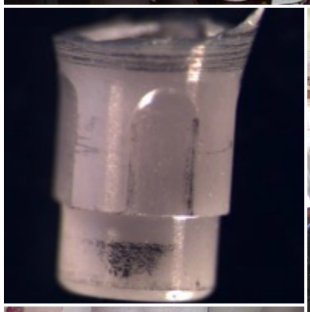
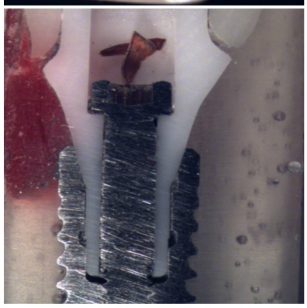
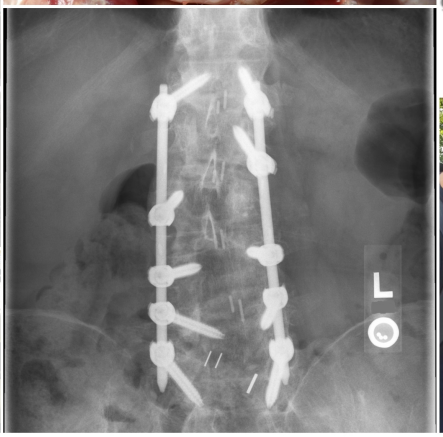
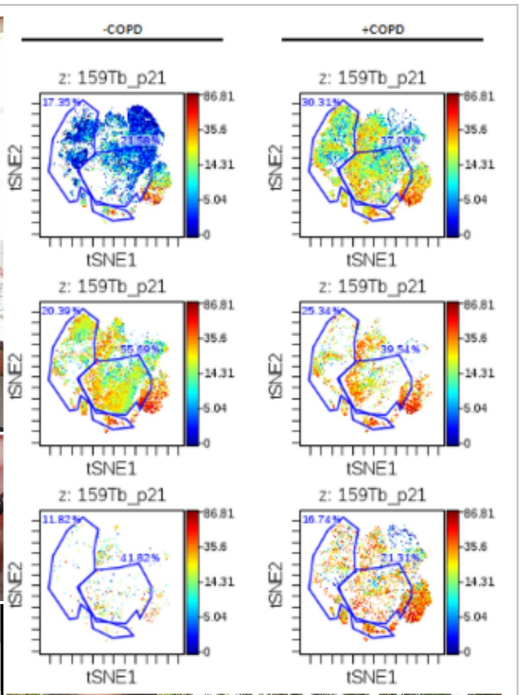
2017 Medical and Dental
STUDENT RESEARCH DAY









Supported by the Irvin H. and Martha L. Lepow Visiting Professorship Fund and the Scholarship Linked to Discovery Fund

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SCHEDULE OF EVENTS

March 13, 2017

POSTER SESSION

2:00-3:30 PM | Academic Rotunda

TALKS

10:15-11:30 AM and 3:45-5:15 PM | Keller Auditorium

KEYNOTE SPEAKER

12PM | Academic Rotunda

"Many Medical Students or One Expert Authority?: The Power of Crowdsourcing to Enhance Public Health Campaigns, Engage Communities, and Spur Action"

Joseph D. Tucker, M.D., Ph.D.

Assistant Professor, University of North Carolina School of Medicine, Director of UNC – Project China, and Co-Director UNC-South China Sexually Transmitted Infection Research Center, Guangzhou, China

ORAL PRESENTATIONS

Session 1: Keller Auditorium 10:15am - 11:30am

10:15 **Systematic Review of Internal Fixation of Osteochondritis Dissecans of the Knee: Bioabsorbable versus Metallic Implants**
Hannah Reuman, Jeffrey Nepple, Christopher Cheng, Carl Nissen, Matthew Milewski

10:30 **DKK1 Expression Over Time in MC3T3-E1 Cells and the Effects of DKK1-Ab on MC3T3-E1 Cell Osteogenic Differentiation**
L. Gormer, T. Peng, J. Alhamdi, M. Hurley, L.T. Kuhn

10:45 **Development and Validation of a CyTOF Antibody Panel for Detection of Circulating Angiogenic Cells in the Peripheral Blood of Patients with and without COPD**
Madeline DeWane, Patty Lee, Maor Sauler

11:00 **Low-dose CBCT Protocol Yields Comparable Diagnostic Information as Conventional Protocols**
Bailey Proft, Riccardo Ambrogio, Alan Lurie, Aditya Tadinada

11:15 **Subacromial Bursa versus Bone Marrow Stromal Cells for Cell-Based Tendon Repair**
Philip Zakko, Felix Dyrna, Leo Pauzenberger, Mary Beth McCarthy, David W Rowe, Augustus Mazzocca, Nathaniel A Dyment

Session 2: Keller Auditorium 3:45pm- 4:45pm

3:45 **Examining the Role of the DNA Repair Protein PARP During the Life Cycle of Herpes Simplex Virus**
Adam Mastrocola, Sandra Weller

4:00 **Establishment of Polarized Acinar-Like Structures as an *in vitro* Model for Salivary Gland Dysfunction**
Sean Burke, Mayank Tandon, Paula Perez-Riveros, Ilias Alevizos

4:15 **The Effects of Social Support, Stigma, and Depression on the HIV Treatment Cascade in the Aging Population**
Christopher Mashiak, Grace Chan, Lisa Chirch, David Steffens

4:30 **Prevalence of *H. pylori* Infection, Symptoms, and Associated Factors in Kisoro, Uganda**
Lyubina Yankova, Kevin Dieckhaus

4:45 **Compressive Loading Rescues the Effects of Botox Injection into the Masseter in the Mandibular Condylar Cartilage and Subchondral Bone**
Candice Logan, Eliane H. Dutra, Alexandro Lima, Mara H. O'Brien, Sumit Yadav

5:00 **Assessing Hydroxyurea Therapy in Pediatric Sickle Cell Disease: A Review at CCMC**
Hunter Terry, Roger Thrall, Donna Boruchov

POSTER PRESENTATIONS

Dental Student Poster Presentations

Student: Blake Bandeff
Mentor: Dr. Ilias Alevizos
Title: Skeletal Characterization of CD146 Deficient Mice

Student: Isabella Chen
Mentor: Dr. Marion Frank
Title: Salty, Sweet and Bitter Tastes of Sodium Salts after Chlorhexidine Rinse

Student: Sundine Chizzonite
Mentor: Dr. Aditya Tadinada
Title: Tablet-Computers And Smartphones Can Reliably Detect Radiographic Tooth Fractures

Student: Roshni Patel, Lisa Fredrickson
Mentor: Petra Clark-Dufner
Title: Addressing the Social Determinants of Health: Strengthening Clinical and Community Partnerships

Student: Basem Gayed
Mentor: Dr. Rajesh Lalla
Title: Assessment of Market Needs for a New Formulation of a Long-Acting Topical Anesthetic Agent for Pain Secondary to Oral Mucositis

Student: Willan Jumbo
Mentor: Dr. Flavio Uribe
Title: Osteogenic Markers in Response to Piezocision in a Rat Model

Student: Lora Manley
Mentor: Dr. J.R. Kelly
Title: Micro-Movement of Full Zirconia CAD/CAM Abutments Within Titanium Implants

Student: Victoria Phu
Mentor: Dr. I-Ping Chen
Title: Characterizing Pain and Inflammation in a Mouse Model for Symptomatic Apical Periodontitis

Student: Matthew Prezioso
Mentor: Dr. Aditya Tadinada
Title: Evaluating the value of a novel foot controlled mouse to navigate between electronic health records and radiographs in a dental clinic setting

Student: Sharon Vincenty-Flores
Mentor: Dr. Frank Nichols
Title: Distribution of Lipid 654 Diastereomers in Porphyromonas gingivalis Isolates

Student: Drew Weyman
Mentor: Dr. Aditya Tadinada
Title: Cone Beam CT is Superior at Diagnosing Maxillary Sinus Pathology

Student: David Wiegard
Mentor: Drs. Preeti Chandhoke and Aditya Tadinada
Title: CBCT Analysis of Impacted Incisors: Bone and Root Parameter Differences

Medical Student Poster Presentations

Student: Samuel Baron
Mentor: Dr. Kevin Dieckhaus
Title: Perceptions and Practice of Shared Decision-Making among Senior Medical Students in Costa Rica

Student: Spencer Beck
Mentor: Dr. Kevin Dieckhaus
Title: Control of High Blood Pressure: Knowledge, Attitude, and Practice Study of Hypertension in Haitian Migrant Farm Communities in the Dominican Republic

Student: Nicholas Bellas
Mentor: Dr. Daichi Morikawa
Title: The Potential Use of Human Bursa Cells for Biologic Augmentation in Rotator Cuff Repair

Student: Jennifer Brewer
Mentor: Dr. Augustus Mazzocca
Title: The Effects of Platelet Rich Plasma And Concentrated Bone Marrow on Growth Factor Release When Added To a Demineralized Bone Matrix Scaffold

Student: Nicholas Caminiti
Mentor: Dr. Augustus Mazzocca
Title: The Impact of the Internal Brace Repair on the Horizontal Instability of the AC Joint Following Ligament Injuries

Student: Sonny Caplash
Mentor: Dr. Kevin Dieckhaus
Title: Evaluation of Recorded Culturally-Appropriate Verbal Dosing Instructions on Medication Adherence in Migrant Farm Workers

Student: Christopher Cheng
Mentor: Drs. Matthew Milewski and Carl Nissen
Title: Predictive Role Of Symptom Duration Prior To Initial Presentation Of Adolescents With Capitellar Osteochondritis Dissecans On Pre- & Post-Operative Measures

Student: Kousanee Chheda
Mentor: Dr. Kevin Dieckhaus
Title: Initial Barriers to Eye Care Access Among Participants of a Mobile Eye Clinic

Student: Madeline Coulter
Mentor: Dr. Elias Michaelides
Title: Eustachian Tube Reconstruction for the Treatment of Patulous Eustachian Tube: Direct Analysis of Symptom Relief and Patient Satisfaction

Student: Robert Cox
Mentor: Dr. Kourosh Parham
Title: Prestin as a Biomarker for Early Detection of Hearing Loss in a Cisplatin-Ototoxicity Model

Student: Brett Diamond
Mentor: Dr. Heidi Greulich
Title: PDE3A Modulation for Cancer Therapy

Student: Michelle Emmanuel
Mentor: Dr. Frederick Anderson
Title: Assessing The Barriers To Compliance With Colorectal Cancer Screening Tests In The Miami Beach Community Health Center

Student: Ryan Farias
Mentor: Dr. Augustus Mazzocca
Title: Early Fixation Strength And Biomechanics of Anatomical Glenoid Reconstruction With The J-Bone Graft For Anterior Glenoid Bone-Loss

Student: Gian Grant
Mentor: Dr. Kevin Dieckhaus
Title: Evaluation Of The ParrotMD Medication Adherence Tool In Patients With Chronic Diseases In Kisoro, Uganda

Student: Matthew Greenwood
Mentor: Dr. Bruce Liang
Title: Peak Caspase-1 p20 Levels During ST Elevation Myocardial Infarction Correlate With Pre-existing Hypertension, Age And Post-infarction Cardiac Dysfunction

Student: Simran Gupta
Mentor: Dr. Lauren Geaney
Title: Initial Fibular Displacement as a Predictor of Medial Space Widening in Weber B Ankle Fractures

Student: Laura Hatchman
Mentor: Dr. Lisa Barry
Title: Unobtrusive Gait Velocity Measurement in a Geriatrics Outpatient Clinic

Student: Edward Hochman
Mentor: Dr. Augustus Mazzocca
Title: Double-Layer Reconstruction of Delaminated Rotator Cuff Tears Using Human Cadavers

Student: Austen Katz
Mentor: Dr. Isaac Moss
Title: Short- and Long-Term Radiographic and Clinical Evaluation of Multilevel Lateral Lumbar Interbody Fusion in Adult Scoliosis Patients

Student: Livja Koka
Mentor: Dr. Charles A. McKay
Title: Discharge of Patients with Alcohol-Related Impairment in the Emergency Department: The Role of Alcohol Tolerance and Acute Injury

Student: Shilpa Kolli
Mentor: Dr. Matthew Milewski
Title: The Effects of Stride Length and Foot Progression on Pelvic Rotation in Collegiate Pitchers

Student: Ardian Latifi
Mentor: Dr. Daniel Rosenberg
Title: Dysbiosis of Adherent Bacteria on Aberrant Crypt Foci with a Synchronous Polyp

Student: Yue Jay Lin
Mentor: Dr. Thomas Manger
Title: Creation of Remote Active Learning Modules (ReALMs) for Delivery of Clinical Care (DOCC)

Student: Michael Lorinsky
Mentor: Dr. Sophia Elissa Altin
Title: Pentoxifylline as a Cause of Drug-induced Liver Injury: A Case Report and Literature Review

Student: Rebecca Maher
Mentor: Dr. Ross Levine
Title: Modeling Human TET2/NRAS Mutant Myeloid Leukemia in THP-1 cells

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

Student: Samuel Milbin
Mentor: Dr. Judy Lewis
Title: Assessing the Acceptability and Usefulness of a Breast Cancer Treatment Booklet for Patients and their Accompanying Partner/Family Members in Haiti

Student: Maschal Mohiuddin
Mentor: Dr. Kristen Zarfos
Title: Education Intervention To Improve Breast Cancer Study Participation By Young African American Women

Student: Anzhela Moskalik
Mentor: Dr. Srdjan Antic
Title: Silencing of the Connexin Genes in Developing Human Neurons by Antisense Oligonucleotides

Student: Matthew Murphy
Mentor: Dr. Augustus Mazzocca
Title: Synergistic And Selective Repair Of The Acromioclavicular Ligament Alongside Coracoclavicular Ligament in AC Joint Dislocations Greatly Enhances Translational And Rotational Stability

Student: James Nolan
Mentor: Drs. John Taylor and Dharamainder Choudhary
Title: Chemotherapeutic Induced Blebbishield Program in Urothelial Carcinoma Cells – A Model System to Identify Chemoresistance Targets

Student: Kwaku Ohemeng
Mentor: Dr. Augustus Mazzocca
Title: (Double vs Single-Row Reconstruction of Fox/Romeo II/III Tear) Preserving the Superior Subscapularis Muscle With Appropriate Fixation

Student: Pooja Patel
Mentor: Dr. Ilana Waynik
Title: Evaluation of a Clinical Pathway for Management of Febrile Infants Ages 29-60 Days at Connecticut Children's Medical Center (CCMC)

Student: Roshni Patel and Lisa Fredrickson
Title: Addressing the Social Determinants of Health: Strengthening Clinical and Community Partnerships

Student: Andrew Polio
Mentor: Dr. Mar Awad
Title: Clinicopathological Characteristics Associated With Increased Mutational Load In Patients With Non-Small Cell Lung Cancer

Student: Khalil Rahman
Mentor: Dr. Henry Smilowitz
Title: IV Injected Gold Nanoparticles (AuNPs) Demonstrate Enhanced Localization to Intracerebral F98 Rat Gliomas Compared to AuNPs Infused Directly Into the Tumor Site by Convection Enhanced Delivery

Student: Kevin Reid
Mentor: Drs. Douglas Oliver and Kuwada Shigeyuki
Title: Neurophysiological Study of Noise Induced Hearing Loss in Mouse

Student: William Santiago
Mentor: Dr. Daniel Rosenberg
Title: Quantitative PCR Analysis of Gene Expression in Aberrant Crypt Foci That Exhibit Gene Methylation Patterns Similar to Those of Cancerous Tumor Cells

Student: Elizabeth Santone
Mentor: Dr. James Feeney
Title: Compared to Warfarin, Direct Oral Anticoagulants are Associated with Lower Mortality in Patients with Blunt Traumatic Intracranial Hemorrhage: A TQIP Study

Student: Kyle Shin
Mentor: Dr. Kevin Dieckhaus
Title: Assessing Child Nutrition and Malnutrition in the Bateyes of La Romana, Dominican Republic

Student: Mary Soyster
Mentor: Dr. Pamela Taxel
Title: The University of Connecticut OsteoNecrosis Numerical Scale (UCONNS): “An Investigation into Predicting Risk for the Development of Osteonecrosis of the Jaw"

Student: Tiahna Spencer
Mentor: Dr. Mariana Kaplan
Title: Rheumatoid Arthritis Fibroblast-Like Synoviocytes Produce IL-9 and Its Production Is Regulated by Pro-Inflammatory Cytokines

Student: Carsen Sulzer
Mentor: Dr. Christopher Nold
Title: Dimethyl Sulfoxide Inhibits Both MyD88 and TRIF Activation in the Cervical Epithelial Barrier

Student: Erik Swanson
Mentor: Dr. Christian Mosebach
Title: Magnesium Deficiency In Chronic Alcoholism

Student: Michael Tassavor
Mentor: Dr. Michael Payette
Title: Estimated Cost Efficacy of US Food and Drug Administration Approved Treatments for Acne: Isotretinoin as First-line?

Student: Ishan Tatake
Mentor: Dr. Renier Brentjens
Title: Investigating a new mechanism for CAR T cell imaging and elimination

Student: Katherine Tian
Mentor: Dr. Phillippe Chavrier
Title: The Effect of CDK5 Inhibitors on Vesicular Transport and Metastasis of Breast Cancer Cells

Student: Kristin Torre
Mentor: Dr. Michael Murphy
Title: Dermatologic Conditions in a Shelter-Based Homeless Population: Lessons Learned from a UCONN Medical Student-Run Dermatology Clinic

Student: Andrew Trinh
Mentor: Dr. Daniel Rosenberg
Title: Characterization of Immune Cell Composition within the Tumor Microenvironment of Colorectal Cancer in Smoking and Aspirin Taking Patients

Student: Carolina Vicens-Cordona
Mentor: Dr. Judy Lewis
Title: Social Factors Influencing Family Planning Knowledge, Attitudes, and Practices in the Ngäbe Population in Bocas del Toro, Panama

Student: Lauren Weaver
Mentor: Dr. Catherine Wiley
Title: Optimizing the Effectiveness of an Ocular History Questionnaire in School Aged Children

Student: Elizabeth Wolfe
Mentor: Dr. Kai Chen
Title: The Lower the Better: Systolic Hypertension is Associated with Diastolic Dysfunction

Student: Katelyn Wong
Mentor: Dr. Timur Durrani
Title: Educating Healthcare Professionals About Endocrine Disrupting Chemicals in Consumer Products

Student: Alan Zakko
Mentor: Dr. Kamal Khanna
Title: The Role Of CD169+ Splenic Macrophages During Systemic Listeria Monocytogenes Infection

Student: Rebecca Zweifler
Mentor: Dr. Kevin Dieckhaus
Title: Pap Smears in Peru: The Impact of Income and Education on Women's Attitudes

Skeletal Characterization of CD146 Deficient Mice

Blake E. Bandeff[1], Luis Fernandez de Castro[1], Andrew J. Maul[1], Brian J. Sworder[1], Paolo Bianco[2], Kenn Holmbeck[1], Pamela G. Robey[1]

[1]National Institute of Dental and Craniofacial Research, National Institute of Health, Bethesda, MD, USA, [2]Sapienza University of Rome, Rome Italy

A subset of bone marrow stromal cells (BMSCs) known as skeletal stem cells (SSCs) or bone marrow-derived mesenchymal stem cells (BM-MSCs) are able to differentiate into osteoblasts, adipocytes, chondrocytes and provide a hematopoietic supportive stroma. These cells have been a major focus in recent research due to their therapeutic potential. SSCs reside as pericytes in the subendothelial microenvironment of the bone marrow, and in humans, have been previously shown to selectively express MCAM/CD146. When transplanted heterotopically, human $CD146^+$ SSCs form a bone ossicle that also supports a hematopoietic microenvironment of host derived blood cells (Sacchetti et al, Cell Stem Cell, 2007). This suggest that $CD146^+$ BMSCs function in the bone marrow as a stem cell source for osteoblast and stromal cells that support hematopoiesis. Therefore, we hypothesized that CD146 knockout (KO) mice would present with a reduced or impaired SSC population, ultimately resulting in an osteopenic phenotype. Surprisingly, no significant differences between CD146 KO and WT mice skeletons were found using micro computerized tomography (μCT) (n=24). For this reason, we further examined the SSC functions of WT and KO mice by performing ectopic bone transplants. Twelve weeks post implantation, WT and KO BMSCs showed no significant differences when analyzed by μCT and hematoxylin and eosin (H&E) staining. Our work reveals that while CD146 may be a useful cell surface marker to identify human SSCs, its functional importance in the murine BMSCs or progeny does not appear to be significant.

