety, nutritional knowledge, and beliefs.

Results: Low caseloads resulted in low statistical power. Descriptive trends included 6 months younger children in the urban Medika Mamba program; and that malnourished children had lower averages for weekly consumption of servings of protein (9 servings per week), fats (3 servings per week), and fruits and vegetables (5 servings per week), but higher consumption of carbohydrates (4 servings per week). There was no difference in Dietary Diversity Scores. Simple carbohydrates such as rice, bread, and pasta comprised the major proportion of the children's diets in both locations. Goat meat, eggs, and beans were major protein sources for both rural and urban families, with the latter also consuming fresh fish and chicken. Socioeconomic status was similar.

Conclusions: This study suggests that a diet high in calories from simple carbohydrates and deficient in micronutrients was associated with malnutrition. Increased food diversity and consumption of proteins and should be promoted but will require further research to understand the nutrition and feeding knowledge and practices of caregivers. Because socioeconomic factors were not significant, Parents with healthy, nourished children with similar economic and situational constraints could provide practical and culturally appropriate strategies to prevent malnutrition.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Ministry of Public Health and Population [le Ministère de la Santé Publique and de la Population] (MSPP), Haitian Childhood Institute [l'Institut Haïtien de l'Enfance] (IHE) and ICF International. 2013. 2012 Haïti Mortality, Morbidity, and Service Utilization Survey: Key Findings. Calverton, Maryland, USA: MSPP, IHE, and ICF International.

Secretome of Resolvin E1-activated Osteoblasts

Jia Liu¹, Yiyang Zhu², Karim El-Kholy², Shevali Kansal², David Shafer¹, Thomas Van Dyke², Markus Hardt²

¹ UConn School of Dental Medicine, Farmington, CT 06030; ² The Forsyth Institute, Cambridge, MA 02142

Objective: Resolvin E1 (RvE1) has potent anti-inflammatory activities and directly impacts bone remodeling in experimental periodontitis. To provide a comprehensive understanding of the actions of RvE1 on osteoblast-mediated organic matrix formation and autocrine and paracrine functions, the impact of RvE1 on osteoblast-secreted proteins was investigated using a proteomic approach.

Methods: Primary bone cell cultures were established with cells isolated from neonatal mouse calvaria. After differentiation, cells were stimulated with IL-6 and IL-6 receptor to simulate inflammatory conditions. The treatment sample was simultaneously incubated with RvE1 for 24 h. Proteins from the conditioned cell medium were digested with trypsin using the filter-aided sample preparation (FASP) approach, followed by nanoLC-MS/MS analysis. Protein identification and quantification were performed using Maxquant. A custom R script was used to determine peptides unique to mouse, their corresponding protein sequences along with their differential expression levels and subcellular localization. Biological functions, pathways and networks were analyzed using the Ingenuity Pathway Analysis tool.

Results: A total of 370 proteins were detected. After filtering out peptides from bovine proteins originating from the FBS media, 247 mouse proteins were identified. Of them 193 proteins (78%) were annotated as secreted proteins. Thirty eight proteins (33 are secreted) were found to be differentially expressed between the two conditions (adjusted $p < 0.05$). Eighteen proteins including 5 cytokines (Ccl8, Cxcl2, Cxcl5, Cxcl1, Csf1) were increased, 20 proteins including 1 cytokine (Spp1) were decreased by resolvin E1 treatment. The differentially expressed proteins are annotated to be involved in multiple biological functions including hematological system development and function, inflammatory response, tissue development, immune cell trafficking and cellular movement.

Conclusions: This pilot study provides the first step toward a deeper understanding of how Resolvin E1 modulates protein secretion from osteoblasts. 193 secreted proteins were identified from osteoblast culture medium of which 33 proteins were found to be differentially expressed in absence or presence Resolvin E1. Therefore, Resolvin E1 had a significant impact on the secretome of osteoblasts in inflammation.

Future Directions: The implications of RvE1 actions in inflammation and bone remodeling need to be studied further.

Support: Supported in part by a 2014 AADR Student Research Fellowship, NIDCR grant DE015566, and a capital grant from the Massachusetts Life Sciences Center.

References:

Hasturk, H. et al. Resolvin E1 regulates inflammation at the cellular and tissue level and restores tissue homeostasis in vivo. *Journal of immunology* 179, 7021-7029 (2007).
Hasturk, H. et al. RvE1 protects from local inflammation and osteoclast- mediated bone destruction in periodontitis. *FASEB Journal* 20, 401-403 (2006).
Gao, L. et al. Resolvin E1 and chemokine-like receptor 1 mediate bone preservation. *Journal of Immunology* 190, 689-694 (2013).

Chondrocyte Progenitor Cells in Osteoarthritis

Michelle Llinas¹, Melanie Fisher², Caroline Dealy^{2,3}

¹UConn School of Dental Medicine; ²Department of Reconstructive Sciences; Center for Regenerative Medicine and Skeletal Development; ³Chondrogenics, Inc.

Objective: Osteoarthritis is a common disease of the joints which affects approximately 27 million Americans. This disease is characterized by the degeneration of the articular cartilage found at the ends of long bones in the joints of the body, including the knee, hip and shoulder. Once damaged, articular cartilage has little regenerative capacity. The loss of the articular cartilage causes pain, and loss of mobility. There is no cure yet for osteoarthritis, but cell-based therapies to repair damaged articular cartilage have been suggested to offer a potential therapeutic approach. However, current cell-based treatments have proven to be an inadequate solution, resulting in poor outcomes and lacking long term benefits. This may be because the source of the cells used, or the delivery method into the joint, is not suitable for cartilage repair and osteoarthritis treatment. The purpose of this experiment was to gather preliminary information on the use of a novel cell-injection approach for the treatment of osteoarthritis, using cartilage cells generated from human pluripotent stem cells.

Methods: Genetically immune-compromised mice (NIH-III strain) were subjected to surgical knee ligament transection to destabilize the joint and induce osteoarthritis. Four weeks after surgery, the knee joints were injected with either precursor chondrocytes or mature chondrocytes that had been derived from human embryonic stem cells; or vehicle control. Four weeks later, the joints were harvested, fixed, and embedded in wax. Sections were cut and prepared for histological examination to assess the degree of cartilage damage present in the joint. Cartilage morphology and proteoglycan accumulation were evaluated using Safranin-O staining, and scored using a semi-quantifiable scale endorsed by the Orthopedic Association Research Society. Cartilage breakdown was assessed using immunohistochemistry with an antibody that recognizes aggrecan fragments.

Results: Eight weeks after surgical induction of osteoarthritis, the joints of vehicle-injected osteoarthritic animals showed mild damage, with localized loss of proteoglycan staining, and presence of small surface cracks in the articular cartilage. Focal regions of matrix turnover were present at the distal and lateral corners of the articular cartilage surfaces. At the same time point, the joints of osteoarthritic animals previously injected with human stem cell-derived cartilage precursor cells or mature cartilage cells tended to show more moderate damage, and more widespread matrix degradation. However, histological scoring of the cartilage morphology did not reveal significant differences among the groups, due to extensive variability from knee to knee within the groups.

Conclusions: This preliminary study revealed that differences in the appearance of the articular cartilage of the joints of the animals did not differ significantly between control and cell-injected groups. The study confirms prior statistical analyses which predicted that 5 control and 10 experimental animals would be required to achieve sufficient power at $p < 0.05$, a sample size outside the scope of this summer project. Surprisingly, a trend was observed towards increased cartilage degradation in cell-injected knees. It has recently been suggested that local inflammation in response to introduction of exogenous cells may lead to localized tissue damage and play a role in osteoarthritis induction in this model. These studies will be useful in developing new strategies for cartilage repair and osteoarthritis treatment.

Future Directions: Future studies will utilize additional control and cell-injected knees, and/or an alternate animal model of osteoarthritis that does not rely on surgical ligament transection, which may reduce variability of cartilage damage within groups. Future studies will also focus on the role of the cells in stimulating endogenous host cartilage progenitor cells to repair damaged cartilage.

Support: Support was from the Connecticut Innovations Stem Cell and Regenerative Medicine Initiative and from the UConn School of Dental Medicine Alumni Fellowship Fund and the UConn-TIP Intern Program.

Albuminuria Leads to Proximal Tubule Damage through a CD13-dependent Mechanism

Robin Lo¹, Claire Gerber², Mallika Ghosh², Linda Shapiro²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Center for Vascular Biology, UConn Health, Farmington, CT

Certain disease states, such as Diabetes Mellitus (DM), damage glomerular function and result in albuminuria which promotes renal damage.^{1,2} Urinary proteins are efficiently resorbed via receptor-mediated endocytosis in the epithelial cells of the renal proximal tubules (PT) by the endocytic protein complex of megalin and cubulin.^{1,2} Although reduction of urinary protein levels is known to be therapeutically beneficial, some studies show that proteinuria-induced lysosomal overload results in cell damage.^{3,4} Furthermore, while albuminuria is considered a clinical biomarker for renal damage, it is generally not detected until damage is quite advanced.⁵ CD13 has previously been shown to be a negative regulator endocytosis and endocytic recycling in other cell types.⁶ Here we show that mouse CD13 knock out (KO) PT cells attenuate the damaging effects of albuminuria by increasing resorption of albumin both in vitro and in vivo. Bovine serum albumin treated mouse primary CD13 KO PT cells exhibited decreased cleaved caspase-3 levels while exhibiting increased albumin uptake compared to primary wild type (WT) PT cells. A 9-day model of albumin overload confirmed similar findings of increased albumin uptake in PT cells of global CD13 KO mice. Furthermore, we show that certain brush border enzymes may be viable surrogate biomarkers to detect early renal damage. A streptozocin (STZ) induced mouse model of DM demonstrated increased urinary levels of proximal tubular proteins – CD13, CD26, and collectrin – by western blot at 4/8/12/16 weeks following onset of DM compared to baseline levels pre-STZ treatment. Our results demonstrate that CD13 serves as a key mediator for albuminuria-induced PT damage and along with other brush border enzymes, as possible biomarkers for early renal damage. We anticipate that our findings serve as a starting point for identifying the role of CD13 in albuminuria-induced renal damage from DM or any other etiology leading to renal injury and that it may lead to novel therapies targeting CD13 to delay or prevent further disease progression from chronic kidney disease to end stage renal failure. Establishing urinary CD13 as a better predictive biomarker for early renal damage and disease progression would aid clinicians in diagnosing patients, establishing therapeutic plans, and monitoring treatment efficacy.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Lopez-Novoa JM, et al. Etiopathology of chronic tubular, glomerular and renovascular nephropathies: clinical implications. *J Transl Med.* 2011;9:13.
2. Mina-Osorio P. The moonlighting enzyme CD13: old and new functions to target. *Trends Mol Med.* 2008;14(8):361-371.
3. Bauer EM, Shapiro R, Billiar TR, Bauer PM. High mobility group Box 1 inhibits human pulmonary artery endothelial cell migration via a Toll-like receptor 4- and interferon response factor 3-dependent mechanism(s). *The Journal of biological chemistry.* 2013;288(2):1365-1373.
4. Saito A, et al. Molecular mechanisms of receptor-mediated endocytosis in the renal proximal tubular epithelium. *Journal of biomedicine & biotechnology.* 2010;2010:403272.
5. Ware LB, et al. Renal cortical albumin gene induction and urinary albumin excretion in response to acute kidney injury. *Am J Physiol Renal Physiol.* 2011;300(3):F628-638.
6. Ghosh M, Subramani J, Rahman MM, and Shapiro LH. CD13 restricts TLR4 endocytic signal transduction in inflammation. *J Immunol.* 2015;194(9):4466-76.

Investigation of the Structural Interactions of the Spectrin and GEF Domains of Kalirin-7 via FRET Assay

Michael Lorinsky¹, Dick Mains², Betty Eipper³

¹*University of Connecticut School of Medicine, UConn Health, Farmington CT*

²*Department of Neuroscience, UConn Health, Farmington CT*

³*Department of Molecular Biology and Biophysics, UConn Health, Farmington CT*

Learning and memory require changes in the structure and function of the excitatory synapses found at the tips of dendritic spines. The *KALRN* gene generates a family of proteins including Kalirin-7, an isoform that localizes to the post-synaptic density. *KALRN* mutations have been linked to neuropsychiatric disorders such as schizophrenia. Kalirin-7, a 195 kDa protein, contains multiple functional domains, including a guanine nucleotide exchange factor (GEF) domain, which activates Rac1 by catalyzing GTP binding. Rac1 regulates actin polymerization, a process central to spine growth. To better understand spine formation, I focused on the regulation of Kalirin-7 GEF activity. Kalirin-7 is less active than its isolated GEF domain, suggesting a folded structure in which the other domains [spectrin repeats (SR) 1 to 9 and a PDZ binding motif (PBM-end)] exert an inhibitory effect. To investigate this hypothesis, PBM-end was appended to the GEF domain (GEF-PBM-end) and an increasing number of spectrin repeats (SR9-end, SR8-end, SR7-end, SR6-end, SR5-end), were appended to the N-terminus of GEF-PBM-end. Each construct was expressed in mammalian cells along with a Rac-1 biosensor. GTP binding to the Rac-1 biosensor produces a conformational change that brings its yellow and cyan fluorescent protein domains close enough together to fluoresce at 525 nm. This is distinguished from GDP bound biosensor, which has minimal fluorescence at 525 nm. Analysis of the GEF activity of the six constructs showed that GEF-PBM-end, SR9-end, and SR8-end were as active as the isolated GEF domain. In contrast, SR5-end, SR6-end and SR7-end were substantially less active. This suggests that the presence of SR7 allows the protein to adopt a folded structure that suppresses GEF activity. Further biophysical and crystallographic studies are under way to characterize this structure and investigate regulatory mechanisms that may modulate Kalirin-7 GEF activity.

