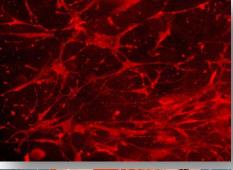
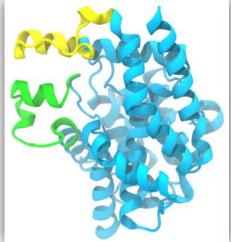
# Medical & Dental Student Research Day 2018







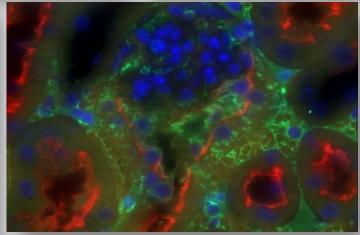












UCONN SCHOOL OF MEDICINE Support provided by the Irwin H. and Martha L. Lepow Visiting Professorship Fund, the UConn Health Discovery Fellowship Fund, and the Hartford Medical Society

UCONN SCHOOL OF DENTAL MEDICINE

# Schedule of Events

# February 26, 2018

#### **TALKS**

9:00 - 11:45AM Academic Rotunda

#### **KEYNOTE SPEAKER**

12:00 - 1:00PM Academic Rotunda

#### **POSTERS**

2:00 – 5:00PM Academic Rotunda



#### **KEYNOTE ADDRESS**

"Hormonal Regulation of Stem Cells and Lineage Development"

David Breault, M.D., Ph.D.

David T. Breault received his BS from Trinity College (USA) and his MD/PhD from the University Connecticut School of Medicine and The Graduate School, followed by clinical and research training at Yale-New Haven Hospital, Boston Children's Hospital and Harvard Medical School, where he is a Clinician Scientist. He is a Principal Faculty member of the Harvard Stem Cell Institute and a Member of the Harvard-MIT Health Sciences and Technology Faculty. His research focuses on understanding the hormonal regulation of stem cells and their lineage development, particularly as applied to tissue regeneration and repair. In 2011, he was a recipient of the Presidential Early Career Awards for Scientists and Engineers, the highest honor bestowed by the United States government on science and engineering professionals in the early stages of their independent research careers.

# Oral Presentations

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9:00 – 11:45AM Ac	cademic Rotunda
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Session 1: 9:00am - 10:15am

- 9:00: A Comparative Analysis between Radiographs and Photographs to Determine the Value-Addition of the Lateral Cephalometric Anjali Dinesh, Aditya Tadinada
- 9:15: Loss of Functional Connectivity Precedes Cortical Thinning in Primary Lateral Sclerosis

  <u>Devin Bageac</u>, Michael G. Clark, Rachel Smallwood Shoukry, Caleb J. Huang, Laura E. Danielian, Mary Kay Floeter
- 9:30: Low Phosphate Diet Partially Corrects the Skeletal Abnormalities in a Mouse Model for Craniometaphyseal Dysplasia

  <u>Eric Ress</u>, I-Ping Chen
- 9:45: Epidemiological Trends In Neuroendocrine Tumors: An Examination of Incidence Rates and Survival of Specific Patient Subgroups Over the Past Decade Paul E. Sackstein, Daniel S. O'Neil, Alfred I. Neugut, Tito Fojo
- 10:00: Sex Tourism, Condomless Anal Intercourse, and HIV Risk Among Men Who Have Sex with Men
  Salem Harry-Hernández, Su Hyun Park, Kenneth H. Mayer, Noah Kreski, William C. Goedel, H. Rhodes Hambrick, Brandon Brooks, Vincent Guilamo-Ramos, Dustin T. Duncan, Bonnie McRee

#### Session 2: 10:30am - 11:45am

- 10:30: Fatalism, Understanding and Barriers to Healthcare for Children with Chronic or Complex Medical Needs in Rural Nicaragua Brooke Schuman, Josue Chavez, Reina Somarriba, Kevin Dieckhaus, Michael Cipoletti, Siddhartha Dante
- 10:45: **Oral Health in Santa Maria de Jesus, Guatemala** Emily Keller, Kevin Dieckhaus, Aditya Tadinada
- 11:00: Should Fecal transplant be Considered Earlier than Fidaxomicin as Therapy for Clostridium difficile Infection?

  Erin Mulry, John Birk, Chia-Ling Kuo, Thomas Devers
- 11:15: In Vivo and In Vitro Analysis of Progenitor Potential of Gli1-expressing Mesenchymal Progenitor cells

  Anastasiya Badziai, Ivo Kalajzic
- 11:30: Identification of Receptors Mediating Serum Amyloid A3 Stimulation of Inflammasome-Dependent Pro-Inflammatory Cytokines in Bone Marrow Macrophages

<u>Rebecca Calafiore</u>, Shilpa Choudhary, Dharamainder Choudhary, Robert Clark, Carol Pilbeam

# Poster Presentations

#### **POSTERS**

2:00 - 3:30 Odd #s; 3:30 - 5:00PM Even #s Academic Rotunda

Dental Student Poster Presentations (#24 - #51)

Student: Yumna Arif #51 Lobby

Mentor: Dr. Peter Maye

Title: TLR Regulation of TGF  $\beta$  Signaling in Cherubism Mutant Myeloid Cells

Student: James Balloch #50 Lobby

Mentor: Dr. Blythe Kaufman

Title: Can Tooth Discoloration Resulting From Contaminated MTA With Blood Be

Reversed by an Internal Bleach Procedure?

Student: Joseph Barbar #49 Lobby

Mentor: Dr. Liisa Kuhn

Title: Model Protein Binding and Release from Hydroxyapatite Crystals

Student: Jillian Bernstein #48 Lobby

Mentor: Dr. Eliane Dutra

Title: Cellular and matrix effects of short- and long-term injection of Botulinum

Toxin into the masseter in the mandibular condylar cartilage of mature

female mice

Student: Erin Bibber #47 Lobby

Mentor: Dr. Deborah Redford-Badwal

Title: Clinical Outcomes of the Furlow Z-Plasty Following Primary Cleft Palate

Repair from 2007-2017

Student: Danielle Brainard #46 Lobby

Mentor: Dr. Aditya Tadinada

Title: Average Height and Width of Posterior Edentulous Sites From An Implant

Planning Perspective

Student: Ross Camiel #45 Lobby

Mentor: Dr. Ivo Kalajzic

Title: Effects Of Notch Inhibition On Fracture Healing Using NRR2 Antibody

Student: Mariamma Chaluparambil #44 Lobby

Mentor: Dr. Liisa Kuhn

Title: Spectrophotometric Assay Of Beta-hydroxyacid (Active) Form Of

Simvastatin In KMNO<sub>4</sub>

Student: Henry Chen #43 Lobby

Mentor: Dr. Caroline Dealy

Title: Regulating Digit Regenerative Potential in a Mouse Model

Student: Tapan Dalal #42 Lobby

Mentor: Dr. Alex Lichtler

Title: Transgenic Reporter Cell Fluorescence Tracking to Monitor the

Differentiation of Murine Cells Along the Osteochondral Lineage

Student: Anthony DeFilippo #41 Rotunda

Mentor: Dr. Mina Mina

Title: Comparison of the Expression of Wnt3a, and Wnt10a in Developing

Odontoblasts in Vivo and in Vitro

Student: Callan Donovan #40 Rotunda

Mentor: Dr. Aditya Tadinada

Title: CBCT Guided Mini-implant placement with Radiographic Guide Yields

Superior Results

Student: Demitria Estrada #39 Rotunda

Mentor: Dr. Ernst Reichenberger

Title: Variant Analysis for Inherited Keloid Formation

Student: Lily Etemad #38 Rotunda

Mentor: Dr. Aditya Tadinada

Title: Prevalence of Incidental Findings in Orthodontic Patients: A Retrospective

**CBCT** Analysis

Student: Brian Greco #37 Rotunda

Mentor: Dr. Frank Nichols

Title: Effect of Novel Porphyromonas gingivalis Glycine Lipids on Osteoblast

Function

Student: Lisa Harris #36 Rotunda

Mentor: Dr. Keri Discepolo

Title: Evaluating the value of an innovative School-Based Dental Clinic in

Connecticut: A pilot study

Student: Maciej Kosakowski #35 Rotunda

Mentor: Dr. Robert Kelly

Title: Compatibility Testing of Obsidian® Lithium Silicate Metal-Ceramic Systems

Student: Abraham Kwok #34 Rotunda

Mentor: Dr. Archana Sanjay

Title: Characterization Of Osteal Macrophages In The Bone Marrow

Student: Grethel Millington #33 Rotunda

Mentor: Dr. Marja Hurley

Title: High Molecular Weight FGF2 in Dentin and Alveolar Bone Mineralization

Student: Robert Morrin #32 Rotunda

Mentor: Dr. Rajesh Lalla

Title: Risk Factors for Severe Oral Mucositis in Head and Neck Cancer Patients

Receiving Radiation Therapy

Student: Chidinma Okafor #31 Rotunda

Mentor: Dr. Sarita Arteaga, Dr. Aditya Tadinada

Title: Reported Oral Health Status of the Adult Population in the Bateye

Communities of the Dominican Republic

Student: Huiyao Ouyang #30 Rotunda

Mentor: Dr. Carol Pilbeam

Title: RANKL-Simulated SOCS3 Expression Depends on Saa3 in Mouse Bone

Marrow Macrophages

Student: Ashley Pacelli #29 Rotunda

Mentor: Dr. Aditya Tadinada

Title: CBCT has Significant Value Addition for Preoperative Implant Treatment

Planning

Student: Daniel Parisi #28 Rotunda

Mentor: Dr. Peter Maye

Title: Examination of TGF  $\beta$  Pathway Signaling Components in Cells Derived

from Cherubism Bone Marrow Stromal Cultures

Student: Nicholas Pray #27 Rotunda

Mentor: Dr. Keri Discepolo

Title: The Effect of Sealants on Six Year Molars Applied at UConn Health: A

Retrospective Cohort Study

Student: Erica Quinones #26 Rotunda

Mentor: Dr. Carol Pilbeam

Title: Parathyroid Hormone Regulates RANKL and OPG in Primary Osteoblasts

via the Protein Kinase C Pathway

Student: Samuel Roh #25 Rotunda

Mentor: Dr. Liansheng Song

Title: Avoidance of Anesthesia Needle Tip Barb Formation to Reduce Risk of

Complications During Administration of an Inferior Alveolar Nerve Block

Injection

Student: Zachary Ward #24 Rotunda

Mentor: Dr. David Banach

Title: Antibiotic Prescription Practices in Outpatient Dentistry: A Descriptive

**Analysis** 

# Medical Student Poster Presentations (#1 - #23: Laboratory, Education; #52 - #89: Clinical, Community and Global Health)

Student: Anne Abbate #55 Lobby

Mentor: Dr. Lisa Chirch

Title: Evaluation of Bone Health Screening Practices Among HIV and Primary

**Care Providers** 

Student: Bayan Abunar #82 Lobby

Mentor: Dr. Hugh Blumenfeld

Title: Analysis Of Interpreter Services Among Arabic Speaking Refugees In

Health Centers In Connecticut

Student: Elizabeth Atteh #68 Lobby

Mentor: Dr. Robert Sherwin

Title: Comparison of Glycemic Variability in Individuals with Normal Weight,

Obesity, Type 2 Diabetes and Type 1 Diabetes

Student: Joshua Baruch Baldino #1 Rotunda

Mentor: Dr. Augustus Mazzocca

Title: In Vitro Characterization of Tissue-engineered Constructs Produced by

Human Subacromial Bursa-Derived Cells and Bone Marrow Stromal Cells

Student: Nicholas Bellas #53 Lobby

Mentor: Dr. Lauren Geaney

Title: Validation of the Single Assessment Numeric Evaluation (SANE) Score as

an Outcome Measure as Compared to the revised Foot Function Index

Student: Patrick Bergamo #2 Rotunda

Mentor: Dr. Anthony Vella and Dr. Stefan Brocke

Title: Targeting Of The Raf-1 Kinase Signaling Complexes In Inflammation

Student: Zachary Boivin #3 Rotunda

Mentor: Dr. Eric Mortensen

Title: Association of Atypical Antipsychotics and Mortality for Patients

Hospitalized with Pneumonia

Student: Jennifer Brewer #67 Lobby

Mentor: Dr. Augustus Mazzocca

Title: Separation Systems Designed for Preparation of Plate-Rich Plasma Yields

Differences in Cellular Viability, Cytotoxicity and Apoptosis

Student: Dylan Buller #54 Lobby

Mentor: Dr. Henry Klar Yaggi

Title: Oxygen versus PAP for Treatment of Sleep Apnea in Chronic Heart Failure

Student: Samuel Crooks #4 Rotunda

Mentor: Dr. Tammy Dugas

Title: Development of a Methylenedianiline Model for Pulmonary Arterial

Hypertension

Student: Sean Cusano #52 Lobby

Mentor: Dr. Beth Taylor

Title: Effects Of Varying Levels Of Physical Activity On HDL, LDL, And

Triglycerides

Student: Quynh-Lan Dao #56 Lobby

Mentor: Dr. David Steffens

Title: Cognitive and Neuroimaging Predictors of Acute Treatment Outcomes in

Late-Life Depression

Student: Antea DeMarsilis #72 Lobby

Mentor: Dr. Stephen Schensul and Dr. Jean Schensul

Title: Patterns of Betel Quid Use Among Women in the Central Province of Sri

Lanka

Student: Shyam Desai #21 Rotunda

Mentor: Dr. Renee Boynton-Jarret

Title: An Evaluation of the CenteringParenting Group Well Child Care Model

Student: Alyssa DiCosmo #73 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Prevalence of Childhood H. pylori Infection, Symptoms, and Associated

Factors in Cyanika, Uganda

Student: Farith Donaghey #74 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Hepatitis C Infection on Guam: Knowledge, Attitudes, and Risk Factors

Student: Michelle Duong #66 Lobby

Mentor: Dr. Stuart Weinzimer

Title: Recent Advances in Type 1 Diabetes Technology: What Do Pediatric

Patients Know And Where Are They Learning It?

Student: Bryan Ferrigno #5 Rotunda

Mentor: Dr. Sangamesh Kumbar

Title: Trans-Differentiation of Human Mesenchymal Stem Cells into Neuronal-like

Phenotype

Student: Alexander Giuliano #75 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Knowledge and Self-Management of Diabetes Among Adults in León,

Nicaragua

Student: Megan Grammatico #65 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Prevalence of H. pylori Infection, Symptoms, and Associated Factors in

Kisoro, Uganda

Student: Nia Harris #77 Lobby

Mentor: Dr. Julian Ford and Dr. Rocio Chang

Title: Filling the Therapeutic Void: Creating Guidelines for "DTD" through Film

Student: Rabale Hasan #78 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Pre-Exposure Prophylaxis Awareness among Primary Partners of HIV+

Populations in Connecticut

Student: Emily Isch #6 Rotunda

Mentor: Dr. Henry Smilowitz

Title: Can a Novel Iodine Nanoparticle Contrast Agent Avoid Contrast Induced

Nephropathy?

Student: Divya Iyer #79 Lobby

Mentor: Dr. Latha Palaniappan

Title: Years of Potential Life Lost Due to Cardiovascular Disease in Asian

American Subgroups 2003-2012

Student: Taylor Jackvony #7 Rotunda

Mentor: Dr. Min Tang-Schomer

Title: Electrical Stimulation Induces Synchronized Activity of Neurons In Vitro

Student: Shaan Kamal #8 Rotunda

Mentor: Dr. Eric May

Title: Computational Investigations into the Structural Characteristics of PDE6

and its Inhibition by PDE6-y

Student: Vijay Kodumudi #10 Rotunda

Mentor: Dr. Caroline Dealy

Title: HBV Vaccine Optimization Via Plasmid Re-engineering

Student: Trisha Kwarko #9 Rotunda

Mentor: Dr. Carol Pilbeam

Title: The COX2 and SAA3 Dependency of LPS-induced NLRP3 Activation and

IL-1β Release

Student: Jennifer Lawson #71 Lobby

Mentor: Dr. Stephen Schensul

Title: Familial Aggregation of CKDu in Endemic Population of Sri Lanka

Student: Robin Lo #20 Rotunda

Mentor: Dr. Linda Shapiro

Title: Role of CD13 in Renal Proximal Tubular Handling of Albumin

Student: Craig Macken #11 Rotunda

Mentor: Dr. Augustus Mazzocca

Title: Novel Source for Cell Augmentation of Murine Patellar Tendon Defect

Student: Forrest Mahony #57 Lobby

Mentor: Dr. Craig Rodner

Title: The Relationship between Shoulder Surgery and the Onset of Cubital

**Tunnel Syndrome** 

Student: Timothy Marquis, Christopher Van Akin and Nicholas Barresi

Mentor: Dr. Thomas Manger #23 Rotunda

Title: Student-Led Educational Quality Improvement (sEQI) of COrE-A, Stage 1,

MDelta Curriculum

Student: Sarah Mattessich #76 Lobby

Mentor: Dr. Sam Soheil Dadras

Title: Characterizing the Expression of Melanoma-related microRNAs in

Dysplastic Nevi

Student: Morgan McCarthy #81 Lobby

Mentor: Dr. Luis Diez-Morales

Title: Neonatal Abstinence Syndrome Comprehensive Education and Needs

Training: A Qualitative Study

Student: Tiffani-Amber Miller #89 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Determining The Relationship Between Knowledge And Attitudes of

Chlamydia Trachomatis Among The Women Of Guam And Their Safe Sex

**Practices** 

Student: Sonal Muzumdar #12 Rotunda

Mentor: Dr. Sam Soheil Dadras

Title: Dicer Expression in Melanocytic Lesions

Student: Kelly Nedorostek #83 Lobby

Mentor: Dr. Christine Ohannessian

Title: Social Media Use and Depression Symptoms in Emerging Adults

Student: Aloys Nsereko #13 Rotunda

Mentor: Dr. Linda Shapiro

Title: CD10, CD13 and CD26 as Potential Biomarkers of early Renal Damage in

Murine models and children with Congenital Ureteropelvic Junction

Obstruction (UPJO)

Student: Deborah Pacik #80 Lobby

Mentor: Dr. Joseph Walker

Title: Controlled Rhythmic Yogic Breathing as Complementary Treatment for

Post-Traumatic Stress Disorder in Military Veterans: A Case Series

Student: Jennifer Park #14 Rotunda

Mentor: Dr. Ariella Shikanov

Title: Biomimetic Hydrogel Based 3D Culture System for Supporting Growth and

Maturation of Primordial Follicles

Student: Christine Parsons #84 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: The Quality and Determinants of Maternal Healthcare in Kisoro, Uganda.

Student: Rashmi Pashankar #58 Lobby

Mentor: Dr. Philip Chan

Title: Barriers to Pre-Exposure Prophylaxis (PrEP) Uptake in Black and

Hispanic/Latino MSM

Student: Colin Pavano #59 Lobby

Mentor: Dr. Robert Arciero

Title: Mid and Long-Term Outcomes for Patients Treated with Distal Femoral

Osteotomy

Student: Brendan Pier #60 Lobby

Mentor: Dr. Agnes Kim

Title: Circulating Biomarkers and Noninvasive Cardiac Imaging Techniques That

Predict Cancer Therapy Cardiotoxicity

Student: Kyle Robey #61 Lobby

Mentor: Dr. Pavlos Papasavas

Title: Healthcare Resource Utilization Associated with Roux-en-Y Gastric Bypass

vs. Sleeve Gastrectomy

Student: Robert Romano #15 Rotunda

Mentor: Dr. Travis Hinson

Title: Assessing Pathogenicity of beta-Myosin Heavy Chain Gene Variants Using

Human Stem Cell-Based Assays

Student: Nicholas Saba #16 Rotunda

Mentor: Dr. Royce Mohan

Title: Peptidyl arginine deiminase-4: A Gliosis-Associated Target for Age-related

Macular Degeneration

Student: Allison Sadowski #70 Lobby

Mentor: Dr. Ted Rosenkrantz

Title: Effect of Study Duration/Time of Day on Studying Respiratory Abnormalities

in Former Preterm Infants

Student: Mohaned Serdah #85 Lobby

Mentor: Dr. Susan Levine

Title: Implementation of a New Residency/Medical School Curriculum in

Refugee Health at UConn Health

Student: Brandon Shore #17 Rotunda

Mentor: Dr. Pablo Romagnoli and Dr. Lynn Puddington

Title: Evaluation of Indole-3-Propionic Acid and Probiotics on the Restoration

and Integrity of the Microbiome in Inflammatory Bowel Disease

Student: Martina Sinopoli #86 Lobby

Mentor: Dr. Valerie Duffy

Title: Electronic Tailored Health Messages and Coordination of Care at

Connecticut Children's Medical Center's Primary Care Center

Student: Samuel Southgate #22 Rotunda

Mentor: Dr. Alise Frallicciardi

Title: Impact of Just-In-Time Emergency Department Simulation Training on

Medical Student Procedural Performance

Student: Kristin Torre #69 Lobby

Mentor: Dr. Michael Murphy

Title: Molecular Testing Practices and Perceptions Among Dermatopathologists

Student: Kodi Udeh #18 Rotunda

Mentor: Dr. Indranil Sinha

Title: Evaluation Of The Hypoxia Pathway in Skeletal Muscle Regeneration

Student: Vruksha Upadhyay #87 Lobby

Mentor: Dr. Kevin Dieckhaus

Title: Prevalence, Symptomology and Associated Factors of Helicobacter pylori

infection in La Romana, Dominican Republic

Student: Rafael Vissepo #19 Rotunda

Mentor: Dr. Nilanjana Maulik

Title: Engineered Nanofibrous Scaffold Loaded with Resveratrol Preserves

Cardiac Function Following Myocardial Infarction

Student: Stephanie Vu #62 Lobby

Mentor: Dr. Lisa Barry

Title: Association Between In-Office Gait Velocity Assessments and Processing

Speed in Geriatric Clinic Patients

Student: Kristina Wagner #63 Lobby

Mentor: Dr. Matthew Ledford

Title: Employing Risk Stratification to Decrease CT Pulmonary Angiogram Usage

for Pulmonary Embolism Diagnosis

Student: Yanbin Wang #64 Lobby

Mentor: Dr. Christopher Morosky

Title: The Effects of Low-dose Aspirin on the Placental Pathology of Women at

Risk for Preeclampsia

Student: Christina (Cheng) Yang #88 Lobby

Mentor: Dr. Judy Lewis

Title: Women's Breast Cancer Knowledge and Beliefs in the Context of a Rural

Haitian Community

# Evaluation of Bone Health Screening Practices Among HIV and Primary Care Providers Anne Abbate<sup>1</sup>, Faryal Mirza<sup>1</sup>, Sabina Zawadzka<sup>1</sup>, Michael C. Thompson<sup>1</sup>, Lisa Chirch<sup>1</sup> \*\*Tuniversity of Connecticut School of Medicine, UConn Health, Farmington, CT

HIV-positive individuals have a higher prevalence of osteoporosis and fractures compared to uninfected matched controls [1]. Causes include viral factors, exposure to antiretroviral therapy (ART) and increased frequency of secondary risk factors [2,3]. Increased life-expectancy makes prevention of bone loss an increasingly important component of HIV care. In 2015, the Infectious Diseases Society of America (IDSA) released screening guidelines for HIV-infected patients [1]. Our goal is to assess provider knowledge about these guidelines and implement an intervention to improve adherence as well as to assess secondary risk factors for fragility fractures.

Surveys sent to primary care and ID providers assessed knowledge of current guidelines for bone health screening. A total of 27 HIV infected patients were surveyed using a questionnaire. Predicted fracture risk was calculated using the Fracture Risk Assessment Tool (FRAX). Notifications were sent to providers for DXA eligible patients. Data including viral loads, CD4 counts, ART and DXA history was extracted. Correlations between secondary risk factors and fragility fracture risk were assessed.

Seventy eight percent of providers were unaware of current IDSA guidelines, although 74% knew that HIV infection was a specific risk factor. Ninety six percent of providers were unaware of specific recommendations pertaining to men with HIV. Patient demographics included a mean age of 54 years; 44% were of African American descent, 33% Caucasian and 22% of Hispanic ethnicity. Seventy percent of patients had a fracture history, with a 42% of these were fragility fractures. All patients with fragility fracture history had a history of tenofovir exposure (p=0.08). Protease inhibitors were protective for fragility fracture (p=0.02). Twenty two patients (81%) met criteria for a DXA; however only 3 of these (14%) had a previous DXA performed.

Initial results reveal low levels of provider awareness of and compliance with guidelines for bone health screening despite this being a high risk population. Knowledge of appropriate screening of HIV infected men was particularly poor. A correlation between tenofovir exposure and fragility fractures was noted, which has been previously described. Interestingly, none of the patients taking protease inhibitors sustained a fragility fracture. Further provider education and additional evaluation of risk factors unique to this high risk population is warranted.

Supported by: UConn School of Medicine Summer Research Fellowship

- 1. Brown, T.T., et al., *Recommendations for Evaluation and Management of Bone Disease in HIV.* Clinical Infectious Diseases, 2015. 60(8): p. 1242-1251.
- Fakruddin, J.M. and J. Laurence, HIV envelope gp120-mediated regulation of osteoclastogenesis via receptor activator of nuclear factor κB ligand (RANKL) secretion and its modulation by certain HIV protease inhibitors through interferon-γ/RANKL cross-talk. Journal of Biological Chemistry, 2003. 278(48): p. 48251-48258.
- 3. Gazzola, L., et al., Association between peripheral T-Lymphocyte activation and impaired bone mineral density in HIV-infected patients. Journal of translational medicine, 2013. 11(1): p. 51.

### Analysis Of Interpreter Services Among Arabic Speaking Refugees In Health Centers In Connecticut

Bayan Abunar<sup>1</sup>, Robert Romano<sup>1</sup>, Hugh Blumenfeld<sup>2</sup>

<sup>1</sup>University of Connecticut School of Medicine, UConn Health, Farmington, CT

Thousands of new refugees have entered the US in search of a safer home, and due to the valiant efforts of organizations in CT such as the Integrated Refugee & Immigrant Services (IRIS) as well as Catholic Family Charities, CT is the 12th largest Syrian resettlement in the nation<sup>17</sup>. Refugees are a vulnerable population in the US<sup>3,14</sup> especially when it comes to health care<sup>9,12</sup>. Numerous literature reviews state language services are a necessary component to health care equity<sup>6,9,16</sup>. Our goal is to evaluate the use of professional interpreters and to further assess if we have improved patient understanding and satisfaction of their care since interpreters have become required by medical professionals. We aim to elucidate the prevalence of interpreter services usage for Arabic refugee patients in the primary care setting and improve our understanding of the efficacy of these services in improving care. Our study aims to show 1) how often interpretation services are offered and used in Arabic refugee populations 2) how well their interpreters are functioning in improving the experience and health for patients and 3) how the provision of interpreter services affects the patients' satisfaction with American Health care. Additionally, we hypothesized that dialects can cause unanticipated miscommunication for patients. As far as we know, this angle has not been explored or reported in recent literature.

<u>Methods:</u> 14 families were provided a questionnaire specifically asking 1) background information 2) their experience with several interpreter services, 3) satisfaction of communication between the provider and patient through the interpreter and 4) understanding the treatment plan.

<u>Results:</u> All participants received health care from local health centers in the Greater Hartford Area. All were offered an interpreter: in-person, telephone, or MARTII. All participants were either "satisfied" or "strongly satisfied" regarding two-way communication between the provider and the patient regardless of mode of interpretation modality. Additionally, 79% of participants understood their treatment and how to use it; however, 21% did not.

<u>Conclusion:</u> Refugees are consistently offered options for interpretation services. As hypothesized, the use of in-person interpreters led to dialect inconsistencies, rendering this modality at a disadvantage compared to others. Furthermore, time spent with medical providers was independent of satisfaction of care. The critical information about how to take medications were not consistently portrayed regardless of how well the interaction between provider and patient was; putting refugees at risk. Patients made special note that medication labels were not in native language.

Supported by: St. Francis Medical Center



<sup>&</sup>lt;sup>2</sup>Family Medicine, UConn Health, Farmington, CT

#### TLR regulation of TGF\$\beta\$ signaling in cherubism mutant myeloid cells

Yumna Arif<sup>1</sup>, Peter Maye<sup>2</sup>

<sup>1</sup>University of Connecticut School of Dental Medicine, UConn Health, Farmington, CT <sup>2</sup>Reconstructive Sciences/Center for Regenerative Medicine, UConn Health, Farmington, CT

Background: Cherubism is a rare genetic disorder that presents in children ages 2-7 characterized by bilateral swelling of the lower face, which is caused by significant erosion of the mandibular and maxilla bones and the overgrowth of fibrous cystic lesions [1]. The genetic basis of cherubism was mapped to chromosome 4p16 [2] and later found to be caused by missense mutations in a gene encoding for a signaling adapter protein SH3-domain binding protein 2 (SH3BP2). Recent work has revealed a strong link between TLR signaling, SH3BP2, and the progression of disease [3] It has been shown that SH3BP2 activates the myeloid differentiation factor-88 (MYD88) pathway in macrophages in response to stimulation [4]. Recent work has also shown a possible role for transforming-growth factor-beta (TGFβ) in cherubism, showing inhibitors of TGFβ signaling that rescue osteoblast differentiation and repress osteoclast formation. Many studies have also found a connection between TGFβ and TLR signaling in other fibrotic diseases such as pulmonary and hepatic fibrosis.

<u>Objective</u>: The objectives of this study was to further investigate the possible connection between TLR and TGF $\beta$  signaling in myeloid cells derived from wild type and cherubism mice.

<u>Methods</u>: Myeloid cells were obtained from wild-type and knock-in cherubism mice and were treated with TLR2 agonists (Heat Killed *Listeria monocytogenes*) and TLR4 agonists (lipopolysaccharide from *E.col* K12 strain). The transcriptional changes of TGFβ were analyzed by using techniques of RNA purification, cDNA synthesis, and real-time PCR. To control that we actually activated TLR2 and TLR4 signaling, we also looked at TNFα expression using the same techniques as TNFα has been shown to be activated by TLR signaling [4]. Results were analyzed using Bio-Rad CFX Manager 3.1.

<u>Results</u>: Our preliminary studies do provide some evidence that TLR activation particularly with LPS did increase TGF $\beta$  signaling. BAMBI, an inhibitor of TGF $\beta$  signaling was down regulated, while Pai1, a target gene of the TGF $\beta$  signaling pathway, increased.

<u>Conclusions</u>: Although TLR activation did have an effect on TGF $\beta$  signaling, there were no significant differences observed from myeloid cells derived from wild-type compared to cherubism mice. Furthermore, demonstrating TLR activation through detection in changes of TNFα gene expression at the transcriptional level proved to be difficult. Surprisingly, the bacterial lipids we initially used did not activate TLR2 and TLR4 receptors very efficiently.

**Future Directions**: Examining changes in gene expression at the transcriptional level may not be ideal for TLR activation studies. Future work will investigate changes in gene expression of TNF $\alpha$  and TGF $\beta$  pathway members at the protein level.

<u>Support</u>: The UConn School of Dental Medicine Summer Research Fellowship References:

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## Comparison of Glycemic Variability in Individuals with Normal Weight, Obesity, Type 2 Diabetes and Type 1 Diabetes.

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<u>Background:</u> Continuous Glucose Monitoring Systems (CGMS) provide comprehensive data about an individual's Glycemic Control (GC) and Glycemic Variability (GV), which are both important factors in assessing risk of developing macro- and micro-vascular complications from diabetes. Previous studies have used CGMS to compare GV in individuals with normal weight (NW) to that in individuals with either obesity, type 1 diabetes (T1D), or type 2 diabetes (T2D), however, the full spectrum of differences in GV across these 4 different groups has not been analyzed in a single study.

<u>Hypothesis:</u> GV, as assessed by CGMS, would vary across and between groups in individuals with NW, OB, T2D and T1D.

Methods: 45 subjects (11 M / 34 F), 9 NW, 16 OB, 14 T2D, 6 TID, were asked to wear CGMS (Dexcom G4®) devices for 5-7 days and maintain a food log during the time of CGMS wear. The EasyGV© program was used to calculate 13 commonly reported indices of GV and GC.

Results: All 13 measures of GV and GC were significantly different across groups (All p < 0.005, one-way ANOVA). As expected, the T1D group had the highest GV, followed by the T2D group, while the NW and OB groups had similarly low indices of GV. Between groups analyses demonstrated no statistically significant difference in all 13 measures between the NW and OB groups. Standard Deviation, Lability Index, J Index, High Blood Glucose Index, Mean of Daily Differences, and Mean Amplitude of Glucose Excursions showed statistically significant different values between the NW and T2D, NW and T1D, OB and T2D, OB and T1D, and T2D and T1D groups (All p < 0.05, unpaired t-test).

<u>Conclusion:</u> Our data demonstrates that as expected, NW and OB individuals did not differ in GV or GC values; however, significant differences exist in all other between group comparisons. Because select individual CGMS tracings from the NW and OB groups highlighted glucose perturbations which may be otherwise missed with measures such as HgbA1c, future studies will include analyzing the corresponding food log data to investigate the relationship between food intake and GV in the 4 groups.