Supported by: NIDCR Summer Dental Student award

References:

Sacchetti B. Oct 2007. Self-renewing osteoprogenitors in bone marrow sinusoids can organize a hematopoietic microenvironment. Cell. 133(5):928.

Perceptions and Practice of Shared Decision-Making among Senior Medical Students in Costa Rica

Samuel Baron[1], Kevin Dieckhaus[1], Mario Tristan[2]
[1]*University of Connecticut School of Medicine, UConn Health, Farmington,CT*
[2]*International Health Central American Institute, San Jose, Costa Rica*

Shared decision-making (SDM) is defined as, "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences."[1] Although SDM has proven beneficial to physicians and patients alike, it is still grossly underutilized as a method of decision-making by the medical community.[2,3] The education and implementation of SDM in Central America is currently not well understood. This study aims to gauge the current perceptions and practices of SDM by Costa Rican medical students. 34 senior students who were, at the time, currently enrolled in Costa Rican medical schools were surveyed from August to December of 2016. The survey illustrated five unidentified models which were intended to represent the spectrum of decision-making methods including SDM, informed decision-making and the paternalistic approach. After reviewing the models, students were asked which model best represented the method they observe physicians using most often, which method they currently use most often and which method they would prefer to use as a physician. The students were asked which model they would use in a variety of clinical situations with different patient competencies and diagnoses. Lastly, students were asked if they have ever had educational or clinical training in SDM. Data was collected and unidentified via participant submission through a survey website. Results showed that only 5.8% (2) of students claim to observing instructors utilizing SDM most often, and only 28.1% (9) and 8.8% (3) have reported to have received educational and clinical SDM training, respectively. Despite the lack of training, the majority of students surveyed at 45.7% (16) currently use SDM most often when interacting with patients, while an astounding 80.0% (28) would prefer to use the SDM model in the future as practicing physicians. The evidence indicates that, as expected, SDM is not routinely modeled by Costa Rican medical faculty or taught in the curriculums of Costa Rican medical schools. However, students are identifying with the SDM method for current practice and intend to do so in the future as physicians. To teach medical students the concepts and skills necessary to practice SDM, medical schools in Costa Rica need to incorporate SDM training into their curricula while enhancing their collection of clinical preceptors who can be role models for SDM in clinical practice.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Elwyn G, Coulter A, Laitner S, Walker E, Watson P, Thomson R. Implementing Shared Decision Making in the NHS. BMJ. 2010;341:c5146. doi: 10.1136/bmj.c5146.
2. Lipkin M. Shared Decision Making. JAMA Intern Med. 2013;173(13):1204-1205. doi: 10.1001/jamainternmed.2013.6248.
3. Lee E, Emanuel E. Shared Decision Making to Improve Care and Reduce Costs. New England Journal of Medicine. 2013,368:6–8i. doi: 10.1056/NEJMp1209500.

Control of High Blood Pressure: Knowledge, Attitude, and Practice Study of Hypertension in Haitian Migrant Farm Communities in the Dominican Republic

Spencer Beck[1], Kevin Dieckhaus[1,2]
[1]*University of Connecticut School of Medicine, UConn Health, Farmington, CT*
[2]*Division of Infectious Diseases, UConn Health, Farmington, CT*

Introduction: Hypertension (HTN) is one of the most common diagnoses in the Dominican Republic, with particularly high prevalence in sugarcane worker communities known as bateyes [1]. As a major risk factor for many life-threatening cardiovascular morbidities including strokes, myocardial infarctions, and heart failure, HTN is a pressing concern for this population [2,3]. Proper management and patient education are crucial for effective treatment of HTN in these patients. This study aims to assess the knowledge, practices, and attitudes that these patients have regarding their condition, and identify barriers hindering effective management.
Methods: Patients were recruited from mobile health clinics in bateyes near the city of La Romana. Enrolled patients with previously or newly diagnosed HTN were administered an IRB-approved survey assessing demographics, risk factors, knowledge of and attitudes toward treatment, management practices, and barriers to care. Composite knowledge scores (K-s) and attitude scores (A-s) were determined from responses. A high A-s indicates a more realistic attitude, a greater sense of control, and willingness to change. A seated right arm blood pressure (BP) measurement was taken as part of standard care. 81 patients (42 males, 39 females; mean age of 59) were enrolled. SPSS v. 22 was used for statistical analysis.
Results: The average BP of participants was 162/98mmHg. Of patients on a HTN medication, 66% could not name it. Only 37% felt confident that they know how to lower their BP. 26% of patients reported frequently missing their medication. The average K-s was 14.9 out of 23 questions. Being a cane worker was associated with a lower K-s ($p<.01$), less confidence in knowing how to lower BP ($p<.01$), less family support ($p<.05$), more frequent missed medications ($p<.1$), and previously undiagnosed HTN ($p<.01$). Education level and confidence in one's ability to make lifestyle changes were positively correlated ($p<.01$), as was K-s and A-s ($p<.01$). Feeling that one's doctor explains HTN clearly was associated with less frequent missed treatment ($p<.1$). Previously undiagnosed HTN was associated with less family support ($p<.01$) and less confidence in knowing how to lower BP ($p<.1$), but was not correlated with overall K-s or A-s. Difficulty refilling medication consistently was associated with missing medication more often ($p<.05$). BP was not significantly correlated with K-s, A-s, barriers, or management practices.
Conclusion: Overall, knowledge of HTN and management practices in the bateyes were poor, most notably among cane workers. The correlations discovered in this study demonstrate an opportunity to improve patient education, promote self-efficacy, and eliminate barriers to achieve better HTN outcomes in this population.

Supported by: The UConn School of Medicine Summer Research Fellowship

References:

1. Ferrara BJ, et al., 2014. Short-Term Global Health Education Programs Abroad: Disease Patterns Observed in Haitian Migrant Worker Communities Around La Romana, Dominican Republic. The American Journal of Tropical Medicine and Hygiene, 91(5):871-5.
2. Levy D, et al., 1996. The progression from hypertension to congestive heart failure. Journal of American Medical Association, 275(20): 1557-62.
3. Psaty BM, et a., 2001. Association Between Blood Pressure Level and the Risk of Myocardial Infarction, Stroke, and Total Mortality. Archive of Internal Medicine, 161(9):1183-92.

The Potential Use of Human Bursa Cells for Biologic Augmentation in Rotator Cuff Repair

Nicholas Bellas[1], Mary Beth McCarthy[1], Bastian Scheiderer[1], Mark P. Cote[1], Augustus D. Mazzocca[1], Daichi Morikawa[1,2]

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

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

[3]Department of Orthopaedic Surgery, Juntendo University, Japan

Connective tissue progenitor cells (CTP) are an effective option for improving outcomes in biologic augmentation of rotator cuff repair with respect to healing and prevention of re-tears. Prior studies have used the iliac crest bone marrow as the source of human mesenchymal cells (hMSCs) for biologic augmentation of rotator cuff repair [1]. The purpose of this study is to determine the best source of hMSCs from the human shoulder for potential use in biologic augmentation of rotator cuff repair. The targeted shoulder tissues include the bursa tissue on the supraspinatus muscle (MB), the bursa on the supraspinatus tendon (TB), and the bone marrow aspirate (BMA) of the humerus. Five (2 males and 3 females) patients (57 + 5.6 years old) with a diagnosed rotator cuff repair (full thickness tear of 17.9 + 12.5 mm) were consented for bone marrow aspiration (IRB# 06-577-2). Human bursa (MB and TB) samples were also collected from the same patient (IRB# 07-224). BMA was concentrated to a 3-4 ml sample (cBMA) using the Angel System (Arthrex Inc., Naples Fla.) to give a final product rich in CTPs. To obtain CTPs from the bursa, MB and TB were digested for three to four hours in alpha-Minimal Essential Medium (□MEM) containing 2mg/ml collagenase. CTPs were then grown in culture to compare the number of colony forming units (CFU) and proliferation index between the shoulder tissue and cBMA samples. There was a greater number of CFUs derived from the TB and MB compared to the BMA, and there was a greater number of CFUs derived from the TB compared to the MB ($p<0.001$). The BMA showed no detectable hMSC colonies when grown on the 1,000 or the 10,000 cells/cm2/60-cm2 dish. The proliferation rate of MB and TB was not significantly different, although both showed a greater proliferation rate in comparison to the cells from the BMA. The findings indicate that hMSCs derived from the bursa tissue on the rotator cuff tendon (TB) have the greatest potential for proliferation and growth. Furthermore, TB and MB both have potential for use in biologic augmentation of rotator cuff repair and may be a preferable source of hMSCs because the use the subacromial bursa minimizes surgical intervention on the patient in comparison to harvesting cells from the iliac crest bone marrow.

Supported by: Department of Orthopaedic Surgery, University of Connecticut, Farmington, CT

References:

1. Hernigou P, Flouzat Lachaniette CH, Delambre J, et al. Biologic augmentation of rotator cuff repair with mesenchymal stem cells during arthroscopy improves healing and prevents further tears: a case-controlled study. Int Orthop. 2014;38:1811-1818.

The Effects of Platelet Rich Plasma And Concentrated Bone Marrow on Growth Factor Release When Added To a Demineralized Bone Matrix Scaffold

Jennifer Brewer[1], Mary Beth McCarthy[2], Augustus D. Mazzocca [2]
[1]*University of Connecticut School of Medicine, UConn Health, Farmington, CT*
[2]*Department of Orthopaedic Surgery, University of Connecticut, Farmington, Connecticut*

Introduction: Millions of Americans seek medical attention for shoulder pain. Of the patients that undergo rotator cuff repair (RCR) re-tear is a common issue. A 30% revision rate is encountered and the quality of the tissue is poor with the surgeries being less successful[1]. New technology is being investigated to increase the success of these surgeries. It has been shown that the growth factors and clotting properties in Platelet Rich Plasma (PRP) and the stem cells contained in concentrated Bone Marrow Aspirate (cBMA) can stimulate regeneration of tissue[1–3]. Demineralized bone matrix (DBM) is a degradable material that can allow for the PRP and cBMA to be delivered, help maintain the cells at the repair site for 6-12 weeks, and does not impede healing. All of which are essential for RCR. We investigated whether a DBM scaffold with the addition of PRP and cBMA can enhance cell activity and differentiation.
Methods: Two samples age 25.5 +/- 2.1 of whole human blood and matched bone marrow aspirate (BMA) was purchased from Lonza Biotech Inc, a Swiss multinational biotechnology company. This was purchased, so that all samples tested were consistent in quality. Blood and bone marrow were processed to obtain PRP and cBMA, using the Angel System from Arthrex. This system is a centrifugation device. It takes whole blood and bone marrow, centrifuges it, and collect the various components into their collection compartments. Once cBMA and PRP are centrifuged down either or both were added to a 5 X 5 mm piece of DBM or a control scaffold (Tissue Culture Plastic). A standard cell culture of alpha minimal essential medium (α-MEM) containing 2% fetal bovine serum (FBS) and 0.1% penicillin/streptomycin was then added to each well. An ELSIA was performed at an optical density of 450 to assess the TGF-β and PDGF growth factor activity for time points 0 hours, 24 hours, 48 hours, 3 days, 7 days, 14 days and 21 days. Time points were determined based on the half-lives of the growth factors and the hypothetical durability of the clot.
Results: Significant differences were seen between the control and the DBM scaffold with the amount of TGF-β and PDGF activity. As well PRP and cBMA added together to the DBM scaffold showed the greatest amount of growth factor activity.
Conclusion: The DBM scaffold maintains adhesion to the growth factors when added with PRP and cBMA. DBM scaffold can stimulate bone regeneration with minimal risk while promoting tendon to bone healing, which can improve the recovery times and outcomes for patients after surgery.

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Arthrex, Inc. 1370 Creekside Boulevard, Naples, Florida 34108-1945

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Establishment of Polarized Acinar-Like Structures as an *in vitro* Model for Salivary Gland Dysfunction

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Sjögren's Syndrome is an autoimmune disorder that affects the salivary and lacrimal glands resulting in decreased tear production and unstimulated salivary flow rate (<1.5mL/15m). Currently, mouse models and human salivary gland cell lines (HSG) are commonly used approaches to research pSS and can provide insight into the multifactorial nature of this disorder. Unfortunately, there is no mouse model that can completely replicate the "disease profile" observed in humans [1]. As a result, there is a need to establish alternative models to study pSS. Previous work has demonstrated the ability to transform mammary epithelial cells into polarized acinar-like structures [2]. Development of polarized acinar-like structures is highly desirable because it indicates that salivary gland cells obtained through biopsy can be manipulated to re-establish their *in vivo* morphology and can then be subjected to various experimental conditions *in vitro*. If successful, this will allow us to evaluate functional differences between pSS and healthy volunteer (HV) cell lines. Therefore, the goal of my research was to establish a manipulable *in vitro* system using salivary gland cells that can be used to recreate the pathological characteristics seen in human pSS.

In this study we sought to optimize culture conditions to achieve polarization of the acinar-like structures formed by salivary gland cells. Three different culture conditions were tested: keratinocyte growth medium-2 (KGM) low calcium, KGM-2 high calcium, and keratinocyte serum-free media (KSFM) low calcium. Initial experimentation with immunofluorescence staining for apical- and basolateral-specific proteins, specifically aquaporin 3 (AQP3), aquaporin 5 (AQP5), and inositol 1,4,5-triphosphate receptor type 3 (ITPR3), was used to monitor polarization in a 3D gel matrix (Matrigel).

Experimental results indicated that media type influences pSG cell polarization of AQP5 in acinar-like structures with KSFM low calcium showing the greatest degree of polarization. It was also demonstrated that pSG and HSG acini showed different patterns of AQP3 and AQP5 localization. Establishment of such acinar-like structures from primary salivary gland cells in a 3D culture provides a functionally representative *in vitro* model for salivary glands that can be altered with standard cell cultures approaches. Such a system can support complex or detailed experimental designs that will yield mechanistic insights into the etiology of salivary gland dysfunction in pSS.

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The Impact of the Internal Brace Repair on the Horizontal Instability of the AC Joint Following Ligament Injuries

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Introduction: The AC joint is frequently injured when athletes fall directly onto their shoulder. Current surgical repair involves only reconstruction of the CC ligament without repairing the AC ligament and fails to achieve optimal results. Specifically current technique fails to adequately stabilize the AC joint in the anterior-posterior plane. There is evidence that addressing the AC ligament during AC joint repair provides increased stability for the joint after reconstruction. Our research focused on the impact of the internal brace repair of the AC ligament on the horizontal stability of the AC joint.
Methods: The posterior translational and rotational stability of the native cadaver shoulders will be measured. These values will then be compared to values obtained after complete severing of the AC joint. To test the importance of different areas on the posterior integrity of the AC joint, the AC ligament will be divided into an anterior, superior, and posterior section. Each cadaver will then have one of these sections repaired and the posterior translational and rotational stability of the AC joint will again be assessed. A second section will then be repaired on each shoulder and the AC joint stability will again be assessed. Finally, the repair of the AC ligament will be completed, but the CC ligament will be severed to determine the impact of the CC ligament on posterior translation and rotation of the AC joint. Finally, the CC ligament will be repaired and the complete repair will be compared to the native shoulder.
Results: Our data indicates that AC repairs that address both the CC and AC ligaments provide more posterior stability than repairs that only address the CC ligament. However, the data is unclear with regards to the posterior stability of the repair compared to the native shoulder. Furthermore, much of the data is does not yet reach statistical significance. Additionally, the data indicates that individual repairs of the anterior and superior aspect of the AC ligament provide the most translation and rotation stability. Finally, repairing both the anterior and superior aspect of the AC ligament provides the most stability to posterior translation while repair of the anterior and posterior aspects of the AC ligament provides rotational stability approaching that of the native AC joints.
Conclusions: Further research is clearly needed to determine whether this effect is clinically significant. However, addressing the AC ligament is addition to the CC ligament during repair of AC joint injuries appears to be a promising avenue to improve repair integrity.

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Evaluation of Recorded Culturally-Appropriate Verbal Dosing Instructions on Medication Adherence in Migrant Farm Workers

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In the state of Connecticut, there are approximately 5,977 farms with approximately 3,654 Migrant Farm workers (MFWs). 64% of MFWs surveyed by Connecticut Area Health Education Council have little to no fluency in English. As healthcare providers, this proves to be a barrier in medication adherence and health literacy. MFWs have shown acceptance of electronic device interventions in previous studies and the purpose of this study was to see the effect of a verbal dosing device (ParrotMD) on health literacy and medication adherence. We used a pre- and post-intervention model for medication adherence and health literacy. The intervention involved use of the verbal dosing device ParrotMD which followed a standardized format in the language of choice for participants. The pre-intervention survey gathered basic demographic information, pre-existing medications and chronic health problems. We measured a baseline medication adherence score and health literacy score with this survey as well. After the pre-intervention survey, we gave the device to the enrollee. Pre-interventional survey n=15. Intervention was 4-6 weeks. In the post-intervention visit, the same surveys were administered for health literacy and medication adherence. For both pre- and post-intervention surveys, a Morisky Medication Adherence survey and a 3-day recall survey were used. Health literacy was modeled after a peer-reviewed published survey studying health literacy in a rural Pakistani population. In addition to these surveys, a Likert Scale feedback survey on the device was administered during the post-interventional survey. Post-interventional survey n=9. The number of enrollees was too small to generate statistical significance of any difference and therefore no significant difference in medication adherence and health literacy were found among pre and post intervention surveys. Feedback surveys on the device showed that the majority of patients liked using the device and would like it to be implemented in more clinics. The device received an average Likert score of 4.7/5 in terms of ease of use and a score of 4.0/5 for reliability. Demographic data showed that all were males, with a median age of 53. Education did not surpass 11th grade for any of the farmers and common primary languages included Spanish and Jamaican. While it is hard to draw substantiative conclusions about the effect of the device, this study did find that the patients sampled did appreciate use of the device and would like the device to be used in clinical settings. Further research will require larger sample sizes and the use of biological markers to correlate the effect with any form of biologic impact. Blinding of subjects to research project may also be required for more accurate results.