Supported by: The UConn School of Medicine Summer Research Fellowship

References

1. Xin-Ming Ma, Megan Miller, KS Vishwanatha, Maegan Gross, Yanping Wang, Thomas Abbott, TuKiet Lam, Richard Mains, and Betty Eipper. "Nonenzymatic domains of Kalirin7 contribute to spine morphogenesis through interactions with phosphoinositides and Abl" *Molecular Biology of the Cell* 2014. 25: 1458-71.
2. Christine Remmers, Robert Sweet, and Peter Penzes. "Abnormal kalirin signaling in neuropsychiatric disorders" *Brain Research Bulletin* 2014. 103:29-38.
3. KS Vishwanatha, YP Wang, HT Keutmann, RE Mains, and BA Eipper. "Structural Organization of the Nine Spectrin Repeats of Kalirin" *Biochemistry* 2012. 51: 5663-73.
4. Peter Penzes. "Kalirin Signaling: Implications for Synaptic Pathology" *Mol Neurobiol* 2012. 45(1): 109–118

Maternal Perception of Child Anxiety Symptoms: The Role of Prolactin

Jelena MacLeod, MHS¹, Wendy Silverman, PhD², Krista Basile, MHS², Alyssa Martino, BA², Eli Lebowitz, PhD²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Yale Child Study Center, Yale School of Medicine, New Haven, CT

Background: Prolactin is an integral primer of the physiological, neurological, and behavioral changes necessary for motherhood¹⁻³. Animal studies have implicated prolactin in modulating maternal responsiveness to distress in offspring. For example, administering prolactin to the central nervous system in rats has been shown to attenuate the responsiveness of the Hypothalamic-Pituitary-Adrenal stress axis in a dose-dependent manner, promoting increased maternal protectiveness during the peripartum period towards pups in distress^{4,3}. Given the neuromodulatory effects of prolactin on various endocrine axes implicated in animal maternal behavior and stress response, there is likely an interaction of the prolactin system with anxiety-related phenomena involving the human mother-child dyad.

A common challenge in the assessment and treatment of childhood anxiety is the discrepancy between a mother's perception of her child's anxiety, and the child's own self-report. Previous studies have linked underreporting of child anxiety to maternal depression, which is associated with a deficiency of the neurotransmitter dopamine^{5,6}. Prolactin is constitutively inhibited through hypothalamic secretion of dopamine¹. In a low-dopamine state such as depression, prolactin levels may be pathologically elevated, and might impact mother-child interactions. Our study builds on previous research and explores the role of prolactin levels on maternal perception of anxiety symptoms in clinically anxious children.

Methods: We measured serum prolactin levels in blood samples from mothers of clinically anxious children (N=65, aged 7-17) with primary anxiety disorders as determined by the Anxiety Disorders Interview Schedule (ADIS IV). Mothers and children also completed anxiety rating scales.

Results: Results show that maternal prolactin was negatively correlated with maternal ratings of child anxiety ($r_{64} = -0.31$, $p < 0.05$), and that mothers with high prolactin levels were significantly more likely to underreport the severity of their child's anxiety relative to the child's self-rating ($\chi^2 = 6.03$, $p < 0.05$). Hierarchical multiple linear regression indicated that maternal prolactin levels significantly contributed to predicting maternal ratings of child anxiety, independent of other predictors including the child's self-rating and the mother's rating of her own anxiety.

Conclusion: Maternal peripheral prolactin levels are associated with mothers' perception of children's anxiety. Prolactin's unique regulation via dopamine inhibition might help explain its dampening effect on maternal perception of child anxiety. More research is needed to further elucidate prolactin's contribution to maternal cognition and behavior, and its subsequent effect on the family system of an anxious child.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Grattan DR. The hypothalamo-prolactin axis. *J Endocrinol*. 2015; 226(2):T101-T122.
2. Larsen CM, Grattan DR. Prolactin, neurogenesis, and maternal behaviors. *Brain Behav Immun*. 2012; 26: 201-209.
3. Torner L, Toschi N, Nava G, Clapp C, Neumann ID. Increased hypothalamic expression of prolactin in lactation: involvement in behavioral and neuroendocrine stress responses. *Eur J Neurol*. 2002; 15: 1381-89.
4. Torner L, Toschi N, Pohlinger A, Landgraf R, & Neumann ID. Anxiolytic and anti-stress effects of brain prolactin: improved efficacy of antisense targeting of the prolactin receptor by molecular modeling. *J Neurosci*. 2001; 21(9): 3207-14.
5. Affrunti NW, Woodruff-Borden J. The effect of maternal psychopathology on parent-child agreement of child anxiety symptoms: A hierarchical linear modeling approach. *J Anxiety Disord*. 2015; 32: 56-65.
6. Dunlop BW, Nemeroff CB. The role of dopamine in the pathophysiology of depression. *Arch Gen Psychiatry*. 2007; 63(3): 327-37.

Chikungunya in Jamaica

Jessica Malcolm, MSII¹, Kevin Dieckhaus, MD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Division of Infectious Diseases, University of Connecticut School of Medicine, UConn Health, Farmington, CT*

Chikungunya is a highly contagious arboviral infection that has begun to rapidly spread throughout many countries of the Caribbean, with a vast outbreak occurring in Jamaica. This study aims to assess the knowledge, attitudes, beliefs, and practices of disease prevention in regards to this viral infection. Chikungunya is transmitted to humans via *Aedes* mosquitoes. The acute phase of the infection lasts for 1 – 2 weeks and often presents with fever, arthritis, and arthralgia. Unfortunately, many individuals who recover then enter into the chronic phase of this infection. These individuals experience recurrent episodes which include mild to severe arthritis and/or arthralgia for months to years post infection. In 2014, the Jamaican government created an Emergency Response team to reduce the number of Chikungunya infections that were occurring on the island. Jamaican Parish Health Departments made increased efforts to address the public lack of knowledge regarding Chikungunya through health education. However, there are currently no scientific studies which fully explore the effectiveness of this spread of public health information within the Jamaican population. This study will remedy this gap in the literature. The data was obtained from standardized questionnaire interviews conducted with Jamaican citizens (ages 18 – 84) at a local medical center in the parish of Kingston, the capital of Jamaica. This location provides care for individuals from many different geographic locations and socio-economic backgrounds in Jamaica. The population of the study included 200 subjects: (53%) female and (47%) male. The mean respondent age = 44 years and the mean education= 16 years. Many participants (66%) reported getting most of their information about Chikungunya from the government. However, of those individuals only (39%) stated that they frequently trusted the government's information. It was shown that individuals who had a decreased knowledge of Chikungunya infection transmission mechanisms had an inversely proportional relationship to their self-perceived risk of acquiring Chikungunya ($p<0.01$). It was also shown that individuals who were of lower socioeconomic status had an proportional association with retention of health promoting messages related to Chikungunya prevention ($p<0.01$).

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Weaver SC, Lecuit M (2015) "Chikungunya Virus and the Global Spread of a Mosquito Borne Disease". *N Engl J Med* 372:1231-1239.
2. Dhar-Chowdhury P, Haque CE, Driedger SM, et al. (2014) "Community perspectives on dengue transmission in the city of Dhaka, Bangladesh". *Int Health* 6 (4): 306-316.
3. Moro ML, Gagliotti C, Silvi G, et al. (2010) "Knowledge, attitudes and practices survey after an outbreak of chikungunya infections". *Int Health* 2 (3): 223-7.
4. Setbon M, Raude J, and Pottraz D.(2008) "Chikungunya on Reunion Island: Social, Environmental, and Behavioural Factors in an Epidemic Context". *Population* 63(3):491-518.

TITLE

Barriers to Oral Health Care in Select Federally Qualified Health Centers in Connecticut: A Comparison of Rural vs. Urban Locations

AUTHORS

Raquel Manley – Affiliated with: University of Connecticut School of Dental Medicine and the Urban Service Track of the Connecticut Area Health Education Network

Geralynn McGee – Affiliated with: Hartford Legal Aide and the Community Health Center Association of Connecticut

OBJECTIVE

Oral health care is a vital aspect of total body health care. Unfortunately, many of Connecticut's underserved populations do not have access to oral health care or face other barriers to utilizing oral health care services. This project investigated the barriers patients of both urban and rural Federally Qualified Health Centers (FQHC) encounter when seeking care as described by FQHC personnel.

METHODS

For this research project we interviewed Dental Directors who practice in Community Health Centers in CT. In preparation for the interviews we reviewed information about FQHCs, how they are financed, organized, and which services they provide to patients. A thorough literature review was conducted to review current barriers to oral health care in this population using the definition of urban vs. rural and access vs. utilization as laid out by the Connecticut State Office of Rural Health and the US Department of Health Resources and Services Administration. A series of questions was developed addressing issues of access and utilization. Three rural and five urban federally qualified community health centers were chosen based on provider availability during project duration and FQHC membership in CHCACT. Conversational interviews with the Dental Directors of eight representative health centers were conducted. The project took place over a period of six weeks from July 1st 2015 until August 21st 2015.

RESULTS

This project found that the dental directors perceived the barriers to receiving oral health care in CHCACT FQHC's were, in descending order #1 – Oral Health and Poverty Culture, #2 – Cost of Care, #3 – Reimbursement Method, #4 – Transportation, #5 – Access, #6 – Health Literacy and finally #7 – Child Care.

In comparing rural vs. urban barriers to care the common issue perceived by dental directors was the prioritizing of oral health care for the patient. From there the issues split. For rural FQHC's the next most common barrier was recruiting dental providers and transportation of patients. For the urban FQHC's the next issue was the cost of care for the underinsured and uninsured.

CONCLUSIONS

The issue of barriers for oral health care is multi-factorial and without a single solution. The difference between the dental provider's expectations of patient behavior and patients' understanding and ability to meet those expectations was the most important and prevalent barrier to oral health care. The research also determined that oral health barriers between rural and urban FQHCs are more similar than they are different.

FURTHER DIRECTION

With the results of this project the Community Health Center Association of Connecticut will develop focus groups to decrease the barriers patients' face when accessing and receiving oral health care.

SUPPORT

This project was supported by the Connecticut Area Health Education Network and the Community Health Center Association of Connecticut.

Title: Lower-Dose 180° CBCT Offers Comparable Information for Mini-Implant Placement when Contrasted to Conventional 360° Protocol

Authors: A. Marczak¹, S. Yadav², S. Tadinada¹

Department/Institution: ¹Department of Oral Health and Diagnostic Sciences, Oral and Maxillofacial Radiology Division; ²Department of Craniofacial Sciences, Orthodontics Division

Objective: Temporary anchorages devices (TADS), also known as mini-implants, are temporarily fixed to bone for enhancing orthodontic anchorage. Accurate surgical placement of TADS without any perforation of the adjacent teeth is critical to its success or a risk of root resorption or nasal cavity or maxillary sinus perforation is possible^{1, 2}. A 360° rotation CBCT is conventionally used to predictably plan surgical TAD placement³. The objective of this study was to compare the outcome of surgical TAD placement by scanning the potential TAD site using a lower-dose 180° acquisition protocol and a conventional 360° acquisition protocol.

Methods: Ten dentate human skulls were used to provide 20 maxillary and 20 mandibular sites for potential TAD placement. The sites were randomly divided into two groups: 360° and 180° CBCT acquisition protocols. A small volume 180° and 360° CBCT scan of each site was acquired using the Morita Accuitomo-170 CBCT machine. For each group, a TAD was placed at the potential sites where the operator was randomly given either a 360° or a 180° acquisition CBCT. A follow-up 360° CBCT was done after TAD placement to serve as a gold standard to evaluate the location of the TAD and root perforation. Two raters, an oral and maxillofacial radiologist and an orthodontist, evaluated the scans.

Results: Ninety eight percent of TADs placed did not perforate any root structure. Two percent of the sites had a questionable appearance of perforation. On the Likert Scale, both the raters agreed that the subjective evaluation of the diagnostic quality between the two protocols, ability to make and read measurements of the sites and preferences for the specified diagnostic task were comparable. Cohen's Kappa showed a high inter and intra rater agreement

Conclusions: One hundred eighty degree acquisition CBCT protocol yields comparable diagnostic information in assessing the potential TAD site and preventing root perforation compared to a conventional 360° acquisition protocol. These results were also superior to those of a study conducted by Landin et al., which demonstrated a 55% occurrence of root perforation during TAD placement without imaging³. This alternate protocol results in a considerably decreased radiation exposure to the patient.

Future Directions: This study may provide important information to aid in establishing imaging protocols that maximize diagnostic efficacy while minimizing radiation dose.

Support: Fellowship support from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving.

References:

- 1) Bonnick AM, Nalbandian M, Siewe MS. Technological advances in nontraditional orthodontics. *Dent Clin North Am.* 2011;55:571–584, ix.
- 2) Cope, Jason B. "Temporary Anchorage Devices in Orthodontics: A Paradigm Shift." *Seminars in Orthodontics* 11.1 (2005).
- 3) Landin M, Jadhav A, Yadav S, Tadinada A: A comparative study between currently used methods and Small Volume-Cone Beam Tomography for surgical placement of mini implants. *Angle Orthod.* 2014 Oct 24. [Epub ahead of print] PMID:25343688

Understanding Predictors of Home Birth in Kisoro, Uganda

Kaitlin Markoja¹, Christine Nimwesiga², Kevin Dieckhaus¹

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Kisoro District Health Office*

Introduction: Maternal mortality for women in sub-Saharan Africa is 47 times greater than for women in the United States [1]. Uganda is among the highest contributors to global maternal mortality, where an estimated sixteen women die each day due to childbirth [2]. A critical way to reduce maternal deaths is to increase use of skilled, hospitalized care for childbirth. In Uganda, many women deliver from home, where necessary care is not readily available. Understanding the etiology for continued home birth even when appropriate facilities are present is important for improving utilization of services and decreasing maternal mortality.