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## In Vivo and In Vitro Analysis of Progenitor Potential of Gli1-expressing Mesenchymal Progenitor cells

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<u>Background:</u> Mesenchymal stem cells (MSC) are of great interest in gene therapy as they are safe and free of ethical concerns (1). Their capacity for multipotent differentiation and immunomodulation have been well-characterized. Several studies support perivascular space as the in vivo location of MSCs. However, a major obstacle in MSCs study is the absence of specific in vivo markers and a defined system to track their fate in vivo. Gli1 protein is specifically expressed in perivascular tissues from arteries to capillaries and presents at low frequency, which supports the hypothesis that Gli1-expressing cells may be of MSC nature. We hypothesized that Gli1+ cells represent mesenchymal progenitors of adult bone tissue in bone marrow. Finding specific identification markers for MSCs is a big step in developing bone remodeling techniques and new pharmacological targets. The knowledge gained in these murine models would ultimately be applicable to studies of human cells and metabolic bone diseases.

<u>Objective</u>: The goal of our project was to examine the ability of Gli1-expressing cells to generate osteoprogenitors during long bone formation and remodeling in mouse long bones. We aimed to explore the fate of Gli1-expressing cells in vivo via lineage tracing techniques. Additionally, we wanted to analyze whether the profile of cell surface markers on these cells correlates with the one typical of bone progenitor cells.

Methods: Gli1-CreER<sup>t2</sup> transgenic were treated with tamoxifen (75 μg/g of weight) on day -1 and day 0 and sacrificed on day 2, 14, and 28 to obtain tibia and femur bone samples for histological studies and bone marrow samples for culture and FACS analysis. Histological samples were fixed, embedded in cryomedium, sectioned and imaged at each time point to trace Gli1-expressing cell lineage in vivo. Bone marrow samples were enzymatically digested to obtain single-cell suspensions and their cell surface profiles were characterized via FACS analysis using commercially available antibodies (Sca1, CD51, Ter 119, CD45, CD31). Additionally, bone marrow cultures were induced to differentiate into osteoblasts using alphaMEM medium/10% fetal calf serum (FCS) supplemented with 50 μg/ml ascorbic and 8 mM b-glycerol phosphate for 2 weeks. Osteogenic phenotype was determined via alkaline phosphatase staining and mineralization.

Results: Lineage tracing experiment via histological imaging of long bones on day 2, 14 and 28 post-treatment revealed that Gli-expressing cells were located in perivascular regions of epiphyseal plates and later formed cell columns characteristic of chondrocytes. Additionally, Gli-expressing cells were expressed in periosteal region. Cell cultures induced to osteoblastic differentiation revealed regions of calcification after 2 weeks and Gli-expressing cells stained positive for alkaline phosphatase. FACS analysis of endostium showed that cells expressing Gli1 were negative for hematopoietic markers CD45, Ter119 and CD31 and expressed Sca1 and CD51 cell markers which is characteristic of progenitor cells.

<u>Future Directions</u>: Further experiments involving fracture models and biomechanical testing of newly formed bone should be done. Additionally, studies involving Gli-expressing cells transplantation as well as ablation of these cells would advance this line of research.

<u>Support:</u> This work has been supported by NIH grant AR55607 to Ivo Kalajzic and The UConn School of Dental Medicine Summer Research Fellowship.

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#### Loss of Functional Connectivity Precedes Cortical Thinning in Primary Lateral Sclerosis

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Primary lateral sclerosis (PLS) is a rare variant of motor neuron disease characterized by the insidious onset of progressive spasticity caused by degeneration of corticospinal neurons.[1] The rate of progression is most rapid in the first years after symptoms begin, often reaching a plateau after seven to eight years.[2] This clinical course suggests a limited time window during which corticospinal neurons degenerate and when potential interventions could be targeted. Unfortunately, the diagnosis of PLS is based on clinical criteria that render it indistinguishable from amyotrophic lateral sclerosis (ALS) until four years after symptom onset.[3] In order to establish the diagnosis of PLS before neuronal degeneration has run its course, a method of differentiating it from ALS during the first few year of symptoms must be developed. Importantly, patients with long-standing PLS have neuroimaging findings, which include cortical atrophy,[4] and changes in resting-state networks.[5] Neuroimaging changes that occur in the first years of symptoms-before the disease is clinically distinguishable from ALS-are unknown. The goal of this study was to examine functional or structural neuroimaging changes in the first years after symptoms of PLS begin. Thirteen (13) patients with pure upper motor neuron symptoms for five years or less underwent MRI scanning and longitudinal follow-up to confirm a clinical diagnosis of PLS. These patients were compared to eighteen (18) patients with longstanding, established PLS. Imaging studies consisted of a seed-based analysis of sensorimotor functional connectivity, diffusion tensor imaging measures of white matter integrity, and measures of cortical thickness. Z-statistic images of functional comparisons were thresholded using clusters determined by Z > 2.0 and a (corrected) cluster significance threshold of P=<0.05. We show that loss of functional connectivity in the sensorimotor network precedes cortical thinning in PLS, and occurs during the first 5 years following symptom onset. Furthermore, sensorimotor functional connectivity exhibits a biphasic pattern in PLS, with early loss and later recovery suggesting functional re-organization. This pattern differs from that described for ALS, in which functional connectivity increases early in disease and decreases with progression. Our findings suggest that distinguishing between these two patterns may be an effective way to differentiate between pre-PLS and ALS patients early in disease. Prospective studies in newly-presenting clinic patients will be needed in order to test this hypothesis.

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### In Vitro Characterization of Tissue-engineered Constructs Produced by Human Subacromial Bursa-Derived Cells and Bone Marrow Stromal Cells

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<u>Background:</u> Research has traditionally focused on bone marrow stromal stem cells (bMSCs) to augment tendon repair. Although the value of bMSCs appears promising within the reported literature (1), results have failed to be consistent. Identification and investigation of alternative sources of mesenchymal progenitor cells would be of tremendous utility and could progress the standard of care. The subacromial bursa, regarded as a source of pain in rotator cuff pathology, is typically debrided or excised during surgery. In revision surgery, bursal tissue has been observed even after previous debridement, indicating its regenerative potential. Cells isolated from subacromial bursa express mesenchymal stem cell surface markers and differentiate into multiple mesenchymal cell lineages both *in vitro* and *in vivo* (2–5), suggesting a cellular milieu that may be used to restore rotator cuff function.

<u>Purpose:</u> To compare the cell migration, cell engraftment, and matrix synthesis and organization of subacromial bursa-derived cells versus bMSCs using controlled in vitro systems.

Methods: Bone marrow aspirate and subacromial bursa were acquired from skeletally mature male or female patients between the ages of 18-70 undergoing rotator cuff repair. The cells were labeled with DiO to confirm human origin during analysis. Three distinct experiments were performed. (A) To assess migratory capacity, harvested cells were immediately placed on a two-dimensional cell migration assay and analyzed via spectroscopy at 24-hour intervals until confluent. (B) Tail tendon scaffolds from NSG mice were used to histologically assess the ability of stem cells to incorporate into decellularized matrix. (C) Production of an organized matrix was measured by placing cells into fibrin gels within the Flexcell Tissue Train® three-dimensional culture and histologically analyzing them at 2 and 3 weeks incubation.

<u>Results:</u> Preliminary data suggest that bursa-derived stem cells exhibit superior migration, better incorporate into tendon scaffolding, and produce more organized matrix compared to bMSCs. This study is still in progress and more data will be gathered to quantitatively confirm these results.

<u>Conclusion:</u> The subacromial bursa appears to be a promising source of stem cells for augmented tendon repair that shows greater differentiation potential and cellular characteristics to bMSCs.

Supported by: The UConn School of Medicine Summer Research Fellowship

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# Can tooth discoloration resulting from contaminated MTA with blood be reversed by an internal bleach procedure?

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<u>Background</u>: Mineral Trioixde Aggregate (MTA) was introduced for endodontic application in 1993 with an initial use as a root end filling due to its tissue compatibility and good seal. The use of bioceramic materials that include MTA has broadened to include placement at the cemental enamel junction (CEJ) within the pulp chamber during pulp regeneration procedures on imature teeth with necrotic pulps. Tooth discoloration with Bioceramic materials has been an undesirable side effect to when used in the esthetic zone. Reports of discoloration using white MTA (wMTA) have also been documented, due most likely to the presence of the opacifying agent bismuth oxide. Interest exists among clinicians as to the reversibility of the tooth discoloration observed after using Bioceramic materials.

<u>Objective</u>: To test in an ex vivo model, the reversibility of discolorations specific to wMTA with Blood, GMTA with Blood, GMTA alone, Blood alone using internal or "walking bleach" procedure via spectrophotometric analysis.

<u>Methods</u>: Twenty extracted premolar teeth previously discolored through treatment with GMTA with blood, wMTA with blood, GMTA, and blood were included in this study.

An initial shade measurement was taken for each tooth using a VITA Easyshade spectrophotometry gun and values for lightness (L), red-green (a), and blue-yellow (b) were recorded. Teeth were then prepared by removing previous composite and bioceramic material to the approximate level of the CEJ. Two iterations of walking bleach were performed in succession for 7 days, respectively. Shade checks were done concurrently with values recorded. Additional shade checks were done extending to 3 months.

Results: Across 4 groups of permanent pre-molar teeth previously stained by GMTA contaminated with blood, wMTA contaminated with blood, GMTA only, and blood only: a relationship was found between groups and the degree of color change ( $\Delta E$ ) that could be induced by internal bleaching (p < .0001). The  $\Delta E$ 's by group were: GMTA with blood ( $\Delta E$  10.6), wMTA with blood ( $\Delta E$  10.0), GMTA only ( $\Delta E$  12.8), and blood only ( $\Delta E$  14.7). More specifically, differences in lightness ( $\Delta L$ ) after bleaching teeth previously stained by contaminated MTA materials, when compared to teeth stained by MTA only and blood only were significant (p < .02), while the degree of red-green color changes ( $\Delta a$ ) and blue-yellow color changes ( $\Delta b$ ) were not significantly different. The  $\Delta L$ 's by group were: GMTA with blood ( $\Delta L$  8.6), wMTA with blood ( $\Delta L$  9.2), GMTA only ( $\Delta L$  12.9), and blood only ( $\Delta L$  11).

<u>Conclusions</u>: In discolored teeth, the presence of GMTA and wMTA when contaminated with blood suggests mild resistance to internal bleaching methods when compared to teeth stained by blood only and GMTA only.

<u>Future Directions</u>: To verify findings, the same procedure must be conducted with larger sample size to increase power and shade checks should be performed ranging from cervical to occlusal aspects of tooth crown.

<u>Support</u>: All mentor support provided by Dr. Kaufman, material support included; handover specimens, use of photobooth setup and access to VITA Easyshade gun.

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#### Model Protein Binding and Release from Hydroxyapatite Crystals

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Background: Recent data shows that Dickkopf 1 antibody (Dkk1 Ab) injections have positive effects on bone fractures in old mice [2]. The Dkk1 Ab neutralizes Dkk1. Dkk1 antagonizes the Wnt-β catenin signaling pathway and the inhibition of Dkk1 thus increases osteoblast activity which rely on Wnt signaling [1]. With age Dkk1 increases [1] and thus there is potentially great potential to improve bone healing from anti-Dkk1 treatment approaches. Calcium phosphate (CaP) has been used to deliver active biomolecules [3] and using it for local delivery would avoid systemic side effects. Binding and release studies of proteins are needed for the type of CaP to be used.

<u>Objective</u>: The goal of this in vitro binding and release study is to establish the characteristics of protein binding and release for nanohydroxyapatite (nHA) crystals using a model protein BSA. The long-term goal is to identify a method that could be used to measure binding and release of Dkk1 antibody from a biomaterial. The BSA protein is much cheaper per microgram compared to the cost of Dkk1 Ab, thus it being used as a model for this project.

<u>Methods</u>: Nanohydroxyapatite: Berkeley Advanced Biomaterials, Inc. Cat #BABI-HAP-N20.

The A280 spectrophotometer measured the absorbance of solutions after binding and release experiments of 1.0mg/ml BSA with 5mg of nHA crystals in .01M hepes/.15M NaCl solution. The recorded absorbance levels were extrapolated via standard curve to determine the concentration of BSA. 1.0mg/ml BSA samples were placed with the 5mg nHA in three replicates of six time intervals (ranging 0.5 to 48 hours) and measured via A280 to quantify binding capacity over time. These nHA pellets were then rinsed, placed in the buffer solution, vortexed, and spun down while the supernatant was syringed through a 0.2 micron filter and quantified using the A280 spectrophotometer.

**Results:** The BSA at [1.0] mg/ml bound to the 5mg of nHA at an average of 84 ug per 5mg of nHA, or 16.8 ug/mg nHA, over the course of one day. After the release experiment over a 48 hour the free BSA was measured with A280 and compared to the bound BSA results. The percent of BSA released results in negligible data in each of the samples.

<u>Conclusions</u>: The data shows cases of negative amounts of protein released from the crystals which is physically impossible. This most likely occurred from the nHA crystal being too fine for the filter, resulting in erroneous data.

**<u>Future Directions</u>**: The protocol conceived in this experiment should be used in future studies as a guideline for testing antibody binding and release from nHA crystals.

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# Validation of the Single Assessment Numeric Evaluation (SANE) Score as an Outcome Measure as Compared to the revised Foot Function Index (rFFI)

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Patient reported outcome measures serve as an invaluable tool in both the clinical and research setting to monitor a patient's condition and efficacy of treatments over time. We aim to validate the Single Assessment Numeric Evaluation (SANE) score for disorders of the lower extremity using the revised Foot Function Index (rFFI) as a reference. The rFFI is a validated 34-question survey tool utilized in the evaluation of patients with foot and ankle related pathology [1], while the SANE score consists of a patient's single numerical rating of the status of their extremity [2]. Given its ease of use and prior validation with shoulder pathology, the SANE score has potential as a practical and effective outcome measure in foot and ankle pathology. Patient age, sex, visit diagnosis by ICD-10 code, SANE score, and FFI score were collected retrospectively from 218 initial patient encounters between January 2015 through July 2017. Patients were included if they were 18 years and older presenting for outpatient evaluation to the University of Connecticut Foot and Ankle Orthopedic Department. The rFFI is a 34-question survey with subscales including pain (7 questions), stiffness (7 questions), activity limitation (3 questions), difficulty (11 questions), and social issues (6 questions). Results of the two scores were compared using the Pearson or Spearman correlation coefficients with correlation defined as excellent (>0.7), excellent-good (0.61-0.7), good (0.4-0.6), or poor (0.2-0.39) [3]. Diagnoses were categorized into 9 subgroups that were analyzed including: forefoot, plantar fasciitis, arthritis, deformity, fracture, tendinitis, OCD, soft tissue trauma and "other". The SANE score had good correlation with the overall rFFI score (r=0.51, p<0.001). When comparing the SANE score to the rFFI subscores, there was good correlation with pain (r=0.42, p<0.001), good correlation with stiffness (r=0.44, p<0.001), poor correlation with activity (r=0.36, p<0.001), good correlation with difficulty (r=0.52, p<0.001), and poor correlation with social issues (r=0.39, p<0.001). Sub-analysis showed an excellent to good correlation between SANE and rFFI score for forefoot pathology (r=0.67, p<0.001), "other" pathologies (r=0.65, p<0.001), and plantar fasciitis (r=0.63, p<0.016), good correlation for arthritis (r=0.49, p<0.038), deformity (r=0.60, p<0.010), fracture (r=0.50, p<0.004), and tendinitis (r=0.47, p<0.017), and no significant correlation for OCD of the talus (r=0.56, p<0.145) and soft tissue trauma (r=0.19, p<0.319). The SANE score demonstrates good correlation with the rFFI overall. However, its correlation varies depending on the subscore of the rFFI and the presenting pathology of the patient.

Supported by: The UConn Orthopedic Department

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#### **Targeting Of The Raf-1 Kinase Signaling Complexes In Inflammation**

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Inflammation plays a crucial role in the pathogenesis of countless human diseases. Phosphodiesterase 8A (PDE8A), one isoform of PDE that controls cAMP levels, is critical in regulating the adhesion of T cells to endothelial cells and their migration to sites of inflammation. Recent studies have shown that PDE8A binds with high affinity in a complex with Raf-1. Raf-1 is at the apex of the MEK-ERK pathway, controlling many fundamental biological processes including cell proliferation, survival, and transformation, as well as cell migration. Raf-1 also complexes with an inhibitory protein termed the raf kinase inhibitor protein (RKIP). Previous research has shown the interaction between PDE8A and Raf-1 as well as RKIP and Raf-1 separately regulate vital steps in inflammation. However it is not known how and to what extent these regulatory proteins interact with and influence each other and thus exert their effects on Raf-1 signaling. Further understanding of this is vital for future pharmacological testing.

We present here a first survey of these molecules in naïve mice and mice challenged with a potent immune stimulus in vivo. We show that the expression of PDE8A changes in response to systemic inflammatory conditions in RKIP knockout (RKIP ko) mice via Western Blot (WB) and flow cytometry. The WB protocol was first optimized over many iterations of various combinations of buffers, antibodies, and transfer protocols. After optimization five wild type (WT) and five RKIP ko mice were immunized with staphylococcal enterotoxin A (SEA) based on weight. One mouse from each group was sacrificed on days 0, 1, 2, 3, and 6. After sacrificing, the number of splenic leukocytes was measured and cells were separated into 10 million cell aliquots. WB blot was then performed with staining for RKIP and PDE8A with secondary staining for GAPDH for standardization and loading control. Flow cytometry was used to confirm T cell expansion by staining for CD4, CD8, TCR Vbeta3 and Vbeta14.

Results indicated a comparable number of splenocytes between WT and RKIP ko on days 0, 1 and 2 followed by a massive expansion of WT over RKIP ko on day 3. WB revealed about a 2-fold higher PDE8A expression in WT compared to RKIP ko on every day of the study, including the spleen of a naïve mouse.

The reduced PDE8A expression in WT vs RKIP ko suggests that RKIP expression exerts an influence on PDE8A expression in T cells in normal and systemic inflammatory states. These results are consistent with a model of complex formation between PDE8A-Raf-1-RKIP in T cells and provide rationale for future studies to directly isolate the complex and target it with selective inhibitors in order to characterize the specific inflammatory function controlled by its molecular components.

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# Cellular and matrix effects of short- and long-term injection of Botulinum Toxin into the masseter in the mandibular condylar cartilage of mature female mice

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<u>Background</u>: Injection of Botulinum Neurotoxin Type A (Botox) into the muscles of mastication have been used to improve the symptoms associated with temporomandibular joint disorders (TMDs), myofascial pain syndrome, tension headache and chronic migraines (1, 2). Botox blocks the cholinergic transmission and acetylcholine release at the neuromuscular junction, resulting in temporary flaccid paralysis of the injected muscle (3).

Several reports have shown deleterious effects of Botox injections into the masseter in the mandibular ramus and condyle (4-7). Our preliminary data showed, in addition to previously reported decreased bone volume, dramatic effects on the mandibular condylar cartilage (MCC) 4 weeks after unilateral Botox injection into the masseter of growing transgenic mice. We observed reduced cartilage thickness, decreased cell proliferation, reduced matrix deposition and decreased expression of proteins important for chondrocyte differentiation and endochondral mineralization (8).

The aim of this study was to evaluate the cellular and matrix changes in the MCC of mature female mice after unilateral injection of Botox into the masseter. We have chosen this model since mature female mice may represent a better model for patients with TMD, given that adult females are more likely to develop this condition (9,10). Our <u>hypothesis</u> was that Botox injections into the masseter of mature female mice would cause decreased mineralization, decreased cell proliferation and decreased matrix deposition.

<u>Objective 1</u>: To study bone volume in the mandibular condyle and bone turnover within the subchondral bone of mature female mice after short- and long-term Botox injection into the masseter.

<u>Objective 2</u>: To analyze the cellular proliferation and cartilage thickness of the MCC of mature female mice after Botox injection into the masseter.

<u>Methods</u>: Botox (0.3 U) was injected into the right masseter of 16-week-old female mice. Bone labels (3 days and 1 day before sacrifice) and the proliferation marker EdU (2 days and 1 day before sacrifice) were intraperitoneally injected into experimental mice. Mice were sacrificed 4 or 8 weeks after botox injection. Mice were dissected and examined by micro-CT and histology. Bone turnover was evaluated by TRAP staining and bone labeling. Moreover, we studied cell proliferation by EdU staining and proteoglycan distribution by toluidine blue staining.

Results: Bone volume fraction, tissue density and trabecular thickness were significantly decreased on the subchondral bone of botox injected side when compared to control side, 4 and 8 weeks after injection. Furthermore, histological analysis revealed decrease in mineralization, matrix deposition, TRAP activity, and EdU positive cells in the MCC of the botox injected side, 4 and 8 weeks after injection. In addition, toluidine blue staining revealed decreased cartilage thickness at the Botox injected side in comparison to contralateral side.

<u>Conclusion</u>: Botox injection into the masseter muscle of 16-week-old mice affects bone volume, cartilage thickness and cell proliferation in the mandibular condyle. These results are consistent with the changes observed in younger mice.

<u>Future Directions</u>: We will compare this results to a matching control group in which only saline solution would be injected into the masseter. In addition, we will further demonstrate these effects in a mouse model for TMD (mouse model with temporomandibular joint degeneration).

<u>Support</u>: The University of Connecticut School of Dental Medicine Summer research grant and award from the American Association of Orthodontic Foundation provided to ED and SY.

#### Clinical Outcomes of the Furlow Z-Plasty Following Primary Cleft Palate Repair from 2007-2017

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<u>Background</u>: Cleft lip and palate are among the most common congenital craniofacial anomalies evaluated by a craniofacial team. Successful treatment depends on accurate diagnostics, surgical experience, knowledge of oral/maxillofacial anatomy, and meticulous operative and postoperative care. Cleft palate surgery is designed to allow for separation of the nasal cavity and the oropharynx, and can transform an individual's quality of life by maximizing feeding, speech, and hearing abilities. If the surgery is unsuccessful, complications in the development of an oronasal fistula and/or velopharyngeal insufficiency (VPI) can occur. There is limited evidence on the rationale for the development of an oronasal fistula following primary cleft palate repair. Many surgical techniques have been described in literature, however reported fistula and VPI incidence rates vary widely. The average percentage of the resulting oronasal fistula, as reported by Krishnamurphy et al. in 2016 was 10-30%. Post-operative data of our patient cohort from 1996-2006 demonstrated a fistula rate of 3.6%. The results of this study yielded the lowest incidence rates reported in literature upon publication.

<u>Objective</u>: To a) describe clinical outcomes, including speech evaluations, following the completion of a primary cleft palate repair using the Furlow Z-plasty technique; b) determine if the age at cleft palate repair, cleft palate type, or the presence of a related syndrome is associated with the development of oronasal fistulas or velopharyngeal insufficiencies, and c) to compare the post-operative incidence rates of oronasal fistulas and velopharyngeal insufficiencies between the current patient cohort and those from the previous study published in 2007.

Methods: A single center, retrospective analysis of approximately 350 children diagnosed with Cleft Palate Syndrome who have undergone a Furlow Z-plasty from January 1, 2007 to June 20<sup>th</sup>, 2016 was performed. Data was obtained by review of the subjects' speech evaluations, operative notes, progress notes, and oral/maxillofacial (OMF) reports that had been previously recorded for each patient during CCMC appointments. The data measured includes quality of speech during development, incidence of oronasal fistula, and the need for corrective surgery to manage velopharyngeal insufficiency. Data has been analyzed from patient charts to determine if the age of cleft palate repair, cleft palate type, or the presence of a related syndrome is associated with the development of a post-operative oronasal fistula or velopharyngeal insufficiency, and, ultimately, speech outcomes of patients who have undergone primary cleft palate repair. Statistical analysis will be performed with JMP Statistics Software (SAS Institute, Cary, NC).

**Results**: We will continue to complete the data analysis phase of this study, but current trends suggest concordance with the previous study published in 2007<sup>2</sup>, with a post-operative oronasal fistula incidence rate of approximately 3.3% (244 charts analyzed as of this date with a fistula incidence of 8).

<u>Conclusions</u>: This study will serve to broaden the knowledge on the outcomes of the Furlow Z-plasty for the successful closure of the cleft palate. The findings will be of use to professionals on craniofacial care teams in order to establish a protocol for future families of infants with cleft palate syndrome who are considering primary cleft palate surgery as a treatment option for their child.

<u>Future Directions</u>: In the future, we hope to complete a meta-analysis between the two CCMC studies comparing post-operative results of the Furlow Z-plasty.

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## Association of Atypical Antipsychotics and Mortality for Patients Hospitalized with Pneumonia

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<u>Background:</u> The use of some antipsychotics have been associated with higher mortality in older adult patients with dementia. These medications, especially the newer antipsychotics known as atypical antipsychotics, are commonly used in patients with psychiatric conditions as well as dementia and delirium. The purpose of this study was to examine whether atypical antipsychotics use prior to hospital admission is associated with increased mortality in patients with pneumonia.

<u>Design:</u> We conducted a retrospective cohort study of hospitalized patients with pneumonia at any Departments of Veterans Affairs (VA) hospital over a 10-year period.

Setting: Departments of Veterans Affairs (VA) hospitals

<u>Participants:</u> Patients 65 years or older who consistently received VA care and who were diagnosed with pneumonia. There were 103,997 patients who met the inclusion criteria, 5,977 of whom were taking atypical antipsychotics. We excluded 1,021 patient taking typical antipsychotics.

<u>Measurements:</u> We used multilevel regression models to examine the association between atypical antipsychotics and mortality after controlling for potential confounders.

Results: Atypical antipsychotic use was associated with an increased odds of 30-day (odds ratio 1.27, 95% confidence interval 1.16-1.38), and 90-day (1.31, 1.22-1.40) mortality. There was also an increased odds of 30-day and 90-day mortality in subgroups of patients with preexisting psychiatric conditions (1.13, 1.01-1.27), (1.12, 1.02-1.24) and preexisting cardiac conditions (1.30, 1.14-1.48), (1.38, 1.23-1.54) respectively. However, we found that atypical antipsychotics were not associated with an increased odds of cardiovascular events (0.83, 0.75-0.91).

<u>Conclusion:</u> In patients over 65 years or older that are hospitalized with pneumonia we found an association between atypical antipsychotics use and an increased odds of mortality. This was particularly pronounced for patients with preexisting psychiatric or cardiac conditions. We suggest minimizing use of these medications in older adult patients.

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# Average Height and Width of Posterior Edentulous Sites From An Implant Planning Perspective

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<u>Background</u>: With dental implants becoming an increasingly attractive choice for restoring edentulous sites, factors that determine their success like bone height and width along with ridge topography are important to consider while treatment planning potential implant sites [1]. Knowing the average alveolar ridge heights and widths provide better understanding of ridge dimensions and help in treatment planning.

<u>Objective</u>: To evaluate the average height and width of potential posterior edentulous sites in the maxilla and mandible. Maxillary sinus pathology, bony septa, and mandibular lingual undercuts were also analyzed.

<u>Methods</u>: A total of 310 de-identified CBCT scans referred for dental implant therapy were evaluated. Maxillary and mandibular edentulous first molar sites were evaluated by generating cross sectional images to obtain height and width measurements of the potential implant sites. The height was measured from alveolar crest to the floor of the maxillary sinus and width was measured half way between crest and the sinus floor. In the mandible, the height was measured from alveolar crest to inferior alveolar nerve canal and width was measured at 2mm and 6mm apical to the alveolar crest. Additionally, bony septations and mucosal thickening in the maxillary sinus and lingual undercuts in the mandible were evaluated.

Results: The average measurements in the posterior edentulous left and right maxilla were 5.635mm and 5.654mm in height and 8.769mm and 8.632mm in width, respectively. In the left mandible, the posterior edentulous sites had an average of 10.835mm in height, 8.265mm at 2mm from the alveolar crest, and 11.086mm at 6mm from the alveolar crest. In the right mandible, the posterior edentulous sites had an average of 10.848mm in height, 7.911mm at 2mm from the alveolar crest, and 10.566mm at 6mm from the alveolar crest. Lingual undercuts were found in 33.84% of left mandibular sites and 25.79% of right mandibular sites. Mucosal thickening was present in 24.34% of left maxillary sites, 13.04% of right maxillary sites. Bony septa were present in 10% of left maxillary sites, 2.2% of right maxillary sites.

<u>Conclusions</u>: From an implant planning perspective, this group of patients did not have adequate bone height in the maxillary posterior sites compared to posterior mandibular sites. Bone width was adequate for the majority of maxillary and mandibular sites.

<u>Future Directions</u>: Additional studies with a larger sample size and from other geographic areas must be done to understand ridge topography across larger population groups.

**Support**: UConn School of Dental Medicine Summer Research Fellowship

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## Separation Systems Designed for Preparation of Plate-Rich Plasma Yields Differences in Cellular Viability, Cytotoxicity and Apoptosis

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<u>Background:</u> Platelet rich plasma (PRP) has great potential to increase tissue healing. However the heterogeneity of its preparation methods cause diverse PRP composition making its healing potential difficult to decipher.

<u>Hypothesis/Purpose:</u> The purpose of this study was to investigate the PRP composition differences between two preparation systems. Our hypothesis was that one device creates healthier more viable PRP product.

<u>Methods:</u> Blood samples were obtained from two healthy subjects. PRP was derived using two automatic systems Angel and SmartPRP (Angel, Arthrex Inc., Naples FL; SmartPRP, Harvest Technologies, Lakewood, CO). Leukocyte-rich PRP settings were used based on the manufacturer's recommendation. For each donor, this yielded an average total leukocyte concentration of  $1.01 \pm 0.10 \times 103$  cells/µL and an average platelet concentration of  $2128.67 \pm 0.34 \times 103$  cells/µL. PRP was added at a concentration of 1:10 to all experimental wells that received PRP. There were seven times points 1, 4, 24, 48, 72, 96 hrs. There were six wells per times point, utilizing two systems creating 72 wells for each patient for a total of 144 wells. At each time point the wells were asses for cellular viability, cytotocity and apoptosis.

<u>Results:</u> Significant differences in cellular viability, cytoloxocity, and apoptosis were seen between the SmartPRP and Angel systems for all time points except for viability between the SmartPRP and Angel systems at timpoints 4, 72, and 96 hours. As well as significant differences were seen over time for both the SmartPRP and Angel systems except for time point four hours for all variables tested and for timepoint 48 hours for cell viability.

<u>Conclusion:</u> We found that the Angel system created more healthy looking cells compared to the SmartPRP system. As well as the Angel system had better cellular viability, cytotoxcity, and apoptosis outcomes. Our study, therefore, revealed, that there are differences between PRP preparation systems and future studies should consider preparation techniques when utilizing PRP.

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#### Oxygen versus PAP for Treatment of Sleep Apnea in Chronic Heart Failure

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Sleep apnea is present in more than 70% of patients with chronic heart failure (HF), with approximately half of these cases being of central rather than obstructive etiology.(1) When compared to heart failure patients without central sleep apnea (CSA), patients with co-morbid HF and CSA have a hazard ratio for mortality of 2.1.(2) Unfortunately, while CSA is associated with a greater mortality risk in patients with HF, sleep apnea in chronic HF typically lacks the daytime sleepiness characteristic of sleep apnea in the general population, which may explain why as few as 2% of patients with newly diagnosed HF are evaluated for the presence of sleep apnea within a year of HF diagnosis.(3,4) Treatment of CSA in patients with HF may thus be a wide-spread, relatively non-invasive, and increasingly tolerable intervention that can both extend and improve the quality of patients' lives. In this study, we aim to establish the efficacies of continuous positive airway pressure (CPAP) and nocturnal supplemental oxygen (NSO) compared to a control group receiving usual care and healthy lifestyle and sleep education. 161 patients with co-morbid HF and CSA will be randomized to receive 3 months of treatment with standard medical management alone, standard medical management plus CPAP, or standard medical management plus NSO. Assessment of improvements in cardiac health and exercise tolerance will be analyzed at baseline and at the end of the treatment period, as determined by the change in left ventricular ejection fraction on echocardiography, and change in peak oxygen consumption as measured by cardiopulmonary exercise testing. Secondary outcome measures. such as 24-hour ambulatory blood pressure profile and biomarkers of ventricular remodeling. will also be assessed. Approximately half of the targeted number of subjects have been enrolled and randomized in the study, with the hope that the data collection phase of the study will be completed by the end of the year. Pending data analysis, this study has opportunity for great clinical impact, and may indicate value for sleep studies and subsequent CSA treatment in newly diagnosed HF patients.