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Salty, Sweet and Bitter Tastes of Sodium Salts after Chlorhexidine Rinse

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Objective: Effects on tastes of sodium-salt concentration series by the bis-cationic biguanide, antiseptic chlorhexidine in the Peridex rinse form used to control periodontal disease were studied. When applied to the anterior part of the tongue, Peridex greatly reduced the perceived salty taste of sodium chloride but had no effect on the sweet taste of sugar (1). Peridex rinse has recently been shown to change the sweet sodium benzoate taste to bitter (2); the means by which the taste qualities are altered is currently unknown (3, 4). In the present project, taste quality (sweet, salty, sour, bitter, tasteless) identification of 4 concentrations ranging from zero to moderate intensity of the sodium salts (benzoate, saccharin, chloride, sulfate) were examined for the first time following rinse with Peridex and results of experimental (Peridex rinse) and control (water rinse) sessions were compared.

Methods: Stock solutions were prepared and applied to five distinct locations on the anterior two-thirds of a subject's tongue using Q-tips (3). The solutions (concentration series of sodium salts, controls) were randomly presented within a session for a subject to identify taste qualities recognized by pointing to a list of taste qualities. Two sessions were performed per subject, one with prior control water rinse first and the second because taste changes can last for days with prior experimental chlorhexidine rinse. Data were collected in an Excel spreadsheet with identification of each quality given a value of 1, non-identification a value of 0. This primary data will be converted to proportions, with differences between experimental vs. control mean proportions statistically analyzed using t-tests.

Results: For all solutions of sodium salts, identification minus non-identification averages were calculated. Identification of the water control was not-significant (t-test $p>.05$) between water and chlorhexidine rinse. For sodium chloride identification, the salty and sour taste average proportions were significant with salty decreasing (an average 8.8) and sour increasing (an average 9) for the concentrations 0.32M, and 1.0M. For sodium saccharin identification, the sweet taste was perceived more frequently (an average 2) after the chlorhexidine rinse. For sodium sulfate identification, the salty taste average proportion was significant and decreasing (an average 4.6) for the concentrations 0.16M, and 0.5M. Lastly for sodium benzoate identification, the sweet and bitter averages were significant with sweet decreasing (an average 8.6) and bitter increasing (an average 12.6) for the concentrations 0.05M, 0.16M, and 0.5M.

Conclusions: Chlorhexidine rinse reduced identification of the sodium chloride and sodium sulfate salty taste and increased the sour taste for sodium chloride. It turned the sweet taste of sodium benzoate to a bitter taste confirming the previous results (4), but did not increase bitterness of saccharin (usually sweet) and sulfate salts.

Future Directions: To advance this research, the next steps would be to devise experiments to find specific concentrations at which taste changes can be identified for the four sodium salts.

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Predictive Role Of Symptom Duration Prior To Initial Presentation Of Adolescents With Capitellar Osteochondritis Dissecans On Pre- & Post-Operative Measures

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Objectives: Capitellar osteochondritis dissecans (OCD) is a disease that mainly affects young athletes who compete in upper-extremity dominant sports.1 Though treatment options are well described in the literature, the impact of symptom duration prior to initial clinical presentation on pre- and post-operative measures is not well documented. This meta-analysis examines correlations between these variables aiming to identify predictive roles of symptom duration on OCD progression – important for providing a framework for earlier injury prevention and intervention to athletes.

Methods: The published literature was searched and screened using the PRISMA template for the concepts of osteochondritis dissecans and elbow. Meta-regression between symptom duration and 17 pre- and post-operative measures were explored using OpenMetaAnalyst with random effects models. Statistical analyses were assessed at a 0.05 alpha level of significance.

Results: Data was available on 208 patients with mean age of 14.5±1.6 years across 20 papers meeting inclusion criteria. Locking as a chief complaint predominated in a greater proportion of patients who present with a longer history of symptoms (p=0.004). Supporting this, patients who had longer symptom durations trended towards greater odds of presenting with more severe lesions and needed longer time for return to initial level of sport (p=0.013). Conversely, OCD symptom duration had inverse relationships with loss of terminal pre-operative extension measurement (p=0.001) and the proportion of patients with chief complaint of decreased ROM (p=0.012). Symptom duration did not correlate significantly with age, skeletal maturity, and many post-operative measures.

Conclusion: Symptom duration prior to initial clinical visit shows significant correlation with several pre-operative parameters. Meta-analysis revealed prolonged symptom durations as predictive of lesion degeneration and longer recovery periods. Surprisingly decreased ROM, often associated with advanced OCD, was found to be an early-onset symptom. This suggests that "playing through pain" may actually play a detrimental role in causing OCD lesions to propagate until surgical intervention is required. Many post-operative outcomes did not correlate with symptom duration, suggesting that for advanced OCD lesions requiring surgery, the specific surgical procedure rather than symptom duration correlates best with whether or not patients return to sport. Taken together, since conservative treatment of early OCD lesions has been reported to yield good results and short return to sport durations,2 these findings further emphasize the importance of heightened awareness and early detection of OCD in young athletes to allow for intervention at earlier disease stages.

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Initial Barriers to Eye Care Access Among Participants of a Mobile Eye Clinic

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Chronic visual conditions are significant contributors to rising health care costs in the United States, and accounted for approximately $139 billion of national costs in 2013 (1). Barriers to health care access present critical challenges to improving eye health that are dynamic and complex (2, 3), yet few studies have been able to qantitatively measure the impact of these barriers. This study aimed to determine the association between initial barriers to seeking care and time since last eye exam. The Casey Eye Institute (CEI) Outreach Van is a mobile screening clinic that provides comprehensive eye exams in Oregon. Screening participants were identified as un/under-insured by partner agencies in the community. Participants (N=1605) from screenings conducted between 2014 and 2016 completed a demographic and subjective visual acuity questionnaire, and received a comprehensive dialated eye exam. Data regarding demographic information, subjective visual acuity, and measured visual acuity were analyzed with respect to time since last eye exam. Participants were divided into two categories based on whether they received at least one eye exam in the past (n=1344) or had never received an eye exam (n=261). A large percentage of Hispanic (34.89%) and uninsured (28.62%) participants had no previous eye exam. Multivariate logistic regression analysis showed that race, insurance status, age, and history of diabetes was statistically significant predictor variables for having a history of eye exams. Ethnicity data ($p<0.0001$) showed that the least time elapsed since last eye exam was found among American Indians/Alaska Natives (mean 2.78 ± 3.59y) and Asians (mean 2.79 ± 2.89y), while the most was found among Caucasians (mean 5.79 ± 7.05y, median 3.00y). Privately insured participants had sought care significantly sooner (mean 2.85 ± 2.89y) than public (mean 4.29y ± 5.15y) and private (mean 4.80y ± 6.92y) insurance holders who previously obtained eye care ($p < 0.05$). Time since last eye exam decreased as age increased ($p<0.01$), from 4.09y ± 4.06y (18-39yo) to 3.57y ± 4.08y (70+ yo). Diabetic participants had eye exams less frequently than the annual screeings recommended by the American Academy of Ophthalmology. Our results indicate that barriers to eye care must be assessed quantitively to gain an accurate understanding of the challenges that specific subpopulations face. Furthermore, it is especially important to improve eye care access for diabetic individuals to detect and treat diabetic retinopathy in a timely manner.

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Tablet-Computers And Smartphones Can Reliably Detect Radiographic Tooth Fractures

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Objective: Traumatic events in the maxillofacial region can benefit from having the ability to acquire and visualize radiographs onsite. This is now possible with mobile x-ray units and mobile screens that include tablet computers and often times smart phones. However, the diagnostic accuracy of these mobile screens has not been very well studied. The objective of this study was to evaluate the reliability of identification of anterior tooth fractures in panoramic and posteroanterior (PA) radiographs on a medical grade monitor and on 2 smartphones (iPhone 5 and Nexus 5x) and 2 tablet computers (iPad 5 and Nexus 7).

Materials and Methods: Thirty anterior human teeth were used in this study. The teeth were randomly distributed between maxillary and mandibular arches, and a variety of commonly occurring traumatic fractures were simulated. Panoramic and PA radiographs were acquired. The presence of fractures was evaluated by two pediatric dental residents on all displays. All images were viewed twice, with an interval of at least two weeks between sessions.

Results: Statistical analysis using multivariate analysis showed no significant difference between the display qualities of a smartphone or tablet computer in diagnosing fractures when compared to a standard medical grade monitor which served as the gold standard. Kappa analysis showed good intra-and inter-examiner reliability for diagnosing fractures on all displays.

Conclusion: Smartphones and tablet computers can reliably show anterior tooth fractures in PA and panoramic radiographs.

Future Directions: In a continuation of this study, cone beam CT (CBCT) images will also be viewed on a medical grade monitor, smartphones and tablet computers. The objective will be to evaluate the reliability of identification of tooth fractures across these different screens, as well as compare the diagnostic accuracy of CBCT images with that of the previously acquired 2-D images.

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Eustachian Tube Reconstruction for the Treatment of Patulous Eustachian Tube: Direct Analysis of Symptom Relief and Patient Satisfaction

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Introduction: Since the first visual of a Patulous Eustachian Tube (PET) by Schwartze 1864, there has been a pattern of failure to resolve these problems through medical therapy alone without surgical intervention. The incidence of PET is 0.3-6.6% of the population, of which 10-20% of patients with PET seek medical resolution of their symptoms (1). It is believed that PET is the result of a defect in the anterolateral wall of the tubal valve of the nasopharyngeal orifice. Further, it seems this defect is due to loss of fat, cartilage, soft tissue, or increased muscle wasting (2,3). At the conclusion of this study, one should be able to demonstrate understanding of Eustachian tube reconstruction with different implantation techniques and compare rates of improvement of patulous symptoms, in patients with Patulous Eustachian Tube (PET).
Study Design: Retrospective analysis of patients who previously failed medical treatment for PET and underwent Eustachian tuboplasty. The use of different surgical materials and site insertion into the nasopharyngeal orifice of the ET is assessed to indicate treatment specific outcome on the basis of patient reported autophony and aural fullness in follow-up.
Methods: Surgically, autologous cartilage was placed into a pocket on the anterior edge of the torus tubarius. In addition, some patients had implantation of acellular dermal matrix into the infero-medial Eustachian tube. Post-operative interviews were conducted and patients were asked to rate their patulous symptoms as: resolved, significantly improved satisfied, significantly improved dissatisfied, unchanged or worse.
Results: 21 patients with 30 patulous ET's underwent surgical implantation. Improvement of autophony and aural fullness is reported as 72.73% and 76.92% in the cartilage only group and 84.62% and 91.67% in cartilage with acellular dermal matrix group respectively. Regarding the improvement of autophony, aural fullness and overall patient satisfaction, patient data is trending towards a greater benefit with the use of a combined acellular derma matrix and cartilage technique as compared to that of only cartilage graft.
Conclusions: PET is often associated with bothersome auditory symptoms, for which there are a multitude of different medical treatments. Cartilage implantation in conjunction with acellular dermal matrix implant shows promise to provide functional restoration to patients with PET.

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Prestin as a Biomarker for Early Detection of Hearing Loss in a Cisplatin-Ototoxicity Model

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Introduction: Disabling hearing loss, defined as a loss greater than 40 dB in adults or 30 dB in children, is a prevalent issue affecting over 5% of the world's population, with broad implications for the patient's functional status.[1] Recent evidence has shown that serum levels of otolin-1, an inner ear protein, increase in patients with benign paroxysmal positional vertigo, thus demonstrating proof of concept for the use of inner ear proteins as biomarkers of inner ear disease.[2] We proposed to extend this idea to sensorineural hearing through measurement of prestin, an outer hair cell specific protein believed to be involved in cochlear amplification.[3] Additionally, it should be determined if prestin levels are sensitive to interventions intended to prevent hearing loss.
Objective: The aim of this study was to determine whether serum levels of prestin are sensitive to both hearing loss and the effects of an otoprotective agent, diltiazem, in an animal model of cisplatin ototoxicity.
Methods: Two groups of 10 guinea pigs were assigned to a saline (control) or diltiazem (treatment) group. Baseline prestin and auditory brainstem response (ABR) thresholds were obtained. Cisplatin was administered to both groups intraperitoneally. Intratympanic injections of saline (control) or diltiazem (treatment) were started on the same day and continued for a total of five consecutive days. Blood draws and ABRs were performed at day 1, 2, 3, 7, and 14 post-cisplatin injection. Animals were euthanized on day 14 and brain, kidney, skeletal muscle, heart, and liver tissue were harvested for comparison of prestin levels with the blood using ELISA.
Results: Mean serum prestin levels in control subjects (intratympanic saline) were significantly elevated above baseline on days 1, 2, and 3 post-cisplatin ($p<0.001$, $p<0.001$, $p=0.022$, respectively) and peaked on day 2. ABR thresholds were not significantly elevated until days 7 and 14. In treatment subjects (intratympanic diltiazem), no significant changes in serum prestin levels or ABR threshold were found in any days following cisplatin administration.
Conclusions: In control (intratympanic saline) subjects, serum prestin levels were significantly elevated on days 1-3, followed by significant changes in ABR on days 7 and 14. These changes were not seen in subjects treated with the otoprotectant diltiazem. Thus, prestin may serve as a biomarker of early cochlear injury which is sensitive to therapeutic interventions.

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Development and Validation of a CyTOF Antibody Panel for Detection of Circulating Angiogenic Cells in the Peripheral Blood of Patients with and without COPD

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Introduction: Chronic obstructive pulmonary disease (COPD) is the 3rd leading cause of death in the US.[1] It is now thought that alterations of the pulmonary vasculature accompany the inflammatory changes known to contribute to COPD pathogenesis.[2,3] Because of their potential role in vascular repair, circulating angiogenic cells have been a focus of recent research.[3] Though flow cytometry was previously the tool of choice for identifying rare cells, advances in cytometry time-of-flight (CyTOF) technology now allow identification of a larger number of surface markers via metal-conjugated antibodies.[4,5] This project aimed to develop a CyTOF antibody panel to be used in analysis of peripheral blood mononuclear cells (PBMCs) collected from patients with and without COPD to better understand COPD pathogenesis.

Methods: An antibody panel was designed to discriminate between PBMC subtypes using surface marker recommendations from the Human Immunology Project.[6] Previously established angiogenic, hematopoietic, and senescence markers were selected. Angiogenic and hematopoietic markers were validated via Human Umbilical Vein Endothelial Cell (HUVEC) dilution with beas-2b epithelial cells. Senescence markers were validated by comparing levels of p53, p21, and pRB in HUVECs incubated in room air versus hyperoxia and confirmed in irradiated and non-irradiated PBMCs. 8 patient samples from current or former smokers (4 with COPD and 4 without) were selected from a cohort of previously recruited adults.[7] Staining was performed according to a revised protocol incorporating Yale Core Facilities' surface antibody staining protocol and Fluidigm's Maxpar nuclear antigen staining protocols. Cell count analysis was performed in CytoBank.

Results: As expected, senescence marker expression increased in HUVECs incubated in hyperoxia versus room air and in irradiated PBMCs versus non-irradiated PBMCs. Angiogenic and hematopoeietic marker expression in HUVECs decreased upon beas-2b epithelial cell dilution. Sample analysis revealed increased expression of p53, p21, and pRB in smokers with COPD as compared to smokers without COPD. Angiogenic (Tie2 expressing) cells also demonstrated increased senescence marker expression in patients who had developed COPD.

Conclusion: This project succeeded in designing, validating, and titrating a CyTOF antibody panel to identify PBMC subtypes, angiogenic and hematopoietic cells, and markers of senescence. Analysis of a small number of patient samples demonstrated increased expression of senescence markers in angiogenic cells of COPD patients. Full application of this methodology may yield a better understanding of COPD pathogenesis and elucidate potential therapeutic targets involving PBMCs.

Supported by: The UConn School of Medicine Summer Research Fellowship

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PDE3A Modulation for Cancer Therapy

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BACKGROUND: Cancer is the second leading cause of death in the United States which highlights the need to develop novel cancer therapeutics to reduce mortality. Traditional approaches to cancer drug discovery take the approach of targeting rapid cell division and more recently targeting oncogenic drivers. Many cancers are unresponsive to these traditional therapies underscoring the need to develop novel approaches to cancer drug discovery. Using predictive chemogenomics in a differential cytotoxicity screen, we identified a novel small molecule modulator of phosphodiesterase 3A (PDE3A) that selectively kills cancer cell lines co-expressing increased levels of PDE3A and Schlafen 12 (SLFN12) (de Waal, Nat Chem Biol, 2016). This cell-selective cytotoxic agent, DNMDP, induces apoptosis through complex formation between PDE3A and SLFN12. Although the exact mechanism of apoptosis induction remains to be elucidated, the degree of complex formation between PDE3A and SLFN12 in response to DNMDP correlates with cytotoxicity. Additionally, cancer cell lines made resistant to DNMDP by prolonged exposure downregulated SLFN12 expression and ectopic SLFN12 expression restored DNMDP sensitivity. Similarly, ectopic expression of PDE3A and SLFN12 in naïve resistance cell lines conferred sensitivity to DNMDP. Overall these data highlight the relationship between PDE3A-SLFN12 complex formation as a potential novel mechanism of DNDMP-mediated cancer cell killing.
OBJECTIVES: Experimentally validate the results of screening data which identified PDE3A and SLFN12 expression as a biomarker correlate for DNMDP sensitivity by profiling cell line sensitivity and PDE3A and SLFN12 expression. Assess "outlier" cell lines that are sensitive but do not express PDE3A and SLFN12 to understand possible alternative DNMDP-mediated cytotoxic mechanisms.