Objectives: This retrospective cohort is the first to investigate factors contributing to home birth and to identify potential interventions in Kisoro, Uganda.

Methods: We surveyed 191 randomly selected women from 16 villages in Kisoro, Uganda; inclusion criteria were age greater than 18 and having given birth within the past three years. Our outcome variable was history of at least one home birth, and statistical analysis was performed in SPSS v.22.

Results: 42% of women surveyed had delivered from home in the past. Of the women who had delivered from home, more than half had experienced greater than one home birth. Multiple indicators of poor socioeconomic status including low education of mother and husband, literacy, and income correlated with incidence of past home delivery. Other factors such as distance between home and birthing facility, and sociocultural issues like perceived respect for home birth also correlated with home delivery. Women who delivered from home or facilities expressed generally positive views of health facility safety, procedures, and healthcare workers, indicating these are unlikely barriers to accessing care in Kisoro, in contrast to reports from other regions in Uganda. Use of prenatal care was comparable among women with and without history of home birth. Most women who delivered from home planned to deliver from a health facility, but failed to reach the facility prior to delivery. Women with a past history of home delivery responded favorably to the proposed concepts of a free ambulance, transportation reimbursement, and maternal waiting homes.

Conclusions: Most women surveyed prefer to deliver in a health facility. Our study highlights the need for improved transportation in order to improve health facility utilization. We also suggest that development of a detailed birthing plan during prenatal visits may increase facility-based delivery in Kisoro, Uganda.

Supported by: The UConn School of Medicine Summer Research Fellowship, The Arnold P. Gold Foundation for Humanism in Medicine Summer Research Fellowship

References:

1. WHO, UNICEF, The World Bank, UNFPA, United Nations Population Division. Trends In Maternal Mortality 1990 To 2013.; 2014.
2. WHO, UNICEF, UNFPA, The World Bank. Trends In Maternal Mortality: 1990 To 2010. World Health Organization; 2011.

Predictive Modeling in Cancer Survivorship

Granger Marsden¹, Nancy Baccaro², Alicia Dugan³, Cheryl Oncken³

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Neag Cancer Center, UConn Health, Farmington, CT*

³*Department of Medicine, UConn Health, Farmington, CT*

Cancer survivorship is intended to address not only post-cancer medical sequelae, but also helping the patient to understand and cope with life changing impacts from cancer. Failure to predict and address patient concerns may lead to a lack of critically important follow-up care for patients who need it most. The UConn Cancer survivorship program lacks a predictive model to assist in determining a patient's risks for experiencing distress prior to the patient directly reporting the distress. Enhanced prediction can lead to proactive rather than reactive follow up care. Distress may take time to develop and occur late in a patient's care. Since the psychological distress screening forms are often completed at the initiation of care, late occurring distress is likely to be missed and go untreated unless the patient directly reports distress. This project had two objectives: 1) gather and perform initial analysis on patient-reported data from UConn's cancer survivorship program to determine if a predictive model for patient distress risk factors was feasible, and, 2) identify the factors most associated with patient distress in the UConn patient population sample set. Sixty-six completed psychological distress screening forms were entered into a database along with de-identified patient data including variables such as distress level, age, type of cancer, treatment received, and other characteristics. Patients were divided into three categories based on their reported distress level. A decision tree model was estimated using the UConn data. The model was able to correctly predict low distress level patients with 85% accuracy, mid distress level patients with 66% accuracy, and high distress level patients with 83% accuracy. The most important explanatory variables in the model predicting distress level were the patient's physical problem score, the patient's emotional problem score, and the patient's age. High physical and emotional problem scores were associated with high degrees of distress. Surprisingly, younger age was also associated with higher distress levels. This initial analysis suggests that it may well be possible to develop a predictive model that would prove helpful in predicting likely patient distress levels during cancer survivorship. Such a model could be used to tailor follow up care and address the factors which put patients at the risk for experiencing high distress. Developing and testing a useful formal model will require the development of a significantly larger data set. While there is never a guarantee of modeling success, our initial results are quite encouraging.

References:

1. "Institute Of Medicine Report: Recognizing Psychosocial Health Needs To Treat The Whole Patient". *Journal of Oncology Practice* 4.3 (2008): 128-130. Web.
2. Archer-Nanda, Elizabeth. "Assessing Quality Outcomes In A Behavioral Oncology Program: Capstone Project". Bellarmine University, 2013. Print.
3. Mitchell, A. J. "Pooled Results From 38 Analyses Of The Accuracy Of Distress Thermometer And Other Ultra-Short Methods Of Detecting Cancer-Related Mood Disorders". *Journal of Clinical Oncology* 25.29 (2007): 4670-4681. Web. 21 Feb. 2016.

Design and Assessment of a Novel Database for Dermatological Images

Sarah Mattessich¹, Justin Finch MD^{1,2}

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Dermatology, UConn Health, Farmington CT*

Clinical photography is an essential tool for physicians and educators in dermatology. While digital images are easily appended to a patient's chart for immediate use, retrospective retrieval of databased photographs for research and didactic use is severely limited. No standardized methods have been used to catalogue digital photographs in the current system, restricting its efficiency for resource discovery.¹ Our goal is to generate a clinical photography database that incorporates medical descriptors into metadata to improve the efficacy of image searches as compared to the current, unindexed database.

The experimental design was conducted in two phases. Phase one included the creation of a new, indexed database. To accomplish this, a standard list of keywords was created based on disease, morphology, anatomical site, and histology; MRN numbers were used to collect images and patient records; and medical descriptors were linked into the image metadata using Adobe Lightroom software. Phase two included assessment of the new database. Eight dermatology residents used keywords to locate 10 specific diagnoses from both the indexed and unindexed databases, and image retrieval times were recorded and analyzed using Student's t-test. These keywords included "psoriasis," "tongue," "linear," "alopecia areata," "infantile hemangioma," "vitiligo," "neurofibromatosis," "granuloma annulare," "squamous cell carcinoma," and "bulla."

Results show that the average time to retrieve 10 images was significantly faster ($p < 0.05$) and more uniform using the new, indexed database (17.2 ± 3.3 sec) as compared to the current, unlabeled database (250.2 ± 122.0 sec), which showed a wider range of response times. The keyword category had no effect on response times. Response times for only two keywords, "linear" and "psoriasis," were not significantly faster using the new database.

We conclude that our novel database which incorporates medical descriptors into metadata is a superior system for retrieving dermatological images. We have shown that image searching with keywords is faster than the current scheme, which is organized by patient name and date of appointment. In addition, our system allows for comparison of specific diagnoses across multiple patients through the keyword search option. Our new database will better assist physicians and educators in identifying and sharing specific images for clinical and educational purposes.

Supported by: *The UConn School of Medicine Summer Research Fellowship*

References:

1. Ratner D, Thomas CO, Bickers D (1999). The uses of digital photography in dermatology. *Journal of the American Academy of Dermatology*; 41:749-56.

Characterizing the Differences in Inflammatory Processes between a Diabetic and Non-diabetic Rat Model of Posterior Glottic Stenosis

Michael Mei¹, Easwar Natarajan², Denis Lafreniere³

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Division of Oral Pathology, UConn Health, Farmington, CT*

³*Division of Otolaryngology, UConn Health, Farmington, CT*

The incidence of posterior glottic stenosis is reported to be as high as 14% of adults intubated longer than 10 days (Whited 1983). Posterior glottic stenosis (PGS) is a major problem involving scarring and narrowing of the larynx at the level of the glottis, most commonly caused by endotracheal intubation. Importantly, insulin-dependent diabetes is a factor associated with increased risk of developing PGS. There is a current paucity of knowledge regarding the inflammatory process in diabetic patients as compared to normal patients with respect to the laryngeal mucosa after trauma due to prolonged intubation. Here we compare the inflammatory processes of the laryngeal mucosa after trauma between diabetics and non-diabetics histologically. We developed a rat model of PGS using a laryngoscopic approach with direct trauma to the posterior glottis tissue. These models were developed in two groups, an experimental diabetic rat and a control non-diabetic rat group. We are currently conducting a preliminary study with H&E. Our pathologist was given de-identified laryngeal samples from both diabetic and non-diabetic rat models. We are currently awaiting results. After receiving the preliminary results, we will conduct immunohistochemical studies on our remaining samples. Our preliminary targets are M1 and M2 macrophages. Their dysregulation has been implicated in the development of fibrosis and abnormal laryngeal wound healing (Hillel 2015). Based on our conclusions, we hope to develop novel biomaterials to be used in endotracheal tubes that will decrease the incidence of posterior glottis stenosis in diabetic patients.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

Hillel AT, Samad I, Ma G, Ding D, Sadtler K, Powell JD, Lane AP, Horton MR. Dysregulated Macrophages Are Present in Bleomycin-Induced Murine Laryngotracheal Stenosis. *Otolaryngol Head Neck Surg.* 2015 Aug;153(2):244-50.
Nakagishi Y, morimoto Y, Fujita M, Ozeki Y, Maehara T, Kikuchi M. Rabbit model of airway stenosis induced by scraping of the tracheal mucoas. *Laryngoscope* 2005. 115:1087-1092.
Whited RE. Posterior commissure stenosis post long-term intubation. *Laryngoscope.* 1983. 93:1314-1318.

Barriers to Early Initiation of Breastfeeding in Rural India

Theresa Meotti¹, Kevin Dieckhaus, MD¹

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

Introduction: Proper breastfeeding practices, including initiating breastfeeding within the golden hour after birth, can have a large impact on the nutritional and health status of children in developing countries. Only 52% of infants in the state of Maharashtra, India met the criteria for early initiation of breast feeding in a study performed by the WHO. Pre-lacteal feeds, which are any food other than breast milk given to infants before breastfeeding, are commonly given to newborns in India and this represents an obstacle to exclusive breastfeeding and may introduce disease.

Purpose: To determine if the rates of proper breastfeeding initiation and administration of pre-lacteal feeds are improved in a rural, marginalized population that has had decades of sustained community health related interventions, and to identify what influences these behaviors.

Methods: A cross sectional study was completed for 50 women ranging in age from 16-35 years old, from 13 different villages in the block of Jamkhed, Maharashtra, India. An oral survey was administered to assess demographics, maternal health and antenatal care, educational exposure, breastfeeding practices including time of initiation and administration of pre-lacteal feeds, breastfeeding beliefs, attitudes, and perceptions, and support systems in relation to breastfeeding.

Results: The average age of women interviewed was 22.7 years (SD 3.91 yrs). 36 (72%) of the women interviewed met the WHO guidelines for timely breastfeeding initiation, meaning breastfeeding was initiated within the first hour postpartum. 43 out of 49 (87.7%) women interviewed met the recommended minimum of 4 antenatal visits, and of these women 32 (74.4%) initiated breastfeeding within the golden hour. 31 (62%) women administered pre-lacteal feeds to their baby, including 28% giving honey, 20% giving supplemental water, 10% giving unspecified medicine, 12% giving goat's milk, 4% giving sugar water and 2% giving cow's milk. Women who received breastfeeding education from a trained village health worker were 2.5 times more likely to avoid prelacteal feeds than those who did not (75% vs 31%, n=50, p=0.41)

Conclusions: There is improvement in rates of timely initiation of breastfeeding in villages with sustained health related interventions compared to the state average. The rates of pre-lacteal feeds administration remains high, however breast feeding education given by community elected village health workers has shown to reduce the likelihood of a mother giving her child prelacteal feeds. This finding demonstrates the positive impact of community members receiving health education and disseminating this knowledge in rural areas where there is poor access to medical providers.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

World Health Organization. "WHO Global Data Bank on Infant and Young Child Feeding (IYCF)-India." Updated June 2009. Accessed March 2015.
<http://www.who.int/nutrition/databases/infantfeeding/countries/ind.pdf?ua=1>

Determining the Effects of Silencing Prolyl Hydroxylase-1 (PHD-1) on Neovascularization and Ventricular Remodeling in the Infarcted Myocardium

Elise Mester¹, Vaithinathan Selvaraju², Mahesh Thirunavukkarasu², Babatunde Oriowo², Lijun Zhan², Nilanjana Maulik²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²University of Connecticut School of Medicine, Department of Surgery, Farmington CT

Prolyl hydroxylase 1 (PHD1) is an oxygen sensor that regulates the stability of hypoxia inducible factor (HIF), which plays an important role in the transcription of proangiogenic factors. Previous research has shown that deletion of PHD1 promotes neovascularization and improves perfusion in hind-limb ischemia, a model for peripheral vascular disease. The objective of this study was to determine if deletion of PHD1 can have a similar impact on cardiac tissue following a myocardial infarction (MI).