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#### Identification of Receptors Mediating Serum Amyloid A3 Stimulation of Inflammasome-Dependent Pro-Inflammatory Cytokines in Bone Marrow Macrophages

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Background: Serum amyloid A (SAA) is a family of acute phase lipoproteins. SAA has been implicated in rheumatoid arthritis, cancer, diabetes, Alzheimer's disease, and amyloidosis. SAA3 is the major inducible SAA in mice. We previously showed that SAA3 is produced by bone marrow macrophages (BMMs) in response to receptor activator of NFkB ligand (RANKL), a critical regulator of bone resorption. Preliminary data showed that (1) RANKL-induced the NLRP inflammasome, a multi-protein complex needed for secretion of IL-1β, and (2) the RANKL induction of II1b and NIrp3 expression and IL-1β protein secretion occurred only in BMMs from wild type (WT) mice and not in BMMs from SAA3 knockout (KO) mice. The goal of this study was to identify receptors on BMMs that mediate the SAA3 activation of the NLRP3 inflammasome. SAA3 acts on osteoblasts via the formyl peptide receptor 2 (FPR2) to inhibit effects of parathyroid hormone. The purinergic receptor P2X7 and the toll-like receptor-2 (TLR-2) can mediate induction of the NLRP3 inflammasome or effects of SAA3 in other tissues. Our initial hypothesis was that SAA3 acted via one of these three receptors on RANKL-stimulated BMMs to induce the NLRP3 inflammasome.

Methods: BMMs were prepared from bone marrow flushed from WT, SAA3 KO, and TLR2 KO mice. Whole marrow was expanded in MCSF (100 ng/ml) for 3 days and then treated with MCSF+RANKL (30 ng/ml) for 6 and 24 h. Treatment with receptor antagonists was begun 1 h prior to RANKL. RNA was extracted (n=3 samples/group) and mRNA measured by qPCR. Statistics were performed using Prism, 1-way ANOVA, p <0.01.

Results: As expected, RANKL stimulated NIrp3 and II1b expression in WT but not SAA3 KO BMMs. In WT BMMs, receptor gene expression of TIr2 and Fpr2 was upregulated by RANKL, while expression of TIr4 and P2x7r was downregulated by RANKL. There was no effect of RANKL on receptor gene expression in SAA3 KO BMMs. Blockade of FPR2 and P2X7R receptors by specific antagonists, WRW4 and KN-62, respectively, or by a TLR4 neutralizing antibody did not inhibit the RANKL-stimulation of II1b mRNA in WT BMMs. Treatment with a TLR2 neutralizing antibody decreased the RANKL-stimulation of II-1b mRNA 97% in WT BMMs. There was no RANKL-stimulation of II1b mRNA in BMMs from TLR2 KO mice, confirming these results.

Conclusions: We conclude that (1) SAA3 may increase RANKL-stimulated TLR2 and FPR2 expression in BMMs and (2) TLR2 is the receptor that mediates the SAA3 stimulation of NLRP3-dependent IL1 $\beta$  in BMMs. Because the NLRP3 inflammasome is implicated in many types of disorders associated with chronic inflammation, identifying the pathways by which SAA3 activates inflammasomes may help us design targeted therapies to reduce the effects of chronic inflammation.

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#### Effects Of Notch Inhibition On Fracture Healing Using NRR2 Antibody

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**Background:** Fracture healing is a complex, multi-step process, which involves hematoma formation, periosteal thickening, callus formation, and osteoclast remodeling. Our work focuses on evaluating the effects of fracture healing in the presence of Notch signal inhibition. This signaling pathway is involved in the transduction of information in the fracture healing process. In order to examine fracture-healing outcomes, Notch receptor 2 signaling was inhibited using an antibody system in a closed fracture mouse model.

<u>Objective</u>: The objective of this study was to specifically inhibit the Notch signaling pathway and assess effect of systemic inhibition of Notch signaling pathway using NRR2 antibody. This study will evaluate callus area and structure (mineralized and cartilaginous area) to determine structural integrity of a fractured bone.

<u>Methods</u>: In this study, we will introduce NRR2 antibody to C57BL/6 mice at age of 8 weeks with experimental and control groups randomly divided. Intra-peritoneal injections of antibody were delivered in dosage of 2.5 mg/kg at three time points: day of fracture, 2 days post fracture, and 4 days post fracture. Control group mice received a GP120 antibody vehicle at the same time points. Fracture healing was assessed by radiography and histology at 7, 14, and 21 days post fracture. Histological analysis was performed on cryostat. Cartilage area was detected using Saffranin O. Mineralized area was detected using Von Kossa. Mineral and cartilage areas were calculated by computer tracing using Zen Microscope Software. All data was expressed as a mean value ± standard error of the mean. Comparison between experimental and control groups was accomplished using 2-tailed, heteroscedastic T-tests. P value < 0.05 was considered to indicate significant differences. The research study consisted of two experiments; experiment 1 included 17 mice (10 female, 7 male), and experiment 2 included 12 mice (12 male).

Results: The result of Notch 2 inhibition was the reduction in total callus area after fracture healing in both experiments. In addition to the results above, in the sample of 10 female mice, Saffranin O stains demonstrated that the NRR2 antibody treated mice have smaller percentage cartilage area within the callus. In the same group, Von Kossa stains demonstrated that the NRR2 antibody treated mice have larger percentage mineral area within the callus. The P-values for the differences in cartilage and mineral area were 0.642 and 0.509 respectively.

<u>Conclusions</u>: In both experiments, Notch 2 inhibition was effective in reducing the total callus area of injected mice. Saffranin O stained groups, NRR2 treated mice exhibited a smaller cartilage percentage of total area. In Von Kossa stained groups, NRR2 treated mice exhibited a greater mineralization percentage of total area. These findings demonstrate improved fracture healing outcomes after Notch 2 inhibition. This model could provide evidence for future therapeutic interventions in skeletal diseases involving Notch 2 dysregulation, such as Hajdu-Cheney and Alagille Syndrome. Additionally, Notch 2 inhibition has potential to accelerate or improve quality in the fracture healing process.

<u>Future Directions</u>: Future work includes using flow cytometry to determine the presence of mesenchymal progenitor cells as well as real-time PCR to assess the expression of downstream genes Hes and Hey.

<u>Support</u>: This work was supported by the Kalajzic Lab and the UConn Dental Summer Research Fellowship.

#### Spectrophotometric Assay Of Beta-hydroxyacid (Active) Form Of Simvastatin In KMNO<sub>4</sub>

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<u>Background</u>: Simvastatin, traditionally administered to treat cardiovascular disease, has been shown to enhance alkaline phosphatase activity and mineralization of bone cells (1), as well as increase the osseointegration of dental implants (2). Localized delivery of simvastatin from a bone graft material would avoid side effects from oral administration yet increase bone formation. There are established methods to measure simvastatin as a pure substance or in serum, but anytime the drug is mixed with other materials then it is necessary to re-validate the method. The Kuhn lab is trying to develop a controlled delivery system for the beta-hydroxyacid (active) form of Simvastatin by adsorbing it on a bone graft like material and then covering it with a calcium phosphate layer. The goal of this project was to evaluate the suitability of a spectrophotometric assay as a measurement technique for the simvastatin released into a calcium phosphate solution.

<u>Objective</u>: The objective of this study was to measure beta hydroxyacid (active) form of Simvastatin using a spectrophotometric assay in KMNO4 as described by Tharpa et al [3]. The standards were then reduced to a narrower low range in order to test if the technique would work to measuring low concentrations of Simvastatin, particularly in a solution used to prepare bioinspired apatite coatings on bone graft.

<u>Methods</u>: The following reagents were prepared: 0.3M NaOH, 0.5M NaOH, 6.328x10^-3M KMNO4, and 9.059X10^-5M Simvastatin. Standards were made according to the table given in 15 ml tubes. 1ml of 0.5M NaOH was added to each tube, and then 1 ml of 6.328x10^-3M KMNO4 was added after. The tubes were kept open for 20 minutes with occasional shaking, and then brought to a volume of 10 mL with water. Each solution was pipetted into three wells of a 96-well plate and absorbance was read at 610 nm against the reagent blank. The experiment was repeated again for data accuracy.

**Results:** The results from the first trial showed that this assay is capable of measuring the Betahydroxyacid form of Simvastatin. R<sup>2</sup> values of 0.97 (active simvastatin) and 0.95 (standard simvastatin) showed the technique was more efficacious for the active form than the standard at a range of concentrations. The results from the second trial showed that at lower concentrations (<1.2 ng/ml), the absorbances were all under 0.004. Since there was not much difference between these and the blank reading, this method cannot accurately measure active simvastatin at lower concentrations.

<u>Conclusions</u>: The data from the experiment shows that this spectrophotometric assay of Betahydroxyacid form of Simvastatin in KMNO<sub>4</sub> is an efficacious measurement method for high concentrations of the drug, but not at lower concentrations. Simvastatin is administered at low doses for maximal therapeutic effect; therefore, this measurement technique would not be ideal for use in measuring low levels released from a drug delivery system.

<u>Future Directions</u>: High performance liquid chromatography (HPLC) is another measuring method that should be tested with Beta-hydroxyacid form of Simvastatin, and may prove to be a better technique for lower concentrations.

Support: The UConn School of Dental Medicine Summer Research Fellowship

#### Regulating Digit Regenerative Potential in a Mouse Model

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**Background:** Limb loss is a clinical challenge in the United States; ~185,000 amputations are performed each year and 1.9M people live with limb loss [1]. The health care costs of limb amputations exceed \$8.3B, not including prostheses or rehabilitation [1,2]. A biological approach to limb regeneration would serve an important clinical need.

Regeneration of limb tissue can occur in mammals including humans, but is restricted to the fingertip (distal terminal phalanx) [3]. Understanding the mechanisms involved in this response might provide insight into ways to promote a regeneration response in more severe limb injuries. The epidermal growth factor receptor (EGFR) is important for cell proliferation, differentiation, and survival [4] and plays a crucial role in skeletal development [5]. EGFR signaling might be important in limb regeneration responses.

<u>Objective</u>: We will determine if activation of EGFR signaling during skeletal development promotes regeneration responses in amputated mouse digits. Our hypothesis is that activation of EGFR signaling will promote and improve the regeneration response following amputation of the digit.

<u>Methods</u>: A transgenic EGFR gain-of-function mouse model was used to activate EGFR signaling. Non-transgenic littermates were used as controls. Digit tips were humanely amputated, and collected at various times. Immunohistochemistry was used to detect proliferation, progenitor cells, and relevant receptors or ligands. Histochemical staining was used to observe growth plates and bone growth. Data was subjected to image analysis (ImageJ) and statistical assessment (Student t-test with SEM) [6].

<u>Preliminary Results</u>: In wild-type digits, multiple receptors were co-localized in skeletal tissue, and activated in stump tissue after amputation. Progenitor and proliferation markers were increased after amputation, indicating presence of a progenitor pool. Surprisingly, regeneration was delayed in our transgenic EGFR-gain-of-function model.

<u>Conclusions</u>: Our results suggest endogenous growth factors are limiting in our model; and that exogenous factors are required for a successful regeneration response.

<u>Future Directions</u>: Based on receptor co-localization, we will identify candidate factors that may promote digit regeneration responses. Future projects will examine the effect of delivery of these factors on digit regeneration responses.

Support: The UConn School of Dental Medicine Summer Research Fellowship

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# **Development of a Methylenedianiline Model for Pulmonary Arterial Hypertension** Samuel Crooks<sup>1</sup>, Tammy Dugas<sup>2</sup>

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Introduction: Pulmonary arterial hypertension (PAH) has an average life expectancy of 2.8 years after diagnosis [1]. It is characterized by vascular smooth muscle cell (VSMC) proliferation resulting in increased pressure in pulmonary arteries. PAH is up to 3-fold more prevalent in women than men. Currently, no animal models reflect this discrepancy. Estradiol is linked to PAH development possibly due to its ability to promote dysregulated vascular uptake of serotonin (5-HT), resulting in VSMC proliferation. 4,4'-Methylenedianiline (DAPM) is an aromatic amine. Treatment of rats with DAPM results in medial hyperplasia of pulmonary arterioles, exclusively in females. The hyperplasia is coupled to increases in pulmonary arterial pressures and a female-specific increase in plasma 5-HT [2]. In vitro, DAPM increases VSMC proliferation. This proliferation is blocked by co-treatment with an SSRI (fluoxetine). Our hypothesis is that DAPM induces PAH in female animals in a manner dependent upon ER-mediated increases in vascular 5-HT synthesis and transport. We propose that the DAPM model will be relevant for delineating PAH disease etiology and may help illuminate new treatments.

Methods: Ovariextomized (OVX) and intact female mice were separated into four treatment groups: vehicle, DAMP, Flu (FLU), and DAMP + FLU. Control animals were gavaged once weekly with a vehicle while DAPM groups were gavaged with 25mg/kg DAPM. FLU animals were administered 10mg/kg/day FLU in drinking water while FLU + DAMP received 25mg/kg DAPM via oral gavage and 10mg/kg/day FLU in drinking water. After 12 weeks animals were sacrificed and tissues collected. Plasma 5-HT and endothelin-1 were assessed using ELISA (Enzo Life). 1-way ANOVA determined if treatment with DAPM or DAPM + FLU resulted in significantly altered levels of plasma serotonin or plasma endothelin-1 (p< .05) when compared to control groups.

Results: There was no significant difference found between the control group and DAPM (P>0.05), control group and OVX (p>0.05), control group and FLU (p>0.05), or control group and FLU with DAMP (p>0.05) when comparing plasma serotonin levels and when comparing plasma endothelin-1 levels. The difference between control group and OVX+DAPM was found to be significant when comparing plasma serotonin (p<0.05) and when comparing plasma endothelin-1 (p<0.05)

<u>Conclusion:</u> No significant differences were found in plasma endothelin-1 or serotonin levels when comparing control groups vs treated groups with the exception of control groups and OVX-DAMP. It is possible the sample size for each group was too small to show significant findings. In future studies, an increase in sample size may show significance. Furthermore, other markers of endothelial disfunction may be analyzed.

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#### Effects Of Varying Levels Of Physical Activity On HDL, LDL, And Triglycerides

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Increased concentrations of LDL cholesterol (LDL-C) particles are associated with increasing rates of accumulation of atherosclerosis [1]. Current ACA/ACC Guidelines suggest that aerobic physical activity (PA) should be encouraged to reduce LDL-C and non-HDL-C [2]. However, the research supporting these claims is not well substantiated. In fact, some research suggests that physical activity has little effect on LDL-C and non-HDL-C, while it is able to increase HDL-C [3,4]. We investigated data from the STOMP clinical trial to assess for the correlation between different levels physical activity measured by accelerometer data, and a change in LDL-C, HDL-C, and triglycerides. Healthy adults (n=440) wore accelerometers for 96 hours to assess their normal PA levels prior to a baseline visit during which blood lipids were collected [5]. Using SPSS statistical software, we ran multiple linear regressions to assess the LDL-C, HDL-C, and triglyceride levels as a function of time spent in sedentary, light, moderate, and vigorous physical activity. We corrected for age, gender, and BMI at the baseline visit. We found that time spent in moderate PA, age, gender and BMI contributed to 28.2% of HDL-C levels (p=0.009), while it was unable to contribute to LDL-C or TG with any statistically significance. Time spent in vigorous PA, age, gender, and BMI contributed to 27.8% of the HDL levels (p=0.038), while similarly it was unable to contribute to LDL-C or TG with any statistically significance. Our results support the hypothesis that increased levels of PA do not contribute as strongly to LDL-C or Triglycerides as they do to HDL-C. This analysis adds to the current data on the effects of PA on cholesterol, and suggests we may want to reconsider the current AHA/ACC lifestyle guidelines with regards to PA as therapeutic treatment for LDL-C, and prevention of atherosclerosis and other cardiovascular events.

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# Transgenic Reporter Cell Fluorescence Tracking to Monitor the Differentiation of Murine Cells Along the Osteochondral Lineage: Validation with qPCR

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**Background:** As we know, there is a massive need for skeletal regeneration, which is crucial in the treatment of bone defects and diseases like osteogenesis imperfect and osteoporosis. An evaluating system for identifying good bio-materials that can support skeletal progenitor differentiation has become urgent. The zonal structure of osteochondral tissue underlies its function. Consequently, it is vital that newly-engineered tissue retains this zonal character. Recently, the development of monolithic multidirectional collagen-based scaffolds that mimic the directionality and composition of the superficial, transition, calcified cartilage, and osseous zones of osteochondral tissue has been reported [1]. These scaffolds may aim to support the formation of new osteochondral tissue with zonal character. We have developed a novel method that enables the real-time evaluation of cell differentiation *in vitro*, based on the onset and expression intensity of different fluorescent reporter genes. To date, studies completed show genetic markers being tracked overtime to show development of the tissue, but the novel method used in this study uses fluorescence markers along with qPCR to validate development.

<u>Objectives</u>: The main objective of the study is to look at the ability of multidirectional scaffolds to support the differentiation of murine bone marrow stromal cells (BMSCs) and murine articular cartilage along osteogenic and chondrogenic lineages, respectively. This sub-study validates the usage of real time fluorescence markers to study cell differentiation with corresponding quantitative gene expression data for chondrogenesis and osteogenesis.

Methods: Primary murine-derived dual fluorescent (bone sialoprotein (BSP-GFPTopaz) and dental matrix protein (DMP-mCherry)) BMSCs and triple fluorescent (type I collagen (Col3.6-GFPTopaz)), (type II collagen (Col2a1-ECFP)), and (type X collagen (Col10a1-mCherry)) articular chondrocytes were seeded atop scaffolds and cultured in defined osteogenic or chondrogenic media. Reporter fluorescence was evaluated *in situ* at days 3, 7, 14 and 21. At days 7 and 21, the scaffold was divided into superficial, transition and calcified cartilage, and osseous layers, homogenized in TRIzol reagent, and frozen at -20°C. RNA was extracted, purified using magnetic beads, reverse-transcribed, and subject to qPCR. For osteogenesis with BMSCs, expression of ALP, BSP, DMP, RUNX2, and OCN were quantified. For chondrogenesis, Col1a1, Col2a1, Col10a1, Aggrecan, and Sox9 were quantified. Fold change was calculated via the ΔΔCT method, relative to day 0 mRNA, and normalized to GAPDH.

<u>Results</u>: Fluorescence microscopy of reporter fluorescence for BMSCs revealed continued expression of BSP-GFPTopaz to day 21 of culture. Expression of mature osteoblast marker DMP had an onset at Day 14 and increased at Day 21, suggesting BMSC osteogenesis. qPCR verified the day 7 findings, but conflicted the Day 21 data. Articular chondrocytes successfully matured on scaffolds and had a dramatic expression of col10a1-mCherry up to day 21. qPCR corroborated this data, showing a near 1000-fold change of col10A1 expression in the osseous zone of the scaffold.

<u>Conclusions</u>: The ability to study the differentiation of BMSCs and chondrocytes *in vitro* by tracking reporter fluorescence was mostly validated by qPCR. The discrepancy between osteogenic markers at Day 21 warrants further investigation.

<u>Future Directions</u>: Future experiments will determine the cause of declined osteogenic gene expression at Day 21 for BMSCs, which may be related to poor mRNA retrieval from mineralized tissue.

<u>Support</u>: University of Connecticut School of Dental Medicine Summer Research Fellowship <u>References</u>: 1. Clearfield D, Nguyen A, Wei M. 2017. Biomimetic multidirectional scaffolds for zonal osteochondral tissue engineering via a lyophilization bonding approach.

## Cognitive and Neuroimaging Predictors of Acute Treatment Outcomes in Late-Life Depression

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Objective: Late-life depression (LLD) affects up to 5% of older adults and is associated with cognitive impairment, including deficits in executive functioning (1) and working memory (2). Cognitive deficits are shown to predict poor response to antidepressant treatment (3). MRI studies have demonstrated that structural brain changes, such as white matter hyperintensities (WMH) and hippocampal volume reduction (4), are also associated with poor treatment response. However, few studies have combined cognitive function and structural imaging as predictors of antidepressant response. Moreover, there is limited literature on the association between memory functioning and treatment outcomes. This study investigated cognitive and structural predictors of antidepressant response in a single LLD cohort. We hypothesized that greater executive dysfunction, memory impairment, WMH, and hippocampal atrophy would be associated with worse acute treatment response in LLD.

Methods: Subjects were participants in the Neurobiology of Late-Life Depression (NBOLD) study at the University of Connecticut School of Medicine. Inclusion criteria were age over 60 years, current psychiatrist-based diagnosis of major depression, and the ability to undergo an MRI. Exclusion criteria were dementia and other neurological or neuropsychiatric illness besides depression. Subjects received a baseline assessment of behavior, emotion, and cognition, which included common measures of executive functioning (i.e., Trail Making Test, verbal fluency) and verbal and non-verbal memory. Subjects also underwent a structural MRI scan (Siemens 3T Skyra). Freesurfer was used to calculate regional volume and WMH volume. Follow-up assessment was done at 12 weeks. Individual regression models tested the association between cognitive and imaging predictor variables and MADRS score, controlling for baseline depression.

<u>Results:</u> Data from 37 individuals was used for the final analyses, mean age 71.9 (SD=7.8), 64% female. Subjects with a larger right hippocampal volume/temporal horn volume ratio had a greater response to antidepressants. Surprisingly, subjects who performed worse on a test of nonverbal (figure) recall also had greater antidepressant treatment response.

<u>Conclusions:</u> Subjects with greater right hippocampal volume respond better to antidepressants. However, worse performance on nonverbal recall also predicted greater response. Future studies should follow LLD patients over a longer time period to examine the clinical utility of neuroimaging findings and cognitive function as predictors of chronic treatment outcomes.

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# Comparison of the Expression of Wnt3a, Wnt5a, and Wnt10a in Developing Odontoblasts in Vivo and in Vitro

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## Background

The Wnt pathway plays a pivotal role in tooth development. Wnt signaling pathways mediate its effect through the canonical and non-canonical pathways. Different Wnt ligands have been implicated in odontoblast differentiation. However, there is a gap in the literature in that Wnt3a, - 5a, and -10a expression levels have been quantified in different matrix producing dental pulp cells except odontoblasts, which produce dentin.

#### Objective

The goal of this research study was to examine the expression of Wnt3a, -5a, and -10a during odontoblast differentiation in vitro.

#### Methods

Total RNA was isolated using TRIzol reagent (Invitrogen) from primary pulp cultures at various time points followed by cDNA synthesis. Gene expression in cultures at day 4, day 7, day 10, day 14, and day 17 were examined by TaqMan qPCR analyses using the following primers: Wnt3a (5'-ATTGAATTTGGAGGAATGGT-3'/5'-CTTGAAGTACGTGTAACGTG-3'); Wnt5a (5'-TCAGAACCAGCCACTTAGG-3'/5'-GCACAAATGGAAAGTCTAAACG-3'); Wnt10a (5'-CCACTCCGACCTGGTCTACTTTG-3'/5'-TGCTGCTCTTATTGCACAGGC-3'); Gapdh (5'-ACCACAGTCCATGCCATCAC-3'/5'-TCCACCACCCTGTTGCTGTA-3').

#### Results

Our results in three independent experiments showed expression of Wnt5a and Wnt10a at D4, D7, D10, D14, and D17 pulp cultures. Wnt3a, although expressed at low levels at day 4, was not expressed at other time points during odontoblast differentiation.

## **Conclusions**

The expression of Wnt5a and Wnt10a, during differentiation in dental pulp cultures, indicates essential autocrine roles of both canonical and the non-canonical pathways in odontoblast differentiation. Quantification of Wnt3a, -5a, and -10a levels in developing dental stem cells and odontoblasts will provide further insight into involvement of Wnt signaling in dental pulp development and homeostasis. It could also enhance the understanding and implication of dentin and pulp regeneration as a therapy after root canals and caries excavation.

#### **Future Directions**

As a next step, expression levels of other growth factors and transcription factors involved in the Wnt pathway of tooth development, including Dspp and RUNX2, could be quantified in vitro for further analysis of odontoblast differentiation

## **Support**

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## Patterns of Betel Quid Use Among Women in the Central Province of Sri Lanka

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Introduction: Betel quid, a combination of betel leaf, areca nut, slaked lime, and often tobacco, is the fourth most used addictive substance in the world [1]. Used by both women and men in Sri Lanka, it is engrained in traditional custom and daily activity, though its adverse health effects are widely documented. Previous studies of betel use in Sri Lanka focused on men; we understand little about women's use, despite increased mortality risk in women who chew tobacco [2]. A better understanding of women's betel quid use has meaningful implications for health. Our study, part of a larger investigation into endemic chronic kidney disease of unknown etiology (CKDu), focused on women in remote communities in Wilgamuwa District, Sri Lanka. This study aims to 1) describe women's patterns of betel use 2) explore women's perceptions of betel harms, benefits, socialization, and cessation, and 3) relate betel use to health.

<u>Methods:</u> 30 female patients of the kidney clinics at the Girandurukotte and Wilgamuwa hospitals who chew betel were administered a survey on demographics, betel use, and health. 11 female patients at Girandurukotte Hospital and Kandy General Hospital in Kandy, Sri Lanka were interviewed. Analysis utilized SPSS v.25 and textual analysis with construction of themes.

Results: Of women surveyed, 33.3% add tobacco to their betel quid. The previously described Betel Quid Dependence Scale [7] revealed significant differences on two indicators in women who include tobacco: they report feeling depressed or drowsy with reduction of use and report chewing non-stop more than those not including tobacco (p=.03, p=.003). Most women expressed habituation in interviews. On average, women spend 8.4% of household income on their betel use per month. They believe betel is medicinal, strengthens teeth during pregnancy and labor, and helps stress (16.7%, 33.3%, and 16.7%). More women expect to use betel at family events than cultural events (p=.01). 93.4% report at least one quit attempt in the past year. Women understand that betel is harmful: 83.3% recall being warned. 80.0% cite health as their top reason to quit. Of 24 women with CKDu, 69.6% reduced their use following diagnosis.

<u>Conclusion:</u> Women in Sri Lanka chew betel quid with and without tobacco. We demonstrate dependence, particularly among women adding tobacco, and women themselves identify habituation. They prioritize betel in family spending. We show that women have been unsuccessful in quit attempts despite education on harms, suggesting a need for alternative interventions.

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## An Evaluation of the CenteringParenting Group Well Child Care Model

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Group well-child care positively impacts the patient experience<sup>1</sup>. The Centering Healthcare Institute, a non-profit organization that works closely with healthcare providers from all sectors, piloted a group well-child care model called CenteringParenting in clinical sites across the United States. The CenteringParenting model aims to educate mothers on healthy child development, effective parenting, and self-care while also providing a space for social support among patients. The current study assesses the efficaciousness of the CenteringParenting curriculum by collecting feedback from providers who are currently implementing the curriculum. No such evaluation of the CenteringParenting curriculum exists to date. Feedback from providers focused on (1) provider self-efficacy (2) patient access to resources, and (3) need for additional trauma informed components in the curriculum. 41 providers across 24 clinical sites across the United States completed our web-based survey between August and December 2017. Respondents demonstrated a mean 'self-efficacy in group care' score of 93.63 (out of 110). On a scale of 1-5, providers demonstrate a mean response of 3.58 when asked about the extent to which the CenteringParenting curriculum/group care setting improves their ability to elicit patient concerns of unmet basic social needs. When asked how strongly they believe the CenteringParenting model achieves each of its 5 published objectives, providers demonstrate mean responses between 3.87 and 4.52, again on a scale of 1-5. Logistical Regression Models demonstrate that increasing provider self-efficacy score is a significant predictor of group members demonstrating understanding of educational content (p<0.01), and curriculum content being discussed with a facilitative approach (p< 0.1). Provider who do not feel comfortable supporting and advising families who experience trauma are less likely to discuss curriculum content with a facilitative approach (p<0.01). Providers who do not feel comfortable delivering "trauma informed" care are also less likely to feel that group members demonstrated understanding of the educational content (p<0.1) and less likely to feel that sessions were more like "peer groups" than "classrooms" (p<0.05). As a whole, the results indicate that providers are highly satisfied with the innovative CenteringParenting curriculum and feel self-efficacious in implementing group care across diverse clinical sites. Providers who are more comfortable in delivering "trauma informed" care exhibit better group facilitation skills and demonstrate better outcomes when using the CenteringParenting model. CenteringParenting is therefore successful in accomplishing a myriad of patient care objectives, but providers using this model may benefit greatly from training in trauma informed care practices.

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# Prevalence of Childhood H. pylori Infection, Symptoms, and Associated Factors in Cyanika, Uganda

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<u>Introduction:</u> Many patients in sub-Saharan Africa suffer from dyspepsia [1]. Despite data suggesting that the cause of such dyspepsia in adults is due to Helicobacter pylori, there is limited data quantifying the prevalence in children. Untreated H. pylori infection can lead to chronic gastritis, gastric MALT lymphoma, peptic ulcer disease, and gastric carcinoma, thus meriting treatment to prevent these complications [2]. Furthermore, the epidemiology of H. pylori is incompletely understood. This study attempts to identify the prevalence of H. pylori in children living in Cyanika, Uganda and identify risk factors for infection.

<u>Methods:</u> Subjects included pediatric patients at the Cyanika Clinic or local primary school. Each patient was tested for H. pylori antigen in the stool and antibody in the blood. Each participant was also administered an IRB-approved survey that assessed demographics, exposure to communicable disease factors, and symptoms of dyspepsia. 130 volunteers were enrolled (88 males, 42 females). Statistical analysis was performed using SPSS v.22.

Results: There was a mean of 7 people per household (SD 1.8). The average distance to water was 25 minutes (SD 22). Only 62% of families reported access to water for sanitation purposes and 50% reported soap for handwashing. Regarding medical morbidities, a high rate of subjective malaria and stomach illness was reported: 54% (71/130) reported being treated for malaria in the past year, 28% (37/130) admitted taking antibiotics in the past year, and 47% (62/130) reported that household members currently had stomach pain. The rates of gastrointestinal disorders based on the Rome III criteria [3] were as follows: functional dyspepsia 50.8%, epigastric pain syndrome 26.1%, and post-prandial distress syndrome 27.7%. Only one participant (1/130) tested positive for H. pylori antibody in blood.

<u>Conclusions:</u> Although there is a high prevalence of crowded living conditions, limited access to quality water resources, and functional dyspepsia, we did not find a high prevalence of H. pylori antibody or antigen in our study participants. We postulate that the high rate of antibiotic use for subjective malaria illness may play a role in the low prevalence observed in these children.

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## A Comparative Analysis between Radiographs and Photographs to Determine the Value-Addition of the Lateral Cephalometric

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Background: Lateral cephalometric radiographs are radiographic images that are routinely used in orthodontics for diagnosis and treatment planning. There is debate regarding whether or not the lateral cephalometric radiograph is truly necessary for proper diagnosis given that the clinical examination has the potential to provide sufficient information for diagnosis<sup>1</sup>. While the radiation dose delivered by lateral cephalometric radiographs is relatively low, the lateral cephalometric still delivers radiation to multiple radiosensitive organs, such as the brain, bone marrow, thyroid gland, and salivary glands<sup>2</sup>. The radiation doses delivered by lateral cephalometrics is a pressing concern especially in the field of orthodontics due to the majority of orthodontic patients being children who are still in the developing stage of growth<sup>2</sup>. Previous studies regarding the topic of whether lateral cephalometric radiographs are necessary for orthodontic treatment have resulted in varying and somewhat uncertain conclusions.

Objectives: The objective of this study is to determine the value-addition of lateral cephalometric radiographs in orthodontic diagnosis and treatment planning.

Methods: This retrospective study had 7 orthodontists and orthodontic residents at various stages in residency training. A total of 100 patient records were evaluated during two separate phases. In the first phase, each observer completed a 9-question survey about diagnosis and treatment planning for each patient given the patient record including extraoral photographs, intraoral photographs, and a panoramic radiograph while excluding a lateral cephalometric. In the second phase, the observers completed the same surveys for the same 100 patient records given the same resources with the lateral cephalometric included. Responses between two phases were analyzed. Intra-rater agreement was calculated using Cohen's Kappa analysis and interrater agreement was calculated using inter-class correlation coefficients.

Results: Kappa values for different observers ranged from 0.386-0.841 for diagnosis of Class-1 malocclusion. For Class-2 diagnoses, Kappa values ranged from 0.340-0.976. For Class-3 diagnoses, Kappa values ranged from 0.634-0.859. With the exception of one observer, there was a high intra-rater agreement between all the participants for all of the malocclusion classes evaluated. Cronbach's alpha values for inter-rater agreement ranged from 0.913-0.959 for all of the malocclusion classes evaluated. The overall agreement amongst all observers was the highest for Class-2 diagnoses in both phase 1 and phase 2.

Conclusions: Based on this data set of patients and a limited number of evaluators, the lateral cephalometric radiograph did not add any significant value to the diagnosis of dental malocclusions evaluated for orthodontic treatment.

Future Directions: Ideally this study will be duplicated on a larger, more national scale.

Support: The UConn School of Dental Medicine Summer Research Fellowship

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## Hepatitis C Infection on Guam: Knowledge, Attitudes, and Risk Factors

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Introduction: Hepatitis C virus (HCV) is the most common blood borne pathogen transmitted in the US [1]. Most affected individuals live for decades without exhibiting any symptoms of HCV infection, which can progress to cirrhosis, and hepatocellular carcinoma [1]. At higher risk for infection are adults born 1945-1965, known as "baby boomers" [2]. HCV infection is a concern across the US, including on the Pacific island territory of Guam. One study found that hepatitis C was linked to 63.3% of liver cancer cases on Guam, more than for either hepatitis A or B [3]. Another report estimates there were 934 reported HCV cases on Guam from 1980-2015 [2], likely to be a significantly under-recognized condition. Lack of resources on Guam have hindered efforts to gather essential population information related to HCV infection. The aim of this study is to assess HCV knowledge, attitudes, and risk factors for infection on Guam.