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Assessing The Barriers To Compliance With Colorectal Cancer Screening Tests In The Miami Beach Community Health Center

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Introduction: Colorectal cancer is the third most common cancer in the United States and the second leading cause of cancer-related deaths in the United States between men and women, yet it is still one of the most preventable cancers. However, even with the high preventability and survival rates associated with screening and early detection, adherence rates to recommended annual screening are dismal, especially in underserved communities such as the Miami Beach area. Objective: To identify and address the barriers to colorectal screening participation in patients in the Miami Beach Community Health Center in order to reach the 80% screening implemented by the American Cancer Association by 2020. It is hypothesized that many of the barriers are influenced by socioeconomic status, education, and healthcare familiarity. Methodology: 36 Patients at MBCHC between the ages of 50 – 75 years old that were overdue for their colorectal cancer screening fecal immunochemical test (FIT) by at least one month were administered a 7 question survey over the telephone. The survey was used to collect information on the obstacles that made it difficult for patients to adhere to their overdue screening requirements. Results: In alliance with our hypothesis, a disproportionate percentage of patients reported obstacles that can be alleviated by the community health center, which included barriers such as Difficulty understanding the directions (58.3%), Unsure of the Purpose of the Test (30.5%), Transportation difficulties (25.0%), and Language Barrier (22.2%). Conclusion: In order to address colorectal cancer screening disparities among the Miami Beach Community, efforts were suggested that aimed at removing barriers that disproportionately affect disadvantaged and underserved communities. Lessening these obstacles should primarily include providing more education to fit each patient's individual needs.

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Early Fixation Strength And Biomechanics of Anatomical Glenoid Reconstruction With The J-Bone Graft For Anterior Glenoid Bone-Loss

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Background: Several studies have demonstrated the importance of addressing instability-associated bony Bankart lesions, as failure to do so often leads to recurrence and/or failure after stabilization surgery addressing glenohumeral dislocation.[1] Many surgical techniques aimed at repair of the Bankart lesion have been described in the literature, with excellent results in terms of prevention of future instability.[2] However, many of these techniques have been shown to lead to progression of dislocation arthropathy, osteolysis, and hardware impingement leading to secondary glenohumeral arthritis. Anatomic restoration of the glenoid using an implant-free J-shaped iliac-crest bone graft offers a promising alternative to these currently used techniques, but there is currently a lack of biomechanical data.
Purpose: To evaluate the initial fixation strength, biomechanical properties, and glenoidal contact pressures after J-bone grafting for anterior shoulder instability with associated glenoid bone loss.
Methods: A total of 8 fresh-frozen cadaveric shoulders and J-shaped iliac-crest bone grafts were used for this study. Glenohumeral contact pressures were measured with the humerus in 30° of abduction, 30° of abduction and 60° external rotation, 60° of abduction, and 60° of abduction and 60° external rotation. Additionally, a compressive load of 50N was applied and the peak force needed to translate the humeral head 10mm anteriorly at a rate of 2mm/s was recorded. All measurements were repeated at the following stages: the intact glenoid, after creation of a 30% anterior glenoid defect, and following anatomic glenoid repair using the implant free J-bone graft. Finally, after glenoid reconstruction each specimen was translated anteriorly for 5mm at a rate of 4 mm/s for a total of 3000 cycles while graft protrusion and medio-lateral bending motions were measured.
Results: After creation of the 30% glenoid defect, there was significantly decreased glenohumeral contact area, with a significantly increased contact pressure at all tested positions. The subsequent reconstruction restored contact area and pressure back to that of the intact glenohumeral joint at all tested positions. The mean force to translate the humeral head anteriorly for 10mm was significantly reduced after creation of the defect, and significantly increased following repair compared to the defect state and baseline. Mean graft protrusion under cyclical translation was 138.3±169.8μm, whereas the mean medio-lateral graft deflection was 320.1±475.7μm.
Conclusion: Anatomical glenoid reconstruction using the J-bone graft was able to restore baseline glenohumeral contact area and pressure, which could potentially avoid progression of dislocation arthropathy in clinical settings.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Addressing the Social Determinants of Health: Strengthening Clinical and Community Partnerships

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Purpose: Our study examined two geographically distinct communities in CT to examine how clinical care agencies and community-based organizations are working collaboratively to address the social determinants of health. Specifically, we identified what current practices are in place within clinical care agencies and community-based organizations to address social determinants health, examined how/if clinical care agencies partner with community-based organizations to comprehensively address social and medical needs of patients/clients, and recognized potential barriers to or gaps in care.

Methods: 1) Defined social determinants of health and examined how they relate to health outcomes; 2) Reviewed community health needs assessments and current literature recommendations; 3) Formulated 12 core interview questions; 4) Identified clinical care agencies and community-based organizations in each community and conducted interviews at selected sites; 5) Analyzed linkages and barriers between clinical and community based organizations.

Results/Discussion: Due to lack of community-specific data in the community health needs assessments, health disparities within populations (in particular income and poverty levels) were not fully accounted for. Absence of data regarding social determinants of health demonstrated a need for clinicians and community-based organizations to further engage with one another to fully assess community needs. Community-based organizations and clinical agencies in both cities reported common barriers in terms of addressing social determinants of health and achieving effective collaboration. From these barriers, key areas of opportunity for growth were identified: access to care, data and assessment, and outreach and accessibility.

Conclusions: In order to best address social determinants of health in practice, there must be a push to mandate education and training of all levels of staff and health professions students working in clinical care agencies and community-based organizations. Change at the policy level may help ensure that various entities are maintaining standards of care, active communication, and following current recommendations in addressing social determinants of health. Future research may build on this project to propose such legislative reform and/or implement educational programming.

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Assessment of Market Needs for a New Formulation of a Long-Acting Topical Anesthetic Agent for Pain Secondary to Oral Mucositis

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Background and Objectives: Oral mucositis (OM), erythema and ulceration of the oral mucosa, is a common toxicity that is seen in almost all head and neck cancer patients receiving radiation therapy and about 20-40% of patients receiving chemotherapy for cancer[1]. Lesions of OM are intensely painful, resulting in nutritional compromise with resultant weight loss and failure to thrive[2]. A short-acting lidocaine rinse is commonly used for oral pain, however, systemic opioids are also needed, with resulting side-effects[3]. The objective of this project is to assess the market need for a new formulation of a more potent and longer-acting topical oral anesthetic and identify desired attributes in such an agent.

Methods: Interview questions were developed for the various customer segments identified: patients, prescribers, and pharmacists. Both structured and non-structured (open-ended) questions were used. Interviews were conducted in the context of customer discovery efforts as part of the NSF-funded Accelerate UConn program. After NSF and IRB clearance, potential interviewees were identified via personal contacts and online searches. No protected health information (PHI) was used or recorded. Interviews were conducted in person, by phone or via online surveys.

Results: Of 10 patients, 75% of those who had used a mouth-numbing mouthwash (n=8) reported low levels of satisfaction. All 10 patients reported interest in using the proposed product. Prescribers (n=8) indicated that there is a moderate-strong need for additional local treatment options for pain secondary to oral mucositis and oral ulcerative conditions. Duration of effect and cost of coverage were identified as important factors for such agent. Of 5 pharmacists, 80% indicated low satisfaction level with current treatments and 100% reported that patients were dissatisfied with current treatments.

Conclusions and Significance: There is a strong need for additional topical treatment options for pain secondary to oral mucositis and other oral ulcerative conditions. Longer duration of effect and cost of coverage are important factors for such an agent. These findings will inform the ongoing development of a novel long-acting topical anesthetic agent.

Acknowledgements and Disclosure: This work is supported by funds from UConn School of Dental Medicine Summer Research Fellowship and Accelerate UConn-National Science Foundation Innovation Corps. Development of the novel long-acting topical anesthetic product is supported by the UConn SPARK Technology Commercialization Fund. Dr. Lalla has a significant financial interest in Logic Biosciences, Inc. which is involved in the development of this product.

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DKK1 Expression Over Time In MC3T3-E1 Cells And The Effects Of DKK1-Ab On MC3T3-E1 Cell Osteogenic Differentiation

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Objective: Dickkopf-1 (DKK1) is a secreted glycoprotein that acts as a potent Wnt antagonist. Wnt ligand treatment leads to intracellular stabilization of β -catenin protein levels and its translocation into the nucleus to promote gene transcription. The Wnt/β-Catenin pathway is one of the critical signaling pathways in positively regulating osteogenesis (1). In contrast, DKK1 inhibits the osteoblast's ability to secrete bone matrix by inhibiting β -catenin (2,3). This study aimed to measure DKK1 expression levels over time during mouse MC3T3-E1 cell proliferation and differentiation. Additionally, we also examined the ability of an antibody that blocks the function of DKK1 (DKK1-Ab) to promote osteoblast differentiation of MC3T3-E1 cells.

Methods: MC3T3-E1 cells were seeded in 6 well-plates at a cell density of 10,000 cells/cm^2. Cells were cultured in proliferative media for 7 days, and then switched to osteogenic media until Day 21. DKK1 mRNA expression was measured by qPCR on Day 1, 7, 14, and 21 and calcium content was evaluated on Day 21. Once the timing of DKK1 mRNA maximum expression was identified, additional MC3T3-E1 cells were cultured. On Day 2, 4, and 7, media was supplemented with 100 ng/ml DKK1-Ab or 350 ng/ml DKK1-Ab or Vehicle (PBS) (N=3 replicates per treatment group per time point). DKK1 mRNA expression was measured on Day 1, 7, 14, and 21 and representative images were taken to visualize mineralization in each well on Day 14 and 21.

Results:

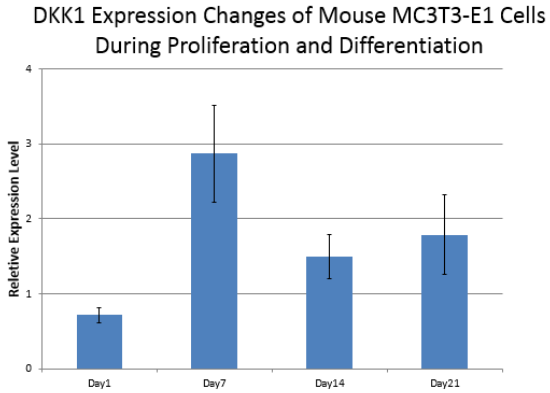

Figure 1. DKK1 relative gene expression (normalized to GAPDH, a housekeeping gene) in MC3T3-E1 cells is lowest on Day 1, peaks on Day 7, and then decreases during osteoblast differentiation on Days 14 and 21. This study identified the approximate timing of DKK1 maximum expression, which was then used to estimate when the addition of DKK1-Ab would have the greatest effect.

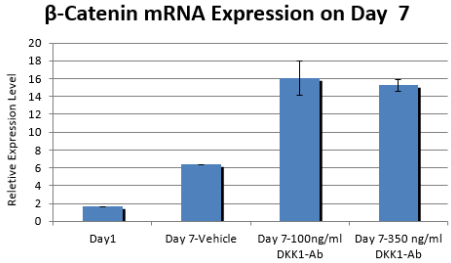

Figure 2. β-Catenin relative gene expression (normalized to GAPDH) in MC3T3-E1 cells significantly increased in both 100 ng/ml and 350 ng/ml DKK1-Ab supplemented treatment groups compared to vehicle. Osteocalcin (OCN) and Collagen type 1 α 1 chain (Col1A1) genes are associated with osteogenic differentiation. OCN increased by 1.4-fold (100 ng/ml DKK1-Ab group) and 1.8-fold (350 ng/ml DKK1-Ab group) compared to vehicle by Day 7. Col1A1 increased by 2.8-fold (100 ng/ml DKK1-Ab group) and 4.5-fold (350 ng/ml DKK1-Ab group) compared to vehicle by Day 7.

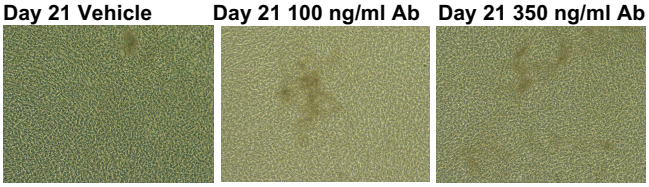

Figure 3. Representative images demonstrate DKK1-Ab treatment groups had increased mineral deposition relative to vehicle at day 21 when cultured in osteogenic media.

Conclusions: Addition of DKK1-Ab effectively neutralized DKK1 produced by MC3T3-E1 cells as demonstrated by a significant increase in β-catenin gene expression which promoted osteogenic gene expression and mineral deposition.

Future Directions: To neutralize DKK1 *in vitro* in human osteoprogenitor cells and *in vivo* in a mouse bone defect model.

Support: Funding provided from the National Institutes of Health, National Institute of Dental and Craniofacial Research (NIDCR) R01DE021103 and the UConn School of Dental Medicine Summer Research Fellowship.

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Evaluation Of The ParrotMD Medication Adherence Tool In Patients With Chronic Diseases In Kisoro, Uganda

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In Uganda, chronic illnesses/diseases (HIV, TB, CVD) is the leading cause of death. These medical diagnoses often require long term pharmacotherapy plans in order to prevent or prolong a decline in a patient's health. The ParrotMD is a recording tool that allows health professionals to place individualized messages that patients can replay at home; it's intended to be utilized as a medication adherence tool. Prior to this study the ParrotMD device had not been tested with patient populations to determine patient satisfaction, usage, and the device effectiveness in improving a patient's adherence. It was our expectation that the usage of the ParrotMD device as an intervention tool would result in an increased adherence compared to subject's baseline. The implementation of this project was done through the Mutolere Hospital in Kisoro, Uganda. The study included a pre- and post- interventional interview which aimed to assess adherence levels and attain patient feedback on the device itself. Patients also received a ParrotMD device for fourteen to twenty-one days after completion of the pre-interventional interview. Each device contained a recording of the names and dosage of each medication the patient was taking for their chronic illness and the date of their post-intervention interview; all of which was recorded in their preferred language (English or local languages). Thirty participants completed the initial interview and received a ParrotMD device, 72% the proceeded to complete the follow up interview and their results are included in this data analysis. No significant change in adherence levels was identified druing this study. Subjects found the instructions on the ParrotMD understandable and the device easy to use. Approximately 91% of participants rated the device as being helpful to them. In addition, we asked each subject to provide suggestions based on their experience with the ParrotMD device. Approximately, 19% felt that the device was fine just the way it was and needed no adjustments. Over 48% of the critiques were in regards to the logistics of the device; access to replacement batteries, and possible accidental HIV status disclosure. An additional, 19% felt that the device should include more health related messages; including the date of their next appointment on the device as a reminder. This project was not able to conclusively determine if the utilization of the ParrotMD can have an impact on medication adherence. However, this may be due to other factors as it appears that our subjects were already adherent to begin with. This study however does Overall further studies should be conducted to analyze other possible roles that ParrotMD may address in resource limited health care settings.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Peak Caspase-1 p20 Levels During ST Elevation Myocardial Infarction Correlate With Pre-existing Hypertension, Age And Post-infarction Cardiac Dysfunction

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Background- Increased inflammation contributes to the development of myocardial infarction (MI) and adversely impacts infarct healing. Caspase-1 is an end effector of inflammasome activation and is an important mediator of systemic inflammation. Caspase-1 is cleaved to produce a 20 kDa (p20) peptide upon activation. Activated Caspase-1 activates downstream cytokines IL-1β and IL-18. Previous work demonstrated that the p20 is elevated in patient serum during and after acute MI.

Objective- The aim of this study was to further elucidate the relationship of Caspase-1 p20 and risk factors for MI. Between 12/10/2007 and 3/28/2016, 170 eligible patients with acute MI were enrolled that had complete information on p20 levels.

Method- Using a solid phase enzyme-linked immunosorbent assay, the 20 kDa peptide was detected in serum during ST elevation (STEMI) and non-ST elevation (NSTEMI) MI as well as after MI. Cardiac function post-MI was evaluated via standard-of-care echocardiography.

Results- There is a positive correlation between age and peak p20 level during acute MI ($P=0.01$, linear regression, $n=170$). In STEMI but not in NSTEMI subjects, pre-existing hypertension (HTN) was associated with a 50.3% higher average circulating peak p20 level during acute MI than those without HTN ($P=0.0056$, Wilcoxon, $n=31$ for both groups-those with HTN and without HTN), suggesting a greater degree of inflammasome activation in HTN patients during STEMI. In these STEMI subjects, the existence of diabetes mellitus or smoking was not associated with a higher peak p20 level during acute MI. There is a trend for all acute MI patients to have a reduced post-MI cardiac function as quantified by LV fractional shortening in echocardiography ($P=0.05$, Spearman correlation, $r=-0.35$, $n=31$).

Conclusion- Older subjects had more elevated peak p20 levels during acute MI, consistent with the concept of a larger inflammasome response to MI as age increases. Inflammasome activation is more pronounced in HTN patients during STEMI, implying a greater degree of inflammatory response in the presence of HTN. A greater extent of inflammasome activation during STEMI may be associated with a worse LV function subsequently.

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Initial Fibular Displacement as a Predictor of Medial Space Widening in Weber B Ankle Fractures

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Introduction: Weber B ankle fractures are distal fibular fractures that extend to the talar dome. They can be stable or unstable, involving the medial malleolus and/or deltoid ligament. Determining stability is important as research shows better long term outcomes with operative fixation in deltoid deficient (unstable) fractures[1]. Manual stress examination is the gold standard to diagnose deltoid disruption[2], but can cause pain to patients. Gravity stress exams are an alternative due to comparable accuracy and ability to impose less discomfort. Fracture displacement can be assessed on plain radiographs, and degree of talar displacement and number of malleoli fractured can be strong predictors of outcome. The purpose of this study was to determine the relationship between initial fibular displacement and medial clear space widening on a gravity stress radiograph to determine its ability to predict medial deltoid instability.

Methods: We conducted a retrospective review of all UConn patients from Aug 2014 to Apr 2016 with isolated Weber B fractures, including only those with both initial injury films and gravity stress view (n=17). On the mortise view, the medial clear space (MCS), lateral fibular displacement (LFD), and fibular shortening (FS) were measured (Fig. 1).On the lateral view, anterior to posterior fibular gap (APFG) was measured. On the gravity stress view, the medial clear space (MCS-W) was measured. MCS-W≥5mm was considered unstable[3]. We used T-tests to calculate mean and standard deviation. Correlation and linear regression analyses were run with each variable relative to MCS-W. ROC analysis was used to determine sensitivity (SN) and specificity (SP).

Results: There were significant differences in the LFD (p=0.047), and APFG (p=0.00001) between stable and unstable fractures, but not FS. Significant correlations with MCS-W were found for LFD (0.69, p=0.002), and APFG (0.72, p=0.001), but not FS (0.34, p=0.18). Linear regression revealed ability to predict MCS-W for LFD (Coefficient=1.12, R2=0.48, p=0.002) and APFG (Coefficient=2.57, R2=0.52, p=0.001) but not FS (Coefficient=0.67,R2=0.11,p=0.18). ROC analysis for APFG showed that a cutoff of 1.0 mm yielded SN and SP of 100% and 100%.

Conclusion: Initial fibular displacement, represented by anterior to posterior fibular gap, is a strong predictor of medial clear space widening in Weber B ankle fractures. This can be assessed on the original injury radiograph. A cutoff of 1mm showed a specificity of 100% and a sensitivity of 100% in predicting deltoid integrity. In the future, it may help avoid patient discomfort with a stress view or the costs of additional diagnostic testing.