Homozygous PHD1 knockout (KO) and wild type (WT) mice were randomized into four groups: 1) WT sham control (sham), 2) KO sham, 3) WT MI, and 4) KO MI. MI was induced by permanent occlusion of the left anterior descending (LAD) coronary artery. Sham groups underwent identical time matched surgical procedures without LAD ligation. HIF-1 α and HSPA12B expression were measured using Gel Shift Assay and SDS-PAGE Western Blot, respectively. Echocardiography measured ejection fraction and fractional shortening 30days post-MI. Capillary density was measured 7 days post-surgery using DAB staining. Arteriolar density was measured 7 days post-surgery using immunofluorescence.

Gel Shift Assay of HIF-1 α and Western Blot analysis of HSPA12B showed expression levels were significantly increased in the KO MI group relative to the WT MI group. Echocardiographic analysis 30 days post-MI showed a statistically significant improvement in ejection fraction and fractional shortening in the KO MI group compared to the WT MI group. Additionally, capillary density and arteriolar density were significantly increased in the KO MI group when compared to the WT MI group.

Silencing PHD1 was shown to increase angiogenesis and decrease the loss of cardiac function following an MI. Thus, silencing PHD1 may provide a novel target for therapy beyond the pharmacological and surgical interventions currently available. Additionally, further study of PHD1 and its involvement in angiogenesis may provide other future potential targets.

Supported by: *The UConn School of Medicine Summer Research Fellowship*

References:

1. Rishi MT, Selvaraju V, Thirunavukkarasu M, et al. Deletion of prolyl hydroxylase domain proteins (PHD1, PHD3) stabilizes hypoxia inducible factor-1 alpha, promotes neovascularization and improves perfusion in a murine model of hind-limb ischemia. *Microvasc Res.* 2015; 97: 181-8.

Gold Nanoparticle Distributions in Rat Brains/Tumors after IV and Direct Injections

Alexandria Meyers¹, James F Hainfeld², Nathaniel Dymant³, Dan Sasso⁴, Crystal Xue⁴, Henry M Smilowitz⁴

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Nanoprobes, Inc.*

³*Department of Reconstructive Sciences, UConn Health, Farmington, CT*

⁴*Department of Cell Biology, UConn Health, Farmington, CT*

Background: More than 22,000 people in the United States are diagnosed with primary brain tumors with 13,000 deaths/year and in addition 130,000 deaths/year due to metastatic brain tumors. More effective treatments are desperately needed. Gold nanoparticles (GNPs) enhance radiation therapy (RT) of tumors (1, 2, 3). In mice with aggressive orthotopic advanced gliomas, the GNPs intravenously injected preferentially leak into tumor tissue versus normal brain tissue (tumor to normal brain tissue ratio of 19:1) leading to an increase in the local radiation dose by up to 400% with 50% long-term survival compared to 0% with RT alone (3). Several pharmacokinetic obstacles have hampered clinical translation including slow whole-body clearance and cost of the gold (4). Our hypothesis is GNPs directly infused into the original tumor site of advanced gliomas will selectively diffuse into the peritumor edema and surround renegade tumor cells thereby enhancing therapeutic RT.

Methods: F98 glioma cells were transduced with FugW:Red Cherry Lentivirus using polybrene; then cloned for the cells producing the brightest fluorescence. F98 cells were injected in the brain of male CD Fischer 344 rats to the LEFT of the bregma, 4 mm in depth. Three weeks later, 10 µl of 200 mg/ml 15 nm GNPs were injected into the brains of three of the rats in the same place and depth, respectively. In a fourth rat GNPs were injected IV via the femoral vein. The brains were extracted following perfusion fixation/euthanasia and preserved in 30% sucrose. The sectioned brains were qualitatively analyzed for nuclei (Dapi, (blue)), edema using an anti-FITC albumin fluorescent tag (green), cherry red fluorescent F98 cells (red), and GNPs after enhancement (black particles).

Results:1. Most of the tumor cells found distal to the main tumor mass were associated with blood vessels. 2. GNP injected IV were found in the endothelial cells and tumor cells lining the blood vessels. 3. GNP injected directly at a depth of 4 mm largely migrated between grey and white matter but also occupied the brain in the greater tumor region. GNPs were found around clumps of migrated tumor cells but not within these regions. 4. More diffuse edema was found in the left hemisphere, and more in the brains that had both tumor and GNP. Bright patches of edema and GNP were seen around some tumor cell containing vessels, but there was a clear correlation between edema and GNPs in brains that received IV GNP versus direct injections

Conclusions: IV injections of GNP should result in greater specific distal tumor localization and therefore greater efficacy for RT enhancement and less toxicity to normal brain.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Hainfeld JF, Slatkin DN, Smilowitz HM 2004. The use of gold nanoparticles to enhance radiation therapy in mice. *Phys Med Biol* 49: N309-N315
2. Hainfeld, J.F., Dilmanian, F.A., Zhong Z., Slatkin, D.N., *Smilowitz, H.M. 2010 Gold Nanoparticles Enhance Radiation Therapy of a Squamous Cell Carcinoma Growing in Mice. *Physics in Medicine and Biology* 55: 3045-3059.
3. Hainfeld, J.F., *Smilowitz, H.M., O'Connor, M.J., Dilmanian, F.A., Slatkin, D.N. 2012. Gold Nanoparticle Imaging and Radiotherapy of Brain Tumors in Mice. *Nanomedicine London (Future Medicine)* 8:1601-1609
4. Hainfeld, J.F., D.N. Slatkin, T. Focella, H.M. Smilowitz. 2006. Gold Nanoparticles: A New X Ray Contrast Agent. *British Journal of Radiology*. 79: 248-253.

Orosomucoid-1 Protein Dynamics Following Ischemic Stroke in Humans and Mice

Hetal Mistry¹, Madeline Levy², Meaghan Roy O'Reilly^{1,2}, Louise McCullough^{1,2}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Neurology, UConn Health, Farmington, CT

Background and Purpose: Orosomucoid-1 (ORM-1) is an abundant protein in humans and mice with important roles in inflammation and immunosuppression. We utilized RNA sequencing to measure mRNA levels in human ischemic stroke patients, with confirmation by serum ORM-1 protein measurements. A mouse model of ischemic stroke was then used to examine post-stroke changes in ORM-1 in the brain itself. As sex differences are important in ischemic stroke, we conducted this study in male and female animals.

Methods: RNA sequencing was performed on whole blood from ischemic stroke patients (n=23) and controls (n=12), with Benjamini-Hochberg correction for multiple testing. Enzyme-linked immunosorbent assay was performed on ischemic stroke patient (n=28) and control (n=8) serum, with analysis by T-test. For brain analysis, mice (n=14) were subjected to a 90-minute middle cerebral artery occlusion (MCAO) surgery and sacrificed 6 or 24 hours after stroke. Control mice underwent parallel "sham" surgery without occlusion. Western blotting was used to detect ORM-1 protein levels in whole brain, with analysis by two-way ANOVA.

Results: RNA sequencing showed a 2.8-fold increase in human ORM-1 at 24 hours post-stroke ($q=.0029$), an increase also seen in serum ORM-1 protein levels ($p=.011$). Western blot analysis of mouse brain revealed that glycosylated ($p=0.0003$) and naive ($p=0.0333$) forms of ORM-1 were higher in female mice compared to males 6 hours post-stroke. Interestingly, ORM-1 levels were higher in the brains of stroke mice at 6 hours ($p=.0483$), while at 24 hours ORM-1 levels in stroke mice were lower than their sham counterparts ($p=.0212$). In both human and mouse data, no sex differences were seen in ORM-1 levels in the brain or periphery at 24 hours post-stroke. **Conclusion:** ORM-1 is a sexually dimorphic protein involved in the early (<24 hour) response to ischemic stroke. This research demonstrates that sex differences exist in post-stroke ORM-1 protein dynamics, and serves as an initial step in determining the mechanism of ORM-1 in the ischemic stroke response and its potential as a future therapeutic target for both sexes.

Supported by: UConn School of Medicine Summer Research Fellowship, NIH Grant 5 R01 NS055215 09, Hartford Hospital

References:

- Manwani B, Bentivegna K, Benashski SE, Venna VR, Xu Y, Arnold AP, McCullough LD. Sex differences in ischemic stroke sensitivity are influenced by gonadal hormones, not by sex chromosome complement. *J Cereb Blood Flow Metab* 2015; 35, 221–229.
- Luo Z, Lei H, Sun Y, Liu X, Su DF. Orosomucoid, an acute response protein with multiple modulating activities. *J Physiol Biochem*. 2015 Jun;71(2):329-40.
- Tian Y, Stamova B, Jickling GC, Liu D, Ander BP, Bushnell C, Zhan X, Davis RR, Verro P, Pevcec WC, Hedayati N, Dawson DL, Khoury J, Jauch EC, Pancioli A, Broderick JP, Sharp FR. Effects of gender on gene expression in the blood of ischemic stroke patients. *J Cereb Blood Flow Metab*.2012; 32(5):780-91.

The Effect of CPOE on CDI Guideline Treatment Adherence and Clinical Outcomes

Emma Polidoro¹, Erik Swanson¹, Jeffrey R. Aeschlimann, Pharm.D.²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²UConn Health Pharmacy Department, Farmington, CT

Introduction: Clostridium difficile infection (CDI) is the leading cause of gastroenteritis-associated death in the US. The UConn Health/John Dempsey Hospital (UCH/JDH) Antimicrobial Stewardship Program implemented a computerized physician order entry (CPOE) set in 2013 to help caregivers make treatment decisions in accordance with the IDSA's 2010 CDI guidelines. The two main goals of this investigation were to: (1) determine if the CPOE set improved adherence to treatment guidelines, and (2) compare the clinical outcomes of patients who received treatment in accordance with IDSA or American College of Gastroenterology (ACG) CDI guidelines to those who did not.

Methods: This is a retrospective case-control study of hospitalized patients treated for CDI who were admitted to UCH/JDH between 2012 and 2015. Data recorded and analyzed included: patient demographics, lab values, hospital course, use of the CPOE set for care, and recurrence of infection. Patients' severity of CDI was stratified based on the ACG and IDSA CDI guidelines, and CDI treatment was compared to guideline-recommended treatment. Clinical outcomes for patients receiving recommended treatment were compared to those receiving alternative treatments.

Results: Prior to the implementation of the CDI CPOE, only 24.6% of CDI patients received treatment in accordance with IDSA guidelines. After CPOE set implementation, adherence to IDSA guidelines improved to 45.6% ($\chi^2 = 5.9$, $p = 0.01$). The pre-CPOE ($n=65$) and post-CPOE ($n=123$) cohort were similar with respect to most demographic variables. In preliminary univariate analysis, the mean length of stay decreased from 15.8 days pre-CPOE implementation to 10.5 days post-CPOE ($t_{obs}=2.67$, $p < 0.01$). However, differences between the groups that will be accounted for during multivariate analyses include: higher burden of NAP-1/B1027 strain in the pre-CPOE vs. post-CPOE groups (10.8% vs. 7.3%) and higher prevalence of severe and complicated CDI disease (IDSA: 36.9% pre-CPOE vs. 28.5% post-CPOE).

Conclusions: Implementation of a CDI CPOE set significantly increased receipt of guideline-concordant therapy for patients with CDI at UCH/JDH. Patient's length of stay also significantly decreased after the CDI CPOE set implementation. Multivariate analysis of the data set is ongoing to delineate all possible factors that could have significantly contributed to these observations.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- Brown, A. T., & Seifert, C. F. (2014). Effect of treatment variation on outcomes in patients with Clostridium difficile. The American Journal of Medicine, 127(9), 865-870.
- Cohen, S. H., Gerding, D. N., Johnson, S., Kelly, C. P., Loo, V. G., McDonald, L. C., ... & Wilcox, M. H. (2010). Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the society for healthcare epidemiology of America (SHEA) and the infectious diseases society of America (IDSA). Infection Control & Hospital Epidemiology, 31(05), 431-455.
- Lessa, F. C., Mu, Y., Bamberg, W. M., Beldavs, Z. G., Dumyati, G. K., Dunn, J. R., ... & Wilson, L. E. (2015). Burden of Clostridium difficile infection in the United States. New England Journal of Medicine, 372(9), 825-834.
- McEllistrem, M. C., McGraw, M., Sahud, A. G., Chan-Tompkins, N. H., Goswami, R., & Bhanot, N. (2014). High frequency of nonadherence to Clostridium difficile treatment guidelines. Southern Medical Journal, 107(9), 597-599.
- Surawicz, C. M., Brandt, L. J., Binion, D. G., Ananthakrishnan, A. N., Curry, S. R., Gilligan, P. H., ... & Zuckerbraun, B. S. (2013). Guidelines for diagnosis, treatment, and prevention of Clostridium difficile infections. The American Journal of Gastroenterology, 108(4), 478-498.

New enzymatic disruption protocol to quantify *in vitro* *Candida albicans* biofilm invasion

Power, J¹; Bertolini, M, DDS PhD¹; Thompson, A¹, BS; Dongari-Bagtzoglou, A, DDS PhD¹

¹University of Connecticut School of Dental Medicine: Division of Periodontology

Objective: Invasion of *Candida albicans* into the oral mucosa is a phenotype associated with increased virulence in humans. Existing protocols used to quantify experimental invasion are suboptimal because tissues are hard to disrupt by mechanical homogenization alone, generating poor homogenates and reducing accuracy on *C. albicans* colony forming unit (CFU) measurements. In order to improve the reliability of CFU counts related to *C. albicans* invasion, we used an *in vitro* invasion model in conjunction with enzymatic digestion to quantify *C. albicans* in single and mixed fungal-bacterial biofilms.