<u>Methods:</u> Participants visiting community health center clinics or outreach events organized by the Guam Department of Public Health and Social Services (DPHSS) were administered an IRB-approved survey that assessed demographics, knowledge, attitudes, and risk factors for HCV infection. Statistical analysis was performed using SPSS v. 24.

Results: A total of 123 participants were enrolled. Composite scores for knowledge and risk factors for HCV infection were calculated. The maximum knowledge score a participant could obtain was 5. There were 2 (1.6%) participants who scored 5/5, while 84 participants (68.9%) scored less than or equal to 2/5. The maximum overall risk score a participant could obtain was 4. The vast majority of participants (96.7%) were at no or low risk (score 0-2) for HCV infection based on survey responses. There was no significant variance in overall risk between "baby boomers" and those younger than boomers (p=0.23). There was also no significant variance in overall risk based on three generated race categories: Chamorro, Chuukese, and other race (p=0.79). There was however, significant variance in knowledge based on birth cohort. Baby boomers demonstrated a mean knowledge score of 2.30, while the mean knowledge score of the younger group was 1.42 (p=0.002). Regression modeling confirmed that the significant difference in knowledge scores was due to birth cohort and was not due to the other demographic factors of race or education level.

<u>Conclusions:</u> Adults in the "boomer" age group demonstrated increased knowledge of HCV compared to younger adults. However, low knowledge scores overall demonstrate a need for improved HCV education on Guam. No differences were observed between major ethnic groups on Guam. Education efforts may be targeted specifically toward adults younger than baby boomers, who may be exhibiting a relative knowledge deficit compared to adults in the baby boomer cohort.

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## CBCT Guided Mini-Implant placement with Radiographic Guide Yields Superior Results

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**Background:** The use of mini-implants (MIs) in dentistry is progressively increasing especially in orthodontics to serve as temporary anchorage devices. Typically, MIs are placed without any preoperative imaging, which increases the risk of perforation to adjacent critical structures. In traditional implants, it is recommended to use a surgical guide along with 3D imaging to mitigate risk and to facilitate accurate placement. This is however not typically done with mini-implants leading to proximal root perforations and failure.

**Objective:** To evaluate the value of a simple radiographic guide modified to be a surgical stent in conjunction with a CBCT scan for Mini-Implant placement (MI).

**Materials and Methods:** Eleven dentate human skulls were used to provide a total of 64 potential mini implant sites .Out of the 64 sites, MIs were placed blindly without any preoperative imaging in 32 sites and a guided method using a radiographic guide made from cast models was used for the remaining 32 sites. A post-operative CBCT was done to assess MI placement. Two raters, a board certified oral and maxillofacial-radiologist and an orthodontist evaluated the scans. The association between successful outcome and use of a radiographic guide was examined by a multivariable logistic regression model fit by the maximum likelihood method. The effects of examiner and site (quadrant) of implant placement was adjusted in the regression model.

**Results:** A total of 128 implant placements by two examiners were examined. 64 sites used a radiographic guide. 77 implant placements were deemed as a successful outcome (87.5% of implants placed with a radiographic guide were successful as opposed to 32.8% success rate in those without a radiograph guide). Following adjustments for the effects of examiner and site of placement, use of a radiographic guide was associated with significantly higher odds for a successful outcome (OR=25.1, 95% CI=7.9 to 79.9, p<0.0001) when compared to placement without a radiographic guide.

**Conclusions:** In this Ex-vivo study, a preoperative CBCT scan along with a modified radiographic guide provided superior outcomes for surgical placement of MIs compared to blind placement without any preoperative radiographic imaging.

**Future Directions**: Future directions should include translating this concept into patients to evaluate the value addition of this method and its contribution to the success of MI placement.

**Support:** UConn School of Dental Medicine, Student Research Program

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# Recent Advances in Type 1 Diabetes Technology: What Do Pediatric Patients Know And Where Are They Learning It?

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New technology for the management of type 1 diabetes (T1D) has become increasingly available to the public, most notably with the first FDA-approved automated insulin delivery system (AID) in September 2016. These devices have the potential to dramatically improve diabetes management and quality of life in pediatric populations. However, how much patients and their families know about these technologies and which people know is unknown. Our goal was to determine the current state of knowledge about diabetes technologies, particularly AID, in our regular clinic population and the sources of information about these technologies. We developed a questionnaire and surveyed 76 parents and 61 patients aged 13 years and older at routine T1D clinic appointments over a 2-month period (patient age 15±4y (mean±SD), 60% male, diabetes duration 7±4y, hemoglobin A1c 8.9±2.1%). We evaluated the relationship between diabetes technology knowledge and sources of information with other demographic (age, gender, race/ethnicity, zip code, health insurance) and clinical (diabetes duration, A1c, diabetes management) parameters. A knowledge score was calculated based on the number of questions answered correctly regarding AID. The average knowledge score was 3.7±2.1 (out of a maximum score of 6). A higher AID knowledge score was associated with pediatric patient respondents (patient: 4.1±1.9 vs. parent: 3.3±2.2, P=0.02), being non-Hispanic white (NHW: 4.1±1.9 vs. minority: 2.4±2.3, P<0.001), and being on private health insurance (Private: 4.0±1.9 vs. Medicaid: 2.6±2.4, P<0.001). Most respondents (97%) relied on their diabetes health care providers as a source of T1D technology information; other sources of information include professional diabetes organizations (53%), other diabetes-related websites (37%), social media (41%), print media (15%), and in-person support groups and friends and family (28%). Variables associated with greater utilization of other professional sources of information for information about diabetes technology included race/ethnicity (NHW: 62% vs. minorities: 29%; P=0.006), insurance type (private insurance: 63% vs. Medicaid: 25%; P=0.001), and diabetes treatment modality (insulin pumps/sensors: 62% vs. injection regimens: 31%, P=0.004). These findings suggest that more outreach to patients of minority backgrounds and on Medicaid would enhance their knowledge and understanding of various T1D technologies available.

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#### **Variant Analysis for Inherited Keloid Formation**

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**Background:** Keloids are a rare wound healing disease and are the result of hyperproliferative wound healing beyond the margin of the original wound<sup>1</sup>. Aside from cosmetic implications, keloids can become invasive, painful, itchy and last for years. The exact etiology of keloids is unclear; however, there is strong evidence for a genetic basis, which is often reported as autosomal dominant with incomplete penetrance. The real catalyst for keloid disease may be anywhere during the wound healing process, and researchers do expect a significant genetic variability and effects of environmental factors. This project used the samples collected in a previous study of the Yoruba ethnic group of Nigeria who have a high prevalence of keloid disease<sup>2</sup>. There were 4,200 samples collected and a total of 103 families. This sample population was chosen because of high prevalence of keloids and large families that can be recruited. Whole exome sequencing with 550 samples from 103 families was performed and candidate variants that segregate in a large family or in several families were identified.

**Objective:** The objectives are to confirm study results by Sanger sequencing variants in entire large families and to test variants in populations that have not been used for whole exome sequencing.

**Methods:** 4,200 samples and 200 variants were identified through whole exome sequencing as relevant to skin biology or wound healing. Out of these 200 variants, 5 to 10 segregated in one or more families and were marked for further analysis. Two families were chosen for PCR and Sanger Sequencing. Family I consists of 11 participating members from 3 generations and Family II consists of 13 participating members from 3 generations.

**Results:** Family I: All affected subjects in Family I were heterozygous for the DPT variant with the exception of two individuals. Phenotypically another unaffected individual was heterozygous for the variant, while all other unaffected individuals did not have the variant present. Family II: All affected subjects were heterozygous for the DPT exon 1 variant with the exception of one individual. One phenotypically unaffected individual was also heterozygous for the variant while the rest of the unaffected individuals in the family did not possess the variant.

**Conclusions:** Sanger sequencing confirmed the presence of the variant in additional family members in Family I and II. The variant identified in Family I was on the fourth exon of the dermatopontin gene, while the variant identified in Family II was the first exon of the dermatopontin gene located on the first chromosome. Dermatopontin is an ECM protein and is located mainly on collagen fibers in the skin and also in the cytoplasm of fibroblasts. Dermatopontin is thought to play a major role in collagen fibril formation, cell adhesion for fibroblasts, and wound healing. Functional studies are ongoing to study the role of variants during wound healing.

**Future Directions:** Going forward this protocol will be useful to test additional families and probands using the primer designed for the variants of interest.

**Support:** The UConn School of Dental Medicine, Student Research Fellowship Program **References:** 

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# Prevalence of Incidental Findings in Orthodontic Patients: A Retrospective CBCT Analysis

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<u>Background</u>: Imaging is a valuable diagnostic tool in the overall assessment of the dental patient<sup>1</sup>. Three-dimensional (3-D) radiographic examination for orthodontic patients is typically done using a large field of view (FOV) CBCT scan. With a large FOV scan, there is an increased potential to encounter several incidental findings<sup>2</sup>. Incidental findings are defined as any and all discovered findings, detected by an imaging modality that are unrelated to the clinical indication for the imaging being performed<sup>3</sup>. Given the recent advent of this technology, many dental clinicians may be unfamiliar with the complex 3-D anatomy of the maxillo-facial area and the cranial base. This could lead to missing major findings of clinical significance as well as misinterpretation of anatomic variants as pathology<sup>4</sup>. Therefore, there is a need for a more comprehensive review of the entire CBCT volume and appropriate reporting and documentation of all findings, regardless of the region of interest. To date, there are not many well-designed studies that have evaluated incidental findings based on clinical significance.

<u>Objective</u>: The objective of this retrospective study was to determine the prevalence of incidental findings in orthodontic patients imaged with CBCT.

<u>Methods</u>: This retrospective study evaluated a randomly selected sample of 250 CBCT images acquired primarily for orthodontic intervention. The inclusion criteria for the study were CBCT scans of patients referred for orthodontic treatment. Exclusion criteria were scans that had patient movement or had metallic artifacts from dental restorations that made the scan non-diagnostic. CBCT scans were acquired using three different CBCT machines, Icat-flex, Jmorita, and Planmeca. All CBCT scans were reconstructed using a CBCT reconstruction program INVIVO-version 5 (Anatomage INC, Irvine, CA). Scans were evaluated in all three orthogonal planes. A dental student and two board certified oral and maxillofacial radiologists evaluated the scans for incidental findings. Findings were classified based on their anatomic region and then were assigned a specific clinical significance with a scale of low, moderate, or high. The data was recorded on an Excel sheet and statistical analysis was performed.

Results: Incidental findings were categorized and placed into one of six subgroups based on anatomic region: sino-nasal, dentoalveolar, nasooropharyngeal airway, temporomandibular joint, neck, non-pathological calcifications, and miscellaneous findings. Of the 250 scans, 1415 incidental findings were identified among the six anatomic regions. The most frequently identified findings were those located in the sino-nasal and dento-alveolar, representing 35.0% and 34.8% respectively. Within the sino-nasal category, nasal septal deviation and mucosal thickening of maxillary sinus had the highest percentage of incidental findings, 54.0 and 47.6% respectively. Within the dentoalveolar category, impacted canines and third molars had the most frequently incidental findings, 81.6% and 79.2% respectively.

<u>Conclusions</u>: This study shows a high occurrence of incidental findings in orthodontic patients imaged with CBCT and highlights the need for a careful evaluation of the entire scanned volume.

<u>Future Directions</u>: Future research can focus on increasing the sample size and collecting the data from a different population to determine prevalence of incidental findings in orthodontic patients.

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## Trans-Differentiation of Human Mesenchymal Stem Cells into Neuronal-like Phenotype

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Peripheral nerve injuries (PNIs) involve injury to nerve fibers causing damage resulting in segmental defects. PNIs occur due to cancer, congenital abnormalities, and most often from trauma [1]. Goals of treatment include structural, sensory, and motor function recovery, however the current therapies often fall short of these aims, resulting in significant impairment and disability [2]. Schwann cells play a key role in the regeneration and repair of peripheral nerves after injury, they are the primary reason peripheral nerve regeneration can occur in the PNS, compared to the very limited regenerative ability of the CNS [3]. These cells secrete several neurotrophic factors including brain derived neurotrophic factor (BDNF) to promote PNI healing [4]. We hypothesize that co-culture experiments involving human Schwann cells and human mesenchymal stem cells (hMSCs) may offer a controlled in-vitro environment to study the potential stem cell differentiation under the influence of neurotrophic factors secreted by cells. Our study investigated the potential trans-differentiation of hMSCs into a neuronal/Schwann cell-like phenotype when co-cultured with Schwann cells and different mixtures of media. Cells were co-cultured for two different lengths of time, 3 days and 7 days, in order to observe and compare potential changes. In a control group study, hMSCs maintained their typical fibroblast morphology throughout the culture time in the basal media.

Our results support that in the presence of Schwann cells and different combinations of media, hMSCs appear to trans-differentiate into non-fibroblast lineages. When subject to treatment, hMSCs begin to express a neuronal-like phenotype with axon-like and dendritic-like processes, as well as a soma-like cell body. Additionally, cultured cells stain positively for both the Schwann cell marker SOX-10 and neuronal marker BDNF. Though Schwann cells are the primary choice in treating PNIs via tissue engineering, research has been hampered due to the difficulty in isolating and expanding these cells. hMSCs provide a clinically relevant and alternative source for cell therapy due to their ease of isolation, expansion, and ability to transdifferentiate into different lineages under the proper stimulation. Ongoing studies are looking at the rate of hMSC proliferation, morphological changes, and Schwann cell/neuronal-like phenotype expression via various techniques including RT-PCR, Western blots, and immunohistochemistry.

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## Knowledge and Self-Management of Diabetes Among Adults in León, Nicaragua

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<u>Introduction:</u> The prevalence of diabetes mellitus in Nicaragua has been measured at 8.1% and is increasing every year.1 Diabetes care is multifaceted. It is critical that patients are well versed in ways to control their blood glucose levels through modes of self-care, such as diet and exercise, in addition to their pharmacotherapy.2 Currently, there are no diabetes self-management education programs implemented by the Nicaraguan government. There is also limited regional data within Nicaragua regarding the behavior and knowledge of its diabetic population.3 This study aimed to provide insight about adult diabetics in León, Nicaragua through the analysis of demographic, behavioral, and biological variables.

Methods: 44 adult diabetic subjects (14 men and 30 women) were surveyed at clinics and home wellness visits within the urban center of León and the adjacent rural town of Chacraseca. Demographic information was collected from the participants. A fingerstick point-of-care glycosylated hemoglobin (HbA1c) test was obtained to assess glycemic control over the past three months. A diabetes knowledge assessment and the Diabetes Self-Management Questionnaire (DSMQ) were verbally administered to each subject. The DSMQ evaluated the diabetic self-management domains of physical activity, health care use, glucose management, and dietary control. These itemized subscales were combined together to form a summary score as a global measure of the subject's self-management efficacy.2

Results: The mean HbA1c of those surveyed was 9.25%. Only 25% had values at or below the American Diabetes Association goal of 7%. Women trended towards having a higher HbA1c score compared to men (M=9.75+/-2.50 vs. 8.18+/-2.21, p= 0.05). Rural and urban populations differed in their DSMQ sum scores and glucose management subscores, with subjects livings in rural areas scoring significantly lower than their urban counterparts (M=6.26 +/- 1.34 vs. 7.23 +/-1.25, p<0.05). Several gaps in diabetes knowledge were also identified. For example, 47% of patients surveyed were uncertain of how they could prevent diabetes and 37% were unaware of the potentially asymptomatic nature of the disease.

<u>Conclusion:</u> A high rate of poor glycemic control was observed. We were able to highlight opportunities for increasing knowledge and self-management skills among diabetic patients surveyed in locations throughout León. Women and rural inhabitants demonstrated fewer diabetes self-management skills and higher HbA1c levels. Ongoing investigations will increase enrollment in order to add strength to the analyses. Ultimately, the information gathered in this study will be used to better direct diabetic self-management education efforts in the region.

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## Prevalence of H. pylori Infection, Symptoms, and Associated Factors in Kisoro, Uganda

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Introduction: Dyspepsia is a common presenting symptom in medical settings in sub-Saharan Africa (SSA) [1]. Helicobacter pylori is a possible contributing factor, and has shown to be highly endemic in populations in SSA. Untreated H. pylori infection can also lead to chronic gastritis, gastric MALT lymphoma, peptic ulcer disease, and gastric carcinoma [2]. Accurate identification of H. pylori infection would facilitate appropriate treatment and may improve clinical outcomes. This study aimed to identify the presence of H. pylori in patients attending outpatient services in Kisoro, Uganda, assess the utility of symptom review as a predictor tool for infection, and identify risk factors for infection.

<u>Methods:</u> Adult patients attending outpatient clinical services at Saint Francis Mutolere Hospital in Kisoro, Uganda, were offered testing for H. pylori antibody (Ab) in blood and H. pylori antigen (Ag) in stool using two point-of-care tests. Each patient was also interviewed using an IRB-approved survey that assessed sociodemographics, risk factors for infection, prior medical problems, and symptoms potentially consistent with H. pylori infection. Symptoms were classified using Rome III criteria [3].

Results: 305 patients (197 females, 108 males) were enrolled over the course of 14 months. Gastrointestinal symptoms were common, with 74.1% reporting functional dyspepsia, 8.2% reporting epigastric pain syndrome, and 52.8% reporting post-prandial distress syndrome. The overall prevalence of H. pylori infection was 32.2% (98/305), with 9.3% (28/301) demonstrating a positive stool Ag and 26.6% (81/305) demonstrating a positive blood Ab test. Of patients with any positive Ab or Ag test, 64% met clinical criteria for a functional GI disorder. Using functional dyspepsia as a predictor tool for H. pylori infection yielded a sensitivity of 73.5%, specificity of 25.6%, positive predictive value of 31.8%, and negative predictive value of 67.1%.

<u>Discussion:</u> There is a high prevalence of functional dyspepsia and H. pylori in Kisoro, Uganda. However, symptoms are dyspepsia alone are imperfect predictors of infection, as demonstrated by point-of-care testing. There are likely multiple other potential causes of GI symptomatology in this cohort that limit history alone as a predictive tool. Additional testing with H. pylori antibody and/or stool antigen would improve diagnostic accuracy of H. pylori infection in this rural SSA setting.

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## Effect of Novel Porphyromonas gingivalis Glycine Lipids on Osteoblast Function

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**Background:** *Porphyromonas gingivalis*, a subgingival organism associated with chronic periodontitis, is a Gram negative anaerobe known to produce serine and glycine lipids. Serine lipids include Lipid 654 and Lipid 430 classes. The enzyme phospholipase A2 (PLA2) has been shown to catalytically hydrolyze Lipid 654 to Lipid 430. However, bone marrow macrophages incubated with Lipid 654 demonstrate two other hydrolysis products, Lipid 567 and Lipid 342. These\_lipids are termed glycine lipids and are generated with the removal of the terminal serine group from Lipid 654 and Lipid 430, respectively.

**Objective**: The objective of this project was to isolate Lipid 342 from *P. gingivalis* grown in culture and to evaluate whether this lipid class affects bone marrow stromal (BMS) osteoblasts. This investigation also sought to determine whether cellular effects by Lipid 342 are mediated through Toll-like receptor 2 (TLR2) engagement.

**Methods**: *P. gingivalis* was grown in broth culture for 3-4 days and pelleted by centrifugation. 16S ribotyping was used to evaluate bacterial purity. Bacterial total lipids were extracted using the method of Bligh and Dyer and the lipids were fractionated using a semipreparative normal phase high-performance liquid chromatography (HPLC). Liquid chromatography-electrospray ionization-mass spectrometry (LC-ESI-MS) was then used to identify fractions containing the four classes of bacterial lipids. Fractions containing Lipid 567 or Lipid 342 were pooled separately and refractionated using the same HPLC solvent supplemented with 0.1% acetic acid. To evaluate the capacity of Lipid 342 to activate or inhibit BMS cell differentiation, wild-type and TLR2-knockout (KO) BMS cells were cultured for 2 weeks and Lipid 342 was exposed to cells during the second week. Osteoblast green fluorescence protein (GFP) expression as well as von Kossa stained mineral deposit formation were quantified on images using Image J software.

**Results**: MS analysis confirmed highly enriched preparations of serine and glycine lipid classes from the total lipid extracts of *P. gingivalis*. BMS cells exposed to Lipid 342 demonstrated significant inhibition of osteoblast differentiation and function in wild type cells but not TLR2 knockout cells.

**Conclusions**: These experiments demonstrate the capacity for *P. gingivalis* L342 to promote bone loss through inhibition of osteoclast function. These lipids, present in elevated levels in diseased gingival tissue at chronic periodontitis sites, are capable of inhibiting osteoblast differentiation in a TLR2-dependent manner.

**Future Directions**: Future directions will evaluate the effects of Lipid 342 and Lipid 567 on osteoclastogenesis mediated through engagement of TLR2.

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# Evaluating the value of an Innovative School-Based Dental Clinic in Connecticut: A pilot study

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<u>Background</u>: Many barriers to receiving dental care exist across the U.S. In addition to lack of dental insurance and inability to pay for expensive procedures, many also lack reliable transportation or are unable to find a dental office in their local area. Children have been one of the most hard-hit demographics from this lack of dental care; one in four children are faced with untreated decay, which is now considered the number one chronic illness among school-aged youth. Many school districts in Connecticut, including Hartford and Danbury, have revolutionized a new system of dental clinics located right in the nurse's offices of their elementary, middle, and high schools. By eliminating transportation barriers for students and decreasing the amount of time spent out of class, the schools aimed to improve dental care and overall health of their students. Two specific school-based dental clinics, S.A.N.D. in Hartford, CT and Rogers Park Middle School in Danbury, CT, were studied, and many comparisons could be made.

<u>Objective</u>: The objective of this study is to investigate the care received by students enrolled in elementary and middle schools in Hartford and Danbury that contain a school-based dental clinic in order to discover the specifics of care provided, funding, and use this information to draw conclusions about the efficacy of such programs.

Methods: A chart audit and program director survey were constructed and employed to obtain data on the two different clinics. The chart audit included demographic information such as grade level of student, gender, race/ethnicity, and then collected data regarding dental status of the students through questions that addressed radiographs, dental prophylaxis, sealants, fillings, extractions, and emergency visits. The program director surveys obtained information about the specific clinics, including days and times of service, presence of hygienists/dental assistants/dentists, and funding. The data was then entered into Microsoft Excel spreadsheets to analyze and chi squared tests were performed to determine validity.

Results: The S.A.N.D. clinic in Hartford, CT employs 3 rotating dental assistants, 9 rotating dental hygienists and 2 rotating dentists while the Rogers Park Middle School clinic in Danbury, CT employs a single dental hygienist. However, even after accounting for this large discrepancy, both clinics were adequate at performing dental prophylaxis, taking radiographs, and placing sealants on the students enrolled in the corresponding schools. One major difference noted was that the S.A.N.D. clinic is able to complete around 50% of oral surgery themselves while the clinic at Rogers Park refers out 100% of oral surgery needs. Additionally, the Rogers Park clinic employs a fixed appointment fee set at \$150.00, while the S.A.N.D. clinic billed to HUSKY insurance as well as some private insurers.

<u>Conclusion</u>: While the 19 school-based dental clinics in Hartford, CT all share many features and provide comprehensive care to the students who attend said schools, other clinics in Connecticut provide differing levels of care. Both a large-scale school-based clinic such as S.A.N.D. in Hartford and a smaller operation at Rogers Park in Danbury were efficient in providing basic prophylaxis, radiographs, and sealants. However, the presence of rotating dentists allowed for more procedures to be completed at S.A.N.D. and allowed for less referrals. In the future, it would be interesting to observe the difference in dental health of students with these clinics in their schools versus students who do not have them.

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## Filling the Therapeutic Void: Creating Guidelines for "DTD" through Film

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<u>Introduction:</u> Over three million cases of child trauma are reported in the United States annually.¹ Currently the "best fit" diagnosis for child onset trauma is PTSD, a diagnosis originally created for adults. However, most traumatized children do not meet PTSD diagnostic criteria.² Moreover, PTSD does not capture the widespread impact of child onset trauma on child development.³ Therefore, a new provisional diagnosis has been proposed: "Developmental Trauma Disorder (DTD)," which encompasses the variable manifestations of trauma on child development.³ The specific goal of this project is to provide "DTD" guidelines to clinicians/therapists working with children who have experienced trauma through short films/webinars. We hypothesize that our webinars will help prevent missed diagnostic opportunities for child onset trauma.

Methods: A team composed of UConn Health/SOM affiliates, a director, and a film crew held conferences, drafted webinar prompts, and recruited actors. Background character information and sample scripts were drafted by UConn affiliates. Dress rehearsals and filming sessions were held in August 2017. Two free webinars have been released on the National Child Trauma and Stress Network (NCTSN) website, and will be released on a rolling basis. Webinar viewers were asked to evaluate webinar quality (7 items) and how well content addressed learning objectives (Likert scale 1 to 5) – average item ranks were calculated. Additionally, viewers were asked if they would recommended the webinar (optional). Lastly, number of enrollment and certificates received by viewers every month, and "roles" of new enrollees were recorded.

#### Results:

TABLE 1:					Webinar 1	Webinar 2	
Evaluations Completed					165	105	
Learning Objectives (Av	verage Rank)				4.075 (4 obj.)	4.1 (3 obj.)	
Quality Rank (7 items)		Speaker knowledgeable in content areas			4.4	4.3	
		Content consistent with objectives			4.3	3.4	
		Speaker clarified content in response to questions			4.4	4,3	
		Teaching aids/audio visuals used effectively			4.3	4,2	
		Teaching style/methods appropriate for subject matter			4.3	4,3	
		Information can be applied to practice			4.3	4,3	
		Information could contribute to achieving professional goals			4.4	4,3	
% Would recommend					98%	99%	
TABLE 2:	Enr	ollments	Certificates	Mos	Most common viewer "roles"		
October	281	L	47		1) mental health clinician/therapist (293)		
November	197	7	52	_			
December	358	3	95		2) student/trai	nee/post doc	
January	153	3	54	54		(88)	

<u>Discussion:</u> Our findings demonstrate that thus far we are targeting the population of interest: therapists, clinicians, and persons in training. Moreover, our findings suggest that we are providing high quality, informative content to our viewers.

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## Sex Tourism, Condomless Anal Intercourse, and HIV Risk Among Men Who Have Sex with Men

<u>Salem Harry-Hernández</u><sup>1,2</sup>, Su Hyun Park², Kenneth H. Mayer³,4 Noah Kreski², William C. Goedel², H. Rhodes Hambrick², Brandon Brooks², Vincent Guilamo-Ramos⁵, Dustin T. Duncan², Bonnie McRee¹

<u>Background:</u> Sex tourism (i.e., traveling to engage in sexual activity) impacts the sexual health of both tourists and locals with whom they interact. However, few studies have examined whether sex tourism is a risk factor for HIV and sexually transmitted infection (STI) among men who have sex with men (MSM)<sup>1,2</sup>, and no such studies have been conducted in Western Europe. The purpose of this study was to examine the association between sex tourism, condomless anal intercourse, other sexual risk behaviors, HIV seropositivity, and STI diagnosis histories among a sample of French MSM.

<u>Methods:</u> Broadcast advertisements were placed on a popular geosocial-networking smartphone application for MSM in Paris, France with a link to a web-based survey. Regression models estimated the relative risk of 1) engagement in condomless anal intercourse (overall, receptive, and insertive); 2) use of alcohol and drugs during and outside of sex; 3) participation in group sex; and 4) self-reported HIV infection and previous STI diagnoses.

Results: Almost 160 (27.7%) of respondents reported engaging in sex tourism in their lifetime. Sex tourism was associated with an elevated risk of engagement in condomless receptive anal intercourse (aRR=1.24; 95% CI=1.00-1.54), use of alcohol and/or drugs during sex (aRR=1.20; 95% CI=1.01-1.42), participation in group sex (aRR=1.14; 95% CI=1.02-1.29) and with an elevated risk of diagnosis with any type of STI over the previous year (aRR=1.50; 95%CI=1.09-2.07), specifically gonorrhea and chlamydia.

<u>Conclusion:</u> Sex tourism was associated with recent diagnoses of STIs and with sexual risk behaviors including condomless receptive anal intercourse among our sample of MSM. Future research among MSM who engage in sex tourism should explore the feasibility and acceptability of the use of episodic pre-exposure prophylaxis (PrEP) for short periods of elevated risk behaviors for both tourists and local sex partners.

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## Pre-Exposure Prophylaxis Awareness among Primary Partners of HIV+ Populations in Connecticut

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Introduction: Pre-exposure prophylaxis (PrEP) is a bio-medical prevention strategy to reduce HIV acquisition among at-risk individuals. Antiretroviral therapy with tenofovir/emtricitabine has shown substantial efficacy for men who have sex with men (MSM), injection drug users (IDU), and heterosexual men and women. In Connecticut, the uptake of PrEP can curb HIV transmission if high-risk populations are aware of this prevention method. PrEP Knowledge and implementation in partners of People Living with HIV (PLWH) is not well understood. This study aimed to identify the relationship between knowledge of PrEP, attitudes, and lifestyle factors (i.e. sexual behaviors, contraception use) among primary partners of PLWH.

<u>Methods:</u> 33 PLWHs, 13 from the University of Connecticut Health Center in Farmington and 20 from Community Health Services Inc. in Hartford, were surveyed from June to August 2017. The survey explored demographic information, reported knowledge of PrEP, HIV virus detectability, partner HIV status, type of relationship, and sexual risk factors including barrier use. Deidentified data was collected via a secure survey website.

Results: 39.4% of PLWH denied knowledge of PreP, 60.6% had heard of PrEP, and 12.1% knew someone who has used PrEP. 50% of participants believed that their risk of HIV transmission to their partner was low. This was identical in both long-term and casual relationships. Age of participants differed significantly according to knowledge of PrEP (Heard or knew someone on PrEP vs. Never hearing of PrEP), t (30.9) = -2.82, p = .008. PLWH who had knowledge of PrEP (M = 41.6, SD = 13.3) were younger compared to those without knowledge of PrEP (M = 52.6, SD = 9.115). 50% of participants believed that their risk of HIV transmission to their partner was low. This was identical in both long-term and casual relationships. 9.1% of seronegative primary partners was reported to be using PrEP. The most common reasons for not using PrEP were that the Partner was HIV+ (18%) and the PLWH believed to have an undetectable viral load (51.9%). Of those primary sexual partners of PLWH not taking PrEP, 45.5% were HIV seropositive.

<u>Conclusions:</u> Knowledge of PrEP is incomplete among PLWH. Only a small fraction of HIV-negative primary sexual partners of PLWH are taking PrEP. PLWH may perceive that their risk of transmission of HIV is lower than it is in actuality. Practitioners caring for PLWH should educate their patients of risky sexual behaviors and the efficacy of PrEP as an HIV prevention intervention for seronegative partners. Based on the input from the PLWH, individuals who refuse PrEP use have other means of limiting HIV transmission through barrier protections (i.e. condoms, dental dams) and the primary partner's viral control.

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## Can a Novel Iodine Nanoparticle Contrast Agent Avoid Contrast Induced Nephropathy?

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Introduction: Worldwide, patients receive more than 75 million iodine doses for radiographic testing each year. Contrast agents enable critical and life-saving procedures, however, current iodine agents are suboptimal for blood pool imaging due to their rapid renal clearance and nephrotoxicity. Contrast induced nephropathy (CIN) is responsible for approximately 11% of hospital-acquired renal failure [3], and development of CIN following contrast exposure significantly increases risk for 30-day mortality [2]. Nanoprobes, Inc. recently developed a novel iodine polymer nanoparticle contrast agent (Niodx™), studied in collaboration with the Smilowitz lab, showing an extended blood half-life of ~40 hrs, that is not renally metabolized, and could expand the use of clinical imaging. We hypothesize that Niodx™ is less nephrotoxic compared to standard iodine contrast agents in the setting of preexisting kidney injury.

Methods: We tested our hypothesis by producing kidney injury in a total of forty-six CD1 outbred male mice using two models: bilateral renal artery clamping [4] and administration of Indomethacin and L-NAME [1], to produce a kidney injury prior to administration of standard contrast agent versus Niodx™. Renal artery clamping: We anesthetized mice and clamped renal arteries with microaneurysm clips [4]. We removed clamps after 30 minutes and closed incisions with sutures. Medication pretreatment: Mice received weight-based doses of Indomethacin + L-NAME [1]. 24 hours after surgery/15 minutes after treatment with medication, mice received doses of Iohexol/Niodx™/PBS. We measured kidney injury with plasma Cystatin-C ELISA/Creatinine assay 24 hours after administering contrast agent/PBS.