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Unobtrusive Gait Velocity Measurement in a Geriatrics Outpatient Clinic

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Objective: Gait velocity is a simple, robust predictor of health outcomes in older persons. It has been shown to be a reliable predictor for poor quality of life, future hospitalizations, nursing home placement, physical and cognitive functional decline, falls, and mortality.[1,2] However, clinicians do not regularly utilize this "5th vital sign" due to the lack of a routine, objective, and unobtrusive measurement method that complements the everyday workflow of clinical settings.[3] We sought to address this problem by establishing the validity and feasibility of using a radio frequency identification device (RFID) to measure gait velocity among geriatric patients.
Methods: We recruited patients from UConn Health's geriatrics clinic over 4 weeks. Participants (N=50) wore an armband containing a RFID tag with a unique ID and were instructed to walk down the clinic hallway at their usual pace. Wall-installed RFID readers recorded the time it took subjects to walk 4.3-meters. Participants' walks were simultaneously timed via a stopwatch, the "gold standard." Two gait velocity measurements, based on RFID and stopwatch recordings, were calculated for each participant and difference scores (RFID gait velocity – stopwatch gait velocity) were plotted. T-tests determined if difference scores varied according to patient characteristics. Participants and 9 clinic staff were also asked questions regarding acceptability of using the device.
Results: Subject mean age was 80.9+8.0 (62-99) and 66% were female. Average gait velocity (m/s) via RFID was 0.849+0.268 (0.132 to 1.471) and via stopwatch was 0.852+0.269 (0.126 to 1.466). Average difference score was -0.003+0.035. Participants who reported difficulty walking a quarter mile (42%), used an assistive device (24%) or reported fair/poor health (18%) had higher (worse) gait velocity using either RFID or stopwatch ($p<0.01$ for each comparison). However, these characteristics did not impact difference in gait velocity. Overall, 50 (100%) and 46 (92%) participants agreed/strongly agreed that they felt comfortable having their gait velocity measured and that they wanted their providers to track this over time. Also, 8 of 9 providers indicated that measuring gait velocity did not interrupt office procedures.
Conclusions: Measuring gait velocity using RFID technology is unobtrusive and provides measurements comparable to the research "gold standard." Integrating gait velocity measurement into "real-world" clinical settings may help to support T2 translation and the Precision Medicine effort.

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Double-Layer Reconstruction of Delaminated Rotator Cuff Tears Using Human Cadavers

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Background: Re-tear rates following rotator cuff repair are reported to range from 11% to 95%.[1,2] Numerous studies have tried to identify the reasons for rotator cuff repair failure, but have yet failed to provide conclusive results. An important morphological factor that has to be considered is the presence of a delaminated rotator cuff tear, in which there is a degenerative tear between the rotator cuff layers.[3] Delamination tearing as a finding in rotator cuff surgery has been reported to be between 38% and 92% in the literature,[4] yet very few studies have described surgical techniques used for delaminated rotator cuff tears, and a biomechanical rationale has not yet been presented.
Methods: The objective of this study was to use a cadaver model to evaluate footprint reconstruction, gap formation under cyclic loading, and load-to-failure of three different repair constructs for delaminated rotator cuff tears. The three repair types used were the knotless double-layer cinch-stitch repair, transosseous equivalent double-row repair with medial row sutures, and a knotless Fibertape double-row repair. These repairs were equipped with optical markers, and using a Tekscan sensor, contact pressure, force, and area measurements were taken.
Results: Contact pressure, contact area, and load-to-failure were similar across all groups. Double layer reconstruction showed the highest percentage of footprint restoration. Also, double layer reconstruction restored displacement under cyclic loading closest to native conditions.
Conclusions: Double layer reconstruction of delaminated rotator cuff tears demonstrated excellent footprint restoration through the whole range of motion, while restoring displacement under cyclical loading closest to the intact tendon. Results suggest a safe earlier start of postoperative rehabilitation with double layer reconstruction compared to other repair techniques. This finding indicates that double layer reconstruction is a viable alternative for treatment of anterior instability with glenoid bone loss in patients with delaminated tears.

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Osteogenic Markers in Response to Piezocision in a Rat Model

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Objectives: Increasing treatment efficiency is a goal of orthodontists that could potentially improve patient satisfaction. Among the surgical procedures proposed to work in conjunction with conventional orthodontic treatment, piezocision is the least clinically invasive procedure. It creates a flapless mucosal incision in the alveolar bone, thus affecting dentoalveolar remodeling and potentially enhancing the rate of tooth movement. The purpose of this study was to evaluate, in the rat model, whether local piezocision results in an increased rate of tooth movement, and to analyze the osteogenic genes activated after experimental orthodontic movement and piezocision.

Methods: Seventeen-week-old male Wistar rats were used as the animal model. In the initial pilot study, animals were divided into 3 groups of 5 rats each: 1) control (CTRL) 2) orthodontic tooth movement (OTM) – only experimental tooth movement 3) orthodontic tooth movement + piezocision (PIEZ) - local piezocision was performed in addition to tooth movement. Orthodontic force (10-15 g) in both OTM and PIEZ groups was delivered by attaching a nickel-titanium coil spring between the right first molar and the incisors. The PIEZ group received one piezotome incision on the mesio palatal aspect of the first right molar in addition to the orthodontic spring. For this part of the research, animals were euthanized 7 days after intervention. The amount of tooth displacement was recorded through Polyvinylsiloxane (PVS) impressions of the interproximal space between the first and second right molars. Additionally, the alveolar bone in the region of interest (molars in the right hemimaxilla) was excised and frozen in liquid nitrogen for RNA analysis. Frozen bone pieces were then homogenized using a mortar and pestle then the polytron. Trizol™ reagent (Thermo Fisher Scientific Inc, Waltham, MA, USA) was added to the bone powder for RNA extraction. For each group, RNA was extracted from individual rats and was pooled for quantitative reverse transcription PCR. We used a Rat Osteogenesis PCR array (RT^2 profiler PCR array, Qiagen, Hilden, Germany) to quantify 84 genes associated with osteogenic differentiation.

Results: The goal of this pilot study was to validate our method of RNA extraction and analysis from alveolar bone of rats after experimental tooth movement and local piezocision. Our preliminary results showed that we successfully extracted RNA from the frozen alveolar bone of rats. Our PCR results revealed different expression of genes among CTRL, OTM and the PIEZ groups. We observed significant decreased expression of Bmp1, Col1a1, Col1a2, Col3a1 in PIEZ in comparison to CTRL group. When comparing OTM and PIEZ groups, we found significant decreased expression of Dlx5, Mmp2, Mmp9, Tgb3 and Tbgr2 in the PIEZ group.

Conclusions: These preliminary results suggest decreased expression of specific genes relevant to bone mineralization and osteoblast differentiation in the PIEZ group. These results confirm the feasibility of this method to evaluate osteogenic gene expression from RNA extracted from alveolar bone.

Future Directions: In addition to performing these experiments in more animals to validate our results, we will compare gene expression of osteogenic markers among CTRL, OTM and PIEZ at additional time points before and after intervention.

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Short- and Long-Term Radiographic and Clinical Evaluation of Multilevel Lateral Lumbar Interbody Fusion in Adult Scoliosis Patients

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Objective: Traditional approaches to correcting spinal deformity are associated with significant morbidity, complications, and costs due to long operative, recovery, and hospitalization times, increased infection, blood loss, and thromboembolism rates, and even persistent neurological deficits and death [1]. Lateral lumbar interbody fusion (LLIF) offers a minimally invasive solution to treat spinal pathology including debilitating degenerative stenosis, spondylolisthesis, scoliosis, and kyphotic deformities. However, long-term literature on multilevel LLIF is scant. We analyzed the long-term clinical and radiographic outcomes of adults with degenerative conditions treated with LLIF at ≥3-contiguous levels of fusion.
Methods: Clinical data was obtained preoperatively (P0) and at 6-weeks (6w), 3-months (3m), 6-months (6m), and ≥1-year postop (P2) via surveys on pain, physical/mental health, and disability (VAS leg/back, SF12, ODI). Radiographic data at P0, immediate-postop (P1), and P2 was measured in Surgimap and confirmed by the senior author, and included pelvic tilt (PT) and incidence (PI), sacral slope (SS), lumbar lordosis (LL), Cobb angle (CA), cage subsidence (CS), and disc-height-index (DHI; via Farfan method) [2,3]. Preop and postop parameters were compared using ANOVA or Wilcoxon-rank test, with Bonferroni correction. All adults from the practice of Dr. Moss who underwent a multilevel LLIF for degenerative pathology and deformity were included, excluding those with previous fusions.
Results: 29 patients were included; mean 4.6 levels were treated per patient (range, 3-9). Mean age at P1 (64y) and mean time from P1 to P2 (1.8y) were controlled for. VAS-back scores decreased from P0 (5.6cm) to 3m (3.2, p=.011), 6m (2.6, p=.003), and P2 (2.8, p=.020). VAS-leg scores decreased from P0 (5.7cm) to 6w (3.9, p=.012), 3m (2.6, p<.001), 6m (3.4, p=.012), and P2 (3.3, p=.025). SF12 scores increased from P0 (26 points, p=.019), 6w (26, p=.026), and 3m (28, p=.047) to P2 (33). ODI decreased from P0 (23) to 6m (16, p=.010) and P2 (15, p=.010), and from 6w (23) to 3m (18, p=.039), 6m (p=.005), and P2 (p=.006). PT, PI, and SS were unchanged. LL increased from P0 (48°) to P1 (52°, p=.005) and P2 (52, p=.038). CA decreased from P0 (21°) to P1 (8°, p<.001) and P2 (9°, p<.001). CS increased from P1 to P2 at L5-4 (p=.014), L4-3 (p=.001), L3-2 (p=.021), and L2-1 (p=.046). DHI decreased from P0 to P2 by 26% (p<.001), and from P1 to P2 by 21% (p<.001).
Conclusions: Patients recovered swiftly with long-term pain improvement, and regained mental-physical functionality, despite subsidence and DHI loss. Stabilized pelvic parameters and greatly improved LL and CA indicate successful deformity correction. LLIF is a viable treatment option for multilevel spinal pathology.

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Discharge of Patients with Alcohol-Related Impairment in the Emergency Department: The Role of Alcohol Tolerance and Acute Injury

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Importance: Ethanol intoxication/chronic alcohol abuse are significant public health issues. Alcohol-related medical, traumatic, and/or psychiatric issues precipitate many ED patient presentations. JAMA states alcohol intoxication is third leading cause of death in US (85,000 deaths/year).
Objective: Hypothesize clinicians' inhibited ability to recognize alcohol intoxication due to confounding distractors, attention to more acute conditions, and patients' varying degrees of tolerance to alcohol results in discharge of legally intoxicated patients(BAC >0.8)
Participants and Setting: Two reviewers independently conducted chart reviews for Emergency Department patients with plasma ethanol measurements >50mg/dL
Design, Outcomes, and Measures: Evaluated evidence of clinical impairment using pre-determined scale, presence/nature of acute medical/surgical conditions, and chronic alcohol misuse. BAC was determined by multiplying plasma ethanol measurements by 0.00085. BAC at time to achieving clinical sobriety or demonstrating symptoms and or signs of withdrawal calculated by decreasing 0.02/hour. Evaluation based on stated presence of alcohol misuse and compared to concurrent estimated BAC. Limitations include the assumed rate of ethanol elimination and the fact that clinicians obtained blood alcohol measurements on 2% of patients; did not capture breathalyzer, only screening measurements. Hypothesis was formulated during data collection.
Results: 220 patient encounters, 27% women, 73% men, aged 17 – 83. 46% presented acute traumatic injuries, 20% head injuries and/or hypotension (BPs < 80mmHg). 14.5% developed withdrawal symptoms while in ED with estimated BACs ranging 0 – 0.304. 60% of patients considered clinically sober and discharged from ED with estimated BACs ranging from 0 – 0.360 (mean BAC: 0.115 median BAC: 0.102). 41% of these patients had BAC >.08. 78% of those developing withdrawal symptoms or discharged with alcohol present were chronic alcoholics. Following a derivation set, inter-rater reliability exceeded 0.8.
Conclusions: Clinicians need to have high suspicion for alcohol when assessing/discharging ED patients. Alcohol tolerance and confounding acute presentations significantly alter clinicians' cursory assessment of alcohol-related impairment. Implications for triage decisions regarding assessment of blood ethanol as well as discharge decisions with responsible parties. Future studies can assess patients BAC at time of discharge. The AMA Task Force to Reduce Opioid Abuse believes up to physicians and policymakers to stop substance disorders. Difficult to treat/educate patients from harmful ethanol use if presence of alcohol isn't recognized

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The Effects of Stride Length and Foot Progression on Pelvic Rotation in Collegiate Pitchers

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In order to deliver a pitch, kinetic energy must be efficiently transferred from the lower body through the pelvis and core to the pitching arm [1]. However, little research has been done to investigate the contribution of the lower extremities to pelvic rotation or forces placed on the pitching arm. The purpose of this study is to determine the relationships between (1) stride length and pelvic rotation and (2) foot progression and pelvic rotation. Ninety nine collegiate pitchers participated in this study and their pitches were analyzed using three dimensional motion analysis. A mixed effects random intercept regression model was used to identify associations between stride length and foot progression and pelvic rotation. There was a five degree decrease in pelvic rotation at FC for every 10 centimeter increase in stride length. There was a three degree decrease in pelvic rotation at MER for every 10 degree increase in internal foot progression. Therefore, if the stride foot lands in a more internally rotated foot position or if the pitcher strides too long, there is a decrease in pelvic rotation. Decreased pelvic rotation has been linked to more force being placed on the elbow and shoulder, thereby increasing the likelihood of pitching arm injuries [2]. Therefore, coaches should work to find an ideal stride length and teach players to step inwards toward home plate in order to improve pelvic rotation and reduce pitching arm injuries.

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Dysbiosis of Adherent Bacteria on Aberrant Crypt Foci with a Synchronous Polyp

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Introduction: The changes in the microbiome along the adenoma-carcinoma sequence in colorectal cancer have been well established. Studies have shown that there are significant shifts in the microbial community composition as the underlying colonic mucosa undergoes neoplastic changes. One explanation for these shifts is the driver-passenger model, which states that there are early changes in the microbiome that drive tumorigenesis that precede a shift to passenger communities that may stall or stop the process. Aberrant crypt foci (ACF) are the earliest detectable dysplastic changes in the colon, and their associated microbiome has never been characterized. These early lesions should therefore express mroe tumorigenic bacteria. An evaluation of the ACF microbiome would both elaborate the adenoma-carcinoma microbial shift sequence and demonstrate the driver-passenger model. Finally, this study presents the first characterization of bacteria specifically adherent to ACF.
Methods: High-definition chromoendoscopies were performed on 23 consenting patients. Biopsies were taken from ACF tissue and adjacent normal mucosa in the proximal colon. The presence of synchronous polyps was noted. Biopsies were submerged in OTC fluid and stored at -80 ^{o}C. DNA was extracted from whole biopsy samples using a soil DNA isolation kit. Partial bacterial 16s rRNA genes (V4) were amplified by a modified MARS 16s processing pipeline method. Sequences were aligned to a library database. Relative abundances of reads were log-transformed for statistical analyses.
Results: Out of 23 patients in the study, ACF were identified in 12, and 3 of those patients had polyps. In every patient, there were no statistically significant differences between the adherent bacteria in ACF and adjacent normal mucosa samples. The overall microbial diversity and abundance of several bacteria were found to be significantly different between patients with and without a synchronous polyp. Of note, known anti-inflammatory genera, Lactobacillus (p-value = 0.0009) and Bifidobacterium (p-value = 0.032), were enriched in ACF with synchronous polyps.
Conclusions: Significant microbial community changes only occurred alongside more advanced dysplastic lesions. In the presence of a local polyp, enrichment of anti-inflammatory bacteria is suggestive of a late passenger-type shift that inhibits further dysplastic development of ACF. This dysbiosis may contribute to why only few ACF progress to the adenoma stage. Yet, because the ACF did not adhere bacteria any differently than adjacent normal mucosa, there may be a widespread field affect taking place. Further studies are needed to elucidate the mechanism of the bacterial community shifts..

Supported by: The UConn School of Medicine Summer Research Fellowship

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Creation of Remote Active Learning Modules (ReALMs) for Delivery of Clinical Care (DOCC)

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In the 2016-2017 academic year, the University of Connecticut Schools of Medicine and Dental Medicine introduced the M-Delta curriculum, which moves away from lectures and focuses on team-based learning and self study. In M-Delta, first year medical and dental students are trained in clinical medicine through the Delivery of Clinical Care (DOCC) course. Currently, DOCC lacks educational video content for students to prepare for their clinical skills experiences. In addition, the previous curriculum for clinical medicine was scheduled to complement the concurrent anatomy course. However, many lessons in DOCC are scheduled before students have any exposure to anatomy. This project filled this need by creating high quality Remote Active Learning Modules (ReALM) which can be accessed online by all students to complement readings and ultimately enhance learning. In addition, there is a focus on introducing relevant anatomy for physical examinations through overlaid digital animation. The ReALMs also used a variety of special effects to enhance delivery of content. ReALMs were created for Introduction to DOCC, Medical History (Parts I, II & III), Adult Vitals, CORE Physical Exam, Pediatric Assessment, Pediatric Measurements, The Write-Up, Mental Status Exam, Smoking Cessation, Pulmonary Exam, Head & Neck Examination, Eye Examination, and Ear Examination. Feedback for the CORE Physical Exam ReALM was collected after the first year students (N=152) completed the module and practiced the clinical skills on a patient instructor (PI). Surveys indicate that students agree that the CORE PE video helped them improve understanding of the proper techniques (M 4.76/5.00, SD 0.55), understand the relevant anatomy and physiology (M 3.75/5.00, SD 1.10) and feel more comfortable working hands-on with PI's (M 4.18/5.00, SD .86).

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Compressive Loading Rescues The Effects Of Botox Injection Into The Masseter In The Mandibular Condylar Cartilage And Subchondral Bone

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Objective: To evaluate whether the effects of botulinum neurotoxin (botox) injection into the masseter in the mandibular condylar cartilage (MCC) and subchondral bone are transient and/or if loading would rescue the osteopenia and cellular changes after injection.

Methods: Botox (0.3 U) was injected into the right masseter of 6-week-old female mice, while 8 mice were used as control and received no injections. 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 and control mice. Experimental and matching control mice were sacrificed 4 or 8 weeks after botox injection. Another group of mice were subjected to temporomandibular joint (TMJ) compressive loading, by forced mouth opening, 4 weeks after Botox injection. Mice were dissected and examined by micro-CT and histology. Sagittal sections of condyles were stained for TRAP, EdU, and toluidine blue.

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 and control mice, 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. However, compressive loading reversed the reduced bone volume and density and the cellular changes in the MCC caused by Botox injection.

Conclusions: The effects of Botox injection into the masseter muscle in the MCC and subchondral bone are not transient, but TMJ compressive loading rescues the negative effects of botox injection in the MCC and subchondral bone.

Future Directions: To evaluate the effects of Botox injections into the masseter in older mice that present MCC degeneration.

Support: The UConn School of Dental Medicine Research Fellowship.