Methods: The *in vitro* tissue invasion model consisted of a fibroblast-embedded collagenous 3D matrix, infected by *C. albicans* (inoculated at 1×10^6 cells/mL) wild-type strain (SC5314). Two pseudohyphal strains (ndt80-/- and rim101-/- mutants), which are non-invasive were used as negative controls. Mixed biofilms with *Streptococcus oralis* strain 34 (5×10^6 cells/mL), which has been shown previously to increase the invasive potential of *Candida*, were also tested. Matrix was collected after 30 hours, washed with PBS, and supernatants were aspirated to remove the surface biofilm. Next, 3 mL of collagenase (or PBS on control groups) was added at 0.1 mg/mL and matrix was disrupted on a shaker at 37°C for 60 minutes. Homogenates were then serially diluted, plated in triplicate for CFU counts and incubated 24 hours. Statistical analyses were performed using a Student t-test.

Results: The recovery of *C. albicans* (SC5314) from single biofilms invading the gels was significantly higher with collagenase compared to mechanical homogenization ($p = 0.0025$), indicating that collagenase digestion allowed *Candida* retrieval from the matrix. When CFU from *C. albicans* and *S. oralis* mixed biofilms were compared, there were higher counts in the mixed biofilm group ($p = 0.0014$), showing that this protocol is sensitive enough to detect differences in single and mixed biofilms with *S. oralis*. The non-invasive pseudohyphal-mutants did not show statistical differences when collagenase-treated and control groups were compared, suggesting that most of the biofilm grew on the surface of the collagen matrix and was removed by PBS washing. Interestingly, the CFU values for the non-invasive mutants were close to the values from SC5314 without collagenase, illustrating how mechanical homogenization alone can underestimate the biofilm invasion.

Conclusions: The enzymatic disruption protocol using collagenase to quantify *Candida albicans* invasion in single and mixed biofilms significantly enhances quantification of *C. albicans* biofilm invasion in this *in vitro* model.

Future Directions: We plan to test this protocol in estimating fungal invasion using mouse models of oral and gastro-esophageal *Candidiasis*.

Support: Fellowship support from the Vernon D. and Florence E. Roosa Family Foundation Memorial Fund at the Hartford Foundation for Public Giving..

Title: Gender variation in palatal bone thickness for mini-implant placement**Authors:** Emily Sachs, Sumit Yadav**Department:** UCONN Health Division of Orthodontics

Objective: Orthodontists are aiming to use palatal temporary anchorage devices in orthodontic treatment to prevent undesired movement of anchor teeth and reduce stress on the molars¹. The palate is an ideal location for the mini-implants as it is easily accessible and there is little danger of damaging anatomical structures¹. The objective of this study was to compare the bone thickness of the palatal areas in males and females to find ideal locations for the mini-implants.

Materials and Methods: Cone-beam computed tomography (CBCT) scans of 356 patients were divided into 99 growing males (12 years and 5 months), 74 non-growing males (31 years and 3 months), 105 growing females (mean age: 13 years and 4 months) and 81 non-growing females (mean age: 27 years and 1 month). The measurements of palatal bone thickness were made in between canine and first premolar, between first premolar and second premolar, between second premolar and first molar and between first molar and second molar. The measurements were made in the center of the palate and 4mm away from the center of the palate. All the measurements were made using InVivo5.0 software (Anatomage, San Jose, California). Analysis of variance was used to analyze the palatal bone thickness in different area within the group and between 4 different groups.

Results: The palatal bone thickness was significantly lower ($P < 0.0001$) as we moved from anterior palate to posterior palate in all the groups. The palatal bone thickness was significantly ($P < 0.001$) more in the center of the palate than 4mm away from the center, except in between canine and first premolar, where the palatal bone thickness was significantly lower ($P < 0.05$) in the center than 4mm away from it (growing male: $8.17 \pm 2.38 < 11.73 \pm 3.16$ mm; growing female: $6.36 \pm 2.17 < 9.74 \pm 2.81$ mm; non growing male: $8.29 \pm 2.88 < 12.63 \pm 3.38$ mm; non-growing female: $6.79 \pm 2.64 < 9.57 \pm 3.01$ mm). The growing male had significantly higher ($P < 0.0001$) bone thickness than growing female in between canine and first premolar and first premolar and second premolar both in the center of the palate and 4mm away from the palate. Similarly, non-growing male had significantly greater ($P < 0.001$) palatal bone thickness than non-growing female in between canine and first premolar and first premolar and second premolar both in the center of the palate and 4mm away from the palate. We were not able to differentiate ($P > 0.05$) the palatal bone thickness between growing male and non-growing male at the sites of measurements, or between growing females and non-growing females ($P > 0.05$).

Conclusions: The palatal bone thickness was significantly less in females. These descriptive findings will help clinicians to decide ideal locations of mini-implant placement in the different regions of the palate.

Future Directions: We are hoping to measure the width of the palate from canine to canine as well as molar to molar and classify our results based on narrow arches or wide arches to see how palatal bone thickness is affected.

Support: None

References: ¹<http://www.dentistryiq.com/articles/2012/05/use-of-temporary-anchorage-devices-for-movement-of-teeth.html>

Peripheral and Central Nervous System Degeneration in Patients with Xeroderma Pigmentosum

Paul Sackstein, BS¹, Deborah Tamura MS, RN², Sikandar G. Khan, PhD², Nicholas J. Patronas, MD³, Edythe Wiggs, PhD⁴, Carmen C. Brewer, PhD⁵, John J. DiGiovanna, MD², Kenneth H. Kraemer, MD², Tanya J. Lehky, MD⁴

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Dermatology Branch, National Cancer Institute, NCI, CCR, NIH, Bethesda, Maryland, USA*

³*Clinical Center, National Institutes of Health, Bethesda, Maryland, USA*

⁴*National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, USA*

⁵*Otolaryngology Branch, National Institute on Deafness and other Communication Disorders, Bethesda, Maryland, USA*

Objective: Xeroderma Pigmentosum (XP) is a rare genetic disorder characterized by defective nucleotide excision repair.¹ XP is classified into 8 different complementation groups (XP A-G and XP V) based on defects in DNA nucleotide excision repair (NER) genes and the polymerase- η gene, respectively. Ventriculomegaly and thinning of the cerebral cortex have been observed in XP-A and XP-D patients with neurodegeneration.² Recently, Totonchy et al. identified sensorineural hearing loss (SNHL) and acute burning on minimal sun exposure as strong predictors of XP-type neurological degeneration.³ However, the frequency of peripheral neuropathy (PN), and its association with central neuropathy, in different XP complementation groups remains unknown. In this study, we reviewed nerve conduction velocity (NCV) and MRI/CT imaging studies to assess the frequency of PN among XP subtypes and whether or not the PN correlates with central neurological abnormalities. Ultimately, we aim to establish PN as a reliable biomarker to help predict the time course of neurodegeneration and enable early therapeutic intervention for these patients.

Design/Methods: Patients with XP were evaluated under protocol (NCT00001813) by genetic and clinical evaluation at NIH. NCV studies were performed on patients referred from this protocol. Brain MRI and/or CT imaging studies, audiological and neuropsychological evaluations were also performed on most subjects in this study.

Results: Of the 33 subjects evaluated, 7 subjects were XP-A, 9 subjects were XP-C, 9 subjects were XP-D, 1 subject was XP-E, 4 subjects were XP-V and 3 subjects were XP-unknown. Ten subjects showed evidence of peripheral neuropathy. XP-A and XP-D had the highest frequency of PN with 71% (5/7) and 44% (4/9), respectively. The PN was strongly associated with the presence of cerebral or cerebellar atrophy by brain MRI/CT imaging studies. SNHL and deep tendon reflexes also correlated with the presence of PN in XP-A and XP-D patients. XP-E, XP-V and XP-unknown patients did not display evidence of PN.

Conclusions: XP-A and XP-D subtypes were predominantly associated with PN. Absent deep tendon reflexes and SNHL may precede PN in XP and therefore serve as valuable clinical indicators of XP patients that will later develop PN.

Supported by: The UConn School of Medicine Summer Research Fellowship, National Institutes of Health Summer Internship Program

References:

1. Bradford PT, Goldstein AM, Tamura D et al. Cancer and neurologic degeneration in Xeroderma Pigmentosum: long term follow-up characterizes the role of DNA repair. *J Med Genet* 2011; 48:168.
2. Lai JP, Liu YC, Alimchandani M et al. The influence of DNA repair on neurologic degeneration, cachexia, skin cancer and internal neoplasms: autopsy report of four Xeroderma Pigmentosum patients (XP-A, XP-C and XP-D). *Acta Neuropathol Commun* 2013; 1:4.
3. Totonchy et al. Auditory analysis of xeroderma pigmentosum 1971-2012: hearing function, sun sensitivity and DNA repair predict neurological degeneration. *Brain* 2012; 136: 194-208.

Predictors of Weight Status and Nutrition in Puerto Rican Children

Verónica Y. Schmidt¹, Kevin Dieckhaus¹

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

Childhood obesity is a major public health concern as there are many negative health consequences. According to the Center for Disease Control (CDC), the prevalence of child and adolescent obesity in the United States is 16.9%¹. The prevalence among Hispanic children and adolescents was much higher than any other ethnic group; Hispanic (22.4%), non-Hispanic black (20.2%), non-Hispanic white (14.1%) and non-Hispanic Asian (8.6%). A study in 2008 demonstrated that the prevalence of childhood obesity in children aged 6-11 years old was 26.8%. The purpose of this study is to examine the current prevalence of childhood obesity in Puerto Rico and examine what factors may be predictive of childhood obesity.

This study surveyed parents/guardians of pediatric patients, ages 2-11 years in a pediatric office in Moca, Puerto Rico. The survey questions included questions regarding family food security, demographics, family food access, parental nutrition knowledge and recent food consumption of the child. A prospective chart review was conducted to collect information about the child's age, weight, height, and body mass index (BMI). SPSS and Microsoft Excel were used to analyze summative data, Pearson's R Correlations, One-way ANOVAs, and Independent T tests.

A total of 64 parents/guardians of (31 male and 33 female) pediatric patients, ages 2-11 years were surveyed. Of the male patients that were examined in the study 51.61% were overweight or obese as compared to 36.36% of the female patients. Only 50% of the parents correctly identified their child's weight status. The children whose parents underestimated their weight status were more likely to be heavier ($M=82.364$, $SE=5.2184$ versus $M=52.154$, $SE=5.7672$) conditions; $t(62)=-3.32$, $p=.001$. The children whose parents underestimated their weight status were more likely to be underweight ($M=.614$, $SE=.3757$ versus $M=71.733$, $SE=3.877$) conditions; $t(57.009)=18.255$, $p=.000$. Parents who correctly identified their child's weight status had a higher educational level ($M=26.68$, $SE=.7342$) compared to parents who incorrectly identified their child's weight status ($M=23.7586$, $SE=1.01304$) conditions; $t(52)=2.270$, $p=.027$. Finally, a parent's belief that "a fat child was a healthy child" and their child's BMI percentile was correlated, $r=.306$, $n=62$, $p=.015$.

This study had limitations due to a small sample size. This study was consistent with other studies that demonstrated that boys were more likely to be overweight in comparison to girls. Parent's perceptions on their child's weight status and their beliefs in regards to a healthy weight status may impact their own child's weight status. These results suggest that parent education on healthy childhood weight statuses may be a target to ameliorate childhood obesity.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*. 2014;311(8):806-14.
2. Rivera-soto WT, Rodríguez-figueroa L, Calderón G. Prevalence of childhood obesity in a representative sample of elementary school children in Puerto Rico by socio-demographic characteristics, 2008. *P R Health Sci J*. 2010;29(4):357-63.
3. Rivera-soto WT, Rodríguez-figueroa L. Childhood Obesity among Puerto Rican Children: Discrepancies Between Child's and Parent's Perception of Weight Status. *Int. J. Environ. Res. Public Health* 2012, 9, 1427-1437.

Evaluation of the Diagnostic Efficacy of Two CBCT Protocols in Reliably Detecting the Location of the Inferior Alveolar Nerve Canal

Sydney Schneider, Sumit Yadav, Aditya Tadinada

University of Connecticut School of Dental Medicine

Background: Cone beam computed tomography (CBCT) is increasingly being used in dentistry to obtain three-dimensional images of the maxillofacial region. Over the last few years several valuable dental applications have evolved. The current conventional acquisition protocol is a 360-degree rotational scan. The evolution of a lower dose 180-degree rotational acquisition CBCT acquisition protocol has opened doors for its use in a variety of diagnostic tasks. The key advantage to this protocol is a significant reduction of the radiation dosage without affecting diagnostic accuracy.¹ A key challenge in implant treatment planning and surgical placement is the ability to reliably localize the inferior alveolar nerve canal.

Objectives: To evaluate the diagnostic accuracy of two CBCT protocols in accurately identifying the location of the Inferior Alveolar Nerve Canal (IANC).

Materials and Methods: Ten dentate and partially edentulous dry human skulls were randomly chosen for this study. All skulls were obtained from Educational Support Services at UCONN Health and imaged using J. Morita's Accuitomo CBCT scanner using a 180-degree and 360-degree rotational protocol. For each individual skull, a total of 4 CBCT scans were acquired: (1) small voxel (0.2-mm) with 360-degree protocol, (2) small voxel with 180-degree protocol, (3) large voxel (0.4-mm) with 360-degree protocol, and (4) large voxel with 180-degree protocol. For each CBCT scan, the length from the inferior cortical border of the mandible to the top of the IANC was evaluated at 4 locations: (1) mental foramen, (2) middle of 1st molar, (3) middle of 2nd molar, (4) middle of 3rd molar. In addition, a fifth length measurement was made from the inferior cortical border of the mandible to the top of the mental foramen. The measurements were then compared to detect if there was a significant difference between the two protocols.