<u>Results</u>: There was no consistent increase in kidney injury markers after either surgical or medical treatments. In mice where injury markers increased, neither iohexol nor Niodx $^{\text{TM}}$  treatment raised injury marker levels further.

Conclusion: In our hands, renal artery clamping and Indomethacin + L-NAME did not successfully produce a consistent and reproducible measurable acute kidney injury, as evidenced by inconclusive data from the assays performed. Therefore, we were unable to compare nephrotoxic effects of lohexol versus Niodx™. Future studies could include changing the parameters of the kidney injury and/or the use of different inbred mouse models, in order to confirm the presence of kidney injury prior to administration of different contrast agents, or the use of an eNOS knockout model that has been described to produce kidney injury in mice [5].

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# Title of Project: Years of Potential Life Lost Due to Cardiovascular Disease in Asian American Subgroups 2003-2012

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<u>Background:</u> Asian American subgroups (Asian Indian, Chinese, Filipino, Korean, Japanese, and Vietnamese) display varied cardiovascular disease mortality patterns, especially at younger ages.

<u>Objective:</u> This study aims to examine the years of potential life lost (YPLL) due to ischemic heart disease (IHD) and cerebrovascular disease among the six largest Asian American subgroups compared to Non-Hispanic Whites (NHWs).

<u>Methods:</u> We used National Center for Health Statistics (NCHS) Multiple Causes of Death mortality files from 2003-2012 to calculate race-specific life expectancy, mean YPLL, and YPLL per 100,000 population for each Asian subgroup and NHWs.

Results: Asian American subgroups display heterogeneity in cardiovascular disease burden. Asian Indians had the highest burden of IHD; Asian Indian men lost 17 years to IHD, and 724 years per 100,000 population in 2012. Respectively, Filipino and Vietnamese men and women lost a mean of 16 and 17 years of life to cerebrovascular disease; Filipino men lost 352 years per 100,000 population in 2012. All Asian subgroups for both genders had higher years of life lost to cerebrovascular disease compared to NHWs.

<u>Conclusions</u>: Cardiovascular disease burden varies among Asian subgroups, and contributes to significant premature mortality in certain subgroups. Asian Indian and Filipino populations have the highest years of life lost due to ischemic heart disease and Filipino and Vietnamese have the highest years of life lost due to cerebrovascular disease Analysis of risk factors and development of subgroup-specific interventions are required to address these health disparities.

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## **Electrical Stimulation Induces Synchronized Activity of Neurons In Vitro**

Taylor Jackvony<sup>1</sup>, Min Tang-Schomer<sup>2,3</sup>, David L. Kaplan<sup>4</sup>, Sabato Santaniello<sup>5</sup>

A neuronal network or circuit is a collection of neurons that fire in a synchronized manner in order to respond to external stimuli (1). As a neuronal network develops, it evolves from a collection of randomly firing neurons into a fine-tuned functional and structural unit that is capable of human experiences, like learning and memory (2). Both internal signaling pathways and external electrical modulation influence the development of these networks (3), and aberrant network connectivity has been implicated in many neurological diseases, such as epilepsy (4). Understanding the neuronal connectivity of the human brain, both healthy and in disease states, relies on understanding the ways that functional clusters of neurons correlate with physical mapping or architecture of neurons in a circuit; however, such information is not known. Here, we used calcium imaging data from an in vitro model of rat cortical neurons to identify clusters of neurons with similar patterns of activity in response to external electrical stimulation of varying conditions (5). We then mapped these clusters onto the calcium images of the neurons to determine whether the functional clusters of neurons correlated with the architecture of the clusters. We hoped to identify large clusters of neighboring neurons that fired in a synchronized manner. Similar methods have been used to identify clusters of synchronized neurons in in vivo studies of epilepsy (6). Among multiple conditions tested, we found that biphasic waves beginning at a frequency of 0.2 Hz and increasing to 200 kHz in 10-fold stepwise increases with 6 minutes per frequency produced large, synchronized oscillations of the majority of neurons tested. Interestingly, when the neurons were organized into clusters based on the intensity of their response to the electrical activity, neurons in the same functional cluster were located in close proximity on the physical map. Because abnormalities in neuronal firing synchrony have been identified in pathologic states like epilepsy, this study is significant in that it provides insight into the development of synchronized, functional clusters of neurons (7).

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# Computational Investigations into the Structural Characteristics of PDE6 and its Inhibition by PDE6-y

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Phosphodiesterase 6 (PDE6) is a critical enzyme in the eyesight signaling pathway. When activated, PDE6 hydrolyzes cGMP to GMP, which deactivates cGMP-gated ion channels, causing hyperpolarization of the cell and activa.ng the sensory neurons responsible for vision [1]. Within the PDE family, PDE6 is the only enzyme known to have an inhibitory subunit (PDE6- $\gamma$ ), which allows for the regulation of cGMP levels [1,2]. When PDE6- $\gamma$  is bound to PDE6, the enzyme is turned "off" and cannot catalyze cGMP [2]. The  $\alpha$  subunit of the G-protein transducin removes the inhibition of PDE6- $\gamma$  and activates PDE6. Mutations in two mobile loops of PDE6 (the H- and M-loops) reduce affinity for PDE6- $\gamma$  interactions despite the loops being distant from the PDE6- $\gamma$  binding site [3]. PDE6 has proven problematic to isolate, making it difficult to study experimentally and preven.ng a structure from being solved [1]. A chimera of the structurally similar PDE5 and PDE6 (PDE5/6) has been used experimentally to study PDE6. PDE5/6's validity as a model has been shown through mild inhibition by PDE6- $\gamma$  [4]. To study the native sequence of PDE6, a computational approach was applied by creating a homology model of PDE6. Using this model has allowed us to understand the structural basis for PDE6's inhibition by PDE6- $\gamma$ .

We investigate correlations in protein dynamics possibly responsible for allosteric properties by running 1 microsecond of simulations and carrying out various analyses. PDE6 and PDE5/6 are both inhibited by the PDE5 inhibitor sildenafil. With this knowledge, systems of the homology model of PDE6, PDE5, and PDE5/6 in apo, sildenafil bound, and PDE6-y bound states were constructed and simulated through equilibrium molecular dynamics simulations and metadynamics simulations for 100-300 nanoseconds each. Our analyses were aimed at validating our homology model of PDE6 and showing the effect of sildenafil and PDE6-y within each system and across different systems. These studies have allowed us to gain insight into the structural characteristics and the specific residues that are involved in allosteric communication and regulation of PDE6's inhibition by PDE6-y. These simulations highlight that sildenafil inhibits the conformational space PDE5 can sample, show that sildenafil and PDE6-y have the same effect on PDE6, and that mutations of PDE6 that are implicated in the development of retinitis pigmentosa also cause reduced flexibility of PDE6. Using the RMSF, cross-correlational analysis, and motions of the first principal component of apo PDE6, we have discovered a novel region, residues 678 to 710 (the KM region), of PDE6 that may be a region of allosteric control and may serve as an allosteric therapeutic target for diseases such as retinitis pigmentosa.

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#### Oral Health in Santa Maria de Jesus, Guatemala

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<u>Background</u>: Oral health is a determinant of overall health and quality of life [1]. In the United States, young adults, defined as older than 18 years of age, are at a greater risk for poor health outcomes. Within this subgroup of young adults, Hispanics have an even higher risk for poor health outcomes [2]. In addition, many other risk factors have been identified that affect overall oral health such as smoking, sugar intake, diet, alcohol use, and social determinants. Before one can implement measures to improve oral health, the oral health status of the community must be evaluated. Within the entire country of Guatemala there are few recorded efforts to evaluate the oral health status of the rural population. The majority of people in the town are living in extreme poverty and 80% of them suffer from malnutrition [3]. This project is significant because the data obtained can be used to advocate for this population and their oral health rights.

<u>Objective</u>: The purpose of this study was to (1) evaluate the oral health of young adults. To the author's knowledge, there have never been research of any kind conducted in this rural community. In general, little to nothing is known about the oral health status of this population. Hypotheses include: (1) General oral health will be poor (2) Individuals with increased risk factors, such as high consumption of sugary beverages, etc., will have poorer oral health.

<u>Methods</u>: Research took place in Santa Maria de Jesus, Sacatepequez, Guatemala using an observation cross sectional study. Data was collected using a WHO oral health questionnaire given orally by the investigator with informed consent through a local nonprofit, Cosechando Felicidad Inc. The survey included questions about demographics, risk factors, lifestyle factors, attitudes about oral hygiene, and access to dental care. 152 young people aged 18-28 were surveyed. This age group was selected due to their increased risk of poor health outcomes as well as their availability for screening. Additionally, the youth of this age group allows potential intervention to help improve their oral health status and access to care in the future. The data collected was then analyzed through cross sectional analysis to determine the oral health status of this population.

**Results:** Aim 1: Of the 77.9% of participants who had visited a dentist in the past 5 years, 53.8% went becase of pain. Aim 2: 45.6% of participants had oral pain in the past 12 months. 62.5% of participants had consumed coffee with sugar at least once daily. This indicates a relationship between frequency of coffee intake and the presence of oral pain in the past 12 months,  $\chi^2(2) = 6.58$ , p < .05 (p=0.04). The percentage of people endorsing pain in the past 12 months was higher among those who reported higher levels of coffee intake with sugar.

<u>Conclusions</u>: Santa Maria de Jesus, Guatemala was successfully determined to be of particular need for oral health interventions in the age group of 18-28. This data highlights the importance of future changes to dietary intake as well as access to care.

<u>Future Directions</u>: Future research should be conducted to evaluate attitudes towards oral healthcare in this community in order to evaluate potential for future interventions.

<u>Supported by</u>: The UConn School of Dental Medicine Summer Research Fellowship References:

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## **HBV Vaccine Optimization Via Plasmid Re-engineering**

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240 million people worldwide are chronically infected with the hepatitis B virus (HBV). HBV infection can lead to liver cirrhosis as well as liver carcinoma. Although there are effective prophylactic vaccines available that can prevent a future infection of HBV, those who are already infected with HBV have few effective therapeutic options available to them. CaroGen Corporation is working on developing a therapeutic HBV vaccine through the use of virus-likevesicles (VLVs). VLVs are self-replicating, infectious nanoparticles that are capable of delivering the RNA of an antigen of interest into cells. VLVs differ from regular viruses in that they do not have a capsid, and they do not follow the typical lytic or lysogenic cycle of virus replication [1]. They simply consist of RNA that is enveloped by a membrane. The VLV's are produced from a plasmid that contains sequences for HBV antigens, as well as structual and replication proteins necessary for VLV function. The sequences within the plasmid are seperated at three sites by self-cleaving enzymes of the 2A family. There are multiple members of the 2A family that can be used in the plasmid, including T2A, P2A and E2A. Recently, CaroGen has been trying to figure out which combination of 2A family members will produce the VLVs that will initiate the greatest immune response against HBV. Two plasmids that have been used in the past include a 3xT2A plasmid and a P2A-E2A-T2A (Mix2A) plasmid. Previous studies at CaroGen have shown that the 3xT2A plasmid yields VLVs that create a stronger CD8+ response in HBV-infected cells than the Mix2A plasmid. CaroGen wants to determine to what extent 3xP2A-derived VLVs can elicit a CD8+ T-cell response against HBV. By the time this study was finished, a P2A-P2A-T2A (2xP2A) plasmid was constructed. The next step is to create a 3xP2A plasmid from the 2xP2A plasmid. After the 3xP2A plasmid is created, its efficiacy can be measured and compared to the Mix2A and 3xT2A plasmid. Final analysis of the 3xP2A plasmid will lead to a greater understadning of the role VLVs can play in HBV treatment.

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## Compatibility Testing of Obsidian® Lithium Silicate Metal-Ceramic Systems

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<u>Background</u>: Modern metal-ceramic restorations have revolutionized the field of dentistry over the past several decades [1]. These materials have been praised for their predictable performance, biocompatibility, and ability to simulate the optical characteristics of natural teeth [2]. First introduced in the 1950's, porcelain fused-to-metal (PFM) crowns set the standard for restoring both anterior and posterior teeth, where either aesthetics or strength are favored, respectively. Despite their proliferative adoption, porcelain dental ceramics had much room for improvement, particularly due to the brittleness of the material, excessive wear on opposing dentition, low repair potential, weakness of the metal-ceramic bond, and great effort and time required for manufacturing [3,4].

Obsidian® lithium silicate is a new ceramic material developed at Glidewell Laboratories. Named after the naturally occurring volcanic glass, this silicon dioxide based ceramic is highly esthetic, cheaper, stronger, and more durable than its porcelain predecessors, particularly when pressed to metal [8]. Several clinical trials have demonstrated the favorable properties of this material, but the studies are limited in scope, and to date, there is a lack of concrete scholarly research on Obsidian® lithium silicate. Further analysis of Obsidian® lithium silicate is needed, using standardized laboratory methods, in order to fully demonstrate its potential to fill a valuable role in a dentist's restorative repertoire.

<u>Objectives</u>: The purpose of this study is to determine the performance of Obsidian® Lithium Silicate metal-ceramic systems for use in dental restorations using standardized laboratory techniques (ISO 6872) [5]. The key variable to be measured is the crack initiation stress at the ceramic-metal interface, which will be compared to industry standards. Various specimens of metal alloys will be used to identify how differences in quality and preperations of the metal component effect the bonding strength of Obsidian®.

<u>Methods</u>: Specimens were prepared by Glidewell laboratories according to the shape and thickness described in ISO 6872. 10 test specimens were manufactured with Obsidian® cermaic for each of 6 varying metal categories being assessed: Net Press Non-Precious (NPNP), Casted Non-Precious (CNP), Casted Semi-Precious (CSP), Casted Precious (CP), 3D Printed Non-Precious (3DPNP), and 3D Printed Semi-Precious (3DPSP). The specimens were placed in the bending apparatus until failure. Crack initiation stress was calculated using peak load and the various elastic moduli of the metal alloys and results were compared using ANOVA and Tukey HSD at 95% confidence level.

Results: The mean and standard deviation values for crack initiation stress obtained were as follows: NPNP  $37.42 \pm 5.49$  MPa (n=9), CNP  $37.35 \pm 8.61$  MPa (n=10), CSP  $32.24 \pm 4.13$  MPa (n=10), CP  $36.30 \pm 7.35$  MPa (n=9), 3DPNP  $46.99 \pm 7.76$  MPa (n=10), and 3DPSP  $26.77 \pm 3.67$  MPa (n=10). The strongest bond was observed for the 3DPSP,  $46.99 \pm 7.76$  MPa. Tukey analysis revealed 3 different statistically significant groups, 1) 3DPSP, 2) NPNP, CNP, CP, CSP, and 3) CSP, 3DPSP. All specimens met the lower limit under ISO 9693 of 23 MPa for commercial use.

<u>Conclusions</u>: Obsidian® Lithium Silicate ceramic-metal systems prove to be up to industry standards with bonding strength above the lower limit for each metal alloy tested. The crack initiation stress observed for the 3D Printed Non-Precious group of  $46.99 \pm 7.76$  MPa showed the greatest bonding strength overall.

#### **Future Directions:**

Future areas of research should be directed at identifying factors and/or technique sensitivity contributing to the wide range of values observed .

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## The COX2 and SAA3 Dependency of LPS-induced NLRP3 Activation and IL-1β Release

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The NLRP3 inflammasome is a multiprotein complex, expressed primarily in myeloid cells, that mediates host immune responses. Activation of the NLRP3 inflammasome by diverse stimuli results in maturation and release of the cytokines IL-18 and IL-18 [1]. Previously, we showed that receptor activator of NF-kB ligand (RANKL), which commits bone marrow macrophages (BMMs) to become bone resorbing cells, stimulates Saa3, Nlrp3, and II1b gene expression and IL-1β protein release in a cyclooxygenase 2 (COX2)-dependent manner [2]. We also showed that inflammasome activation was dependent on RANKL-produced serum amyloid A3 (SAA3). SAA3 belongs to the SAA family of acute phase apolipoproteins and has been implicated in diseases associated with chronic inflammation [3]. The goal of this study was to determine if the lipopolysaccharide (LPS) induction of Saa3, Nlrp3, and II1b expression is COX2 dependent and if the LPS activation of NLRP3 is SAA3 dependent. Methods: Bone marrow was flushed from the long bones of WT, COX2 KO, and SAA3 KO mice. BMMs were prepared from the marrow by expanding with MCSF (30 ng/ml) for 3 days. BMMs were then cultured with MCSF+LPS (10 µg/ml) or vehicle for 1, 3, 6, and 24 h. Gene expression was measured by quantitative PCR and protein release by ELISA. Results: First, we showed that LPS increased Cox2 expression in BMMs relative to MCSF treated groups at all timepoints with the initial induction at 1 h. Next, we assessed the dependence of Saa3, Nlrp3 and II1b expression on COX2 using BMMs from WT and COX2 KO mice. LPS induced their expression in WT but not COX2 KO BMMs. We then determined that SAA3 was not needed for the LPS induction of Cox2 because LPS could induce Cox2 expression in SAA3 KO BMMs. Next, we determined that SAA3 expression was necessary for LPS to induce NIrp3 and II1b expression by showing that LPS increased their expression in WT but not SAA3 KO BMMs. Lastly, to determine if the NLRP3 inflammasome activation, which results in secretion of IL-1β, was dependent on COX2 or SAA3 expression, we measured IL-1β protein release by ELISA in culture media from LPS treated WT, COX2 KO, and SAA3 KO BMM cultures. IL-1β protein was only released from LPS-treated WT BMMs, indicating that the release required both SAA3 and COX2. Conclusion: COX2 was required for the LPS induction of Saa3, Nlrp3 and II1b. COX2 and SAA3 were required for the LPS induction of mature IL-1β. Understanding the role of COX2 and SAA3 in the LPS activation of the NLRP3 inflammasome increases our understanding of the basic mechanisms regulating this important component of the innate immune system and may help us design therapies to treat inflammation due to LPS.

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## **Characterization Of Osteal Macrophages In The Bone Marrow**

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#### Background

While the study of monocytic lineages differentiation into macrophages and osteoclasts is well studied, the role of osteal macrophages and their recent role in maintaining bone homeostasis is not well established. Given the location of osteal macrophages on bone surfaces and their proximity to osteoblasts *in vivo*, they are believed to play a significant role in the course of bone modeling and remodeling. Surface expression of CD169 is a marker for osteal macrophages. Characterizing the role of CD169<sup>+</sup> macrophages will establish its role in bone homeostasis and during the repair process.

#### **Objective**

CD169 is hypothesized to be a critical marker in maintaining bone homeostasis. The aim of the study is to characterize the role of CD169<sup>+</sup> macrophages derived from the bone marrow from mice and cultured bone marrow macrophages. Flow cytometric analysis was done to ensure accurate representation of the monocytic populations. By flow cytometry, we determined whether in addition to F4/80<sup>+</sup>, a well known monocytic marker, CD169 was also expressed on bone marrow derived macrophages.

## **Experimental Design**

Wild type mice and mice in which PI3 Kinase activity was upregulated were used. To visualize monocytes, these mice were bred with Csf1r<sup>EGFP+</sup> reporter mice. Bone marrow cells were isolated from the femur and tibia of mice. Cells were stained immediately after isolation or were cultured in with Macrophage colony stimulating factor for 72 hours. Cells were incubated with fluorescently conjugated antibodies against CD45, CD11b, F480, and CD 169+. Following gating for live dead staining and background staining using isotype controls, the percentage of cells expressing monocyte macrophage markers were examined.

#### Conclusions

Flow Cytometric showed

- A population of monocyte co-expressing F4/80+, CD11b+ was present in both freshly isolated monocytes and those obtained from in vitro culture
- In mice with increased PI3 Kinase activity, CD169+ monocytes numbers were augmented.

## **Future Directions**

With continued investigation, CD169+ can serve as a notable marker in identification of active osteal macrophage activity within the bone marrow microenvironments. Additional flow cytometric analysis of antigen markers for CD45R, CD3 epsilon, and CD11c will clarify specific lineage and progeny.

#### Support

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## Familial Aggregation of CKDu in Endemic Population of Sri Lanka

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Introduction: Over the last two decades there has been a rapid increase in chronic kidney disease (CKD) in association with rising rates of hypertension and diabetes in low and middle income countries. At the same time, chronic kidney disease of unknown etiology (CKDu), not associated with hypertension or diabetes, has emerged in rural, arid, agricultural lowland regions in multiple countries including Sri Lanka. These countries report 15 to 20% prevalence among men and women between the ages of 30 to 60, particularly among field and agricultural workers. CKDu is a progressive and irreversible disease resulting in renal failure and death unless dialysis or a kidney transplant is available, both of which are highly limited in endemic areas. Primary research efforts addressing CKDu have focused on identification of distinct etiological factors but these efforts have been frustratingly inconclusive. Familial aggregation of CKDu has been reported, but investigation of the possible genetic contribution to CKDu pathogenesis has yet to be systematially studied.

<u>Methods:</u> In this study pedigrees were obtained from individuals who had at least two family members affected with CKDu. Survey questions were administered through interview either at a renal clinic or in home. 86 pedigrees met inclusion criteria and demographic data for 1573 individuals was collected.

<u>Results:</u> Segregation analysis is being performed by the Department of Genetics at UConn Health to investigate the presence of a distinct inheritance pattern of CKDu in these families. Preliminary data suggests that a likely mode of transmission may be autosomal dominant inheritance with incomplete penetrance.

<u>Conclusion:</u> CKDu is an endemic disease plaguing rural areas of Sri Lanka. Determining the etiology will have a transformative impact in combating this public health crisis. Systematic evaluation of familial aggregation suggests there may be a heritable component of CKDu pathogenesis.

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## Role of CD13 in Renal Proximal Tubular Handling of Albumin

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Certain disease states, such as Diabetes Mellitus, damage glomerular function and result in albuminuria, which further promotes renal damage and may progress to chronic kidney disease or end stage renal failure.[1-5] Urinary proteins are normally efficiently resorbed via the Megalin-Cubilin receptor complex and the neonatal Fc Receptor (FcRn) on epithelial cells in renal proximal tubules.[4,5] CD13 has previously been shown to be a negative regulator of endocytosis in a variety of cells including endothelial cells, macrophages, dendritic cells, fibroblasts and epithelial cells. [6] Also, loss of CD13 in two different murine models of albuminuria, streptozotocin (STZ) induced diabetic nephropathy and albumin overload, has previously demonstrated increased albumin uptake by proximal tubule cells. (Shapiro Lab, unpublished data). Here we show that even basal CD13 KO proximal tubules exhibit increased albumin uptake by immunofluorescence and flow cytometry. Furthermore, we identify several possible mechanisms by which CD13 may regulate albumin endocytosis, including 1) colocalization of CD13 and FcRn, 2) elevated levels of cubilin at the brush border of CD13 KO proximal tubules, and 3) maintenance of cristae integrity in CD13 KO mitochondria after a 20 week model of STZ-induced diabetes nephropathy. Our results demonstrate that CD13 serves as a key mediator for albumin endocytosis in the proximal tubule and may be a potential therapeutic target for preventing albuminuria-induced damage in renal disease.

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## **Novel Source for Cell Augmentation of Murine Patellar Tendon Defect**

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Tendon injury is a common pathology that incurs a significant disability to the patient and is a socioeconomic burden. However, the cellular physiology of healing tendon is poorly understood. After surgical repair, the enthesis fails to regenerate a native tendon-to-bone interface and instead heals with a fibrous scar. This fibrocartilaginous construct contains misaligned collagen fibers and lacks a mineralized matrix, leading to a biomechanically inferior construct (1). The current gold standard has failed to demonstrate an improvement in re-tear rates. Therefore, techniques to improve the tendon healing biology must be developed in order to advance the tendon repair field. Mesenchymal stem cells (MSCs) are commonly used for cell-based tendon repair. Bone marrow stromal cells (bMSC) are an abundant and easily accessible source of MSCs; however, inconsistent and inadequate results have been reported for tendon healing (2). Investigators have described a potential source of regenerative cells within the subacromial bursa, which demonstrated express of similar markers to mesenchymal stem cells, and have the ability to differentiate into cells of mesenchymal lineages (3). A subpopulation of multipotent cells residing within the subacromial bursa therefore presents a potential source of mesenchymal stem cells that may promote tendon healing. The purpose of this study is to compare the ability of bursa-derived cells to improve tendon to bone repair via cell engraftment and matrix synthesis compared to bone marrow stromal cells. The central hypothesis is that subacromial bursa-derived mesenchymal stem cells will improve tendon to bone healing versus bone marrow-derived MSCs by engrafting into host tissue and synthesizing more organized and biomechanically superior matrix within a murine patellar tendon defect. In the present study, bone marrow aspirate and subacromial bursa were harvested from consenting patients undergoing rotator cuff repair. The cellular contents were immediately processed, fluorescently tagged, and implanted into NSG murine patellar tendon defects. Atomic force microscopy was performed to assess the alignment of collagen fibers within the stem cell augmented repair, while histological analysis was used to confirm the incorporation of the fluorescently labeled, human cells into the tendon defect. Terminal biomechanical stress testing was also performed to assess the structural integrity of the repair. The load to failure results for the tendon groups are as follows: cut only (8.188 ± 1.832 N), suture & fibrin (5.946 ± 0.651 N), suture & bursa  $(7.204 \pm 3.346 \text{ N})$ , suture & bone marrow  $(7.008 \pm 2.725 \text{ N})$ , cut & bursa  $(5.190 \pm 1.130 \text{ N})$ , and native (10.580 ± 3.970 N). This study is ongoing and it is anticipated that defects treated with subacromial bursa-derived MSCs will show superior alignment, engraftment, and physical resilience compared to defects treated with bone marrow derived MSCs.

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# The Relationship between Shoulder Surgery and the Onset of Cubital Tunnel Syndrome Forrest Mahony<sup>1</sup>, Craig Rodner<sup>1,2</sup>

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Cubital tunnel syndrome appears to be a prevalent sequelae (as observed by Dr Craig Rodner) of previous shoulder surgery. Cubital tunnel syndrome is a type of distal peripheral neuropathy, especially in relation to shoulder surgery. It causes distal peripheral pain and parasthesias that frequently require surgery. Our goal is to search the data for a possible correlation between patients who receive cubital tunnel syndrome surgery with a previous orthopedic shoulder surgery. Furthermore, once we determine which of the cubital tunnel syndrome surgery patients listed had a previous shoulder surgery we plan to explore any commonalities amongst the patients that may indicate a potential cause of the development of peripheral neuropathy. The aim here would be to potentially avoid any aspect of the surgery and/or recovery process that may increase the likelihood of developing a distal peripheral neuropathy. Our last goal would be to apply an anova type statistical study to the data to determine the presence of any risk factors that may be present in the data that contribute to development of cubital tunnel syndrome.

We recently collected the medical record numbers (MRN) and CPT codes from all of the cubital tunnel surgeries performed between May 2007 and May 2017 by Dr Craig Rodner and Dr Jennifer Wolfe. This search resulted in 803 pings. Once we were able to collect the patient information and medical records related to these search results our next step was to look at each of the medical records, locate the charts related to the surgery, and determine how many of the patients had a previous shoulder surgery. The 803 pings for the given CPT codes for cubital tunnel syndrome correlated to the charts of 408 cubital tunnel syndrom surgery patients. Of these patients, 95 of them had orthopedic shoulder surgery listed in their medical records before the cubital tunnel syndrome surgery.

Before we began the project we expected around 200 patient charts to result from the CPT search, but due to that number doubling, the project was not able to be completed in the summer and was expanded into the Scholarship Capstone Project.

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## Student-Led Educational Quality Improvement (sEQI) of COrE-A, Stage 1, MDelta Curriculum

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Team-based learning (TBL) is an active-learning pedagogy (1), and has been shown to yield equal or better academic performance than traditional pedagogies (2,3,5). In 2016, The University of Connecticut School of Medicine (UCONN SOM) introduced the MDelta Curriculum, which integrated the TBL pedagogy across all pre-clerkship courses. As with any new and current curricula, it is critical to perform quality improvement on a regular basis to ensure efficacy, quality and consistency. In this study, we report a new quality improvement model for the constructive review, evaluation, and refinement of pre-clerkship medical education courses, called Student-Led Educational Quality Improvement (sEQI). All US medical schools have curriculum committees consisting of faculty and administrators (and students in some instances) and incorporate student involvement and feedback as part of the Liaison Committee on Medical Education (LCME) 'Self-Study' accreditation process (6). However, students that have recently and successfully completed pre-clerkship medical courses are uniquely situated and highly qualified to be co-drivers of curricular change and refinement along with their faculty and administration. As a pilot program, we specifically focused on the quality improvement of the first ten-week block (Block A) of the main course of the MDelta Curriculum, Case Oriented Essentials (COrE). Three students, who were part of the first class to experience the new curriculum, comprehensively reviewed and evaluated the efficacy of COrE syllabi, objectives, learning materials, and exam questions, and provided detailed constructive feedback and recommendations in collaboration with the faculty and administration. Based on the average student evaluation data for COrE Block A after our sEQI intervention, class satisfaction increased 17% for objectives being communicated well; increased 20% for objectives being achieved during class; increased 19% for classes being educationally effective; increased 14% for class preparatory workload being manageable; and increased 12% for the appropriate preparatory resources being provided. Our data suggests that sEQI is an effective medical education quality improvement model leading to significantly greater student satisfaction, and that current medical students should necessarily be intimately involved in this process. In summary, we are the first to design and implement the novel quality improvement program, sEQI, for pre-clerkship medical curricula. As an easily implementable and versatile model, we hope that sEQI will serve as a foundation for student leadership in transforming the next generation of medical education across the United States.

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## Characterizing the Expression of Melanoma-related microRNAs in Dysplastic Nevi

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The biological relationship between common nevi (benign mole), dysplastic (atypical) nevi, and melanoma remains unclear. A current tumorigenesis model suggests that dysplastic nevus may be a premalignant lesion; however, the specific molecular events are not yet identified [1]. A distinct set of microRNAs (miRNAs)--miR-203, miR-205, and some let-7 family members--with tumor suppressive activity are deregulated in cutaneous melanoma compared to common nevi [2-5]. Here, we measured the expression of these miRNAs directly in histologically defined dysplastic nevi and compared their levels to common nevi, in-situ and invasive melanomas (n= 75) by real-time quantitative RT-PCR (gRT-PCR). ANOVA and Kruskal-Wallis analyses, followed by adjusted pairwise comparisons showed significantly increased expression of miR-203, miR-205 and let-7b and decreased expression of let-7i in dysplastic nevi compared to common nevi and melanomas. Only let-7e (P=0.0018) and let-7g (P=0.0063) were significantly associated with the degree of cytological atypia, where moderate to severe atypia correlated with their decreased expression in dysplastic nevi. Although these results showed that specific melanoma-related miRNAs were also deregulated in dysplastic nevi, their measured expression levels were unique when compared to common nevi and melanomas. The presence of individual miRNA profiles supports a divergent relationship between common nevi, dysplastic nevi, and melanomas.

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## **Neonatal Abstinence Syndrome Comprehensive Education and Needs Training: A Qualitative Study**

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Introduction: Non-medical use of opioids has reached epidemic levels in the US [1]. Neonatal Abstinence Syndrome (NAS) occurs when newborns go through withdrawal because their mothers were addicted to opioids during pregnancy. Symptoms of newborns suffering from NAS include: tremors, seizures, feeding difficulties, respiratory complications, autonomic dysfunction, and failure to thrive [2,3,4]. Neonatal Abstinence Syndrome Comprehensive Education and Needs Training is a project designed to decrease the prevalence of NAS. The goal is to standardize the recognition and support of women of childbearing age who abuse opioids. Methods: We conducted an exploratory qualitative analysis by conducting community meetings and individual in-depth interviews of health care practioners, community outreach members, and women of childbearing age who have struggled with the use of opioids. Participants were recruited from the Harriot Home Heath, the Center for Health Equality, NICU at Saint Francis, the InterCommunity Recovery Center, the U.S. Pain Foundation and The Greater Hartford Harm Reduction Center. Permission was given by all participants to audiotape-record the sessions. A discussion guide was used and the meetings were transcribed verbatim from the audiotapes. Specific quotations were chosen to support the main themes analyzed. Information collected from interviews and community meetings will be used to create an educational module for health care practioners.

Results: Many participants noted the need for practitioners to recognize the polychotomy in opioid use among different populations abusing opioids in different manners. Improvements in care included asking specific questions to recognize high-risk patients. A continuous theme throughout the meetings was to make non-opioid alternatives for pain more financially and practically available: "My opioid prescription is \$5, my non-opioid prescription is \$50, a back injection it is \$100, acupuncture is \$40. The problem comes from that opioids are cheap and easy...it is hard to give other options, because they cannot afford them, they cannot access them, there is not enough education about them." Another recurrent theme included altering DCF strategies away from scare tactics towards continued support for the mother and family after the birth: "When DCF is no longer a scare program, but a help program then we will start to see some change in people willing to come forth and be engaged."

<u>Conclusion:</u> The main themes derived from the meetings included: addressing the different forms of opioid abuse among different populations, including alternatives for pain management, and using DCF as a helping program. Information gained from these meeting will be used as an educational module for healthcare practitioners.