Pentoxifylline as a Cause of Drug-induced Liver Injury: A Case Report and Literature Review

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Pentoxifylline is a methylated xanthine derivative used in the treatment of intermittent claudication due to peripheral vascular disease. The use of pentoxifylline in the treatment of claudication is controversial, with studies demonstrating from minimal to moderate efficacy[1]. Generally the drug is well tolerated, with the most common side effect being gastrointestinal upset[2]. Pentoxifylline has been consistently linked to drug induced hepatitis, however only one case report[3] exists describing this phenomenon.

The patient is a 66 year-old male presenting to the emergency department with severe weakness, lightheadedness, icterus, and lower extremity edema. His past medical history is significant for coronary artery disease, peripheral vascular disease, type II diabetes mellitus, and COPD. Of note he started taking pentoxifylline three months prior for claudication symptoms, which, since its initiation, has been causing significant nausea, vomiting, and diarrhea. Despite this, he continued use of the drug. On presentation he was found hypotensive at 70/40 mmHg, with elevated liver function tests (LFTs), including AST 203 u/L, ALT 94 u/L, alkaline phosphatase 337 u/L, total bilirubin 5.29 mg/dL and direct bilirubin 4.02 mg/dL. Ultrasound confirmed an enlarged and echogenic liver, but a surgically removed gallbladder and no evidence of biliary disease. His symptoms were alleviated with fluid administration, but his LFTs remained elevated. He was worked up extensively for causes of his transaminitis, but hepatitis A serology, hepatitis B serology, hepatitis C serology, HFE gene, ANA, anti-Smooth muscle antibodies, mitochondrial antibodies, and cerulloplasmin levels were all within normal limits. Drug induced liver injury was ultimately diagnosed, with pentoxifylline being the only likely culprit. His LFTs returned to baseline three weeks after terminating the drug.

The diagnosis of drug induced liver injury (DILI) is a diagnosis of exclusion, but rises on a differential when an extensive workup is unremarkable. Liver injury is reported as a rare but serious complication of pentoxifylline therapy. The single reported case from Saez-Royuela[3] described hepatitis in an 81-year-old female weeks after starting pentoxifylline. Laboratory tests revealed a total bilirubin of 20.1 mg/dL, ALT 577 u/L, AST 293 u/L, and alkaline phosphatase 1387 u/L. These two cases show great similarities—both have cholestatic LFT elevations, with negative workup for other possible causes, and a slow return to baseline over weeks after stopping the drug. A liver biopsy would be required for definitive diagnosis.

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Modeling Human TET2/NRAS Mutant Myeloid Leukemia in THP-1 cells

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The co-occurrence of mutations in epigenetic modifiers and signaling molecules is a common phenomenon in the development of myeloid leukemia. TET2, involved in active DNA demethylation, is one such epigenetic modifier lost in hematologic malignancies, notably in 37% of chronic myelomonocytic leukemia cases. Mutation of the RAS signaling factor, specifically NRAS in 14% of myeloid malignancies, can occur in conjunction with TET2 loss during leukemogenesis. Our lab has previously shown the deleterious effects of TET2 loss and NRAS mutation in a mouse model. Tet2 cKO mice and NrasG12D mice produce double mutant progeny that present with a lethal CMML/JMML-like disease after induction of TET2 loss and Nras mutation by PIPC treatment. Tet2/Nras mutant mice show increased activation of the MAPK and PI3K/AKT signaling pathways, and bone marrow cells from these mice show hypersensitivity to GM-CSF. In this study, we attempt to translate our murine model to human cells using the THP-1 cell line. THP-1 is a human AML cell line that carries the NrasG12D mutation, in addition to other genetic abnormalities like the MLL translocation. By knocking down TET2 expression in this cell line, we seek to recapitulate the Tet2/Nras double mutant genotype in human cells. Methods: THP-1 cells were infected with virus directed against TET2 or a scramble control. Successfully infected cells were sorted by flow cytometry based on GFP positivity. GFP+ cells were grown in liquid culture in RPMI 10% FCS P/S with L-glutamine. The TET2 KD THP-1 cells and scramble controls were analyzed via flow cytometry, Western blot, liquid culture growth curve, CellTiter-Glo luminescence assay, and methocullulose colony formation assay. Results: Knockdown of TET2 in THP-1 cells skewed differentiation from the granulocyte to the monocyte lineage, with a significant increase in expression of CD14, a monocytic surface protein, and significant decrease in expression of CD15, a granulocyte marker. TET2 KD THP-1 cells showed increased signaling through the MAPK and PI3K pathways, as evidenced by increased phosphorylation of Raf1, Erk1/2 and Akt signaling molecules. TET2 KD cells showed increased sensitivity to the MEK inhibitor, binimetinib, with a significant decrease in the number of viable cells at the end of 8 days and a left-shifted survival curve when cultured with increasing doses of the drug. Finally, GM-CSF stimulation significantly increased colony formation in TET2 KD THP-1 cells compared to scramble controls. Conclusion: We have shown that TET2 KD THP-1 cells resemble Tet2/Nras double mutant mice, and that the experimental data previously collected in our mouse model is also true in human leukemia cells. These data may also be true in human leukemia patients with TET2 and NRAS mutations.

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Micro-Movement of Full Zirconia CAD/CAM Abutments Within Titanium Implants

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Objective: Implant dentistry is trending towards aesthetics, leading to the development of ceramic abutments. One ceramic material of choice is zirconia due to its flexural strength, fractural toughness and white color. Failure behavior and origins of commercially available CAD/CAM abutments have been examined in cyclic fatigue to gain insights into the role of abutment design. One potential failure mechanism involves micro-movement at the screw seat (or elastic bending) allowing contact between the zirconia and the inner implant surface. This research aims to determine if failure of zirconia abutments is attributable to micro-movement at the screw seat or internal binding leading to an increased lever arm.
Methods: The primary method of data collection in this study was qualitative. Previously tested (Kelly & Rungruanganunt, 2016) commercial CAD/CAM zirconia abutments were re-examined following dynamic fatigue testing. These abutments were removed from the implants, measured, and looked at physically under stereo light microscope to examine for possible differences in dimensions and design. The full zirconia abutments (Straumann and Atlantis) were further examined to evaluate binding within the abutment. One Straumann abutment-implant system was sent to Dr. Sumita Ho at the University of California San Francisco to perform 3D x-ray evaluation to look for differences in bending contact (Results pending). An intact specimen was cut, measured, and constructed in SolidWorks 3D CAD Design Software and tested under static load of 200N to evaluate stress concentration.
Results: Side by side comparison of all four abutments demonstrated significant design differences that correlate with fatigue results. Notably, optical examination of Straumann and Atlantis abutments showed markings clearly indicating binding within the implant and a cross section cut of the Straumann abutment illustrates binding leading to failure at the screw seat due to the increased lever arm.
Conclusions: Due to the elastic moduli differences (titanium/zirconia), bending leads to binding below the screw seat and fracture involving an increased lever arm. It can be concluded that stress concentration happened at the screw seat/thinnest wall of zirconia.
Future directions: A valuable future direction to advance this line of research would be to design Straumann CAD/CAM zirconia abutments with shortened abutment lengths and reinforced screw seats and to repeat the fatigue testing to evaluate the best design for calculated stress reduction.
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The Effects of Social Support, Stigma, and Depression on the HIV Treatment Cascade in the Aging Population

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Introduction: HIV treatment has been conceptualized as a care cascade where patients progress from diagnosis to viral suppresion. Unfortunately, many leaks within the care casade result in only 25% of the HIV-positive individuals in the US reaching viral suppression [1]. The purpose of this study is to determine how social factors like social support, stigma, depression, and locus of control effect patient's movement through the care continuumm. Older HIV-positive individuals is a growing demographic [2]. Therefore, this study specifically looks at how older patients are affected by these social factors as they travel through the cascade.
Methods: A convenient sample of English speaking HIV-positive patients were surveyed during their appointment at the UCHC Infectious Disease Clinic. The survey included assessments of social support, HIV stigma, depression, and locus of control [3-6]. Patients older than 50 completed an ageism assessment [7]. Successful progresion through the care cascade was marked by patients appointments, viral load, and CD4 count. A patient was considered retained if they made 2 or more appointments and had no no-shows in the previous year.
Results: A total of 58 subjects were enrolled in the study. Of the subjects, 57% were male, 45% White non-Hispanic, 29% non-Hispanic AA, and 26% Hispanic. The mean age was 53.4 years (sd=11.8), and 78% of subjects were above the age of 50. More than a third of subjects reported significant depressive symptoms. Most (62%) of the subjects had an undetectable viral load in the previous year, and 74% of subjects had a CD4 count higher than 350. Only 47% of patients were retained in care. There was no statistical difference between outcome variables and age groups or sex. Virally suppressed subjects had a higher external locus of control ($p=0.07$) and higher levels of social support ($p=0.13$). Patients with a CD4 count less than 350 had a higher internal locus of control ($p=0.06$). Patients retained in care were associated with lower levels of social support ($p=0.09$), lower levels of internal locus of control ($p=0.09$), and a corespondingly higher levels of external locus of control ($p=0.10$). There was no significant associations between outcome measures and depression, stigma, or ageism.
Conclusions: Locus of control is a marker for success in HIV care. It is possible patients with a high extrenal locus delegate control to health care providers and are more compliant. Parodoxally, patients with higher social support were not retained in care but reached viral suppression. Furthermore, age did not appear to be a factor in patients success in care. Assesements on locus of control and social support may be used to identify patients who are unlikely to remain in the HIV care cascade regardless of age.

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Examining the Role of the DNA Repair Protein PARP During the Life Cycle of Herpes Simplex Virus

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Herpes simplex virus 1 (HSV-1) is a member of the herpesviridae family and is a common human pathogen (1). HSV-1 has a linear double-stranded DNA genome that is replicated in the nucleus of host cells and results in the formation of branched concatamers, most likely through DNA recombination and repair processes that require cellular factors (2). Research over the past decade has illuminated a complex interaction between HSV-1 and the cellular DNA damage response (DDR), which comprises pathways involved in DNA repair, cell cycle regulation, apoptosis, and transcription. While many DDR proteins are utilized by HSV-1 during its life cycle, a growing list of these factors are inherently antiviral (3). Here, we investigated the role of Poly(ADP-ribose) polymerase (PARP) during HSV-1 infection. Given that PARP-1 is essential for a variety of cellular functions including DNA repair and transcription (4), we hypothesized that PARP-1 would be required for efficient HSV-1 replication. Interestingly, using a glioblastoma cell line that was engineered to stably express shRNA against PARP-1 or a non-targeting (NT) control, we found that depletion of PARP-1 lead to a slight increase in viral yield. These data suggested that PARP-1 activity was potentially antiviral. To combat many of the host cell antiviral strategies, HSV-1 utilizes an ubiquitin ligase, ICP0, to degrade cellular factors. Therefore, to test a potential role of ICP0 in combating a PARP-dependent antiviral mechanism, we examined the yield from the knockdown cells infected with an ICP0-null virus. We found that PARP-1 depletion significantly increased viral yield, supporting the notion that PARP-1 activity is antiviral and is constrained by ICP0. In addition, we found that PARP-1 is not degraded during HSV-1 infection. The viral genome that enters the cell is thought to contain multiple nicks and gaps; therefore, we hypothesized that PARP-dependent DNA repair of the incoming genome may inhibit subsequent steps in the viral life cycle. We examined if PARP was recruited to the incoming viral genome using immunofluorescence; however, we did not observe colocalization of PARP with markers of the viral genome, suggesting that PARP is not associated with this stage of the viral life cycle. We also examined the expression of viral genes in cells depleted of PARP and found a substantial increase in the protein expression of viral early genes ICP8 and UL12, without impacting the immediate early gene ICP4. Taken together, these data have identified PARP as a novel antiviral factor that directly and/or indirectly restrains the expression of a subset of viral genes. Future research will aim to further elucidate the antiviral activities of PARP during the HSV-1 life cycle.

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

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Posterior glottic stenosis (PGS) is a major problem involving scarring and narrowing of the larynx at the level of the glottis, most commonly caused by endotracheal intubation. Importantly, insulin-dependent diabetes is a factor associated with increased risk of developing PGS. In a previous study, we developed a rat model of PGS using a laryngofissure technique described by Nakagishi (2005). In this study, we harvested larynges from diabetic and non-diabetic rat models of PGS and conducted histological analysis of the tissue to look for inflammatory cells. The qualitative nature of the inflammatory reaction, characterized by presence of polymorphonuclear cells, plasma cells, or both, was then determined by an oral pathologist for each sample. High quality images of our histology samples were then created, and our data will guide future histological studies looking for more specific markers of inflammation in the hopes of creating medical devices designed to address the challenges of prolonged intubation in diabetic patients.

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Assessing the Acceptability and Usefulness of a Breast Cancer Treatment Booklet for Patients and their Accompanying Partner/Family Members in Haiti

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Background: Breast cancer is the leading cause of cancer-related death for women worldwide. In low and middle-income countries (LMICs), such as Africa or the Caribbean, recent studies have demonstrated that there is an increase in both incidence and mortality rate related to breast cancer. The relative survival rate, which is based on the mortality-to-incidence ratio, is low in LMICs due to the advanced stage at presentation and the lack of resources to combat the disease. In Haiti, 79% of women with breast cancer present with an advanced stage III or IV and 28% have metastatic breast cancer.
Objectives: 1. Assess the knowledge of women and their family members after provision of an educational booklet with the goal of improving their understanding of the disease and its treatment. 2. Identify potential causes of knowledge deficits among patients and their families.
Methods: Pre and Post-Booklet interviews were conducted at the Project Medishare Cancer clinic in Port Au Prince, Haiti. The IRB-approved surveys included questions about demographics, knowledge, and attitudes regarding breast cancer treatment. The pre and post-booklet surveys included similar questions allowing assessment of changes in the participants' knowledge and the efficacy of the booklet.
Results: A total of 20 subjects participated in the pre-booklet surveys. Of the initial interviewees, 16 believed that "being hit" is a risk factor in the development of breast cancer; but it is worth noting that most of the interviewees were unaware of additional risk factors. Almost all (19) of the patients reported not being taught about breast cancer from any sources and as a result, they had to rely on self-learning with limited resources available to them. In response to the early signs of breast cancer, most reported growing masses and nearly half of the participants believed that "itchiness" and "pain" were early signs of cancer. Regarding treatment, 19 of the initial subjects were aware that breast cancer is treatable and while every participant was aware of chemotherapy as an option, approximately half (9) of the participants believed natural remedies, including teas or concoctions, are effective means of treatment. Seven participants returned for a post-booklet interview. All improved in knowledge related to the different types, side effects, and prognosis of breast cancer treatments.
Conclusion: It is vital that patients have a clear knowledge of their prognosis and the necessary treatments because it is strongly impacts their willingness to continue treatment. The results showed a positive shift in knowledge for the patients who were exposed to the booklet. And the feedback from the participants regarding the booklet has been reported to the program to improve quality of care.

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Education Intervention To Improve Breast Cancer Study Participation By Young African American Women

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Importance: Breast cancer is the most commonly diagnosed cancer among African American women [1]. The Center for Disease Control and Prevention (CDC) found black women had a 41% higher breast cancer death rate than white women [2]. Black women under the age of 40 are found to have more aggressive cancer cell characteristics resulting in a poor prognosis [2,3].
Objective: To enhance education and understanding of the need for breast cancer screening in African American women and assess the willingness of these women to participate in the larger breast cancer screening trial. It was hypothesized that an education intervention will (1) decrease anxiety about breast cancer screening, (2) increase knowledge about personal risk of breast cancer, and (3) result in greater willingness to participate in the breast cancer study among women who show an increase in knowledge of breast cancer risks.
Participants and Setting: Open recruitment was conducted by targeting relatives of women with breast cancer. Participants were African American currently aged 25-39. An education intervention was conducted within local communities such as churches and community centers.
Design: A pre and post-education survey was administered with questions aimed at assessing rates of prior breast cancer screenings, anxiety, and knowledge about breast cancer risks in African American women between the ages of 25-40.
Results: 254 participants in the education programs completed pre and post-education surveys. 63% of the participants had previous breast cancer screenings. 24% of the participants initially indicated anxiety about breast cancer screening. Of these, 13% indicated a decrease in anxiety after the education program. 61% of the participants exhibited an increase in knowledge about breast cancer and screening. The mean score for knowledge of breast cancer risks increased from 1.84 to 2.12, with a t value of -4.97 and a p value of 0.00, indicating statistical significance. Of the participants who showed an increase in knowledge of breast cancer risks, 76% were more willing to participate in the long term breast cancer study.
Conclusions: An educational intervention for African American women between 25-40 years of age is beneficial in increasing knowledge about the risks of breast cancer in general. Of these women who have learned the importance of breast cancer screening, most are willing to participate in a breast cancer study. The educational intervention is a useful recruitment tool for enrolling participants in the larger breast cancer study. Further studies will be conducted to enhance retention of participants in the larger study in order to conduct annual screenings to detect breast cancer at an earlier and more treatable stage in this population.

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Silencing of the Connexin Genes in Developing Human Neurons by Antisense Oligonucleotides

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Introduction: Spontaneous electrical activity plays an important role in newborn neurons by supporting their differentiation, maturation and synaptic connectivity (1). Hypothesis: We hypothesize that connexin hemichannels provide depolarizing currents in this process (2).
Methods: Experiments were designed to: Proliferate human fetal cells in vitro; silence individual connexin genes using antisense oligonucleotides (ASOs), and determine the effect of this gene silencing on the physiological activity. In the first series of experiments, an ASO designed against the housekeeping gene HPRT, was tested at different time-points (days in vitro, DIV 10 - 13) to establish a time point which produced the most robust gene knock down. “ASO-HPRT” was compared to the control (no ASO treatment) by real-time PCR. Based on the above experiment, a 48-hour time point was chosen. Next, two different ASO sequences, targeting gene Cx26, were tested. Real time PCR was performed to determine the knock down of the four connexin genes of interest: Cx26, Cx36, Cx43, and Cx45. Beta-actin (ACTB) was used as a housekeeping gene. Lipofectamine and Mirus oligo transfection reagent were used to increase ASO penetration into neurons.
Results: In the control experiment, the expression of HPRT showed a 12% knockdown, while 60%-70% knockdown has been detected when cationic lipids were used. Transfection agent Lipofectamine increased gene knockdown efficacy to as much as 60 fold decrease in expression, while Mirus agent produces a 1.5 fold decrease. Expression of Cx 26 was delayed by 5 cycles in the stable ACTB expression group, indicating a knockdown.
Conclusions: At 48 hours in vitro, a sizeable knockdown in connexin gene Cx26 was achieved compared to the control ASO sequence (scrambled ASO). We will continue working with Lipofectamine as a transfection agent to silencing human connexin genes in vitro, to understand the significance of connexin proteins Cx26, Cx36, Cx43, and Cx45 in the development of the human neurons.