Results: Comparison of the IANC length measurements for the two protocols as well as for the two voxel sizes revealed no significant difference. Length measurements were identical when comparing the 180-degree and 360-degree protocols, and between the small voxel and large voxel protocols.

Conclusion: The 180-degree CBCT acquisition protocol was able to accurately evaluate the location of the IANC with very high reliability and was comparable to a 360-degree CBCT rotational acquisition. The size of the voxel did not have a significant impact on the ability to localize the IANC. Using a 180-degree protocol and a smaller voxel exposes patients to the least amount of radiation when comparing the four types of CBCT scans taken.

Future Directions: The future aim of our work is to further support these findings by completing another study with a larger sample size as well as translating the project to patients and evaluating those results.

Reference:

¹Yadav, Sumit, Ledjo Palo, Mina Mahdian, Madhur Upadhyay, and Aditya Tadinada. "Diagnostic Accuracy of 2 Cone-beam Computed Tomography Protocols for Detecting Arthritic Changes in Temporomandibular Joints." *American Journal of Orthodontics and Dentofacial Orthopedics* 147.3 (2015): 339-44.

Steps in Development of an Innovative Mouse Model for Cisplatin-Induced Chronic Kidney Disease

Ayibatari Sikpi¹, Xiaojia Guo², Heino Velazquez², Robert Safirstein^{2,3}, Gary Desir^{2,3}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Internal Medicine, Yale University School of Medicine, New Haven, CT

³Department of Nephrology, VA Connecticut Healthcare System, West Haven, CT

One well-known side effect of the antineoplastic agent cisplatin is renal toxicity. Less is known, however, about the specific cellular changes that occur in the kidneys to impair function and how these changes may be targeted for prevention and/or treatment of nephrotoxicity (1). Researchers in the laboratory of Dr. Gary Desir at Yale University School of Medicine are already employing a mouse model to study cisplatin-induced chronic kidney disease (CKD). Traditional histologic methods, however, provide limited information about the pathologic mechanism of cellular injury in cisplatin-induced CKD (2). A goal of the Desir laboratory is to develop an improved disease model in which mouse renal cells can be tagged with fluorescent markers and then examined microscopically for fate-tracing and other studies inaccessible with customary histological methods (such as hematoxylin and eosin staining). Research teams studying topics such as neuronal networks (3) and focal segmental glomerulosclerosis (4) have previously used methods of genetic recombination to produce mice that express particular cellular markers of interest. For the cisplatin-induced CKD model, mouse breeding pairs have been established and offspring have been genetically analyzed through the use of polymerase chain reaction and gel electrophoresis. The research described here outlines the genetic recombination pathway and accompanying genetic analysis that will ultimately lead to a model that may expand knowledge of the pathogenesis of renal toxicity in cisplatin therapy.

Supported by: Summer Research Fellowship, George O'Brien Kidney Center at Yale

References:

1. Arany, Istvan, and Robert L. Safirstein. "Cisplatin nephrotoxicity." *Seminars in nephrology*. Vol. 23. No. 5. WB Saunders, 2003.
2. Torres, Richard, et al. "Three-Dimensional Morphology by Multiphoton Microscopy with Clearing in a Model of Cisplatin-Induced CKD." *Journal of the American Society of Nephrology* (2015): ASN-2015010079.
3. Tao, Jianling, et al. "A multicolor podocyte reporter highlights heterogeneous podocyte changes in focal segmental glomerulosclerosis." *Kidney international* 85.4 (2014): 972-980.
4. Weissman, Tamily A., et al. "Generating and imaging multicolor Brainbow mice." *Cold Spring Harbor Protocols* 2011.7 (2011): pdb-top114.

Systemic Inflammation Reverses Stroke-induced Changes in Astrocytic Aquaporin-4 Expression

Ye Sun¹, Matthew D. Howe², Monica Spychala², Rachael Rosow³, Louise D. McCullough²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Neurology, University of Texas*

³*Bates College*

Introduction: Aquaporin-4 (AQP4) is a perivascular water channel that plays a key role in regulating the blood-brain barrier (BBB). Stroke acutely reduces expression and polarization of AQP4 on astrocytic endfeet, and these vascular changes might persist chronically and evolve with systemic inflammation. Reduced polarization of AQP4 after traumatic brain injury (TBI) leads to impaired perivascular clearance of debris and cognitive decline in mice, and if similar changes occur after stroke, then they may also contribute to post-stroke dementia.

Hypothesis: Stroke will cause lasting changes in vascular organization, reducing astrocytic AQP4 expression and polarization in the area of injury.

Methods: Thirty male Balb/cJ mice were subjected to distal middle cerebral artery ligation, allowed to survive for 28 days, and sacrificed 24 hours after injection with lipopolysaccharide (LPS, 0.33 mg/kg i.p.) or saline to model systemic inflammation. Three sequential coronal sections (20 μ m) near the site of infarct (0.25 mm from Bregma) were stained with lectin, AQP4, and glial fibrillary acidic protein (GFAP) to evaluate BBB organization. Vessel density was evaluated with AngioTool. AQP4 expression was evaluated by Western blot.

Results: Stroke increased vascular density in the injured hemisphere ($11 \pm 0.8\%$ vs $7.6 \pm 0.8\%$ in sham mice, $p < 0.05$). Decreased AQP4 expression and polarization near the site of the infarct was observed, which were reversed with LPS. LPS increased AQP4 protein levels in stroke (2.5 ± 0.37 fold-increase, $p < 0.05$), but not sham mice.

Conclusions: Stroke caused a chronic increase in vascular density, with peri-infarct vessels displaying decreased expression and changed polarity of AQP4. However, with systemic inflammation, this is reversed, potentially contributing to neuroinflammation and worsened cognitive outcomes in stroke patients who encounter infections via increased permeability of these abnormal vessels.

Supported by: The UConn School of Medicine Summer Research Fellowship, NIH NINDS

References:

- Friedman B, Schachtrup C, Tsai PS, et al. Acute Vascular Disruption and Aquaporin 4 Loss After Stroke. *Stroke* 2009;40(6):2182–2190.
- Nicchia G, Nico B, Camassa L, et al. The role of aquaporin-4 in the blood–brain barrier development and integrity: Studies in animal and cell culture models. *Neuroscience* 2004;129(4):935–944.
- Fukuda AM, Adami A, Pop V, et al. Posttraumatic reduction of edema with aquaporin-4 RNA interference improves acute and chronic functional recovery. *Journal of Cerebral Blood Flow & Metabolism J Cereb Blood Flow Metab* 2013;33(10):1621–1632.

Quantitative NMR for Evaluation of Metabolic Changes in EMT-induced Epithelial Breast Cancer Cell Lines

Patrick Svrcek¹, Denisse Tafur-Cortiz², Dr. Bruce White², and Dr. Jeffrey Hoch³

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Cell Biology, UConn Health, Farmington, CT

³Department of Molecular, Microbial, and Structural Biology, UConn Health, Farmington, CT

One of eight females will suffer from breast cancer in their lifetime. In breast cancer, an important distinction that affects prognostic outlook for patients is whether a cancer is in situ or has become invasive. To understand this analogously at a cellular level, masses in situ are akin to epithelial breast cancer cells and invasive masses are epithelial breast cancer cells that have become mesenchymal in phenotype, allowing the cells to effectively intravasate from their site of origin. These two phenotypes are linked by a process called Epithelial-to-Mesenchymal Transition (EMT). Our research focused on key differences between these two phenotypes in terms of lactate metabolism. Lactate is critical due to its role in the classic Warburg effect seen in a cancer metabolism and its usage as a building block and signaling molecule for rapidly dividing cells. Lactate metabolism was explored through endogenous cell surface membrane lactate receptor gpr81, which regulates the expression of lactate transporters and subsequent intracellular lactate levels. The two cell lineages used in our research are the standardized epithelial breast cancer cell line MCF-7 and its EMT-induced mesenchymal variant LMS. Both of these cell lines were subjected to 2-D/3-D growth culture and converted into lysates for quantitative Nuclear Magnetic Resonance analysis (qNMR) to evaluate intracellular metabolite levels. While both of these cell lines undergo the Warburg effect, MCF-7 and LMS have different isotypes of the MCT transporter. MCF-7, an epithelial cell that forms spherical tumor colonies in 3D culture, expresses high levels of MCT1 (lactate importer) and MCT4 (lactate exporter). In contrast, LMS forms loose connective networks as tumors in 3-D culture and loses expression of MCT1 while retaining high levels of MCT4 expression. We have found a key regulator of these transporters to be gpr81, which upon knockout, severely reduce the levels of MCT1 in MCF-7 and subsequently its intracellular lactate. We have developed a protocol to quantitatively evaluate the intracellular levels of metabolites in our cell lines to analyze the cell lines' metabolic profiles as well as monitor for metabolic changes after knockout of key regulatory factors such as gpr81. We have determined that MCF-7 has a significant fourfold increase in intracellular lactate compared to LMS ($p < 0.01$). Knockdown of gpr81 in MCF7 lines also showed reduction in intracellular lactate by up to 50%, implicating gpr81 regulation of MCT transport of lactate.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- Bi H, Krausz KW, Manna SK, Li F, Johnson CH, Gonzalez FJ. Optimization of harvesting, extraction, and analytical protocols for UPLC-ESI-MS-based metabolomic analysis of adherent mammalian cancer cells. *Anal Bioanal Chem.* 2013;405(15):5279-89.
- Boidot R, Végran F, Meulle A, et al. Regulation of monocarboxylate transporter MCT1 expression by p53 mediates inward and outward lactate fluxes in tumors. *Cancer Res.* 2012;72(4):939-48.
- Guttilla IK, Phoenix KN, Hong X, Tirnauer JS, Claffey KP, White BA. Prolonged mammosphere culture of MCF-7 cells induces an EMT and repression of the estrogen receptor by microRNAs. *Breast Cancer Res Treat.* 2012;132(1):75-85.
- Kondaveeti Y, Guttilla reed IK, White BA. Epithelial-mesenchymal transition induces similar metabolic alterations in two independent breast cancer cell lines. *Cancer Lett.* 2015;364(1):44-58.
- Van der graaf M. In vivo magnetic resonance spectroscopy: basic methodology and clinical applications. *Eur Biophys J.* 2010;39(4):527-40.
- Ward PS, Thompson CB. Signaling in control of cell growth and metabolism. *Cold Spring Harb Perspect Biol.* 2012;4(7):a006783.
- Wu W, Zhao S. Metabolic changes in cancer: beyond the Warburg effect. *Acta Biochim Biophys Sin (Shanghai).* 2013;45(1):18-26.
- Yang Q, Qiu H, Guo W, et al. Quantitative ¹H-NMR Method for the Determination of Tadalafil in Bulk Drugs and its Tablets. *Molecules.* 2015;20(7):12114-24.

The Relationship between Maternal and Child Psychosocial Stress and a Novel Biomarker of the Stress Response

Franklin Sylvester¹, Mary Ojukwu¹, Dr. Christine Trapp, MD², Dr. Jessica Hollenbach, PhD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Children's Center for Community Research/Asthma Center, CT Children's Medical Center*

Exposure to chronic psychosocial stress markedly increases vulnerability to adverse health outcomes. The physiological changes involved in the response to chronic stressors alter the regulation of the hypothalamic-pituitary-adrenal (HPA) axis(1). Although maternal depression, poverty, and related stress are often associated with a dysregulated HPA axis in offspring(2), few studies have examined this relationship among racial and ethnic minorities who are at a disproportionately higher risk of exposure.

Cortisol is the final effector of the HPA axis, which is a neuroendocrine system known to be activated by stress exposure (3). Historically, salivary and plasma cortisol levels have been utilized to assess stress, but both measures only provide point estimates of HPA axis activity. This makes them impractical for assessing chronic stress responses. Hair cortisol has emerged as an accurate index of the intensity and course of the stress response over time(4). However, more research is needed to better understand hair cortisol as a marker for stress, especially in the realm of maternal and child psychosocial stress among minority populations.

This study evaluated the relationship between subjective maternal chronic stress and hair cortisol levels in both mothers and their children. Mothers and their children (ages 7-14) were recruited to participate in the study, in which they were asked to complete questionnaires and provide hair samples. Separate surveys were given to the mothers and children so that each could be given a score of subjective chronic stress. Additionally, both mother and child provided hair samples that were examined using ELISA to determine hair cortisol concentrations. The subjective stress score and hair cortisol levels will be compared through statistical analysis to evaluate the relationships between the subjective measure of stress and maternal hair cortisol, the subjective measure of stress and the child's hair cortisol, and correlations between maternal hair cortisol and child's hair cortisol. When the study is completed, the results can be used to help develop a better understanding concerning the role of hair cortisol and subjective stress in minority populations.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Kirschbaum C, Tietze A, Skoluda N, Dettenborn L. Hair as a retrospective calendar of cortisol production-Increased cortisol incorporation into hair in the third trimester of pregnancy. *Psychoneuroendocrinology*. 2009 Jan;34(1):32-7.
2. Dunkel Schetter C. Psychological science on pregnancy: stress processes, biopsychosocial models, and emerging research issues. *Annual review of psychology*. 2011;62:531-58.
3. Entringer S, Buss C, Shirtcliff EA, Cammack AL, Yim IS, Chicz-DeMet A, et al. Attenuation of maternal psychophysiological stress responses and the maternal cortisol awakening response over the course of human pregnancy. *Stress (Amsterdam, Netherlands)*. 2010 May;13(3):258-68.
4. Russell E, Koren G, Rieder M, Van Uum S. Hair cortisol as a biological marker of chronic stress: current status, future directions and unanswered questions. *Psychoneuroendocrinology*. 2012 May;37(5):589-601.