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# Determining The Relationship Between Knowledge And Attitudes of Chlamydia Trachomatis Among The Women Of Guam And Their Safe Sex Practices

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<u>Introduction:</u> Chlamydia trachomatis is the most commonly reported Sexually Transmitted Infection (STI) according to the Center of Disease Control (more than 1.5 million cases reported in 2015)[1]. Guam is currently ranked fifth in the U.S. for C. trachomatis prevalence (586 per 100,000) [2]. This study aimed to explore the relationship between knowledge and attitude of C. trachomatis among women in Guam and their safe sex practices.

<u>Methods:</u> This study was conducted at the Department of Public Health and Social Services in Mangilao, Guam and in the field during public health outreach efforts. Women between the ages of 18-24 years old were administered an IRB- approved survey that assessed their demographic information, personal sexual history and knowledge about STIs. A total of 133 women were included in the study. Data obtained was analyzed using SPSS v.22.

Results: A majority of participants identified their race as either Chamorro (38%) or Chuukese (26%). The "STI Knowledge" portion of the questionnaire included twenty questions and the total score for the participants was M=6.97 (SD= 4.21). Total scores differed significantly between the two most represented groups, Chamorro and Chuukese, t (97) = 6.02, p < .001. Participants who identified as Chamorro had higher results on the "STI Knowledge" assessment (M=8.6, SD = 3.9) compared to those who identified as Chuukese (M=4.2, SD = 3.0). Within the last year, 51% of respondents noted that they "Never used condoms" with the most common reasons being "It just happened" (29%) and "I trust my partner" (25%). Self-reported number of sexual partners within the last year was categorized as either "1," "2," "3," or "4+" partners. Number of self-reported partners was not related to total knowledge scores. Although STI knowledge increased with increased numbers of reported sexual partners, this association was not statistically significant. Safe practices, like being tested for STIs, was not related to race but was trending with 47% of Chamorro reported being tested in the past compared to 28% of Chuukese, x2(1)=3.37, p=.066.

<u>Conclusion:</u> Knowledge of STIs was low in women attending DPHSS clinical and outreach services in Guam. Chukeese participants had significantly lower levels of knowledge compared to the overall cohort and Chamorro women in Guam. Condom use and STI testing was limited in the survey participants. Limited access to health resources may be contributing to differences in testing rates between Chuukese and Chamorro women. Recognition of baseline limitations of STI-related knowledge, ongoing risk behaviors, and testing in specific minority cohorts may help inform health education and STI prevention programs in Guam.

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### High Molecular Weight FGF2 in Dentin and Alveolar Bone Mineralization

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Background: X-linked Hypophosphatemic rickets (XLH) is the inherited form of rickets and is the most common genetic disorder of bone mineralization due to phosphate wasting. XLH causes deficient calcification of bones and teeth and is characterized by short stature, leg bowing, hypophosphatemia, hyperphosphaturia, and abnormal vitamin D metabolism. The dental complications associated with XLH include: severe dental pains, dentin hypomineralization, enlarged pulp chambers and spontaneous periapical infections. XLH is caused by loss of function mutations in PHEX (phosphate-regulating gene with homologies to endopeptidases on the X chromosome) gene. PHEX is expressed in the parathyroid gland, bones and teeth and encodes metalloproteases that cleaves small proteins. PHEX functions to downregulate fibroblast growth factor 23 (FGF23) through its metalloprotease activity. FGF23 is a counterregulatory hormone which inhibit phosphate reabsorption by the sodium/ phosphate co-transporter (NPT2a) in the proximal renal tubules via the FGF receptor 1c (FGFR1c)/ Klotho pathway. FGF23 is elevated in XLH and mediates the renal phosphate wasting phenotype. Inorganic phosphate reabsorption is required for many biological systems including bone matrix mineralization and dentinogenesis. Mice harboring a *Phex* gene deletion (*Hyp* mouse) photocopy human XLH. Fibroblast growth factor 2 (FGF2) is critical for regulating bone matrix mineralization and FGF23 expression. Interestingly, Hyp mice were previously shown to have increased expression of high molecular weight (HMW) nuclear isoforms of FGF2 and increased FGF23 activity.

<u>Objectives</u>: Our unpublished work showed that transgenic mice overexpressing the High Molecular Weight FGF2 isoforms in osteoblast lineage (*HMWTg*) exhibited decreased dentin and alveolar bone mineralization with increased FGF23 expression in mandibular molars. To examine if the alveolar bone and dentin mineralization defects were caused by the increased FGF23 expression, we aimed to rescue the dentin and alveolar bone mineralization defects by utilizing a neutralizing antibody against FGF23.

<u>Methods</u>: *HMWTg* and *VectorTg* control mice were given subcutaneous injections of FGF23 neutralizing antibody (FGF23Ab, 10mg/kg, twice/week) starting at postnatal day21 for 6weeks. In addition, since Vitamin D have direct effects in promoting bone mineralization, we aimed to determine if Vitamin D protects against the defective dentin and alveolar bone mineralization in *HMWTg* mice. Therefore, *HMWTg* mice were given subcutaneous injections of Calcitriol (175pg/g daily) alone for 6 weeks or both Calcitriol and FGF23Ab. Mice were sacrificed and X-ray, Micro-CT, histological, and immunohistochemistry analyses were performed.

**Results:** Our results showed that similar to human XLH and the *Hyp* mouse homologue of XLH, *HMWTg* mice exhibited an enlarged pulp chamber. When we neutralized FGF23 activity in *HMWTg* mice we partially rescued the enlarged pulp chamber phenotype. Additionally, histological analyses show that the FGF23 neutralizing antibody also rescued the dentin and alveolar bone mineralization defects observed in *HMWTg* mice. Interestingly, we found that Calcitriol has a summative effect in promoting dentin and alveolar bone mineralization, in which *HMWTg* mice treated with both the FGF23 neutralizing antibody and Calcitriol further rescues the enlarged pulp chamber, dentin, and alveolar bone mineralization defect phenotypes. **Conclusions:** Together, our data suggest that the dentin and alveolar bone mineralization defects in *HMWTg* mice are caused by the increase in FGF23 expression. Our results further indicate that the HMW nuclear isoforms of FGF2 play a critical role in dentin and alveolar bone mineralization by regulating FGF23 activity.

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### Risk Factors for Severe Oral Mucositis in Head and Neck Cancer Patients Receiving Radiation Therapy

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<u>Background</u>: Oral Mucositis (OM) refers to erythematous, erosive, and ulcerative lesions of the oral mucosa, as a side-effect of systemic chemotherapy or radiation therapy (RT) to the head and neck (H&N) region. It is estimated that 400,000 people suffer from OM each year in the United States alone, including nearly all patients receiving RT for H&N cancer. Patients with severe OM experience significant oral pain and dysphagia, needing systemic opioids, are often unable to eat by mouth, and have to be fed through a stomach tube. OM can cause unwanted treatment breaks resulting in poor prognosis and negatively impacts quality of life. A number of factors have been postulated to affect the risk for OM. A better understanding of risk factors for severe OM can help identify the patients at greatest risk and guide the use of prophylactic and supportive measures.

<u>Objective</u>: The objective of this study was to identify which patient-related and treatment-related factors are associated with 1) greater severity of OM, as measured by OM scores, and 2) greater morbidity of OM, as measured through surrogates such as use of opioids for pain management and rates of hospitalization.

<u>Methods</u>: This study used data contained within the UConn Health OM Research Registry, which included data on up to 50 patients aged 27-96 who had received RT with or without chemotherapy for H&N cancer. Patient-related factors examined were age, gender, history of smoking and alcohol use. Treatment-related factors examined were unilateral vs bilateral RT, total dose of RT, and chemotherapy regimens, specifically types of drugs and timing of administration. A linear regression model was fitted to associate risk factors and severity of OM, assessed using Oral Mucositis Assessment Scale (OMAS) scores. A logistic regression model was fitted to associate risk factors and morbidity of OM, assessed using recorded data on use of opioids and rates of hospitalization for OM. For both tests, p< 0.05 was considered statistically significant.

**Results**: The only patient-related or treatment-related factor that was statistically significant for increased OM severity was the use of induction chemotherapy prior to RT, with an adjusted Odds Ratio (OR) of 2.33, 95% CI [0.71,3.95], p=0.008. The only patient-related or treatment-related factor that was statistically significant for increased morbidity, measured through systemic opioid prescription for pain, was the total dose of RT, with an adjusted OR of 1.004, 95% CI [1.001, 1.010], p=0.038.

<u>Conclusion and Future Directions</u>: These results indicate that the use of induction chemotherapy several weeks prior to the start of RT, significantly increases the risk of severe OM during H&N RT. Although any clinical OM from the induction chemotherapy is typically healed by the start of RT, these findings indicate that subclinical tissue damage persists, resulting in increased risk of severe OM from future cancer therapy. This finding may help inform the risk-benefit analysis concerning use of induction chemotherapy and help tailor prophylactic measures (such as placement of stomach tubes) to patients at greater risk for severe OM.

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### Should fecal transplant be considered earlier than fidaxomicin as therapy for *Clostridium difficile* infection?

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In 2011, C. difficile was responsible for almost half a million infections and about 29,000 deaths, with management costs in the US reaching \$12.4 billion in 2015 (1,4). Current therapy regimens include metronidazole, vancomycin, or fidaxomicin and fecal microbiota transplant (FMT) for refractory *C. difficile* infection (CDI)(3,2). Though FMT is reserved for fulminant CDI, it has a cure rate of over 90%(2). This project seeks to investigate risk factors associated specifically with fulminant CDI requiring fecal microbiota transplant (FMT), including choice of antibiotic therapy, in order to optimize prevention and treatment. A retrospective chart review was conducted to collect data on patients with CDI responding to antibiotic therapy alone (Group A) vs patients with fulminant recurrent CDI requiring FMT (Group B). The data was analyzed using a logistic regression model to associate the two groups with multiple variables including age, sex, comorbidities, antibiotic use as therapy for CDI, number of recurrences, inpatient status at time of initial infection, and PPI use. Odds ratios corresponding to each covariate were reported with a 95% confidence interval and significance level of 0.05. 152 total subjects were reviewed with 87 in Group A and 66 in Group B. No significant differences were found between the two groups regarding age, sex, diabetes, hypertension, CVA, chronic kidney disease, appendectomy status, and PPI use. Differences between Group A and Group B were found to be significantly associated with history of ASHD, type of antibiotic used, inpatient status at initial infection, and number of recurrences (the latter having no estimated odds ratio due to sparse information). History of ASHD and inpatient status at initial infection were significantly associated with a 0.08X and 0.43X risk, respectively, of fulminant CDI requiring FMT. However, these findings were potentially confounded by the possibility that patients with comorbidities may be less likely to be eligible for FMT and thus excluded from this study. metronidazole to treat CDI is associated with a 0.3X risk of developing fulminant CDI while use of vancomycin and fidaxomicin are associated with a 16.29X and 6.71X higher risk. While current guidelines recommend use of vancomycin for mild to moderate CDI and fidaxomicin for severe or complicated CDI, the results of this study suggest using these two medications could lead to the need for FMT. Of note, fidaxomicin is guite expensive with a 10-day supply retailing for over \$3,000. Given the risk of therapy failure of vancomycin and fidaxomicin, the high cost of fidaxomicin, and the high cure rate of FMT, greater consideration may be warranted for FMT as therapy earlier in the disease course.

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### **Dicer Expression in Melanocytic Lesions**

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<u>Introduction:</u> Dicer, a ribonuclease III enzyme, is a rate-limiting step in the processing of immature microRNAs into their functionally active, mature counterparts. Abnormal levels of Dicer have been demonstrated in a number of human cancers, including cervical cancer, prostate cancer, bladder cancer and melanoma. There are conflicting reports in the literature about how Dicer expression varies with the progression of melanoma. In this study, we used a large cohort of patients (n = 217) to see how Dicer expression varies between different melanocytic lesions. In addition, we explored how Dicer expression correlated with histological parameters in patients with primary cutaneous melanoma (n = 116).

Methods: 217 cases from the UConn Department of Dermatology archives were incubated with a monoclonal anti-Dicer antibody. A semi-quantitative scale was used to score the lesions. A "0" was given for a lack of Dicer immunoreactivity; a "1" was given for weakly positive staining; a "2" was given for moderate granular staining; a "3" was given for strongly positive, homogenous staining. To see how Dicer expression varied between diagnostic categories, we analyzed Dicer expression in samples of primary cutaneous melanoma (n = 116), melanoma in situ (n = 49), dysplastic nevi (n = 29) and common nevi (n = 23). Exploratory analyses were conducted to determine how different histological and clinical parameters varied with Dicer expression in patients with primary cutaneous melanoma from the University of Connecticut (n = 116). Parameters that were explored included gender, age, anatomic site, thickness, ulceration, tumor mitotic index, Clark's level, regression, lymphovascular invasion, solar elastosis and tumor infiltrating lymphocytes. Kruskal-Wallis (k = 3) and Mann Whitney (k = 2) tests were used for statistical analyses.

<u>Results:</u> Dicer expression was significantly different between types of melanocytic lesions, with common nevi demonstrating less Dicer expression than dysplastic nevi, melanoma in situ and primary cutaneous melanoma (p = .0001). Dicer was also positively correlated with progressive histological markers of melanoma including thickness, ulceration, mitoses, Clark's level, regression, lymphovascular invasion and solar elastoses (p < .05). Dicer expression was not significantly associated with age, gender or anatomical site of lesion.

<u>Conclusion:</u> Our study demonstrated that Dicer expression is significantly elevated in melanomas and dysplastic nevi as compared to common nevi. In addition, we showed that Dicer expression is positively correlated with progressive histological parameters of melanoma. Further studies should be conducted to explore the role Dicer plays in clinical outcomes for patients with melanoma.

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### Social Media Use and Depression Symptoms in Emerging Adults

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In the United States, depression constitutes a major public health concern, prevalent in 14-22% of young adults [1]. The onset of depressive disorders is highest in adolescents and emerging adults, making emergent adulthood an important time period for clinical intervention [2]. This study investigated the association between depression symptoms and social media use in a nationally representative sample of emerging adults (N=598; 50% females; 63% Caucasian; Age: M=20, SD=1.41). Participants self-reported Facebook, Snapchat, Tumblr, Twitter, and Instagram use and were administered the CES-D to assess depression symptomatology. Increased overall time spent using social media was positively associated with depression symptoms (β=.23; p<.001) and when each platform was analyzed separately, all were positively associated with depression symptoms. No gender differences or differences due to education level were found, however, there was a significant race difference for Twitter (β=.21; p<.05) and Snapchat (β=.20;p<.05). Twitter and Snapchat use were positively associated with depression symptoms for Caucasians ( $\beta$ =.21; p<.05;  $\beta$ =.19; p<.001, respectively), but not for African Americans. However, the mean time spent per day on Twitter and Snapchat was higher in African Americans than in Caucasians. These findings highlight the need to consider race and specific platform use when examining the associations between social media use and depression symptoms in emerging adults. Additionally, these findings demonstrate that social media platforms have the potential to serve as an effective avenue for outreach aimed at emerging adults with depressive symptomatology.

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### CD10, CD13 and CD26 as Potential Biomarkers of early Renal Damage in Murine models and children with Congenital Ureteropelvic Junction Obstruction (UPJO)

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Ureteropelvic junction obstruction (UPJO) is a form of congenital nephropathy that affects 1 in 500 children and can vary in clinical manifestation<sup>1</sup>. The blockage of ureters due to UPJO can results in a wide range of damage, with surgery reserved for those patients with the greatest loss of renal function. Currently, it is difficult to diagnose the level of damage occurring during the blockage to determine when surgical intervention is required. This is done using serum creatinine levels, which remain unchanged until 50% of kidney functional units are lost, and often inconclusive renal scans. Identification of reliable protein biomarkers present in UPJO patient urine are may potentially provide an earlier and more reliable diagnosis, and would be non-invasive. A number of biomarkers have already been proposed, but these biomarkers are proteins produced in response to injury (NGAL, IL8, KIM-1) and therefore the accuracy varies with the etiology of the renal damage<sup>2</sup>. During presentation of UPJO, the blockage of the ureter leads to hydronephrosis, damaging the delicate structures including the proximal tubule. Within each proximal tubule exists a brush border, composed of apically expressed proteins shed due to pressure from the blockage. In particular, proteins containing a single pass within the proximal tubule membrane are more likely to be shed, which is the focus of this study. Based on proteomic analysis of brush border lysates, three proximal tubule metallopeptidases (CD10, CD13, and CD26) were chosen. Bladder urine samples from 12 UPJO patients and 12 control samples were tested for levels of NGAL, KIM-1, CD10, CD13, and CD26 by ELISA. Each of the metallopeptidases outperformed the previously published biomarkers, with the levels being significantly higher in the UPJO patient samples compared to the control<sup>3</sup>. An additional 14 UPJO samples have since been attained, further demonstrating the significance. Because in human patients it is rare for a biopsy to be performed on the renal tissue, it is difficult to make a direct comparison between urine biomarker levels and the levels of damage. To assess this relationship fully, the mouse model of unilateral ureteral obstruction (UUO) was utilized. Urine and kidneys were collected at 2, 3, 4, 5, 7, 10 day (s) post-ligation from both the ligated and unligated kidney. Biomarkers as described above were analyzed using ELISA, and damage quantified using histological techniques including H&E, Trichrome, PAS, Lotus lectin, and ApoTag. Damage increases with time in all measurements, and was synthesized into a single score. These scores were compared to each ELISA biomarker measurement, showing the predictability of each with increasing damage, and further supported the hypothesis CD10, CD13, and CD26 are reliable biomarkers of the associated damage with UPJO.

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### Reported Oral Health Status of the Adult Population in the Bateye Communities of the Dominican Republic

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UNICEF statistics state "61.7% of the [Haitian] population are below the international poverty line of US\$1.25 per day." [4] For this reason, the Dominican Republic receives thousands of Haitian immigrants seeking employment. These workers and their families are concentrated in areas known as the bateyes with no running water, electricity, school facilities or social services from the government. [1] The bateves are an underserved community with a "rapidly increasing level of oral disease...creating the need to assess the oral health status of the population. [2] According to the World Health Organization (WHO) Oral Health Surveys, "data on oral health status are important for surveillance of disease patterns." [3] This study will aim to assess the oral health status of the bateyes by utilizing a standardized WHO Questionnaire for Adults with additional social questions pertaining to this population. 180 community members in over 20 bateyes were interviewed. Persons of all genders and health statuses were included, while those younger than 18 years were excluded. People who completed the survey received a toothbrush, toothpaste, and a brief oral health educational pamphlet. Collected data was entered in MS Excel and imported into SPSS v. 25. For all measures of a continuous nature, descriptive statistics such as sample size, means, medians, and standard deviations were produced. For measures of a discrete (nominal) nature, descriptive statistics such as sample sizes and percentages were created. Of the total survey participants, 57.2% present with 20 teeth or more, while 42.8% have less than 20 teeth and 50.6% have experienced pain in their teeth/mouth in the past 12 months. Those with 20 or more teeth, were significantly younger (M age = 34.41, SD = 13.896) as compared to those with less than 20 teeth. (*M* age= 54.27, *SD* = 13.260), t(178) = 9.68, p < .001. Among the 42.8% with fewer than 20 teeth, 15% had no teeth. Though 28.3% of the total have never received care from a dentist, 71.7% have received care from a dentist in the past 5 years, with 25% of those visits being in the past six months. Of those who have visited the dentist, 70.7% obtained treatment, which the participants identified as extractions. About one-third of the total sample (35.8%) reported specifically visiting a dental mission clinic. At these clinics, the main form of treatment involved extractions (64.3%) while cleanings represented 32.1% of the treatment received. In conclusion, there is a deficit in the oral healthcare of this population, and those who are able to access dental care tend to seek extractions as the prevalent treatment option. To move further, it will be important to establish an assessment of the prevalent oral disease that plagues the community. This will allow for a tailored foundation in the designing of preventative educational programs.

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### RANKL-Stimulated SOCS3 Expression Depends on Saa3 in Mouse Bone Marrow Macrophages

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Background: Suppressor of cytokine signaling 3, SOCS3, regulates cytokine signaling and plays a role in the pathogenesis of many bone diseases, such as osteoarthritis and periodontitis (1). Bone marrow macrophages (BMMs), when committed to become osteoclasts by receptor nuclear factor kappa-B (NFκB) ligand (RANKL), express SOCS3 (2). However, the role of SOCS3 in cytokine signaling remains obscure. In a previous microarray study, the lab found SOCS3 as one of the most highly differentially expressed genes (>35 fold induction) in RANKL-stimulated BMMs compared to non-RANKL-stimulated BMMs. Additionally, the expression of SOCS3 was 26-fold elevated in wild type (WT) BMMs + RANKL compared to cyclooxgenase2 (COX2) knockout (KO) BMMs + RANKL. Serum amyloid A3 (Saa3), an apolipoprotein upregulated in chronic inflammation, was also highly differentially expressed in these cell types (3).

<u>Objective</u>: We want to determine if RANKL-stimulated SOCS3 in BMMs is COX2 and Saa3 dependent.

<u>Methods</u>: WT, COX2 KO, and *Saa3* KO BMMs were collected from long bones of 2 month old mice. BMMs were grown in 6-well dishes with macrophage-colony stimulating factor (M-CSF) +/- RANKL. *Socs3* gene expression was measured at 1, 3, 6, and 24 hours by quantitative PCR. Results were analyzed by two-way ANOVA, followed by post-hoc Bonferroni test.

**Results**: SOCS3 expression was found to be significantly elevated by RANKL stimulation in WT BMMs but not in COX2 KO and *Saa3* KO BMMs. However, a significant elevation was also observed when recombinant human SAA (rhSAA) was added to WT, COX2 KO, and *Saa3* KO BMMs in the absence of RANKL.

<u>Conclusions</u>: The upregulation of SOCS3 in the presence of rhSAA but the absence of RANKL suggests that Saa3 is an intermediate step in RANKL-induced SOCS3 expression in BMMs.

<u>Future Directions</u>: We will continue to investigate the role of SOCS3 in cytokine signaling by knocking it down in BMMs and measure the impact on cytokine production.

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### Evaluating Treatment Planning Outcomes for Dental Implants: A Comparison Between Cone Beam Computer Tomography (CBCT) and Periapical Radiography

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<u>Background</u>: Radiographic imaging is an important adjunct while successfully planning surgical placement of dental implants. Traditionally, two-dimensional periapical radiographs have been the standard of care to aid clinicians in the diagnosis and treatment planning for implant site evaluation, but more recently, three-dimensional imaging has changed this trend. Periapical radiographs are limited in their ability to represent maxillo-mandibular structures while three-dimensional Cone Beam CT (CBCT) offers more advanced imaging to determine the available bone height, width and bone density for implant placement. It is important to evaluate the value addition of 3-D imaging in preoperative implant planning and the perspective of care providers in evaluating these potential implant sites.

<u>Objective</u>: The objective of this study is to (1) determine the value addition of three-dimensional CBCT imaging compared to two-dimensional periapical imaging at the pre-operative planning stage for the success of dental implant placement.

<u>Methods</u>: This retrospective study was done by evaluating 47 cases of patients referred for dental implant therapy. Inclusion criteria was to have an intra oral periapical, an extra oral panoramic and a CBCT scan. An oral and maxillofacial surgeon, a periodontist and a restorative dentist evaluated both the periapical and CBCT images alongside a panoramic imaging for implant treatment planning. All raters had full access to the scans with the full ability to scroll through the entire scan and make site specific measurements. All raters were given a questionnaire with 10 questions evaluating height, width, cortical structure, and pathology.

<u>Results</u>: Inter and Intra operator reliability were used to test if three-dimensional imaging value addition. Cronbach's alpha ranged between 0.499-0.67 showing that there was a good inter observer agreement. A chi-Square test showed that the responses were strongly associated between the periapical and CBCT imaging modalities. The most value addition that the CBCT scans provided were associated with cortication of the bone plates, trabecular pattern, ridge width and bone augmentation.

<u>Conclusions</u>: In the small data set of patients evaluated in this study, 3-D imaging using CBCT offered a significant value addition in the selection process and treatment planning of potential dental implant sites.

<u>Future Directions</u>: Future directions of research will include larger sample size and greater evaluator pool of participants.

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### Controlled Rhythmic Yogic Breathing as Complementary Treatment for Post-Traumatic Stress Disorder in Military Veterans: A Case Series

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<u>Background:</u> Post-traumatic stress disorder (PTSD) is a cluster of symptoms in which a person persistently relives a traumatic event, through recurring thoughts, nightmares, and flashbacks for at least 1 month or more. There are various behavioral and medical treatment options for PTSD. Mind-body techniques, such as biofeedback and breathing-based stress reduction, have shown some promise in the treatment of PTSD symptoms. The purpose of this case series was to examine controlled yogic breathing as a complementary treatment of PTSD in military veterans.

<u>Method:</u> A retrospective review was performed from 2012 to 2016 in 3 cases, and participant demographics, member statements, and PTSD Checklist—Military Version (PCL-M) scores, pre-and-post course, were extracted.

<u>Cases:</u> Three military veterans with PTSD participated in a standardized 5-day course designed to teach them controlled rhythmic yogic breathing exercises.

<u>Results:</u> Subjectively, all 3 participants reported a decrease in PTSD symptoms after the course. Objectively, all 3 participants had a reduction in their overall PCL-M scores after the course. Among all 3 participants, there were score decreases in the Avoidance and Increased Arousal categories. The most dramatic improvement occurred in the participant with the most severe symptoms.

<u>Conclusions:</u> Controlled yogic breathing, specifically Sudarshan Kriya (SKY), appeared to reduce the symptoms of PTSD in 3 veterans of the Armed Services.

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### Examination of TGFβ Pathway Signaling Components in Cells Derived from Cherubism Bone Marrow Stromal Cultures

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**Background:** Cherubism is a rare genetic disorder that presents as large abnormal growths in the upper and lower jaws. These growths are a result of bone erosion and fibrous tissue overgrowth that can cause severe facial deformity. The disorder usually appears in early childhood between ages 2-5 and the symptoms gradually subside with puberty. In some patients, symptoms that do subside on their own and require surgical intervention. The cause of cherubism has been associated with a gene encoding for SH3BP2, an adaptor protein associated with multiple signaling proteins. The most common mutation found in cherubism patients, a proline to arginine mutation was engineered into the mouse *Sh3bp2* gene (P416R) to create an animal model for this disease (*Sh3bp2*<sup>KI/KI</sup>).

By studying bone marrow stromal cultures derived from cherubism mice, Dr. Maye's lab has generated evidence that TGF $\beta$  signaling may have an important role in the presentation of cherubism. Bone marrow stromal cultures derived from  $Sh3bp2^{KI/KI}$  mice inherently display impaired osteoblast differentiation and robust osteoclast formation. However, when cultures were grown in the presence of antagonists against TGF $\beta$  ligands or TGF $\beta$  Receptor 1 (T $\beta$ R1), osteoblast differentiation was rescued, and osteoclast formation was markedly reduced.

<u>Objective</u>: The objectives of this study were to further understand how a cherubism mutation in Sh3bp2 can result in changes in TGF $\beta$  signaling.

<u>Methods</u>: Bone marrow stromal cultures were grown for seven days and FACS sorted for the hematopoietic cell surface markers CD45 and CD11b. RNA was purified from CD45<sup>+</sup>, CD11b<sup>+</sup> and CD45<sup>-</sup>, CD11b<sup>-</sup> FACS sorted cell populations and gene expression analyses for members of the TGFβ signaling pathway were carried out by real-time PCR. Results were analyzed using Bio-Rad CFX Manager 3.1 software.

<u>Results</u>: Gene expression analyses of TGF $\beta$  signaling components does indicate that the cherubism mutation in Sh3bp2 leads to augmented TGF $\beta$  signaling. Pai1, a target gene of the TGF $\beta$  signaling pathway was on average increased 2-fold in CD45-, CD11b- mesenchymal cherubism cells, while BAMBI, an inhibitor of TGF $\beta$  signaling was significantly down-regulated in both the hematopoietic and mesenchymal cell fractions derived from cherubism mice.

Conclusions: Cherubism mutations in Sh3bp2 do lead to changes in TGFß signaling.

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### Biomimetic Hydrogel Based 3D Culture System for Supporting Growth and Maturation of Primordial Follicles

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A common complication from cancer treatment for girls is premature ovarian insufficiency (POI), which results from follicle toxicity and subsequent degeneration. Thirty percent of survivors who were treated with alkylating agents with abdominopelvic radiation later developed premature menopause from toxin-induced POI (1). POI can lead to a wide spectrum of disease such as delayed puberty, infertility, osteoporosis, depression, heart disease, and dementia (2).

The only current option in restoring fertility is cryo-preservation of harvested eggs prior to treatment (3). Cryopreservation of mature eggs may not be suitable for prepubescent children or when treatment cannot be delayed. Additionally, the survival and success rate of maturing primordial follicles *in vitro* is low. We hypothesized that the low survival rates from previous studies were due to a lack of paracrine signals, ECM, growth factors, and reconstitution of the native 3D tissue microenvironment.

Due to these limitations, we designed and developed a novel method for fertility restoration. The overwhelming majority of all ovarian follicles consist of primordial follicles at any reproductive age. However, the survival and success rate of maturing primordial follicles *in vitro* is low. This project aimed to optimize the *in vitro* reproductive potential of primordial follicles.

We designed an artificial ovary in a mouse model via dynamic and tunable hydrogel formulation. 4 day old mouse pup ovaries were retrieved and follicles were individually isolated. Each hydrogel network was composed of 6% 8-arm polyethylene glycol – vinyl sulfone (PEG-VS) crosslinked via Michael type addition with trifunctional crosslinking YKNS/VPMS peptide. Follicles were inserted into the hydrogel network and grown on growth media for up to 20 days. Hydrogel systems were tracked for 20 days and yielded growing and maturing follicles up to the late secondary stage.

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### The Quality and Determinants of Maternal Healthcare in Kisoro, Uganda.

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Obstetrical, prenatal, and peripartum conditions continue to be important causes of preventable morbidity and mortality in sub-Saharan Africa. The World Health Organization (WHO) has issued guidelines on the recommended standard of care in developing nations [1]. Within Uganda, there is wide regional variation in delivery of maternal healthcare. The purpose of this evaluation was to assess maternal healthcare delivery to women in the rural village of Cyanika, Kisoro District, Southwestern Uganda, where the Clare Nsenga Foundation (CNF) operates a level 2 health center and is undergoing an expansion of maternity-related services.

Women attending the CNF clinic were administered a survey assessing sociodemographic information and healthcare received during the last pregnancy within 5 years. Reported care was compared with WHO-defined standards to determine rates of compliance with each recommendation.

One hundred twenty-six women participated. Mean age was 27.7 +/- 6.5 years, with 76.9% receiving some formal education (83.5% primary level, 15.5% secondary level, 1.0% higher education). The average number of pregnancies was 3.0 +/- 2.2. All women reported some level of antenatal care, with a mean time of presentation to ANC of 3.9 +/-1.4 months of gestation, and 55.6% meeting the WHO guideline of first ANC visit within the first trimester. Women reported 3.4 +/-0.8 total prenatal visits, with 47.6% meeting the guideline of 4 visits total. Fortysix percent of women received prophylactic antimalarial medication during pregnancy, with 19.7% receiving the recommended dosing. HIV testing was completed in 94.5%, whereas 78.5% were informed about the risk of transmission of HIV from mother to child during birth. Fifty-three percent of women were administered medicine for intestinal worms, 89.7% received iron supplements, and 87.9% received a tetanus toxoid vaccination. Economic status was significantly related to both giving birth in a hospital (r=0.179, p=0.022) and to the level of postnatal care received (r=0.155, p=0.049). Level of education was negatively correlated with the number of pregnancies, r = -0.235, p = 0.01. Women who received antenatal care were more likely to give birth in a hospital (r=0.260, p=0.003) and receive postnatal care (r=0.394, p=0.000).

This data provides a baseline measurement of antenatal care in Cyanika, Uganda. It identifies a number of areas where delivery of care can be improved. Specifically, time to presentation, number of ANC visits, and administration of antimalarial and deworming medication fell outside of WHO guidelines in this cohort. Both economic status and education level correlated with the level of care received. Entry into the healthcare system early during the pregnancy correlated with better postnatal care.

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### Barriers to Pre-Exposure Prophylaxis (PrEP) Uptake in Black and Hispanic/Latino MSM Rashmi Pashankar<sup>1</sup>, Kevin Dieckhaus<sup>1</sup>, Philip A. Chan <sup>2,3</sup>

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Pre-exposure prophylaxis (PrEP) is a daily antiretroviral medication used to prevent HIV infection that has shown to be more than 90% effective among men who have sex with men (MSM). Black and Hispanic/Latino men who have sex with men (MSM) are two groups with high rates of HIV incidence; however, in both communities, PrEP uptake has been slower than PrEP uptake among white MSM. It is important to understand why this disparity exists and how best to engage with these communities. This project interviewed 20 Black and Hispanic/Latino MSM at a STD clinic in Providence. RI to determine the barriers to PrEP uptake, how future PrEP formulations would be received, and other barriers that prevent these communities from accessing care. The main barriers to PrEP uptake were low perceived risk (30%), cost (25%), lack of knowledge on PrEP (15%), and dislike of daily medications (10%). When considering future PrEP formulations, participants preferred the implant (60%), followed by the daily, currently available, oral pill (20%), rectal microbicide (10%), and antibody infusions (10%). Other barriers to engaging in PrEP included different treatment in health care settings due to their sexual or racial identity, the immense stigma around HIV in their communities, and medical mistrust. The project's goal is to better understand these communities so the best health care and HIV prevention can be provided.