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Synergistic And Selective Repair Of The Acromioclavicular Ligament Alongside Coracoclavicular Ligament in AC Joint Dislocations Greatly Enhances Translational And Rotational Stability

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There is an overwhelming vulnerability of the acromioclavicular joint due not only to the lack of understanding of its complete anatomic and physiologic function, but more importantly, the method by which its dislocation is repaired. Recent literature on the ligamentous distribution of the AC joint has revealed a misconception that the AC ligament is linear in its course(1). Thus, its role in anterior-posterior translation, as well as in rotational stability—especially through elevation of the humerus—has been ambiguous and surgical technique has focused solely on repair of the coracaclavicular ligament, without AC ligament repair. Due to recent elucidation of the AC ligament distribution as oblique in nature, as well as having distinct anterior, superior and posterior facets, our research aimed to define, the unique and synergistic roles of each aspect of the AC ligament during a/p translational and rotational stress(2). It is the hope that selective repair of the AC ligament, synergistic with the CC ligament, will yield a more stable AC joint status post-surgery. 16 AC cadaver specimens were tested with a servohydraulic testing system (MTS 858 Bionix II), 3 specimens were discarded—2 with severe deformities and 1 with os acromiale. Specimens were attached to the MTS by means of a custom fixture that allowed for rotational and axial cyclic loading without taking the specimen out of reposition. Native AC ligaments were used as controls and experimental specimens were treated in the following manner: Group 1 AC joint completely cut. Groups 2, 3 and 4: AC ligament completely cut followed by anterior (0-60°, n=4), superior (60-120°, n=4) and posterior (120-180°, n=5) ligament repair respectively. Next, combination surgical repair was performed and tested in the following manner: Control group and complete cut specimens remained the same. Groups 2, 3 and 4: AC ligament completely cut followed by anterosuperior (0-120°, n =4), superoposterior (120-180°, n=4) and anterior+posterior (0-60° + 120-180°, n=5) ligament repair respectively. Turkey test was used in order to determine significant between experimental AC joint repairs and the control. Anterior and posterior translation, as well as anterior and posterior rotation were tested. The results of our study reveal that synergy between the anterior and superior facets of the AC ligament significantly contributed to posterior translation however do not reach the full integrity of an uninjured AC joint. Synergistic repair of the anterior anterior and posterior ligament showed significant improvement in posterior rotation, coming close to the integrity of an uninjured AC joint. Investigation into AC and CC ligament synergy repair may even further shine light on how to best approach AC dislocation repairs.

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Chemotherapeutic Induced Blebbishield Program in Urothelial Carcinoma Cells – A Model System to Identify Chemoresistance Targets

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Introduction: Current therapy for muscle invasive bladder cancer is cisplatin based chemotherapy but as many as 60% of patients do not respond to treatment.[1] The mechanism by which the cancer cells become resistant to chemotherapy is not yet clear. Treatment with LiCl, a known gsk-3β inhibitor, and cisplatin, a DNA damaging agent, in serum starved media led to transformation of low grade bladder cancer cells through initiation of the blebbishield program. The resultant cells demonstrate increased chemoresistance and a cancer stem cell phenotype suggesting a possible drug evasion mechanism.[2] The aim of this study was to determine the effects of LiCl and cisplatin treatments individually and in combination on various cell death mechanisms in urothelial carcinoma cells to identify potential chemotherapeutic targets in this evasion process.

Methods: RT4, a low grade bladder cancer cell lines, and T24, a high grade bladder cancer cell line, were cultured with varying doses of cisplatin, LiCl, or a combination of the two. Apoptosis, autophagy, cell count, and cell cycle were then analyzed by flow cytometry at 24h, 48, and 72 hours. Cell viability was analyzed by XTT assay. Total RNA was extracted and analyzed by qPCR.

Results: Treatment with LiCl demonstrated dose and time dependent decreases in cell viability and cell count in the T24 cell line. Additionally there was increased evidence of apoptosis but no changes in cell cycle distribution and only basal levels of autophagy with LiCl treatment. In comparison, cisplatin treatment also led to dose and time dependent decreases in viability and cell count, as well as increased apoptosis, but additionally resulted in increased s phase arrest and autophagy in the T24 cell line. Combination treatment led to further decline in cell viability at 72 hours in T24 cells but decreased the level of autophagy in comparison to cisplatin treatment alone. Results in RT4 cells were inconclusive. Cisplatin treatment led to increased expression of inflammatory cytokine SAA1 and apoptotic marker BAX, while LiCl treatment led to increased BAX expression but decreased SAA1 expression.

Conclusion: The data supports that LiCl decreases viability of high grade bladder cancer cells, at least in part through apoptosis. In combination with cisplatin there is evidence that LiCl decreases viability further than cisplatin alone potentially through decreasing autophagy induced by cisplatin. Combination treatment decreased expression of the inflammatory cytokine SAA1 which was previously found to be upregulated in human bladder tumors. It is not yet clear how the apoptotic and autophagy processes associated with these treatments contributes to the blebbishield program and development of chemoresistance.

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(Double vs Single-Row Reconstruction of Fox/Romeo II/III Tear) Preserving the Superior Subscapularis Muscle With Appropriate Fixation

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Objective: The subscapularis (SSC) has the largest footprint and is the most powerful rotator cuff muscle. SSC tears commonly merge from the cranial aspect of the tendon and progress inferiorly. Several studies demonstrate a significant improvement of shoulder function after SSC repair but also show a partial re-tear rate and progressive atrophy especially of the superior aspect of the muscle, demonstrating an unsatisfactory footprint restoration. This study aims to evaluate contact pressure, displacement, and pressurized footprint area differences between double-row (DR) and single-row (SR) repair techniques for full thickness SSC defects focusing on the superior lateral (leading) edge.
Methods: On 15 pairs of human cadaveric shoulders, the native footprint was measured. According to the Fox/Romeo classification, a (A) 25% and (B) 50% defect in a superior inferior directions were introduced. A servo-hydraulic test system was used to analyze contact variables at 0º and 20º of abduction with a force controlled ramped program up to 50N. Additionally, each specimen was cyclically loaded natively, with defect, and repaired. The tears were repaired with one of three constructs: a two anchor-based conventional SR or lateral row construct (LR) or a three anchor based DR. Outcome variables were displacement, pressurized footprint coverage, contact pressure and ultimate tensile load.
Results: The mean native footprint area among all groups was 476.1mm2 ± 69.5 and did not show a significant difference (p=0.31). The 25% defect equaled a mean area of 117.1mm2 ± 32.2 and could equally be restored with either a SR or LR construct revealing adequate load to failure stability and a pressurized reconstruction of the footprint of SR 84% ± 8.9 and LR 95.1% ± 7.9. If focusing on the leading edge, creating a 10% region of interest (ROI) of the total defect size, the SR could reconstruct 25.5% ± 14.8, whereas the LR repair restored 100% ± 0 pressurized contact area (p=0.01). The created 50% defect could be restored with the SR construct up to 72.8% ± 14.2, LR 93.5% ± 10.6 (p=0.02) and DR 90.6% ± 11.8 (p=0.04). With significant differences on the leading edge ROI, SR covered 38.9% ± 31.4, LR 76.8% ± 24.4 (p=0.04) and DR 70.2% ± 26.1.
Conclusion: The biomechanical advantage of a superior-laterally placed anchor increases with defect size. In order to restore the leading edge of the subscapularis muscle and therefore prevent tear progression, it is recommended to add a superior lateral anchor.

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Evaluation of a Clinical Pathway for Management of Febrile Infants Ages 29-60 Days at Connecticut Children's Medical Center (CCMC)

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INTRODUCTION: While fever in infants is most commonly attributable to benign bacterial or viral sources, missing a serious bacterial infection (SBI) can have fatal consequences. Guidelines on the management of febrile infants older than 28 days differ in the recommendations for work-up and treatment. This has the potential to result in unnecessary laboratory testing/invasive procedures and courses of antibiotics, as well as discrepancies in care among providers.(1) The use of a clinical pathway, defined as an algorithm offering evidence-based recommendations to providers, for the management of febrile infants has previously been shown to improve outcomes while decreasing the prevalence of unnecessary testing and the cost of care.(2) We hypothesize that implementation of a clinical pathway for the management of febrile infants 29-60 days at CCMC will reduce the number of invasive lumbar punctures (LPs), antibiotics given and hospital admissions, especially in low-risk infants, without compromising patient outcomes.

METHODS: Our clinical pathway was created based on modified Rochester criteria(3) with input from an interdisciplinary group including emergency and hospitalist providers at CCMC, and implemented in July 2016. Management of the infants was assessed retrospectively for two years leading up to implementation and prospectively following implementation. Variables of interest included the use of LP, administration of antibiotics, hospital admission, missed SBIs and adherence to the pathway.

RESULTS: Prior to implementation of the pathway, 47.3% of the febrile infants studied underwent LP (total n=220). 136 of the 220 met criteria for the low-risk category (where the pathway recommends no LP or antibiotics); 32% of the low-risk infants received an LP, 30% were administered antibiotics, and 17% were admitted. The most recent data for post-pathway implementation shows a decrease in the overall rate of LP to 42% (total n=59). The infants considered low-risk (n= 28) received less non-indicated testing with 0% of low-risk infants undergoing LP or admission, and only 4% receiving antibiotics. Furthermore, the rate of missed SBIs did not vary significantly, with one missed SBI before and after implementation.

CONCLUSION: Implementation of the clinical pathway at CCMC corresponded with improved adherence to evidence-based guidelines. The overall use of the invasive LP procedure declined in these patients, and the infants at low risk for an SBI were less likely to receive antibiotics or be admitted as inpatients. Post-pathway data collection is ongoing and will allow for continued monitoring of care and outcomes for these patients.

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Addressing the Social Determinants of Health: Strengthening Clinical and Community Partnerships

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Purpose: Our study examined two geographically distinct communities in CT to examine how clinical care agencies and community-based organizations are working collaboratively to address the social determinants of health. Specifically, we identified what current practices are in place within clinical care agencies and community-based organizations to address social determinants health, examined how/if clinical care agencies partner with community-based organizations to comprehensively address social and medical needs of patients/clients, and recognized potential barriers to or gaps in care.
Methods: 1) Defined social determinants of health and examined how they relate to health outcomes; 2) Reviewed community health needs assessments and current literature recommendations; 3) Formulated 12 core interview questions; 4) Identified clinical care agencies and community-based organizations in each community and conducted interviews at selected sites; 5) Analyzed linkages and barriers between clinical and community based organizations Results/Discussion: Due to lack of community-specific data in the community health needs assessments, health disparities within populations (in particular income and poverty levels) were not fully accounted for. Absence of data regarding social determinants of health demonstrated a need for clinicians and community-based organizations to further engage with one another to fully assess community needs. Community-based organizations and clinical agencies in both cities reported common barriers in terms of addressing social determinants of health and achieving effective collaboration. From these barriers, key areas of opportunity for growth were identified: access to care, data and assessment, and outreach and accessibility.
Conclusions: In order to best address social determinants of health in practice, there must be a push to mandate education and training of all levels of staff and health professions students working in clinical care agencies and community-based organizations. Change at the policy level may help ensure that various entities are maintaining standards of care, active communication, and following current recommendations in addressing social determinants of health. Future research may build on this project to propose such legislative reform and/or implement educational programming.

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Characterizing Pain and Inflammation in a Mouse Model for Symptomatic Apical Periodontitis

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Objective: Symptomatic apical periodontitis (SAP), which accounts for pain in 26% of patients with toothache, is characterized by inflammatory periapical pain as a result of endodontic infection[1]. The mechanisms and management of the devastating periapical pain remain largely unknown due to lack of appropriate animal models for SAP. Although apical periodontitis has been generated by exposing pulp in mice to study inflammation and osteolysis, pain levels in these mice are not analyzed. The purpose of this project was to characterize pain and inflammation in apical periodontitis in mice.
Methods: To identify pathogenic factors that differentiate between symptomatic and asymptomatic apical periodontitis, a systematic review of the literatures searched from database (ex: Scopus and Google Scholar) was conducted. Markers strongly associated with SAP will be examined in mice with dental infection. Female mice (8-10 week-old) were analyzed 3, 7, 14 and 21 days after pulp exposure in right mandibular first molars by weight measurement, radiographs, histology, and quantitative PCR (qPCR). Left molars and molars from mice without pulp exposure were used as controls.
Results: Review of the literature revealed that IL-6 is most consistently highly enriched in human SAP. Mice showed significant weight loss within 3 days after the operation but recovered afterwards. Radiographs taken by Faxitron showed detectable apical lesions in 44%, 50%, 75% and 100% of mice at day 3, 7, 14 and 21, respectively (d3, 7, 14 and 21: n=9, 4, 4, 5). H&E staining of paraffin sections showed periapical inflammation as early as 3 days after pulp exposure. RNAs from periapical tissues and trigeminal ganglia (TG) were isolated by laser capture microscopy (LCM) and whole tissue extracts, respectively. Results of qPCR showed that levels of *TrpV1*, a receptor for capsaicin, and *CGRP*, a vasodilator, were significantly increased at days 3 and 7 but reduced at day 21. No significant changes were found in *P2X3*, *TRPA1* and *TrkA* following dental infection for 21 days.
Conclusion: Pulp exposure alone results in apical periodontitis with mild to moderate elevation of pain markers only at early time points in mice.
Future Directions: An automated measure of pain behavior will be implemented and the results will be correlated with expressions of pain markers. Stronger stimuli such as intracanal placement of lipopolysaccharide or bacteria strains identified in endodontic infection may be needed to enhance periapical pain in mice. This project is a significant contribution to developing a mouse model for SAP, which will further lead to mechanistic and translational studies to better understand the mechanisms and identify therapeutic targets suppressing pain and inflammation in SAP.

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Clinicopathological Characteristics Associated With Increased Mutational Load In Patients With Non-Small Cell Lung Cancer

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Introduction: Lung cancer remains the leading cause of cancer deaths in the United States. Inhibitors of program cell death receptor 1 (PD-1) or its ligand, PD-L1, have emerged as promising immunotherapies for treatment of non-small cell lung cancer (NSCLC). Unfortunately, PD-L1 immunohistochemical (IHC) staining does not always predict response to PD-1/PD-L1 inhibitors, suggesting other factors may be involved. Increased nonsynonymous mutation number has been associated with improved response to PD-1/PD-L1 inhibition, signifying mutational load as a potential predictor of therapeutic response. The aim of this study was to identify clinicopathologic features associated with PD-L1 expression and increased mutational load.

Methods: 1,011 patients were identified from a retrospective cohort of lung cancer patients via an institutional database in an IRB approved process. Patient characteristics collected included age, gender, race, smoking status, oncogenic mutation, stage of disease, mutational load, and PD-L1 expression status. Mutational load was determined by next-generation sequencing performed via OncoPanel, an advanced sequencing platform at Brigham and Women's Hospital Molecular Pathology. PD-L1 expression was determined via archival tissue samples using a standard IHC assay and defined as positive with greater than 1% expression of membranous staining. Study data was analyzed for statistical significance through use of Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables.

Results: Mutational load (mutation count per megabase) was significantly associated with smoking status (current (8.9+/-6.5) vs. former (6.8+/-4.4), $p < 0.0001$, vs. never (5.3+/-4.1), $p < 0.0001$; former (6.8+/-4.4) vs. never (5.3+/-4.1), $p < 0.0001$), stage of disease at diagnosis (stage IV (6.9+/-5.0) vs. stage I (6.2+/-4.6), $p < 0.05$), and oncogenic driver (KRAS (6.9+/-3.9) vs. EGFR (5.7+/-4.5), $p < 0.001$, vs. MET (4.8+/-2.2), $p < 0.0001$, vs. ALK (4.7+/-3.5), $p < 0.001$; BRAF (8.0+/-5.9) vs. EGFR (5.7+/-4.5), $p < 0.01$, vs. MET (4.8+/-2.2), $p < 0.01$, vs. ALK (4.7+/-3.5), $p < 0.01$).

Conclusion: Increased mutational load is associated with smoking status, advanced stage of disease at diagnosis, and cancers with KRAS or BRAF mutation alterations, confirming mutational load is associated with distinct clinicopathological characteristics.

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Evaluating the value of a novel foot controlled mouse to navigate between electronic health records and radiographs in a dental clinic setting

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Introduction: During most dental procedures the use and access to electronic health records (EHR), clinical notes, and radiographs is essential for the treatment task at hand. Most computer systems use a monitor, keyboard and mouse system or a laptop computer to access these records. Since cross contamination and infection control are important concerns, the keyboard and mouse are covered by a barrier when the procedure being performed has a susceptibility to a higher chance of infection multiple glove changes are done to maintain infection control standards. The objective of the study was examine the value of a foot controlled mouse in the dental clinic setting and compares it with a conventional workstation (mouse and keyboard) to access EHR, clinical notes, and radiographs.

Materials and Methods: A customized workstation was built using a laptop computer and a foot controlled mouse (Boomer Foot Controlled mouse that operated through Bluetooth technology). The normal workstation was setup using the same laptop computer and a wireless mouse (Logitech M335). Clinicians were divided into two subsections a clinical subsection, which involved performing a procedure in general dentistry and an endodontic procedure, and a non-clinical subsection, which involved reviewing radiographic images. The clinicians were given an initial training lesson on the use of the foot controlled mouse and were allowed 15 minutes to become familiar with the foot controlled mouse before beginning the assigned tasks. The clinicians completed their tasks using both the conventional workstation and the customized workstation. The clinicians were timed on how long it took to complete the procedure from start to finish and the number of glove changes during the procedure. After completing the assigned task using the conventional workstation and the customized workstation, the clinicians answered a modified Likert Scale survey valued 1-5; 1 correlated to 'Strongly Disagree' and 5 correlated to 'Strongly Agree'. The survey questions addressed the maintenance of a sterile environment, learning curve, practicality, time to complete the procedure using the Boomer Foot Mouse in comparison to the conventional mouse, and the overall experience with Boomer Foot Mouse in comparison to the conventional mouse.

Results: For the general dentistry procedure the time to complete the simulated procedure with the Boomer Foot Mouse was 1 min and 45 seconds faster than the conventional mouse and required 3 fewer glove changes. The endodontic procedure performed using the Boomer Foot mouse was 4 seconds slower than the conventional mouse and required 1 lesser glove change. Two radiographic images were reviewed and a report was typed for both images by two oral radiologists. The procedure with the Boomer Foot Mouse was 31 seconds slower than the conventional mouse for the first rater and 4 minutes and 18 seconds slower than the conventional mouse for the second rater. The clinicians all completed a customized Likert Survey and the results were analyzed using a Wilcoxon Rank Sum test to determine if there was a difference in the distribution of answers given by clinicians who were performing clinical procedures and the clinicians performing non-clinical procedures. The distribution showed that raters in the clinical procedure subgroup agreed or strongly agreed with the statements from the Likert survey in comparison to the non-clinical raters. The test showed a p-value of $< .0001$ at a significance level of .05 showing that there was a statistically significant difference between the groups

Discussion and Conclusions: The results of the study show that the foot controlled mouse was able to reduce the time of clinical procedures and reduce the number of glove changes during a procedure, but was not very efficient for the non-clinical tasks that required more typing and switching between screens and images and text.