Primary Pectoralis Major Repair Configurations: How to Optimize the Repair Biomechanics

Michael Tassavor¹, Cory M. Edgar MD, PhD², Hardeep Singh MD², Elifho Obopilwe MS, BME², Andreas Voss MD², Jessica Divenere BA², Matthew T. Provencher MD³, Augustus D. Mazzocca, MS, MD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Department of Orthopaedic Surgery, New England Musculoskeletal Institute, University of Connecticut School of Medicine, Farmington, CT*

³*Department of Orthopaedic Surgery, Massachusetts General Hospital, Boston, CT*

Background: Musculotendinous tears of the pectoralis major tendon are difficult to repair with existing techniques. New surgical techniques are explored to better restore the anatomical length of the musculotendinous unit in a robust manner that approximates native anatomy.

Purpose/Hypothesis: The new techniques explored will demonstrate improved initial resistance to cyclic and maximum tensile loads compared to previously described techniques utilizing the Cortical Button.

Study Design: Controlled laboratory study.

Methods: Eighteen fresh-frozen cadaveric shoulders were randomized equally to three repair techniques. The pectoralis muscle was extracted with a portion of the humerus with myotendinous tears simulated in the sternal head of the pectoralis muscle with subsequent repair with three techniques utilizing an endosteal Cortical button (Arthrex, Naples, Florida). The specimens were tested under cycling loads ranging from 10 N to 125 N with a final load-to-failure test occurring at 1 mm/s. All specimens were digitally analyzed using optical markers with failure modes visually classified to determine the location and cause of the rupture.

Results: After cyclic loading, the # 5 Fiber Wire and FiberTape repair group had the lowest mean displacement with 1.09 ± 0.47 mm and 1.14 ± 0.39 mm for the superior and inferior markers, respectively. The same group also had the highest peak and load yield, with 640.48 ± 165.07 N and peak load of 794.09 ± 168.45 N respectively. The FiberTape repair group most closely approximated the native tendon width following repair, with a native tendon width of 55.38 ± 4.77 mm and a repaired tendon width of 47.57 ± 4.66 mm, with a mean difference of 7.82 ± 5.75 mm. All constructs uniformly failed at the musculotendinous junction distal to the repair.

Conclusion: The Fibertape method best restored native anatomy in terms of tendon width. However, the # 5 Fiber Wire & Fibertape method of repair yielded the best load to failure and cyclic loading displacement properties. The biomechanical properties of all three methods using the Pec Button were inferior to native anatomy.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Hart, Nathan D., Derek P. Lindsey, and Timothy R. Mcadams. "Pectoralis Major Tendon Rupture: A Biomechanical Analysis of Repair Techniques." *Journal of Orthopaedic Research J. Orthop. Res.* 29.11 (2011): 1783-787.
2. Sherman, S. L., Lin, E. C., Verma, N. N., Mather, R. C., Gregory, J. M., Dishkin, J., . . . Romeo, A. A. (2012). Biomechanical Analysis of the Pectoralis Major Tendon and Comparison of Techniques for Tendo-osseous Repair. *The American Journal of Sports Medicine*, 40(8), 1887-1894.

Enhanced Chemosensitivity of Urothelial Bladder Carcinoma Cells to a Combination of Cisplatin and Dichloroacetate (DCA), a PDK4 Inhibitor

Cassandra Trammel¹, Dharamainder Choudhary, Ph.D.², Andrew Mikhalyuk¹, John Taylor, M.D.²

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Department of Surgery, University of Connecticut Health Center

Introduction: Muscle invasive bladder cancer (MIBC) is associated with poor prognosis. Standard treatment for these tumors typically includes cisplatin based chemotherapy in spite of only modest improvements in survival. Hence, new molecular targets and inhibitory agents of potential therapeutic use are needed. Our group has shown upregulation of pyruvate dehydrogenase kinase 4 (PDK4) in MIBC patients, indicating that PDK4 may be a therapeutic target (1). PDKs are tissue specific regulatory enzymes with a key role in cellular metabolism. PDK4 inhibitor Dichloroacetate (DCA) has been shown to inhibit proliferation of bladder cancer cells. In vivo, DCA treatment alone does not effect tumor growth, but shows a decrease in growth when given with chemotherapeutic agents (2). The aim of this study was to evaluate the efficacy of cisplatin in combination with DCA on bladder cancer cell proliferation using cell culture and xenograft tumor models.

Methods: HTB9 bladder cancer cells shown to overexpress PDK4 were cultured with varying doses of DCA and cisplatin. Apoptosis and cell cycle analysis were evaluated by flow cytometry. Mice were divided into treatment (100 mg/kg daily oral gavage, n=6) and control groups (water, n=6) and inoculated with HTB9 cells in bilateral flanks. Tumor growth was monitored until tumors reached .55 cm³, at which point the animals were euthanized and tumors excised, weighed and fixed. Total RNA was extracted and qPCR performed.

Results: Treatment of HTB9 cells with DCA (10-50 mM) for 24-72 h showed an increased proportion of cells in G1-arrest and a decrease in S-phase. 10mM DCA did not significantly change cell cycle distribution. Treatment with cisplatin (0.2-10 μ M) caused S-phase arrest. 10mM of DCA and 3 μ M of cisplatin were used for further studies. 3 μ M cisplatin treatment alone for 24 h had a 25% increase in S-arrest relative to controls, while combined 3 μ M cisplatin and 10mM DCA had a 49.6% increase in S-arrest relative to controls. The apoptotic study showed a modest increase in number of early apoptotic cells with combination DCA-cisplatin compared with cisplatin alone. The pilot study to evaluate DCA-only cytotoxicity in a xenograft nude mice model showed no difference in tumor size or weight between groups after 7 weeks. The groups had no difference in gene expression of PDK4, HIF-1 α , PPAR γ , Bax, Bcl2 or IL10. Investigation of the in vivo effect of combination DCA and cisplatin is ongoing, with initial results showing a lower rate of tumor growth in cisplatin-treated mice groups at week 2.

Conclusion: We established a preclinical cell culture model and observed enhanced cytotoxicity of bladder cancer cells on cotreatment with cisplatin and DCA, which may provide a better therapeutic outcome compared to cisplatin alone.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Choudhary D, Mikhalyuk A, Pilbeam C, Taylor JA. Increased Expression of PDK4 in Bladder Cancer Cells. Proceedings of the 106th Annual Meeting of the American Association for Cancer Research; 2015 Apr 18-22; Philadelphia, PA. Philadelphia (PA): AACR; 2015. Abstract nr 1171.
2. Kumar A, Kant S, Singh SM. Antitumor and chemosensitizing action of dichloroacetate implicates modulation of tumor microenvironment: A role of reorganized glucose metabolism, cell survival regulation and macrophage differentiation. Toxicology and Applied Pharmacology. 2013. 273; 196-208.

Improving Vision Screening Rates of 3-year-olds in a Primary Care Clinic

Whitney Washburn, BS¹, Patricia Garcia, MD², Catherine Wiley, MD²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*Primary Care, Connecticut Children's Medical Center, Hartford, CT*

Background/Objective: Early detection of refractive amblyopia results in better long-term visual outcomes. Therefore, a goal of Healthy People 2020 is to increase vision screening rates in preschool aged children from 40% to 50%. We aimed to improve our vision screening rates to >90% of 3-year-old children.

Design/Methods: We obtained baseline vision screening rates for 3-year-olds by a 1-month retrospective chart review. Using successive improvement cycles (plan-do-study-act) and run charts, we monitored vision screening attempts, successful completion, and time to screen over the improvement period for all 3-year-olds presenting for well child appointments. We introduced an autorefractor to supplement testing with visual acuity charts. Screening rates and mean time to screen were compared using chi square and t-tests.

Results: Over the 12-month project period, 520 3-year-old children presented for well child visits (mean age 37.5 months, 51% male, 84% Medicaid, and 9% uninsured). Screening was attempted for 305 of these children. Attempted vision screening rates increased from <2% in August 2014 to 83% in August 2015 ($P < .001$). Successful screens increased from <2% to 57% ($P < .001$, see figure). During the study period only 18% of patients were able to complete screening with visual acuity charts but 63% were successfully screened using the autorefractor ($P < .001$). Average time spent screening decreased during the intervention period from 5.4 minutes in June 2015 to 2.6 minutes in July 2015 ($P < .001$).

Conclusions: Using quality improvement methodology, vision screening in our practice became more consistent, efficient and effective. Key interventions to successful implementation included optimizing use of the autorefractor, one-on-one training, and at-the-elbow support for staff. Ongoing barriers include time-pressure and variable tester confidence. Future study will analyze referral outcomes made during this project.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. American Academy of Ophthalmology. Joint Policy Statement on Vision Screening for Infants and Children, 2013. Found at: http://www.aapos.org/client_data/files/2014/337_visionscreeningforinfantsandchildren_2013.pdf
2. American Academy of Pediatrics. Eye Examination in Infants, Children, and Young Adults by Pediatricians. *Pediatrics* 2003; 111(4): 902. DOI: 10.1542/peds.111.4.902-907.
3. American Academy of Pediatrics. Instrument-Based Pediatric Vision Screening Policy Statement. *Pediatrics* 2012; 130(5): 983-986. DOI: 10.1542/peds.2012-2548.
4. Cotter, SA., Cyert, LA., Miller, JM., & Quinn, GE. Vision Screening for Children 36 to <72 Months: Recommended Practices. *Optometry and Vision Science* 2015; 92(1):6-16. DOI: 10.1097/OPX.0000000000000429
5. Duncan, Paula. Appendix C: Recommendation for Preventative Pediatric Health Care. From *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents*; Ed. 3 (2008); pg. 591. Also accessible at: http://brightfutures.aap.org/pdfs/Guidelines_PDF/20-Appendices_PeriodicitySchedule.pdf.
6. Duncan, Paula. *Bright Futures: Guidelines for Health Supervision of Infants, Children, and Adolescents*; Ed. 3 (2008); pgs. 442 & 453. Also accessible at: http://brightfutures.aap.org/pdfs/Guidelines_PDF/16-Early_Childhood.pdf (pgs.62 & 73)

The Effect of Neuropeptide Substance P Interaction with Neurokinin-1 Receptor in Rhesus Monkeys following Pathogen Exposure

Ashley Wenger¹, Amanda Burmeister², Ian Marriott²

¹*University of Connecticut School of Medicine, UConn Health, Farmington, CT*

²*University of North Carolina at Charlotte Department of Biological Sciences, Charlotte, NC*

Microbial infection of the central nervous system (CNS) can cause a substantial inflammatory response. Although inflammation can have a protective role in pathogen elimination it can often lead to CNS damage, such as astrogliosis, resulting in neurological dysfunction. The neurokinin substance P (SP) has been identified as a potential player in the neuroinflammatory process due to its role in the augmentation of inflammatory responses at peripheral sites such as the skin and gastrointestinal tract, and due to its abundance in the brain (1). Previous studies have demonstrated that administering an antagonist for the SP receptor neurokinin-1 (NK-1R) causes an attenuated inflammatory response following CNS infection with the clinically relevant bacterial pathogen *Borrelia burgdorferi* in mouse models (2), however non-human primate models have yet to be studied. Using immunohistochemical staining for glial fibrillary acidic protein, an astrocyte marker, we assessed the amount of astrogliosis that occurred following rhesus monkey CNS infection with *B. burgdorferi* in both the presence and absence of an NK-1R antagonist. Contrary to our hypothesis, we found that infection with *B. burgdorferi* caused astrocyte death, not astrogliosis, and that blocking the interaction between SP and NK-1R may reduce this cell death. These results could have important implications for the future treatment of meningitis and other diseases involving damaging neuroinflammation.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

- I. Marriott. 2004. The role of tachykinins in central nervous system inflammatory responses. *Front. Biosci.* 9: 2153–2165.
- Chauhan, V. S., D. G. Sterka Jr., D. L. Gray, K. L. Bost, I. Marriott. 2008. Neurogenic Exacerbation of Microglial and Astrocyte Responses to *Neisseria meningitidis* and *Borrelia burgdorferi*. *J. Immunol.* 180: 8241–8249.