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### Mid and Long-Term Outcomes for Patients Treated with Distal Femoral Osteotomy

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Distal femoral osteotomy (DFO) has been utilized for realignment of the knee joint with valgus deformity or symptomatic unicompartmental osteoarthritis in young and active patients. In North America, the use of osteotomies has decreased due to improved technology within arthroplasty. such as the unicondylar knee arthroplasty technique. However, interest in joint preservation, such as meniscal transplant or cartilage procedures in the younger patient, has revived the popularity of osteotomies for joint preservation, or adjunctive procedures. The medial-closing wedge and the lateral opening wedge techniques have been described for the distal femoral osteotomy; however no study has directly compared these techniques. Two recent systematic reviews of the literature through November 2015 have demonstrated that the literature lacks clear long-term outcomes for these procedures. 1,2 These studies typically are retrospective small case series with mid-term follow-up data reporting outcomes such as accuracy of correction, pain and function outcomes<sup>3</sup>, complication and reoperation rates, and the extent to which misalignment pre-op can predict a decline in activity level.<sup>4</sup> Overall, existing literature describing long-term outcomes of distal femoral osteotomies is limited, and largely reports on a small patient cohort. This outcome study will examine clinical and radiographic mid- to long-term outcomes of distal femoral osteotomy performed by two surgeons since 2000 with at least 2 years follow-up. Though data collection and patient follow up is ongoing, we anticipate that the results with show that the distal femoral osteotomy offers good clinical and radiographic outcomes in the cohort examined. This outcome may offer insight into the use of distal femoral osteotomies in a younger patient population suffering from unicompartmental osteoarthritis, and potentially encourage the preservation of native knee joints in young, active patients.

Supported by: The UConn School of Medicine Summer Research Fellowship
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### Circulating Biomarkers and Noninvasive Cardiac Imaging Techniques That Predict Cancer Therapy Cardiotoxicity

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The use of some chemotherapy drugs, such as anthracyclines and trastuzumab, increases the risk that a patient will develop cardiovascular complications.1 The incidence of heart failure in patients receiving a cumulative dose of 550 mg/m2 of anthracyclines may be as high as 26%, and cardiac dysfunction has been reported in approximately 3-12% of patients who received trastuzumab.2 When trastuzumab is combined with anthracyclines, the risk of heart failure climbs to 18-34%.3 The central question that this project addresses is how to detect evidence of chemotherapy-induced cardiotoxicity before the patient experiences irreversible damage to cardiac myocytes. Techniques such as speckle tracking-derived measures of global longitudinal strain (GLS) may offer measures of myocardial deformation that precede permanent changes in ejection fraction. Studies have also shown that biomarkers in blood may serve as prognostic indicators for patients at risk for developing cardiotoxicity.4 This study uses a longitudinal experimental model to monitor patients at different intervals during and after their chemotherapy treatment. Currently, 46 out of an anticipated 100 patients have been enrolled in the study. Patients in the study receive baseline echocardiography measures and blood samples, and these measures are repeated at various checkpoints. For patients receiving anthracyclines chemotherapy, biomarkers from the blood and echocardiography measures are obtained at baseline, at the end of the patient's chemotherapy regimen, and 3-6 months after their chemotherapy has been completed. For patients receiving trastuzumab, biomarkers from the blood and echocardiography measures are obtained at baseline and after 3 months of treatment. Additionally, echocardiography measures are obtained at 3-month intervals for the duration of a year, and biomarkers from blood are obtained 3-6 months after trastuzumab therapy has been completed. Data collection is still ongoing, but preliminary trends suggest that myeloperoxidase (MPO) and brain natriuretic peptide (BNP) serum levels increase as chemotherapy regimens progress. Additionally, global longitudinal strain (GLS), measured by echocardiography, appears to increase during the course of the chemotherapy regimen. Further data collection and analysis is needed to determine if there is a correlation between levels of BNP, MPO, and GLS. To determine the clinical relevance of these changes, long-term follow up may be needed to determine whether changes in BNP, MPO, or GLS can be used to predict symptoms of left ventricular dysfunction later on in the patient's life.

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### The Effect of Sealants on Six Year Molars Applied at UConn Health: A Retrospective Cohort Study

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<u>Background</u>: The effectiveness of sealants on six-year molars conducted by UConn Health has never been studied. As an institution, it is unknown if current protocols regarding sealant recommendations are currently optimal for patients health. In recent years, the benefit of recommending sealants as routine in pediatric caries have been brought to question. The rates of caries have declined over 75% and the economic burden of sealants must be considered <sup>1,2</sup>.

<u>Objective</u>: With the previously discussed studies in mind, as well as the rapidly declining caries rate, there is precedence to discover the effectiveness of sealants on 6-year molars treated by UConn Health.

Methods: A Retrospective cohort study was implemented by utilizing past patient files contained in UConn Health's Axium electronic health record. Inclusion into the study will include six year old pediatric patients enrolled at UConn Health's pediatric dentistry clinic in 2014. Preliminary DMFT score calculations and cut off classifications between "high", "low", and "medium" DMFT was conducted utilizing methods done previously<sup>3</sup>. Patients who stopped attending regular appointments during the four-year period were excluded from the study as well as patients who attained dental treatment outside of UConn Health's Dental clinic.

**Results:** A total of 232 teeth were analyzed for sealant efficacy. At some point in each patient's stay at UConn Health's Pediatric Clinic, a third (36%) of all teeth needed some form of re-treatment after the sealant was placed. Within the patient pool at UConn, the majority had two preventative visits per year (59%), followed by one preventative visit a year (32%). Patients fluorinated drinking water intake as well as tooth brushing frequency was high (98%). The majority of patients had a caries risk assessment of a medium level (41%) followed by low (31%) then high (28%). The majority of patients had public health insurance (95%) in comparison to private (5%).

<u>Conclusions</u>: Our study highlights the need for vigilant recall and repair of sealants placed at the University of Connecticut's Pediatric Dental Clinic. The rate of repair of sealants is high in comparison to other previous studies done at different health clinics<sup>4</sup>. The results, however, may be difficult to compare between different clinics due to the varying epidemiology of each patient pool.

<u>Future Directions</u>: To make appropriate conclusions concerning sealant placement repair at UConn Health, it is imperative that we communicate with nearby Pediatric Health Clinics to see their respective repair rate results. Once attained, we can compare repair rates to clinics with a similar patient population as UConn health. Furthermore, we can compare UConn Health's repair rates to populations known to be dissimilar, like private pediatric practices.

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### Parathyroid Hormone Regulates RANKL and OPG in Primary Osteoblasts via the Protein Kinase C Pathway

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Background and objectives: Parathyroid hormone (PTH) is capable of stimulating both bone formation and bone resorption. When PTH is given continuously, resorption is greater than formation and there is a net bone loss. PTH mediates its effect on resorption by increasing receptor activator of nuclear kappa-β ligand (RANKL) expression and decreasing osteoprotegerin (OPG) expression in osteoblast lineage cells.<sup>1</sup> Previously, this lab identified serum amyloid 3 (SAA3), a factor that blocks PTH-induced cAMP production in osteoblast lineage cells.<sup>2</sup> Preliminary data indicates that the anabolic effects of continuous PTH in vitro are inhibited by SAA3, but it had no effect on resorption i.e. RANKL and OPG expression. This suggests that PTH does not stimulate bone resorption via a cAMP and protein kinase A (PKA) signaling pathway but via different pathway stimulated by PTH. The goal of this study was to determine if PTH-induced RANKL and OPG induction was independent of cAMP pathway and dependent on protein kinase C (PKC) pathway.

<u>Methods</u>: Freshly isolated primary osteoblasts (POBs) were cultured in osteoblast differentiation medium for 5 days and then treated with PKA or PKC inhibitors 45 minutes prior to induction with vehicle or PTH or other agonists for 2 hours. RNA was extracted and gene expression studies were performed.

Results: POBs treated with PTH alone showed an increase in RANKL and a decrease in OPG gene expression, critical regulators of bone resorption. PTH also showed an increased in RAMP3 gene expression, a cAMP dependent gene. PTH induction of RAMP3 was blocked by a PKA inhibitor while RANKL and OPG induction were unaffected. Contrastingly, PTH induction of RAMP3 was unaffected by a PKC inhibitor while increase of RANKL and decrease of OPG by PTH were completely blocked.

<u>Conclusions</u>: These findings suggest that PTH mediates its effects on RANKL and OPG independent of a cAMP signaling pathway and instead, depends on the PKC pathway.

<u>Future Directions</u>: Future investigations can explore the role of specific PKC isoforms and downstream effectors of PKC signaling, such as MAP kinases, in stimulating the expression of *Rankl* and *Opg*.

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### Low Phosphate Diet Recovers Increased Osteocyte Density in a Mouse Model for Craniometaphyseal Dysplasia

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<u>Background</u>: Craniometaphyseal dysplasia (CMD) is a rare genetic bone disorder characterized by life-long progressive thickening of craniofacial bones and widened metaphyses of long bone. Mutations in the progressive ankylosis gene (ANKH, murine homologue Ank) have been identified in the autosomal dominant form of CMD [1, 2]. We previously generated a CMD knock-in (KI) mouse model expressing a Phe377del mutation in *Ank* [3]. Homozygous mice (*Ank*<sup>KI/KI</sup>) replicate many features of human CMD and exhibit impaired osteoblastogenesis and osteoclastogenesis [4]. Whether osteocytes, the most numerous bone cells, are affected in CMD has not been investigated.

**Objective:** Osteocytes respond to phosphate (Pi) challenges [5]. Here, we aim to examine skeletal phenotypes, focusing on the changes of osteocyte density, in  $Ank^{+/+}$  and  $Ank^{KI/KI}$  male mice fed with normal (0.7%) and low-Pi (0.3%) diet for 13 weeks from born. **Methods**:  $Ank^{+/+}$  and  $Ank^{KI/KI}$  mice were injected intraperitoneally with calcein and alizarin

<u>Methods</u>:  $Ank^{+/+}$  and  $Ank^{K/|K|}$  mice were injected intraperitoneally with calcein and alizarin complexon at an interval of 7 days. Two days after the second injection, mice were sacrificed at age of 13 weeks and femurs/mandibles were subjected to  $\mu$ CT and histomorphometry. Frozen embedded femurs were sectioned ( $7\mu$ m) and stained with enzyme-labeled fluorescence 97 and Hoechst for tartrate-resistant acid phosphatase (TRAP) stained osteoclasts and cell nuclei, respectively. Sections were imaged. Osteocyte numbers as well as TRAP signals were determined with Adobe Photoshop and ImageJ software.

**Results**: Low Pi diet partially ameliorates CMD phenotypes in  $Ank^{\text{KI/KI}}$  mice by decreasing the diaphyseal trabeculation, reducing the cortical porosity of femurs, and decreasing high bone mass of mandibles. In an area between 400 and 2000  $\mu$ m distal to the growth plate, TRAP signals and osteocyte numbers normalized to bone surface were significantly increased in  $Ank^{\text{KI/KI}}$  mice. Low Pi diet significantly reduced osteocyte density in both  $Ank^{+/+}$  and  $Ank^{\text{KI/KI}}$  mice. TRAP signals were higher in  $Ank^{\text{KI/KI}}$  mice but not significantly changed by low Pi diet. Interestingly, the TRAP signals measured in the area immediately below the growth plate were significantly reduced in  $Ank^{\text{KI/KI}}$  mice fed with low Pi compared to normal diet.

<u>Conclusions</u>: Based on our findings, low Pi diet partially ameliorates a high bone mass phenotype in CMD, which may mainly be mediated by effects on osteocytes since TRAP signals were not significantly altered and bone formation rate was mildly decreased by low Pi diet.

<u>Future Directions</u>: Future studies will investigate molecular pathways affected by the CMD mutant Ank in osteocytes.

Supported by the UConn School of Dental Medicine Summer Research Fellowship **References**:

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### Healthcare Resource Utilization Associated with Roux-en-Y Gastric Bypass vs. Sleeve Gastrectomy

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Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) together account for the majority of all bariatric surgeries in the US. RYGB tends to be more efficacious than SG in terms of outcomes, but is associated with a greater frequency of adverse effects and complications [1-3]. While the post-operative complication rates of the two procedures have been well characterized, the different healthcare needs of patients undergoing RYGB and SG have not. Our objective was to quantify healthcare utilization after RYGB and SG.

We compared non-routine (NR) visits made and associated services provided up to two years post-surgery for patients undergoing primary RYGB and SG between March 2013 and April 2015 at a single site. NR visits were defined as a visit to the surgical weight loss center, emergency department, or another healthcare facility that was not previously scheduled as part of the standard of care after bariatric surgery and was necessary in order to address a side effect, symptom, or complication judged by the investigators to be related to the primary bariatric procedure.

A total of 258 and 461 patients had primary RYGB and SG, respectively, during the study period. Follow-up rates for the groups at one and two years post-surgery did not differ. Rates for all NR visits, expressed as the number per 100 patients, were 68.6 in RYGB vs. 33.4 in SG patients (p<0.0001). Emergency department visits with subsequent admission (EDA) or without subsequent admission (ED-only), and outpatient visits (OPV) were more frequent in RYGB vs. SG: EDA, 15.1 vs. 8.2 (p<0.0103); ED-only, 17.8 vs. 8.2 (p<0.0001); and OPV, 29.8 vs. 14.1 (p<0.0001). RYGB required more services than SG, 120.9 vs. 75.5, respectively (p<0.0001).

Surgery type remained a significant predictor of healthcare utilization even after controlling for other factors, such as patient comorbidities. Imaging services were the most often used resources for both RYGB and SG patients. Healthcare utilization peaked at 1 to 6 months after the surgery. RYGB required twice as much follow-up care relative to SG, corresponding to previous reports of more frequent complications in RYGB. Physicians should carefully consider this when discussing surgical management of obesity with patients.

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### Avoidance of Anesthesia Needle Tip Barb Formation to Reduce Risk of Complications During Administration of an Inferior Alveolar Nerve Block Injection

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**Background:** The inferior alveolar nerve block (IANB) is the most commonly utilized anesthetic technique used in dentistry and is particularly prone to failure (15-20% failure rates). Severe complications such as facial palsy, irreversible paresthesia, and hematoma may arise due to improper injection technique or lack of patient-specific anatomical considerations. Previous studies have identified specific mechanistic causes, one of which concerns needle tip barb formation upon contact with bone during injection as a potential cause for lingual and inferior alveolar nerve damage or vessel rupture. Preliminary experiments that were conducted have determined that the average amount of force required to blunt the tip of a needle >1mm upon impact with a mandibular bone is only 0.5 N. The proposed project is significant because it will generate new knowledge in hopes of reducing complications and adverse outcomes for the patient. Additionally, such data on optimal force of needle penetration and impact on the mandibular bone during IANB injections have not been measured previously. It is our hope that clinicians can apply this information in their practices to reduce the risk of complications during administration of an inferior alveolar nerve block injection.

**Objective:** The proposed study seeks to measure the various parameters and factors that affect needle tip barb formation upon bony contact, and to ultimately create a set of guidelines for optimal needle size, thickness, and bevel orientation in order to reduce barb formation during an inferior alveolar nerve block. A second aim of this study is to suggest improvements to the standard inferior alveolar nerve block technique. The long term goal of this project will be to reveal the most effective modes of anesthesia administration as it pertains to mandibular nerve blocks, with the hopes that this data will help to improve the standard technique and impact future clinical decision making.

**Methods:** The experimental apparatus consisted of a mandible attached to a weight scale and a needle attached to a dental anesthesia syringe to simulate a clinically accurate model of an IANB injection. For each trial, the needle was positioned to hit the bony prominence of the medial aspect of the ramus with varying forces. The study variables consisted of needle size (long, short), needle luminal thickness (25, 27, or 30 gauge), and bevel orientation (bevel facing bone, bevel turned away from bone). 10 trials were conducted for each combination of needle gauge size and bevel orientation (N=60). Needle tips were visualized and measured to scale using a high power light microscope with a functional screen display. Statistical analyses were performed using Microsoft Excel and SPSS.

**Results:** Average forces were calculated for each of the six conditions. Forces ranged from 0.343N to 0.46N. 30 gauge needle away from bone produced an average force of 0.343N, and 25 gauge away from bone produced an average force of 0.46N. Average needle tip barb distances were measured for each of the six conditions. Barb lengths ranged from 0 to 0.75mm. 30 gauge with bevel facing away from bone created the largest barbs ( $\mu$ =0.43mm) and 25 gauge with bevel facing bone created the smallest barbs ( $\mu$ =0.21mm).

**Conclusions:** The results show that thick 25 gauge needles produce the highest amount of impact force on the bone, whereas thin 30 gauge needles produce the least amount of impact force, as expected. The needle tips of each of the six conditions post-injection demonstrate that 25 gauge needles with the bevel facing away from bone produce the smallest degree of barb formation, while 30 gauge needles with the bevel facing toward bone produce larger barbs. Additionally, we observed an inverse relationship between impact force and needle barb formation. Although his effect was not anticipated, it may highlight the importance of other factors, such as needle thickness and bevel orientation, and their influence on barb formation.

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### Assessing Pathogenicity of beta-Myosin Heavy Chain Gene Variants Using Human Stem Cell-Based Assays

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Heart failure (HF) is an epidemic that affects 5 million patients in the United States and has a mortality rate of 50% at 5 years (cdc.org). The most commonly inherited risk factor for HF is mutation of genes encoding force-producing components of the cardiac sarcomere, such as the beta-myosin heavy chain gene (MYH7) [1]. Notably, individuals with MYH7 mutations may develop hypertrophic cardiomyopathy (HCM) or dilated cardiomyopathy (DCM), which has implications for patient prognosis and therapy [2]. However, how and which MYH7 variants lead to HF is incompletely understood. The majority of the more than 500 rare MYH7 missense variants observed in HF patients are of uncertain significance (VUS), which presents a considerable challenge to clinical genetics and drug development. Recently, our isogenic human cardiac tissue models of HCM identified hypercontractility as a mechanical consequence of MYH7 HCM mutations. To determine how MYH7 variants lead to DCM, I took steps towards engineering an isogenic DCM model with MYH7-S532P using human induced pluripotent stem cell technology, ultimately to analyze comparatively to previous MYH7 HCM models by interrogating a 3-dimensional cardiac tissue assay resembling cardiac architecture and mechanics. Our cardiac tissue models also identified HF-specific cellular phenotypes and molecular markers, providing the foundation for predicting pathogenicity of clinically-observed MYH7 VUS. However, these "gold standard" models of HF lack the throughput necessary to assess the burden of sarcomere variants in the population; therefore, I also initiated the production of a highly scalable functional iPSC-based assay using lentivirus technology, in order to characterize other MYH7 mutations into HCM, DCM or benign variants. To control for MYH7 expression dosage, mutant MYH7-2A-mCherry plasmids will be used to generate lentivirus in order to sort homogenous populations of cardiomyocytes for tissue assays. Importantly, we will generate the first isogenic MYH7 DCM model for the HF field. Comparative analysis of the MYH7 DCM to previous MYH7 HCM mutations, in an isogenic background, will provide a critical piece to understanding how specific MYH7 mutations cause cardiomyopathy. Furthermore, these gene-targeted models will provide the foundation for high-throughput screening of VUS to advance diagnostics and uncover novel targets for drug development.

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### Peptidyl arginine deiminase-4: A Gliosis-Associated Target for Age-related Macular Degeneration

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Citrullination is a protein posttranslational modification (PTM) involving the irreversible modification of arginine residues on proteins to citrulline. Citrullinated proteins have been recognized as biomarkers in several major autoimmune and inflammatory diseases, such as rheumatoid arthritis and multiple sclerosis. Moreover, targeting the peptidyl arginine deiminases (PADs), the enzymes responsible for protein citrullination, with small molecule inhibitors has been shown to be effective in reducing disease burden in several preclinical models. We recently reported that mice subjected to corneal chemical injury elicits retinal gliosis, wherein activated Muller glia displayed elevated levels of citrullinated glial fibrillary acidic protein (GFAP) (1). Inhibition of PAD activity using a small molecule inhibitor potently decreased expression of citrullinated targets, identifying PADs as potential druggable targets for retinal pathology. Chemical injury to the cornea causes inner retinal pathology, initiating GFAP polymerization at Muller glial end feet. We found that the isozyme PAD4 was induced and localized along glial processes (2). As retinal gliosis, including altered citrullinated proteins, have been reported in tissue from age-related macular degeneration (AMD) patients, we explored the idea that PAD4 may be responsible for the altered citrullinated proteome in AMD. Here we have exploited a laser injury model of AMD in mice, where laser ablation in the retinal pigment epithelium (RPE) causes focal lesions. We employed this model to determine if PAD4 expression is co-regulated with retinal gliosis, and to localize PAD4 activity. Our findings show GFAP expression is induced as early as 1-day post injury, as evidenced by western blot analysis. Time course studies using immunohistochemical analysis to examine polymerization of GFAP filaments show that this process initiates at the end feet of Muller glia and progresses into longer filaments that stain in the outer layers of the retina. Surprisingly, PAD4 distribution overlapping with GFAP reveals this polarized staining pattern despite the focal injury activating gliosis occurs in the RPE. Our findings reveal for the first time a previously unrecognized feature about the polarized distribution of PAD4 in retinal pathology, suggesting that a signal relay from the outer retina to the inner retina drives these events. Towards future studies, two questions can be asked. One, because the retina is accessible for non-invasive optical imaging, can PAD4-targeted biomarker probes help inform early retinal pathology? Two, because PAD4 inhibitors are currently available, can this newly discovered localization be exploited for delivery of precision medicine for AMD?

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### Epidemiological Trends In Neuroendocrine Tumors: An Examination Of Incidence Rates And Survival Of Specific Patient Subgroups Over The Past Decade

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<u>Introduction:</u> Neuroendocrine tumors (NETs), neoplasms derived from neuroendocrine cells present throughout the body, represent a small proportion of cancers, but a growing clinical problem as they are increasingly discovered by routine clinical imaging. We sought to examine the incidence and survival of patients with diverse clinical presentations in order to provide the necessary information on which to base clinical decisions in the management and follow up of these patients and identify areas of need for future pharmaceutical research and development.

<u>Design/Methods</u>: The Surveillance, Epidemiology and End Results (SEER) database for the November 2016 submission was used for our research study.1 SEER\*Stat software program was used to compile the SEER 13 and SEER 18 datasets in order to analyze incidence rates over time. Kaplan Meier survival curves and Cox regression analysis, were performed using SPSS and SAS, respectively.

Results: Our cohort included 85,133 patients with NETs and was predominantly female (52.4%) with a median age of diagnosis of 63.0 years. The age-adjusted incidence rates of NETs showed the greatest increase in the jejunum/ileum, pancreas, rectum and lung over time. Patients with grade I, local NETs had the best median overall survival (OS, 233.0 months) and the worst survival was observed in patients with grade III, distant NETs (6.0 months). While the median OS of those with local and distant NETS have not meaningfully changed in the past two decades, the median OS of those with regional NETS has improved. Surprisingly we found the median OS decreased with age across the entire spectrum of ages, with patients >70 years of age having a particularly poor prognosis (28.0 months, p<0.0001). The latter often had distant (34.3%) or grade III disease (40.8%) both of which occur at higher rates in the elderly, but even elderly patients with lower grade and/or stage disease had worse median OS compared to younger subjects. For all age groups, grade and stage the OS did not reach a plateau.

<u>Conclusions:</u> The increase in NET incidence rates over time is most pronounced in the GI tract and lung, which parallels the rising rate of abdominal and chest imaging studies. Patients with grade I NETs often do well, but patients with distant and/or grade III NETs continue to have a poor prognosis and represent an important area for future drug development. The improvement in the OS of patients with regional NETS cannot be explained by stage migration and predates the development of systemic therapies whose benefit is not yet proven. Better, more aggressive surgical management is the most likely explanation for this improvement. Age appears to be associated with a worse prognosis independent of stage and grade at the time of diagnosis.

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### Effect of Study Duration/Time of Day on Studying Respiratory Abnormalities in Former Preterm Infants

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Rationale: There is no standard for the timing or duration of multichannel sleep studies in the NICU population. The IBRP (Infant Breathing and Reflux Program) program at the Connecticut Children's Medical Center NICU uses a 20 hour study time when evaluating neonates for apnea and GER. The studies begin at approximately 12 noon and run for 20 hours to 8 AM the following morning. The long duration of the study results in a large quantity of data which must then be completely analyzed.

<u>Objectives:</u> We sought to determine the most appropriate duration of a multi-channel sleep study in a population of former preterm infants in order to properly diagnose the etiology of the patient's clinical events. The benefit of a shorter study time is less discomfort for the infant and reduced work effort on the part of staff. We also sought to determine whether time of day influenced the data.

<u>Hypothesis</u>: We hypothesized that data would show that sleep study duration of 10 hours, independent of time of day, is sufficient to collect adequate data to diagnose the underlying etiology of the infant's ongoing episodes of apnea, O2 desaturation and/or bradycardia at term corrected gestational age (CGA).

Methods: 50 infants who had studies completed between January 2012 and January 2016 for ongoing abnormal cardiorespiratory events were randomly selected. Birth statistics, GA and WT at study time, and co-morbid conditions were recorded. Data from the 20 hour period included number and duration of periodic breathing(PB) events, number of obstructive, central and mixed apnea events, number of O2 desaturation events and bradycardic events. Each infant's study was divided into two 10 hour epochs which were compared to one another and to the total 20 hour study using ANOVA and paired T-tests with a Scheffe's post hoc correction for multiple comparisons. Data from the pH/impedance probe that was simultaneously performed in a subpopulation is not presented.

Results: The study group was composed of 50 infants, 50% male, with a GA of 32±5.7 wks and WT of 1863±1082 g at birth. At study time infants were 39.6±1.6 wks CGA and weighed 2966±452 g. Major morbidies (n) were BPD(15), IVH(4), PVL(2), HIE(1).

There were no differences in any of the results when each epoch is compared to the other or the total study. 10% of the study time, independent of epoch, was spent in PB, the average duration of each central apnea episode = 30±40 sec, obstructive apnea = 182±212 sec and mixed apnea = 87.5±84 sec.

<u>Conclusions:</u> A 10 hour study is sufficient to capture the data needed characterize the abnormalities in respiration in this population of infants. The results also show that the timing of the study, AM vs. PM, does not affect the results.

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### Fatalism, Understanding and Barriers to Healthcare for Children with Chronic or Complex Medical Needs in Rural Nicaragua

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A report on the Nicaraguan healthcare system estimates that 35 – 40% of the population lack health care access, and lack of access is greatest in rural areas. For families with children with complex medical needs, there may be many additional barriers to meeting the needs of the child. "Salud Para Todos Los Niños" (SPTLN) is a program developed to work with clinics in and around León, Nicaraqua to identify and enroll children with complex medical needs in a longitudinal program to provide consultations and pediatric specialty clinics. SPTLN also seeks to coordinate follow-up care and collaborate with the existing local pediatric medical community. The purpose of this study was to determine barriers to healthcare access and assess beliefs and attitudes of families enrolled in SPTLN. Study participants were recruited from the SPTLN program. A comprehensive survey was administered as an interview in Spanish with families. The survey assessed severity of child's illness, impact on quality of life, perceived barriers to healthcare access, and a fatalism belief scale. Fatalism, the attitude that one's situation is beyond one's control, is highly reported in Latin American communities. A total of 38 families were surveyed out of 51 contacted. The average age of the child was 6 years old (10 months to 18 years) with conditions varying from asthma to cerebral palsy to craniosynotosis. Average income was approximately \$115/month. Families expressed acceptance and understanding of their child's illness but face perceived barriers to care including: finances (37%), transportation (16%), effort to mobilize/bring child (13%), availability of physician consult (11%), distance to clinic (11%), and clinic wait times (11%). Families expressed high rates of fatalistic attitudes which correlated with severity of child's illness as assessed by the caretaker (R=0.43, p = 0.008). Families with children with complex needs in developing countries are particularly vulnerable as poverty and lack of access to quality care can affect growth, development, and future outcomes. The efforts of SPTLN to coordinate quality care must address the barriers identified by this study. However, a high level of fatalism was noted in all families regardless of the self-reported barriers to care. This suggests that other factors, such as poverty in general, influence attitudes. Fatalism can directly affect preventative health behaviors, which may include a family's willingness to seek care. The study provides a strong foundation for outcome measures for our program to include perceived barrier reductions and changes in caretaker's beliefs and attitudes. It is our hope that this study can be repeated in the future to evaluate the impact of the program in this population.

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### Implementation of a New Residency/Medical School Curriculum in Refugee Health at UConn Health

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Refugee health care has become an emergent topic within the healthcare community. In recent years, as many as 75,000 people across the globe become refugees every year (1). The state of Connecticut currently accepts about 400 refugees each year, and requires refugees to undergo health assessments within 30 days of arrival (2). In order to properly treat refugees, physicians must be particularly skilled in identifying/treating their unique medical needs. Examples include detection of specific diseases, familiarity with catch-up vaccination schedules, identification of mental and physical abuse/trauma, and understanding family/social structures (3). It is believed that there is a significant knowledge gap between physicians, and their ability to properly treat refugees (3). This study aims to validate the effectiveness of a novel residency/medical school refugee health curriculum at UConn Health. Interested Internal Medicine residents and medical students at UConn Health were enrolled in the refugee health curriculum. Prior to their exposure to the curriculum, a pre-curricular multiple-choice assessment, and a qualitative survey were administered to each individual. Learners were then provided with an electronically based refugee health curriculum, which contained all of the necessary materials required for mastery of 15 core topics. Following completion of the curriculum, learners completed an identical post-curricular multiple-choice assessment, and another qualitative survey. Assessment data were collected, and the means and standard deviations of the pre and post curricular assessments were utilized to determine if there was a significant increase in assessment performance following completion of the curriculum. Furthermore, the qualitative data was utilized to determine if there was an increase in the desire to work with refugees. Since this study is currently ongoing, there is no definitive statistical data to report on. We anticipate having more data to analyze within the next year as we increase enrollment of interested residents/medical students. However, our preliminary data suggests that there is an interest in refugee health care amongst residents/medical students at UConn Health, there is a knowledge gap in refugee health care, and the curriculum may be positively impacting post-curricular assessment scores. Overall, we believe this research is significant because it has led to the development and implementation of a new refugee health curriculum at UConn Health. This refugee health curriculum will be crucial in training the next generation of physicians to meet the needs of a historically neglected population. The hope is that with this training, physicians will be more competent with treating this growing population.

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### **Evaluation of Indole-3-Propionic Acid and Probiotics on the Restoration and Integrity of the Microbiome in Inflammatory Bowel Disease**

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Inflammatory Bowel Disease (IBD) is an autoimmune disorder of the gastrointestinal tract that affects over 1.4 million people in the United States alone [1]. Many individuals diagnosed with IBD live with pain, discomfort, and severe cramps [2]. Normally, the microbiome protects against mucosal damage and inflammation, however a combination of genetic and environmental factors predispose the microbiome to the pathologic basis seen in IBD [3]. This study aims to establish the relationship between restoring the microbiome associated with Intestinal Epithelial Cells (IEC's) as a cure for IBD through the action of Indole-3 Propionic Acid (IPA) and/or Probiotics. To accomplish this, several genes thought to play a role in the integrity of the intestinal tract are studied in mice before and after administering these metabolites. The first trial of the experiment was completed in Cordoba, Argentina and a follow up trial was conducted at UConn Health. Mice were administered these metabolites for 4 days and then euthanized on the 5th day. The intestinal Epithelial cells (IEC's) were subsequently collected and analyzed through real time PCR for levels of gene expression in previously selected genes thought to play a role in the restorative capacity of the microbiome. Results show varying levels of gene expression in the two trials. Overall, there is a consistent increase in gene expression of IPA induced E-cadherin (485x), a cell adhesion molecule involved in the integrity of the GI microbiota. Two tight junction regulators, TJP1 and OCLN, also show significant increase in gene expression (58x) after given the IPA in the experiment done at UConn Health. There is negligible change in the gene expression from the Probiotics. Overall, IPA has the potential to aid in restorative capacity of the GI tract in patients with Crohn's disease to prevent inflammation from occurring, rather than superficially treating the symptoms with immunosuppressants.