A Cross-sectional Study of Helmet Usage Behavior among Motorcyclists in Connecticut

Meghan Wilson¹, Robert Brown², Karyn Butler², Brendan Campbell^{1,2,3}, Susan DiVietro^{1,2,3}, D'Andrea Joseph^{1,2,3}, Garry Lapidus^{1,2,3}, Eric Klein^{1,2,3}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Hartford Hospital, Hartford, CT

³Connecticut Injury Prevention Center at Connecticut Children's Medical Center, Hartford, CT

Motorcycles place riders at significantly increased risk of head and facial injuries as compared to enclosed vehicles. The long-term burden of motorcycling injuries is poorly documented beyond early death or initial hospitalization.¹ Wearing a helmet significantly decreases the injury burden that a rider suffers as a result of a crash.²⁻³ When not required by law, approximately half of riders choose not to wear a helmet.⁴ Reasons for not wearing a helmet have been well documented in multiple studies, although they differ by country.⁵ The purpose of this study is to identify the prevalence of motorcycle riding among the emergency department patient population and to examine factors that may influence riding behaviors, including helmet use, crash history, and attitudes towards helmet laws among riders. Our specific aims are to: 1) determine the prevalence of and demographic characteristics associated with motorcycle riding among the ED patient population; 2) estimate helmet use among motorcycle riding patients and to identify attitudes, beliefs, and behaviors pertaining to helmet use and helmet laws; and 3) examine associations between retrospectively reported motorcycle crashes and rider health and behaviors. Our preliminary results show that of participants who ride motorcycles 40.5% have always worn a helmet in Connecticut, Rhode Island, or New Hampshire, which are states that do not have a universal helmet law. 16.7% and 11.9% reported that they have family members or close friends hospitalized after a motorcycle crash. Additionally, 66.7% think the government should make wearing a helmet mandatory for all riders. Factors that increase motorcycle helmet usage, other than legal mandate, are not well understood.⁶ A better understanding of the factors that influence helmet use can help guide strategies to increase helmet usage and decrease the injury severity of Americans who are involved in motorcycle crashes.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Centers for Disease Control and Prevention (CDC). Helmet use among motorcyclists who died in crashes and economic cost savings associated with state motorcycle helmet laws--United States, 2008-2010. *MMWR Morb Mortal Wkly Rep*. 2012 Jun 15;61(23):425-30.
2. Cavalcante JR, Oka SC, de Santana Santos T, Dourado E, de Oliveira E Silva ED, Gomes AC. Influence of helmet use in facial trauma and moderate traumatic brain injury victims of motorcycle accidents. *J Craniofac Surg*. 2012 Jul;23(4):982-5.
3. Crompton JG, Oyetunji TA, Pollack KM, Stevens K, Cornwell EE, Efron DT, Haut ER, Haider AH. Association between helmets and facial injury after a motorcycle collision: an analysis of more than 40 000 patients from the National Trauma Data Bank. *Arch Surg*. 2012 Jul;147(7):674-6.
4. McCartt AT, Blunar L, Teoh ER, Strouse LM. Overview of motorcycling in the United States: a national telephone survey. *J Safety Res*. 2011 Jun;42(3):177-84.
5. Germei E1, Lionis C, Davou B, Petridou ET. Understanding reasons for non-compliance in motorcycle helmet use among adolescents in Greece. *Inj Prev*. 2009 Feb;15(1):19-23.
6. Ranney ML, Mello MJ, Baird JB, Chai PR, Clark MA. Correlates of motorcycle helmet use among recent graduates of a motorcycle training course. *Accid Anal Prev*. 2010 Nov;42(6):2057-62.

Propensity Analysis of Mortality One Year after Acute Myocardial Infarction

Karen Xiao¹, John Spertus, MD, MPH, FACC^{2,3}, Garth Graham, MD, MPH^{4,5}

¹University of Connecticut School of Medicine, UConn Health, Farmington, CT

²Health Outcomes Research, St. Luke's Mid America Heart Institute. Kansas City, MO

³Washington University School of Medicine, St. Louis, MO

⁴Aetna Foundation, Hartford, CT

⁵Department of Cardiology, University of Connecticut Health Center, Farmington, CT

It is well known that there is variation in acute myocardial infarction (AMI) outcomes by race (1-2). However, it is unclear whether race is the primary mediating factor effecting such outcomes or whether other factors such as socioeconomic status (SES), psychological support, social support, and overall health have a significant role in influencing mortality one year post-AMI. The purpose of this research is to compare the patient characteristics of black and white patients using propensity analysis and to determine the extent to which other factors attenuate the effect of race on mortality one year post-AMI.

The patient population was pulled from the Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER) study, in which patients with MI were prospectively screened and enrolled from 19 US centers. The baseline profile of white and black patients with AMI were analyzed using chi-square testing for categorical variables. We then created propensity scores for being of black race, creating groups that were phenotypically black and white. One year outcomes of survival±health status were generated across these groups, and propensity scores for mortality 1 year post-AMI were generated for each patient based on 4 validated surveys for SES, psychological support, social support, and overall perceived health. Each of the 4 variables was analyzed independently for their effect on 1 year outcomes post-AMI.

Baseline patient data was gathered from PREMIER yielding white (n=1335) and black (n=514) patients with a mean age of 61.7 and 57.3, respectively (p<0.001). The difference in unadjusted mortality 1 year after AMI was 1.86 (p<0.001) between black and white patients. However, 1 year mortality post-AMI for propensity-matched patients was 1.05 (p = 0.71). Individual analysis of SES revealed that 1 year mortality for white patients vs. black patients was 4.5% and 7.8% respectively for the 1st quintile; 4.5% vs. 7.2% for the 2nd quintile, 5.3% vs 9.3% for the 3rd quintile; 8.4% vs. 7.8% for the 4th quintile; and 11.1% vs. 12.5% for the 5th quintile. In all quintiles but the 4th, black patients were found to have a higher 1 year mortality post-AMI. Independent analysis of psychosocial support and health did not produce significant results.

When other variables such as SES, psychological support, social support, and overall health are accounted for, the effects of race on one year mortality post-AMI are attenuated. The effect of SES on one year mortality is particularly significant because it suggests that race plays a larger role in mortality in higher SES quintiles compared to lower quintiles where SES has a larger effect. Thus, clinical intervention should be modulated not by race, but by disparities in SES.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Brown TM, Deng L, Becker DJ, et al. Trends in mortality and recurrent coronary heart disease events after an acute myocardial infarction among Medicare beneficiaries, 2001-2009. *Am Heart J.* 2015;170(2):249-55.
2. Singh JA, Lu X, Ibrahim S, Cram P. Trends in and disparities for acute myocardial infarction: an analysis of Medicare claims data from 1992 to 2010. *BMC Med.* 2014;12:190.

RESEARCH AWARDS

SCHOOL OF DENTAL MEDICINE

DEAN'S AWARD: Awarded by Dr. Monty MacNeil in recognition of an outstanding presentation demonstrating clinical application and technique relating to dentistry. The award consists of an expense-paid trip as the School of Dental Medicine representative to the Hinman Student Research Symposium, and the student's name engraved on a plaque.

ASSOCIATE DEAN'S AWARD: Awarded by Dr. Rajesh Lalla in recognition of an outstanding presentation in basic, clinical or behavioral science. The award consists of round trip travel and accommodations to attend the ADA Annual Dental Students' Conference on Research in Gaithersburg, Maryland.

ADA/DENTSPLY STUDENT CLINICIAN AWARD: Awarded by Mr. Joel Monteiro in recognition of an outstanding presentation. It includes round trip coach fare to city of annual session of American Dental Association as school representative, allowance for lodging, food and other expenses, and ADA/Dentsply plaque.

COLGATE-PALMOLIVE STUDENT RESEARCH AWARD: An award of \$1000, present by Ms. Diane S. Peterson, to a second year dental student at the School of Dental Medicine, in recognition of exemplary knowledge, understanding and presentation of basic and clinical dental research at Student Research Day.

CONNECTICUT HOLISTIC HEALTH ASSOCIATION: This annual award, presented by Dr. Michael Basso, was established to recognize excellence in research in Integrative/Complementary and Alternative Medicine. A medical student and a dental student will receive \$100 and have their names engraved on a plaque.

GUSTAVE PERL MEMORIAL AWARD: A monetary award of \$100, for outstanding original research, and the student's name engraved on a plaque.

UNIVERSITY OF CONNECTICUT SCHOOL OF DENTAL MEDICINE SOCIETY OF ALUMNI & FRIENDS: A monetary award of \$150, for original research having a direct application to dental practice, and the student's name engraved on a plaque.

JOHNSON & JOHNSON RESEARCH EXCELLENCE AWARD: Awarded by Ms. Nikki Caesar in recognition of an outstanding research project relating to the field of periodontology. This award consists of an engraved plaque to be displayed at UConn, a small plaque for the recipient, and a \$150 UCHC Bookstore gift card.

DENTAL STUDENT RESEARCH SOCIETY: A monetary award of \$100, for excellence of science presentation by an undergraduate student.

OMICRON KAPPA UPSILON AWARDS: In recognition of excellence in the art, science, and literature of dentistry, Dr. Reza Kazemi, Vice President of the UCONN Health Chapter of Omicron Kappa Upsilon, the national dental honor society, presents \$25 gift certificates to the UCHC Bookstore to all dental students who have participated in Research Day activities.

SCHOOL OF MEDICINE

DEAN'S AWARD: In recognition of two outstanding medical student researchers and their faculty mentors. Awards of \$250 each will be presented to the four awardees. The awards to faculty mentors will be used for travel to a scientific meeting.

DR. AND MRS. JEFFREY GROSS: Dr. and Mrs. Jeffrey Gross established this award. Jeffrey Gross, M.D., is Professor and Chair of the Department of Anesthesiology at UCHC. Awards of \$250 each will be given to two medical student researchers who presented excellent studies. One award will go to an oral presentation and one award will go to a poster presentation.

LAWRENCE G. RAISZ AWARD FOR EXCELLENCE IN MUSCULOSKELETAL RESEARCH: In honor and memory of Lawrence G. Raisz, M.D., this award of \$250 will be given to a medical student researcher who presented outstanding work in the field musculoskeletal research.

CONNECTICUT HOLISTIC HEALTH ASSOCIATION: Awarded by Dr. Michael Basso, this annual award was established to recognize excellence in research in Integrative/Complementary and Alternative Medicine. A medical student and a dental student will each receive an award of \$100. Special thanks go to Dr. Michael Basso of the Connecticut Holistic Health Association.

WILLIAM M. WADLEIGH MEMORIAL AWARD FOR INTERNATIONAL HEALTH RESEARCH: This award of \$150 was established in honor of Bill Wadleigh, former Assistant Director of the Center for International Community Health Studies, at the University of Connecticut Health Center, for commitment to diversity.

CONNECTICUT ACADEMY OF FAMILY PRACTICE: Two medical students will receive this \$200 monetary gift for excellence in Primary Care Research.

ACKNOWLEDGEMENTS

In acknowledgment of the efforts of our Medical and Dental student researchers, their faculty mentors, the members of the Medical and Dental Student Research Committees and all those involved in making this day possible.

Medical/Dental Student Research Committees

School Of Medicine

Dr. Lynn Puddington, Co-Chair

Medical School Judges

Dr. Robert Cushman

Dr. Anne Delaney

Dr. Kevin Dieckhaus

Dr. Judith Fifield

Dr. Jeffrey Gross

Dr. John Harrison

Dr. Laura Haynes

Dr. David Henderson

Dr. Marja Hurley

Dr. Barbara Kream

Dr. Joseph Lorenzo

Dr. Bruce Mayer

Dr. Carol Pilbeam

Dr. Pam Taxel

Dr. Jane Ungemack

The Biomedical Science Postdoctoral
Scholars

School Of Dental Medicine

Drs. Art Hand and Aditya Tadinada, Co-
Chairs

Dental School Judges

Dr. Deborah Redford-Badwal

3rd year Dental Student, Mr. Christopher
Haxhi

Dr. J. Robert Kelly

Dr. Liisa Kuhn

Dr. Peter Maye

Dr. Easwar Natarajan

3rd Year Dental Student, Mr. David
Remiszewski

With Special Appreciation To:

Dr. Bruce Liang, Dean, School of Medicine

Dr. Monty MacNeil, Dean, School of Dental Medicine

Dr. Suzanne Rose, Senior Associate Dean for Education, School of Medicine

Dr. David Henderson, Associate Dean, Medical Student Affairs

Dr. Christine Thatcher, Associate Dean for Medical Education and Assessment

Amy Chmielewski, Curriculum Coordinator, Clinical Education

Lisa Ramsdell, Administrative Program Coordinator, School of Dental Medicine

Lina Smith, Administrative Program Coordinator, Community Based Education

Darice Schroeder, Administrative Assistant, Clinical Education

Laura Didden, Administrative Officer, School of Dental Medicine

Abigail O'Brien, UConn Foundation

Schools of Medicine and Dental Medicine Awards Acknowledgments

Students (and in some cases, mentors) receive monetary gifts; travel awards, journals and/or their names engraved on plaques.

School of Medicine - A very special thanks to:

Irwin H. and Martha L. Lepow Visiting Professorship Fund
The Scholarship Linked to Discovery Fund
Dean's Award, School of Medicine
Dr. and Mrs. Jeffrey Gross Award for Excellence in Research Achievement
Lawrence G. Raisz Award for Excellence in Musculoskeletal Research
William M. Wadleigh Memorial Award for International Health Research
Connecticut Academy of Family Practice
Connecticut Holistic Health Association, Dr. Michael Basso
Sigma Xi Research Society

School of Dental Medicine – A very special thanks to:

Dr. Monty MacNeil, Dean's Award
Dr. Rajesh Lalla, Associate Dean's Award
Mr. Joel Monteiro, ADA/Dentsply Student Clinician Award
Dr. Barry Rosenberg, UCONN School of Dental Medicine Society of Alumni & Friends
Dr. Michael Basso, Connecticut Holistic Health Association
The Perl family for the Gustave Perl Memorial Award
Dental Student Research Society
Ms. Nikki Caesar, Johnson & Johnson Health Care Products, Research Excellence Award
Ms. Diane S. Peterson, Colgate Palmolive Award
Dr. Reza Kazemi, Vice President, Omicron Kappa Upsilon Awards

We are especially grateful to the medical and dental dean's offices for their continued support.

Thanks to the Cover Art Contributors: Syed Alam, Daniel Cheong, Andrew Duarte, Benjamin Liba, Jonathan Lis, Sarah Mattessich, Theresa Meotti and Alexandria Meyers