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### Electronic Tailored Health Messages and Coordination of Care at Connecticut Children's Medical Center's Primary Care Center

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Childhood overweight and obesity rates have been increasing dramatically over the past 30 years and many factors influencing this increase have been and are being actively studied. Connecticut has lower obesity rates for children than average rate for all children in United States, but in some areas like Hartford, CT, obesity rates exceed that of the national average [1]. Children that are overweight or obese may have an increased risk of developing type II diabetes, asthma, cardiovascular disease, shortened life expectancy, behavioral problems, depression and poor self-esteem [1]. "Food/ Activity liking" or preference surveys have been shown to more accurately predict adiposity in both children and adults, compared to daily intake recall or other commonly used methods [2]. Liking surveys have also been shown to accurately estimate dietary intake of fats, sugars, fiber, fruits and vegetables [3]. Electronic tailored health messages as an early intervention are currently being used after the liking survey to educate parents and children on healthy diet and lifestyle choices [3]. The effectiveness of the tailored health messages in promoting coordination of care when they are shared with physicians remains to be determined. The purpose of this study is to assess the impact of electronic tailored health messages on the coordination of care in the outpatient pediatric setting. In August 2017, 20 parents at the CCMC primary care office in East Hartford, CT completed a "Food/activity liking" survey for their child at the well child visit, where they were asked to comparitively rate how much their child liked/disliked certain foods and activities (some were healthy behaviors and some more unhelathy behaviors). The surveys are web based so the parent and child immediately received tailored feedback based on the parent's responses to the survey. The feedback is meant to promote positive eating practices and other positive behaviors that promote healthy eating and lifestyle. The parent was then asked to bring the tailored feedback into their appointment with the child's pediatrician; the primary care provider is then able to focus their counseling/education on the tailored feedback. Results showed that 70% of parents reported that they learned new information from the messages, 90% of parents reported that the health messages were helpful, and 60% reported they would like to receive more messages like this in the future. The pediatricians found that using the tailored health messages at the appointment were helpful, because it was able to help focus on the areas where the child may need improvement in.

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### Impact of Just-In-Time Emergency Department Simulation Training on Medical Student Procedural Performance

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The progressive utilization of mannequin- and model-based simulation in medical education has greatly expanded opportunities for training future physicians. These modalities have special utility in the teaching of procedural skills where there is a risk of harm to patients.[1] Recent studies have combined simulation with a just-in-time (JIT) training approach in order to assess the efficacy of simulated practice of a procedure immediately prior to its performance in patient care.[2] In these studies, JIT training has demonstrated promising results in improving resident and faculty performance.[3,4] This prospective randomized trial uses a self-directed simulationbased JIT training module in an academic center emergency department (ED). It aims to assess whether JIT simulation training improves procedural performance of medical students. The bespoke module incorporates videos, images, and written instructions that fourth year medical students follow while performing a suturing procedure on a high-fidelity model. Students undertaking their emergency medicine rotation are randomized to this intervention, which they are asked to complete immediately prior to performing their first suture on a patient in the ED. Students' suturing performance is assessed by observing faculty using validated tools and all participants complete a brief self-assessment. This is a longitudinal study that is projected to run through spring 2020. As such, we are at an early stage in data collection, with 9 students having been enrolled in the project thus far. Descriptive data already suggests broad competency in suturing skills among fourth year medical students. All students had prior exposure to suturing, with 87.5% reporting that they had performed suturing on patients at least twice before, though only 37.5% agreed with the statement: "I feel confident in my ability to perform basic suturing of a wound" prior to their EM clerkship. After completing their first suture in the ED, however, 86% of students agreed with this same statement. All students who were randomized to the suturing module reported that the module increased their confidence in performing the suture, improved their performance, and was a useful addition to their training. Due to the small sample size, at this stage no inferences can be made regarding the effect of the suturing module on procedural performance. Data gathering will continue with later statistical analysis in order to determine the efficacy of the intervention.

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### **Molecular Testing Practices and Perceptions Among Dermatopathologists**

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<u>Background:</u> Innovative molecular diagnostic assays offer clinicians the tools to provide high quality, cost-effective patient care. We sought to assess how dermatopathologists employ molecular testing strategies in their clinical practices and their opinions of the broader role and utility of molecular technologies in dermatopathology.

<u>Methods:</u> A 15-question online survey was sent to Fellows of the American Society of Dermatopathology.

Results: One hundred and thirty-six dermatopathologists completed the survey. The most commonly utilized molecular tests were T-cell and B-cell clonality studies (92%) and BRAF gene testing in melanoma (66%). The least commonly employed techniques were next generation sequencing (16%) and TERT promoter mutation analysis of melanocytic tumors (6%). Sixty-two percent of dermatopathologists order more than 12 molecular tests per year, and 6% do not order these assays in their clinical practice. Fifty-three percent of dermatopathologists are extremely or very confident in incorporating the results of molecular tests into histopathological assessments. When ordering specific tests, respondents place high value in scientific publications / conference presentations (84%) and prior personal experience (58%), with 23% of dermatopathologists emphasizing malpractice concerns. Reported barriers to wider adoption of molecular technologies among dermatopathologists include test costs / insurance coverage (86%), physician knowledge and training (76%), required paperwork (40%), and test turnaround times (40%).

<u>Conclusions:</u> Ninety-four percent of responding dermatopathologists reported use of molecular testing strategies in their clinical practice. Wider use of molecular testing may be limited by a number of factors. The importance of longitudinal education in molecular technologies and their applications during medical school through graduate training and post-fellowship activities was highlighted in this study.

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### **Evaluation Of The Hypoxia Pathway in Skeletal Muscle Regeneration**

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Sarcopenia, or age-associated loss of skeletal muscle mass and function, affects 13% of adults above the age of 60 and nearly 50% of adults above the age of 80 [1]. As such, these patients are at increased risk for incident disability, all-cause mortality, mobility disability, and loss of independence [2,3]. The Regenerative Medicine Laboratory (Sinha Lab) has identified derangements of the hypoxia signaling pathway which occur in aging: a pathologic decline of aryl hydrocarbon receptor nuclear translocator (ARNT) in aging skeletal muscle results in a loss of hypoxia signaling. Of particular interest, ARNT was previously considered to be constitutively expressed and independent of changes to hypoxia levels or injury [4]. This study found that ARNT levels are dramatically decreased in the skeletal muscle of old mice. ARNT is required for the hypoxia-pathway mediated transcription of vascular endothelial growth factor A (VEGF-A), which, in turn, directly activates muscle regeneration, independent of its pro-angiogenic effects. Collected data further demonstrates that transgenic mice with a muscle-specific loss of ARNT exhibit decreased VEGF-A levels in skeletal muscle and impaired muscle regeneration. Future goals of this project are to (1) identify interventions to improve ARNT signaling to preserve skeletal muscle myogenic potentia and mititage/reverse muscle loss, and (2) determine whether muscle hypertrophy in response to exercise, which requires hypoxia signaling and regenerative capacity, improves with restoration of hypoxia signaling in aging.

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### Prevalence, Symptomology and Associated Factors of *Helicobacter pylori* infection in La Romana, Dominican Republic

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<u>Introduction:</u> Dyspepsia is a common complaint amongst patients in Latin America and can result from various ailments including GERD, anxiety/depression, and the focus of this study, the bacteria *Helicobacter pylori* (*H. pylori*) [1,6]. Due to high correlation of dyspepsia and H. pylori infection, there was an initiative to conduct this research. The study aimed to research the prevalence of *H. pylori*, while determining the efficacy of the symptomology, associated factors, and blood antibody test in determining infection. The focus population were the local bateys, a term for sugar plantations, located on the outskirts of La Romana, Dominican Republic. The research design consisted of a questionnaire to determine the symptomology and socioeconomic status, which was quantitatively assessed with serum antibody (Ab) test to detect exposure to *H. pylori*.

<u>Methods:</u> Interested adults in the sugar plantations fields of La Romana, Dominican Republic were consented and enrolled in the study with help of trained translator in Spanish and Creole. Patients first completed an IRB-approved survey gathering information on their socioeconomic status including exposure to risk factors of *H. pylori* and symptomology of functional dyspepsia. The patient were then requested to participate in finger-stick blood draw to check positivity for *H. pylori* antibodies.

Results: Over the eight weeks, 102 participants were enrolled with a balanced gender distribution (53.9% males, 46.1% females). Functional dyspepsia criteria (early satiety, bothersome fullness, or heartburn) were met by 67 of 102 participants. Of these participants with functional dyspepsia, 25 of 67 noted having all three symptoms. In total, 16 of the 101 tested positive on finger-stick antibody test. There were 12 out of 16 participants who tested positive for blood antibody test and met the criteria of functional dyspepsia. The correlation of functional dyspepsia criteria as an indicator for positive antibody testing showed to be statistically insignificant with a p-value of .376.

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### **Engineered Nanofibrous Scaffold Loaded with Resveratrol Preserves Cardiac Function Following Myocardial Infarction**

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In the United States, it is estimated that around 790,000 people suffer from a myocardial infarction (MI) each year. The diagnosis and treatment of MI have been improving, but the actual repair of the injured cardiac tissue has not been successful. Recently, the creation of biodegradable scaffolds that mimic the structure and architecture of the native extracellular matrix has been expanding. The use of these products in combination with biologically active compounds that can be loaded into the scaffold and be released in a slow and steady manner have shown promising results. Resveratrol is a compound found in grapes, berries, and red wine that has been proven to provide cardiovascular health benefits. Studies have shown that resveratrol (Res) has antitumor, antioxidant and anti-inflammatory properties. In the present study, we created a nanofiber scaffold made from polycaprolactone (PCL), loaded with resveratrol, and investigated how the PCL scaffold without resveratrol and PCL with resveratrol would influence cardiac function following an MI in a murine model. ICR-CD1 mice ages 8-12 weeks were used for this investigation. The mice were divided into four different groups, which included a sham group, an MI group, an MI + PCL without resveratrol (MI+PCL), and MI + PCL loaded with resveratrol (MI+PCL+Res). All of the mice underwent ligation of the LAD or sham surgery and scaffolds were sutured onto the myocardium at the time of the surgery. Four weeks after the MI surgery, echocardiogram was performed to assess function of the heart. The parameters used to assess cardiac function included ejection fraction (EF), fractional shortening (FS), stroke volume (SV), and cardiac output (CO). Results of the study showed significant improvement in EF (45.28  $\pm$  3.7 vs. 32.67  $\pm$  2.97%; p<0.05), FS (22.85  $\pm$  2.15 vs. 15.59  $\pm$ 1.54%; p<0.05), SV (50.9  $\pm$  3.94 vs. 33.86  $\pm$  3.04 $\square$ ; p<0.05), and CO (22302  $\pm$  2464 vs. 14090 ± 1316 \(\subseteq\)/min; p<0.05) in the MI+PCL+Res compared to the MI+PCL group. To our knowledge, this is the first study in which resveratrol is loaded into a bioengineered scaffold in order to use it as therapeutic treatment following an MI. In conclusion, the function of the heart significantly improved when the PCL scaffold that was loaded with resveratrol supported the infarcted myocardium compared to groups in which no scaffold was placed or no bioactive compound was added to the scaffold. The combination of a structural support for the myocardium, in this case provided by the PCL scaffold and the use of an active biological compound, here the resveratrol, is showing promising results as a future therapeutic intervention following myocardial infarctions.

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### Association Between In-Office Gait Velocity Assessments and Processing Speed in Geriatric Clinic Patients

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Background: Gait velocity is a simple, robust predictor of health outcomes, including cognitive impairment, in older persons. Despite being described as the "5th vital sign," gait velocity is rarely measured as a routine part of geriatric patient care. Recent research has shown that radio frequency identification device (RFID) technology offers a valid, feasible, and unobtrusive means of assessing gait velocity in geriatrics clinic patients.<sup>2</sup> Yet, research is still needed to demonstrate the potential added value of incorporating in-office RFID gait velocity assessments into routine clinical practice. As a first step towards demonstrating the potential utility of in-office RFID gait velocity assessments, we sought to determine if gait velocity was associated with processing speed in geriatrics clinic patients. We hypothesized that higher gait velocity would be associated with faster processing speed. Methods: A total of 35 geriatrics clinic patients were recruited over 6 weeks. Participants wore an armband containing a RFID tag with a unique identification number and were instructed to walk down the clinic hallway at their usual pace. Wall-installed RFID readers recorded time to walk 4.3-meters. There were 27 participants who completed the Symbol Digit Modalities Test (SDMT) which measures graphomotor processing speed. This test requires participants to pair specific numbers with their corresponding geometric figures within a 90-second timeframe. Pearson correlation coefficients and linear regression were used to determine the association between gait velocity and processing speed. Results: Mean age (N=27) was 82.0±7.8 (65 to 94) and 67% were female. Average gait velocity (m/s) was 0.825±0.244 (0.406 to 1.255). In unadjusted analyses, gait velocity was significantly correlated with SDMT score (r=0.42; p=0.01). Analyses adjusted for age indicated that SDMT scores increased (improved) with increasing gait velocity (beta = 15.20; standard error = 7.79; p=0.06). Conclusions: These findings indicate that measuring gait velocity as part of routine care using RFID technology may provide insight regarding older patients' processing speed. Because slow processing speed has been shown to predict future cognitive decline, in-office RFID gait velocity assessments may offer the added value of providing information regarding patients' cognitive status, especially at preclinical stages. Further research is needed to determine if the availability of gait velocity data via in-office RFID translates to changes in clinical practice (e.g., prescribing of physical therapy, vitamin D, myostatin inhibitors).

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### **Employing Risk Stratification to Decrease CT Pulmonary Angiogram Usage for Pulmonary Embolism Diagnosis**

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Introduction: Pulmonary embolism (PE) is a mechanical obstruction of the pulmonary vasculature that produces clinically nonspecific signs and symptoms, such as chest pain and dyspnea. Physicians can use validated clinical decision algorithms, such as Wells criteria and the pulmonary embolism rule-out criteria (PERC), as well as a D-dimer test to help determine a patient's risk for PE (1). Prior research has shown that many physicians may not follow the risk stratification tools and order CT pulmonary angiograms (CTPAs) due to the fear of missing a potentially deadly diagnosis (2,3). Overuse of CTPAs increases patient exposure to radiation and contrast media, resulting in an increased risk of cancer, contrast-induced nephropathy, and allergic reactions. This study will determine the number of CTPAs ordered in a year at a single Emergency Department that could have potentially been avoided if clinical decision algorithms were used, with a long-term goal of reducing the number of unnecessary CTPAs ordered.

<u>Methods:</u> A retrospective chart review was performed on all patients who received a CTPA for suspected PE at a single site Emergency Department between 7/1/15 and 6/30/16. 255 charts were examined. Data was collected on the ordering physician, documentation of Wells or PERC scores, usage of D-dimers, and CTPA results. Wells and PERC scores were determined for each patient based on clinical presentation and risk factors. Using SAS statistical programming, frequency tables were created to determine the number of cases where a CTPA may have been unnecessary if a risk stratification algorithm had been followed.

Results: Of the 255 charts examined, 247 were included in the data analysis. Eight charts were excluded, four due to inconclusive testing results and four due to the diagnosis of a chronic clot. 34 cases (13.77%) were CTPA positive for PE. Out of the 148 low-risk patients who received a CTPA during the period, providers did not follow risk-stratification algorithms in 107 cases (72.30%). Only six of the 107 (5.61%) were positive for PE. In 89 of these cases (83.18%), providers deviated from the algorithm by not ordering a D-dimer and proceeding directly to CTPA.

<u>Conclusion:</u> This data shows that providers at this Emergency Department are not consistently using risk stratification algorithms when working up patients for potential PE, resulting in a potential excess number of CTPAs ordered. In order to reduce these numbers, it is important to educate physicians on risk stratification methods that could lower the rate for patients at low-risk for having a PE. Future steps are to educate physicians and implement the risk-stratification algorithm into the electronic medical record. Data will be reassessed to determine if this changes CTPA ordering.

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### The Effects of Low-dose Aspirin on the Placental Pathology of Women at Risk for Preeclampsia

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<u>Introduction:</u> Preeclampsia is among the most serious pregnancy complications. If left untreated, it can lead to severe maternal complications such as coagulopathy, renal and liver failure, stroke, and maternal death (1). A daily 81 milligram aspirin (ASA) is recommended for pregnant women who are at risk for preeclampsia (2). However, the exact prevention mechanism is unclear. The hypothesis of this study was that ASA is associated with gross and microscopic changes in placental pathology more consistent with normal placentas rather than preeclampsia placentas.

Methods: We performed a retrospective matched observational study by identifying all women exposed antepartum to ASA due to an increased risk for preeclampsia by searching the outpatient medical record from October 1, 2015 until July 15, 2017. The placental pathology of these ASA patients were compared to a cohort of normal controls and preeclampsia controls, matching for maternal age, gestational age and similar timeframe for delivery. Antepartum and delivery data were abstracted from the outpatient and inpatient medical records. Placental pathology data were abstracted from final pathology reports. Inferential statistics were computed using t test, chi square and Fisher exact tests with R Studio, version 3.0.2.

Results: A total of 32 ASA exposed, 45 preeclampsia control and 87 normal control placentas were identified for comparison. Maternal age (p=.856) and gestational age (p=.311) were similar across all groups. Preeclampsia patients showed significantly more accelerated villi maturation (p<.001), more placental infarction (p=.072), less persistent trophoblasts (p=0.087) and more mild calcification (p=.090) compared to both ASA exposed and normal placentas. Thrombosis (p=.569), hemorrhage (p=.406) and intervillous hemorrhage (p=0.588) were similar across all groups.

<u>Conclusions/Implications:</u> Future studies should focus on villous maturation, infarction, persistent trophoblasts and calcification when examining the effects of low-dose aspirin on placental pathology in women at risk for preeclampsia.

Supported by: The UConn School of Medicine Summer Research Fellowship

- 1. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet 2005; 365:785-99.
- 2. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. Washington, DC: American College of Obstetricians and Gynecologists; 2013. Accessed at www.acog.org/Resources\_And\_Publications/Task\_Force\_and\_Work\_Group\_Reports/Hypertension\_in\_Pregnancy.

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### Antibiotic Prescription Practices in Outpatient Dentistry: A Descriptive Analysis

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<sup>2</sup> Department of Infectious Disease, University of Connecticut Health Center

**Background:** Antibiotics are often prescribed in the treatment of odontogenic infections. Increasing awareness of antibiotic-associated adverse effects, including *Clostridium difficile* and allergies, and the emergence of antibiotic resistance has prompted assessing antibiotic prescribing patterns in medical practice and initiating the practice of antibiotic stewardship. Although medical providers account for the majority of antibiotic prescribing, dental professionals also frequently prescribe antibiotics. Currently, the literature on this subject mainly focuses on medical prescribing patterns. Little is known about antibiotic prescribing in dental practice and the potential role of dentists in antibiotic stewardship.

**Objectives:** The main objective of the study is to describe and analyze antibiotic prescription practices in an academic outpatient dentistry practice. The study will analyze antibiotic prescribing in both treatment and prophylactic settings, and highlight differences or trends in prescribing practices between specialties, providers, and antibiotic indications.

**Methods:** A retrospective analysis of dental prescriptions in outpatient practices from July 1, 2014 – June 30, 2017 was performed. We describe the frequency of different antibiotics prescribed in the practice, as well as specialty and provider information. In a subset of 400 patients treated between January to June in 2017, we analyzed additional clinical data to describe the clinical presentation, medical history, and indications for antibiotic prescribing. The health records also provided data on what type of specialty treated the patient, and whether the provider was a resident, student, or faculty member. Collected data was then analyzed to highlight any trends or patterns between specialties, types of antibiotics, antibiotic indications, and comorbidities.

**Results:** 5632 prescriptions for antibiotics were analyzed. Among these prescriptions, the most frequently prescribed antibiotics were amoxicillin (n=4070, 72.3%), clindamycin (n=785, 13.9%), amoxicillin clavulanate (n=272, 4.8%), and penicillin v potassium (n=254, 4.5%). Other antibiotics that were frequently prescribed include azithromycin, doxycycline, fluoroquinolones and metronidazole. Among the subset of 400 patients for which clinical data was analyzed, 284 (71%) were prescribed for treatment and 44 (11%) were prescribed for prophylaxis, with 72 (18%) records not indicating. Among prescriptions written for treatment, the most common indications were symptomatic apical periodontitis (n=55, 24.9%), necrosis (n=39, 17.6%), and irreversible pulpitis (n=33, 14.9%). Pain was the most common presenting symptoms (172, 52.5%) and the most common abnormal physical exam findings were periapical lesions, indicated by pain on percussion (n=141, 51.46%), generalized or discrete swelling (n=80, 29.2%), and periodontal symptoms including abscess formation and attachment loss (n=38, 13.9%). Of the 284 treatment indications, 153 received a dental intervention, with the most common interventions being extractions (n=73, 47.7%), implant placement (n=12, 7.8%), and incision and drainage of abscesses (n=11, 7.2%).

**Conclusions:** Antibiotics are frequently prescribed by dentists in outpatient practice for several different indications. The duration of antibiotic prescriptions for the treatment of infections varied substantially and several different classes of antibiotics were prescribed.

**Future Directions:** There is a need to improve the understanding of antibiotic prescribing among dentists in outpatient practice. Ensuring that dentists are well educated regarding antibiotic prescribing should be a public health priority. Indications for antibiotics prescribed other than amoxicillin, penicillin v potassium, clindamycin, and amoxicillin clavulanate warrants further research. Development of structured guidelines detailing antibiotic indication, selection, dose and duration may be useful in standardizing clinical practice when treating odontogenic infections.

Support: University of Connecticut School of Dental Medicine Summer Research Fellowship

### Women's Breast Cancer Knowledge and Beliefs in the Context of a Rural Haitian Community

Christina (Cheng) Yang<sup>1</sup>, Judy Lewis<sup>2</sup>, Bette Gebrian<sup>3</sup>

<u>Introduction:</u> Haiti has an estimated annual breast cancer (BCA) incidence 4.4/100,000 (30/100,000 all LMICs), and 2/100,000 mortality. BCA is under-reported with high fatality (45%) due to late entry into care. This study focused on understanding BCA cultural, religious, and socioeconomic factors in rural Haiti to improve education and screening.

<u>Methods:</u> In-depth qualitative interviews were conducted with 120 women recruited through four churches.

Results: Respondent mean age was 40, average household size 6.1, and first pregnancy age 23. 72% were involved in ≥1 church groups and 86% reported visiting the sick as part of church activity. Years of church attendance was positively associated with types of social support during sickness (R=.268; p=.003).

13% had first-degree family history of BCA. 51% knew someone outside the family with BCA. 38% first knew about BCA from someone with BCA, the majority (82%) of whom died. Women reported a mean of 2.4 BCA symptoms (pain 78%, lumps 78%, swelling 18%, itching 19%); mean correct symptoms was 0.9, mean false 1.5. Accuracy of BCA symptoms was related to housing wealth (R=.220; p=.016) but not to education or literacy. 83% believed that hitting or falling on the breast causes BCA; followed by diet 23% and baby burping in the breast 23%. 51% believed that BCA was destined, but this was associated with believing that it was curable (X2=4.8; p=.025).

Major sources of health information were doctors (92%), church (89%), radio (85%), family (63%), school (65%), text (43%). Sources associated with correct symptoms were family (X2=10.7; p=.005) and radio (X2=7.0; p=.03). Primary sources of health social support were doctors/nurses (88%) and women in church (73%). 53% reported some type of health screening, but 86% of these were routine prenatal care. 65% of women reported performing BSE, but only 37% of these had received instruction.

<u>Conclusion:</u> Cultural, religious, and social beliefs must be incorporated in BCA education to promote screening and improve knowledge. BCA symptom knowledge was poor. Health screening outside of prenatal care was not common. Women were willing to perform BSE, which is important in a LIC where CBE and mammography are not available. Based on the high levels of church participation, churches provide a major community resource for BCA outreach, education and support.

Supported by: The UConn School of Medicine Summer Research Fellowship

- 1. Anderson BO, Yip CH, Smith RA, et al. Guideline implementation for breast healthcare in low-income and middle-income countries: overview of the Breast Health Global Initiative Global Summit 2007. Cancer 2008; 113 (suppl 8): 2221–43
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<sup>&</sup>lt;sup>2</sup>Community Medicine and Health Care at University of Connecticut

<sup>&</sup>lt;sup>3</sup>Grand Ans Health and Development Association

# Research Awards

#### SCHOOL OF DENTAL MEDICINE

**2018 AADR STUDENT RESEARCH DAY AWARD:** Award consists of a monetary award of \$500 to assist with travel expenses and a complimentary meeting registration to attend the 2018 AADR/CADR General Session & Exhibition in Ft. Lauderdale, Florida in March, 2018.

**2019 AADR STUDENT RESEARCH DAY AWARD:** Award consists of a monetary award of \$500 to assist with travel expenses and a complimentary meeting registration to attend the 2019 IADR/AADR/CADR General Session & Exhibition in Vancouver, Canada in June, 2019.

**ASSOCIATE DEAN'S AWARD:** Awarded 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 Student's Conference on Research in Gaithersburg, Maryland.

**COLGATE-PALMOLIVE STUDENT RESEARCH AWARD:** Awarded by Ms. Diane Peterson of Colgate-Palmolive, a second-year dental student will receive an award of \$1,000 in recognition of exemplary knowledge, understanding and presentation of basic and clinical dental research at Student Research Day.

**CONNECTICUT HOLISTIC HEALTH ASSOCIATION:** Awarded by Dr. Michael Basso, this monetary award of \$100 was established to recognize excellence in research in Integrative/ Complementary and Alternative Medicine. Special thanks go to Dr. Basso of the Connecticut Holistic Health Association.

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

**DENTAL STUDENT RESEARCH SOCIETY:** Awarded by Dr. Arthur Hand, a monetary award of \$100, for excellence in a science presentation by an undergraduate student.

**DENTSPLY-SIRONA STUDENT CLINICIAN AWARD:** Awarded by Mr. Joel Monteiro of Dentsply Sirona, in recognition of an outstanding presentation. This award includes round-trip coach airfare, lodging and registration fees to attend the AADR/Dentsply Sirona SCADA Program in Vancouver, Canada in June, 2019 as the UConn School of Dental Medicine's representative; a Dentsply Sirona crystal and their name 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.

# Research Awards

**JOHNSON & JOHNSON RESEARCH EXCELLENCE AWARD:** Awarded 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 UConn Health Bookstore gift card.

**OMICRON KAPPA UPSILON – PHI CHI CHAPTER AWARD:** A monetary award of \$200, in recognition of outstanding research.

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

### Faculty Award

**OUTSTANDING RESEARCHER AWARD:** Awarded to a School of Dental Medicine Faculty member who has demonstrated outstanding research accomplishments in the previous calendar year. Supported by Colgate-Palmolive, this award consists of a certificate and a monetary award of \$1,000 for academic enhancement presented by Ms. Diane Peterson of Colgate Oral Pharmaceuticals.

## Research Awards

#### 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 AWARD FOR EXCELLENCE IN RESEARCH ACHIEVEMENT**: 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.

**HARTFORD MEDICAL SOCIETY AWARD**: An award of \$500 will be given to the medical student whose project represents the most effective research performed to advance community medicine.

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.

WILLIAM M. WADLEIGH MEMORIAL AWARD FOR CROSS-CULTURAL AND INTERNATIONAL HEALTH RESEARCH: The award is in honor of William M. Wadleigh, PhD, anthropologist and Associate Director of the Center for International Community Health Studies in the Department of Community Medicine and Health Care, committed to global health education, who passed away from AIDS. The \$250 award is given annually to the medical student whose research best exemplifies international and cross-cultural understanding of health issues.

**CONNECTICUT ACADEMY OF FAMILY PRACTICE**: One medical student will receive this \$200 monetary gift for excellence in Primary Care 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.

# 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 Day Organizing Committee:

Dr. Lynn Puddington, Co-Chair, Director of Medical Student Scholarship and Research Dr. Aditya Tadinada, Co-Chair, Director of Dental Student Research Christine McNally, Academic Curriculum Coordinator, School of Medicine Curricular Affairs, Stage 1 Curriculum Manager

Lisa Ramsdell, Administrative Program Coordinator, School of Dental Medicine Darice Schroeder, Administrative Assistant, School of Medicine, Curricular Affairs Laura Didden, Business Service Manager, School of Dental Medicine

### Medical School Reviewers/Judges

Dr. Steven Angus

Dr. Lisa Barry

Dr. Stephan Brocke Dr. Audrey Chapman

Dr. Kai Chen

Dr. Lisa Chirch

Dr. Dharamainder Choudhary

Dr. Kevin Dieckhaus

Dr. Judith Fifield Dr. Jeffrey Gross

Dr. Rosa Guzzo

Dr. Marja Hurley

Dr. Evan Jellison

Dr. Barbara Kream

Dr. Patrick Murphy

Dr. Doug Oliver

Dr. Joseph Lorenzo

Dr. Kourosh Parham

Dr. John Peluso

Dr. Carol Pilbeam

Dr. Stephen Schensul

Dr. David Steffens

Dr. Roger Thrall

Dr. Pam Taxel

Dr. Priya Kailasan Vanaja

The UConn Health Postdoctoral

**Scholars** 

### **Dental School Reviewers/ Judges**

We would like to thank the judging panel for their tremendous efforts and timely evaluations.

### With Special Appreciation To:

Dr. Bruce Liang, Dean, School of Medicine

Dr. Monty MacNeil, Dean, School of Dental Medicine

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

Dr. Steven Lepowsky, Senior Associate Dean for Education and Patient Care, School of Dental Medicine

Dr. David Henderson, Associate Dean for Medical Student Affairs, Associate Dean

for Multicultural and Community Affairs, School of Medicine

Dr. Sarita Arteaga, Associate Dean for Students, School of Dental Medicine

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

Lina Smith, Administrative Program Coordinator, School of Medicine

Amy Chmielewski, Academic Curriculum Coordinator, School of Medicine

Aaron Frankel, UConn Foundation

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UConn Health Discovery Fellowship Fund

Dr. Bruce Liang, Dean's Award

Dr. and Mrs. Jeffrey Gross, Award for Excellence in Research Achievement

Hartford Medical Society, HMS Summer Research Fellowship, Award for Excellence in Research to Advance Community Medicine

Lawrence G. Raisz Award for Excellence in Musculoskeletal Research

William M. Wadleigh Memorial Award for Cross Cultural and International Health Research

Connecticut Academy of Family Practice

Dr. Michael Basso, Connecticut Holistic Health Association

Drs. Kevin Dieckhaus and Lynn Puddington, Global Health Summer Research Fellowships

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Dr. Monty MacNeil, Dean's Award & Research Day Reception

Dr. Rajesh Lalla, Associate Dean's Award

Mr. Joel Monteiro, Dentsply-Sirona Student Clinician Award

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

Ms. Janet Finkle, Johnson & Johnson Health Care Products, Research Excellence Award

Ms. Diane S. Peterson, Colgate Palmolive Student and Faculty awards

American Association of Dental Research (AADR) Student Research Day Award Omicron Kappa Upsilon – Phi Chi Chapter Award

Dr. Arthur Hand, Dental Student Research Society Award

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The Connecticut State Dental Association for their donation and support of student research

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### \*Dylan Buller

#### **Medical Student Posters**

#### Academic Rotunda Hallway

#### Poster# First Name Last Name Joshua Baruch Baldino 1 2 Bergamo Patrick Boivin 3 Zachary 4 Crooks Samuel 5 Ferrigno Bryan 6 Emily Isch Jackvony Taylor 7 8 Kamal Shaan 9 Kwarko Trisha 10 Kodumudi Vijay 11 Macken Craig 12 Muzumdar Sonal 13 Nsereko Aloys 14 Park Jennifer 15 Romano Robert 16 Saba Nicholas 17 Shore Brandon 18 Udeh Kodi 19 Vissepo Rafael 20 Lo Robin 21 Desai Shyam 22 Southgate Samuel 23 Barresi Nicholas V 23 Marquis Timothy J. 23 Van Akin Christopher

### Academic Lobby

	Academic	LODBY
Poster #	Last Name	First Name
52	Cusano	Sean
53	Bellas	Nicholas
55	Abbate	Anne
56	Dao	Quynh-Lan
57	Mahony	Forrest
58	Pashankar	Rashmi
59	Pavano	Colin
60	Pier	Brendan
61	Robey	Kyle
62	Vu	Stephanie
63	Wagner	Kristina
64	Wang	Yanbin
65	Grammatico	Megan
66	Duong	Michelle
67	Brewer	Jennifer
68	Atteh	Elizabeth
69	Torre	Kristin
70	Sadowski	Allison
71	Lawson	Jennifer
72	DeMarsilis	Antea
73	DiCosmo	Alyssa
74	Donaghey	Faith
75	Giuliano	Alexander
76	Mattessich	Sarah
77	Harris	Nia
78	Hasan	Rabale
79	lyer	Divya
80	Pacik	Deb
81	McCarthy	Morgan
82	Abunar	Bayan
83	Nedorostek	Kelly
84	Parsons	Christine
85	Serdah	Mohaned
86	Sinopoli	Martina
87	Upadhyay	Vruksha
88	Yang	Cheng
89	Miller	Tiffani-Amber
85	Serdah	Mohaned
86	Sinopoli	Martina
87	Upadhyay	Vruksha
88	Yang	Cheng
89	Miller	Tiffani-Amber

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