Future Directions: Future studies could include a voice recognition software that will allow clinicians to dictate notes and reduce the need for a keyboard in the dental operatory lowering the chance of cross contamination more significantly

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Low-dose CBCT protocol yields comparable diagnostic information as conventional protocols

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Objective: Implant-based reconstructive dentistry is increasingly becoming the treatment method of choice for management of edentulous spaces. In preoperative evaluation of a potential dental implant site, it is crucial to assess specific site parameters to ensure treatment success. While 3-D imaging using CBCT has become a preferred imaging technique over 2-D imaging, radiation dose still remains a major consideration. Evolution of lower dose protocols is ongoing but whether the lower dose and modified acquisition protocols yield comparable diagnostic information is still not well established for many diagnostic tasks. The objective of this study was to evaluate the diagnostic efficacy of a low dose, 180˚ rotational CBCT acquisition protocol for evaluating a potential implant site in comparison with a conventional 360˚ rotational acquisition. Our hypothesis was that this 180˚ CBCT would reveal comparable diagnostic efficacy to the 360˚ scan.

Methods: Ten dry partially dentate skulls, yielding 82 randomized potential implant sites (40 Maxilla, 42 Mandible), were imaged twice, first using a 360˚ rotational CBCT acquisition, then a 180˚ rotational protocol. Measurements with respect to bone integrity, proximity to crucial structures, and width of potential placement site were measured. An oral surgeon and an oral radiologist rated the diagnostic efficacy of the scans evaluating the above characteristics. To evaluate linear accuracy of measurements between both the acquisition protocols, the raters were also asked to measure distance from alveolar crest to a correlating critical structure to test linear accuracy of measurement.

Results: Linear regression showed significant agreement between both protocol measurements. Kappa analyses yielded good inter-observer agreement.

Conclusion: 180˚ CBCT acquisition protocol demonstrates a significant radiation dose reduction with its decreased exposure time in comparison to the 360˚ protocol. This study demonstrated that both the 180˚ and 360˚ acquisition protocols have comparable diagnostic efficacy.

Clinical significance: CBCT imaging using the lower dose, modified arc, 180˚acquisition protocol should be considered as the preferred CBCT acquisition protocol for implant treatment planning.

Future Directions: Future directions for this study could compare diagnostic efficacy of 180˚ continuous acquisition compared to pulse mode acquisition CBCT. Further studies with varying technique factors like tube current and voltage must be explored to establish a low dose but a scan of optimal diagnostic value.

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IV Injected Gold Nanoparticles (AuNPs) Demonstrate Enhanced Localization to Intracerebral F98 Rat Gliomas Compared to AuNPs Infused Directly Into the Tumor Site by Convection Enhanced Delivery

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It has previously been shown that IV injected Heavy Atom Nanoparticles (HANPs), in this case gold nanoparticles (AuNPS), greatly enhance radiation therapy of advanced orthotopic gliomas in mice[1]. Local radiation dose enhancements of four-fold are possible with tissue concentrations of 2% by weight AuNPs. If this enhancement can be confined to areas within and immediately surrounding the tumor, it may offer a novel means of targeted radiotherapy to limit loss of healthy brain tissue. In this study we compared the biodistribution of AuNPs with respect to tumor cells and tumor edema after either IV injection or direct infusion into the orthotopic tumor site by convection-enhanced delivery (CED). We have shown that IV injected AuNPs reach a large proportion of the tumor cells, including tumor cells that have migrated far away from the main tumor mass. While directly injected AuNPs have the advantage of being stereotactically injected into the tumor site, they show little penetration into the main tumor mass and do not localize well to tumor cells that have migrated distant to the primary site. Conclusions: IV injection shows improved localization of HANPs to the tumor compared to direct injection with CED. Therefore, IV injected HANPs would be expected to enhance radiation therapy of gliomas better than CED directly infused HANPs. Further, lower dose radiation therapy to a larger area of the brain after IV HANP treatment is expected to be more effective than current high dose focused radiation therapy in the absence of HANPs.

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Neurophysiological Study of Noise Induced Hearing Loss in Mouse

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Introduction: An estimated 48 million Americans experience some degree of hearing loss, and exposure to loud noises can induce hearing loss (1). There are two types of hearing loss, a temporary shift of the hearing threshold and a permanent threshold shift. Depending on the type of damage in the cochlea, this hearing loss may be partial or complete. For example, brief broad spectrum sounds such as gunshots or bombs may produce a permanent threshold shift across a large frequency spectra due to damage to the Organ of Corti (2). Meanwhile, a loud narrow spectrum noise may produce a temporary or permanent hearing loss at a specific frequency range, which may be due to damage to hair cell stereocilia without cell death (3). The objective of this study was to measure the effects of non-lethal explosive devices on hearing thresholds. Ideally, these devices would cause a temporary threshold shift that returns to baseline quickly, without producing permanent damage.

Methods: This experiment was completed using 25 CBA/J mice of either sex, aged between 5 and 8 weeks. The mice were anesthetized using a mixture of ketamine, xylazine, and acepromazine. A craniotomy was performed, and an electrode was placed directly on the inferior colliculus of the mouse. The baseline hearing threshold for the mice was determined by measuring the Amplitude Modulation Following Response (AMFR) at 1/3 octave noise bands centered at 12 kHz and 24 kHz. Next the mice were exposed to one of five experimental conditions: a single, short duration, broad spectrum noise at 150 dB SPL, the same sound at 160 dB SPL, three repetitions of the same sound at 150 dB SPL, three repetitions of the same sound at 160 dB SPL, or no blast as a control (n=5 for each group). Next, the hearing thresholds of the mice were measured for 400 minutes. The mouse was considered to have "recovered" if the adjusted post-exposure threshold returned to within 5 dB SPL of the pre-exposure baseline level.

Results: The single pulse at 150 dB SPL did not produce a threshold shift. The single pulse at 160 dB SPL produced a moderate threshold shift with no recovery over 400 minutes. The triple pulse at 150 dB SPL produced either no threshold shift or a small delayed threshold shift, with recovery after approximately 125 minutes. The triple pulse at 160 dB SPL produced a large threshold shift with no recovery after 400 minutes.

Conclusion: The 160 dB SPL noise, both single and triple pulse, was too loud to produce a threshold shift that returned to baseline within 400 minutes. The single 150 dB SPL pulwas not loud enough to produce a temporary threshold shift. The triple pulse at 150 dB SPL was the only experimental condition to produce a threshold shift that returned to baseline within 400 minutes.

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Systematic Review of Internal Fixation of Osteochondritis Dissecans of the Knee: Bioabsorbable versus Metallic Implants

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Background: Surgical management of osteochondritis dissecans (OCD) of the knee is indicated for unstable lesions or stable lesions that fail to heal despite a prolonged period of non-operative treatment.[1] Internal fixation techniques for lesions generally involve implants made of either metal or bioabsorbable materials.[2] No direct comparison evaluating post-operative outcome of bioabsorbable versus metallic fixation is available in the literature, despite a contrasting set of risks and benefits with each.
Methods: The published literature was searched using a combination of standardized terms and keywords. Only original articles describing surgical management with internal fixation for OCD lesions of the knee were included. Outcome metrics assessed included rate of radiographic healing, validated knee functional outcome survey results, overall complication rate, and rate of unexpected additional procedures.
Results: Thirty-three studies reporting outcomes in 526 patients (mean age 19.86 ± 5.93) were analyzed. Across the included studies, 285 lesions were treated with bioabsorbable fixation and 253 lesions with metallic fixation. There was no significant difference in rate of radiologic healing between the two fixation techniques (bioabsorbable: 81.3%, metallic: 86.5%) or mean Lysholm score postoperative (bioabsorbable: 87.58, n=66; metallic: 89.86, n=37). However, significantly higher mean Hughston scores were reported by patients treated with bioabsorbable fixation (89, n=78) compared to those with metallic implants (67, n=89, $p = 0.034$). While there was no significant difference in overall complication rate between the two groups (bioabsorbable: 18.6%, metallic: 14.2%), the rate of unplanned additional surgeries was significantly higher in the bioabsorbable implant group (11.2%) than the metallic implant group (5.3%, $p = 0.02$). In the metallic fixation group, planned hardware removal was performed for 152 lesions (60% of all metallic lesions). The metallic implant group therefore had a relative 82.8% increase in the rate of return to OR (planned or unplanned).
Conclusion: Bioabsorbable and metallic fixation produced similar outcomes, in regards to rate of radiologic healing, Lysholm scores, and overall complication rates. Interestingly, Hughston scores were significantly higher for those treated with bioabsorbable fixation. There was greater likelihood for patients treated with bioabsorbable fixation to undergo an unplanned return to the OR. However, the likelihood of patients treated with metallic fixation returning to the OR was still significantly higher due to routine hardware removal ($p < 0.001$). These findings may help providers to better educate patients and their families when deciding on which method of internal fixation is optimal.

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Quantitative PCR Analysis of Gene Expression in Aberrant Crypt Foci That Exhibit Gene Methylation Patterns Similar to Those of Cancerous Tumor Cells

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It is projected that 135,400 new cases of colorectal cancer (CRC) and 50,200 CRC-related deaths will be reported in 2017. Currently, CRC is the third most common cancer diagnosis, the second leading cause of cancer-related death in men, and the third leading cause of cancer-related death in women, in the US. The current mainstay of CRC prevention is endoscopic screening and surgical resection of pre-cancerous polyps. Despite the overall success of colonoscopy screening programs, the high incidence of CRC and the frequency with which certain polyp subtypes are missed during examination underscore the need for additional prevention strategies. Aberrant crypt foci (ACF) are the earliest putative precursors to CRC and serve as surrogate biomarkers of future cancer risk. Insights into the molecular changes underlying ACF formation may facilitate the development of novel strategies for the early detection and prevention of CRC. We have previously demonstrated that the genes B4GALNT2, EYA2, GXYLT2, DPP6, GRIN2A, and GABRB3 become progressively hyper-methylated during the progression from ACF to CRC. Transcriptional profiling by RNAseq revealed that DPP6, GRIN2A, and GABRB3 were downregulated in CRC alone, while B4GALNT2, EYA2, and GXYLT2 were downregulated in both ACF and CRCs. The goal of this study was to validate these preliminary findings using rtPCR, a second independent technique for the quantification of gene expression. Analysis by rtPCR confirmed our previous findings: B4GALNT2, EYA2, and GXYLT2 are downregulated in ACFwhile the expression of DPP6, GRIN2A, and GABRB3 is unchanged, despite promoter hyper-methylated. This study validates our previous RNA sequencing data and supports the hypothesis that ACF harbor a subset of cancer associated DNA methylation changes that are insufficient to alter gene expression at early stages of neoplastic progression.

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Compared to Warfarin, Direct Oral Anticoagulants are Associated with Lower Mortality in Patients with Blunt Traumatic Intracranial Hemorrhage: A TQIP Study

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Falls represent the leading cause of traumatic brain injury in adults older than 65, with nearly one third experiencing a fall each year. Evidence suggests that up to 0.5% of anticoagulated patients suffer from ICH annually. Direct oral anticoagulants (DOACs) have become an increasingly popular alternative to warfarin for anticoagulation, however, there is a dearth of research regarding the safety of DOACs, in particular on the outcome of traumatic ICH while taking DOACs. We queried our Trauma Quality Improvement Project registry for patients who presented with traumatic intracranial hemorrhage during anticoagulant use. Patients were grouped into those prescribed warfarin and patients prescribed DOAC medications. The groups were compared with respect to age, gender, Glasgow Coma Score (GCS) on arrival, Abbreviated Injury Scale (AIS) (head), Injury Severity Score (ISS), mortality, need for operative intervention, hospital and ICU lengths of stay, proportion of patients transfused (and their transfusion requirements), and rates of discharge to skilled nursing facility. Poisson regression was conducted to determine the relationship between mortality and treatment group while controlling for covariates (comorbidities, ISS). There were no differences between DOAC and warfarin groups in terms of age, gender, median ISS, median AIS head, or median admission GCS. Mechanisms of injury, median hospital and ICU lengths of stay, ICU free days, and transfusion requirements were also not significantly different. DOAC use was associated with significantly lower mortality (4.9% vs. 20.8%; $p<0.008$), and a lower rate of operative intervention (8.2% vs. 26.7%; $p=0.023$) when compared with warfarin. Excluding patients who died, the observed rate of discharge to skilled nursing facility was lower in the DOAC group (28.8% compared with 39.7%; $p=0.03$). Multivariate Poisson regression analysis demonstrated that warfarin use was associated with an increased mortality when controlling for injury severity, and comorbidities. We report improved mortality and reduced rates of operative intervention in patients with traumatic ICH associated with DOACs compared with a similar group taking warfarin. We also noted an association with decreased rate of discharge to SNF in patients taking DOACs compared with warfarin.

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Assessing Child Nutrition and Malnutrition in the Bateyes of La Romana, Dominican Republic

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Introduction: Government surveys in the Dominican Republic found that children living in bateyes generally had a greater level of malnutrition correlated to decreased socioeconomic status. Our survey found that BMI of children in the bateyes matched the global average with no correlation to socioeconomic status or food availability.
Methods: Surveys were conducted over seven weeks in fourteen bateyes around La Romana in the Dominican Republic. Families were interviewed through an interpreter on questions pertaining to socioeconomic status, food availability, breastfeeding habits, and specific food intake. Children were assessed to determine weight and height, which along with BMI were compared to WHO global averages by gender. BMI z-scores were determined and compared to socioeconomic status and food availability using Pearson R correlations.
Results: 132 children were surveyed from 2 to 90 months of age (72 female, 60 male). BMIs were calculated for the children and z-scores relative to WHO standards based on age and gender were calculated. The average z-score was .25 with a standard deviation of 1.3. Pearson R correlation of BMI to food security resulted in a correlation of .2, with a significance of .816, displaying no significance. Pearson R correlation of BMI to socioeconomic status displayed a correlation of .003 with significance of .972, which is also not significant.
Conclusion: There is no significant correlation between socioeconomic status or food security and BMI among children in the surveyed bateyes, and average BMIs fell within normal ranges of WHO standards.

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The University of Connecticut OsteoNecrosis Numerical Scale (UCONNS): An Investigation into Predicting Risk for the Development of Osteonecrosis of the Jaw

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Objective: Osteonecrosis of the Jaw (ONJ) is a clinical condition defined by the American Society for Bone and Mineral Research in which there is uncovered maxillofacial bone that does not heal for 6-8 weeks despite identification and conservation therapy by a dental provider. The cause of ONJ is not currently well defined and the pathophysiology is not understood. Many clinical and genetic risk factors are currently thought to contribute to the development of ONJ, one of which is bone-modifying agents. Using current literature and theories on causation of ONJ, we developed an instrument, the University Of Connecticut OsteoNecrosis Numerical Scale (UCONNS) to assess and look at effects of different factors on the development of ONJ. This is an ongoing retrospective study to determine the utility of this scale to identify those at high risk of developing this condition. Methods: A retrospective chart review was performed to extract data on 36 patients with documented ONJ seen at the Dental Clinic at UConn Health, and 65 non-ONJ subjects seen at the UConn Health Osteoporosis Clinic and Cancer Canter. These 65 non-ONJ patients were further categorized based on whether they had a malignant or benign condition. Malignant conditions included breast, prostate cancer and multiple myeloma. Benign conditions included patients treated for osteoporosis. Five categories were used to assess the patient's risk factors including: Bone modifying agents, history of dental/oral surgical procedures, oral health conditions, medical conditions and comorbidities. Subjects were assessed in each category and given a score that contributed to their overall UCONNS score. Using SPSS statistical analysis program, the data was analyzed for a mean score amongst groups and a Receiver Operating Characteristic curve was created to determine the discrimination threshold. Results: The mean UCONNS score for the 36 ONJ patients was 23.97 with a standard deviation (SD) of 6.570. The mean UCONNS score for the 65 non-ONJ patients was 13.11 with a SD of 6.006. This mean comparison has a p value = 0.000. The ROC analysis found a UCONNS score of higher than 17.5 to determine high risk patients with a sensitivity of .861 and a specificity of .8. The area under curve (AUC) was .888, with a p value of 0.000 demonstrating accuracy of the diagnostic test. Conclusions: The UCONNS scale is a sensitive and specific predictor of ONJ risk in patients at based on their dental and medical health. A score greater than 17.5 on the UCONNS scale indicated high risk for patients to develop ONJ.

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Rheumatoid Arthritis Fibroblast-Like Synoviocytes Produce IL-9 and Its Production Is Regulated by Pro-Inflammatory Cytokines

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Objective: Rheumatoid Arthritis (RA) is a debilitating autoimmune condition characterized by the chronic inflammation of the joints, leading to the destruction of cartilage and bone. Fibroblast-like synoviocytes (FLS) are cells that line the synovium of a joint, and have been shown to play an important role in the pathogenesis of RA (1). Recent work has shown interleukin-9 (IL-9) to co-localize with FLS inside the synovium, but the role of this cytokine has not been explore in the pathogenesis of RA, or which cells in the synovium can produce it (2). IL-9 is a cytokine that promotes the proliferation and survival of synovial fluid T cells and neutrophils, enhances the inflammatory cascade and increases inflammatory cytokines such as tumor necrosis factor α (TNF α), interferon γ (IFNγ) and interleukin-17 CD+ T cells (IL-17). It has been shown that IL-9 has been found at enhanced levels in the synovial fluid of RA patients when compared to osteoarthritis (OA) patients (2). Therefore, the aim of this study was to elucidate the role of IL-9 in the pathogenesis of RA by determining if FLS from RA and OA synovium produce IL-9, and if so, if IL-9 expression is regulated by pro-inflammatory cytokines.
Design: Since osteoarthritis is a non-autoimmune condition, OA FLS were used as the control to RA FLS. OA and RA FLS were stimulated with IL-17A, IL-17B, IFNγ, and TNFα for 24, 48 and 72 hours. Gene expression was determined by qPCR using isolated RNA and probes against IL-8, IL-9 and TNFα. IL-8 was used as a positive control to show that the FLS were capable of responding to the stimulatory cytokines.Treated OA and RA FLS supernatants were collected and proinflammatory cytokines IL-8, IL-9 and TNFα were analyzed by ELISA.
Results: While OA FLS showed limited IL-9 gene expression in all treatment conditions for 24, 48 and 72 hours, there were elevated levels of IL-9 protein in response to IL-17B, IFNγ and dual stimulation of TNFα and IFNγ in comparison to untreated OA FLS. RA FLS upregulated IL-9 expression after treatment with TNFα for 24 hours, IFNγ for 48 hours and IL-17B for 72 hours when compared to non-stimulated RA FLS. IL- 9 protein was found at elevated levels in RA FLS treated with IL-17A, IFNγ and TNFα for 72 hours.
Conclusions: These results suggest that IL-9 is produced by FLS and regulated by pro-inflammatory cytokines in a time dependent manner. IL-9 protein was regulated by TNFα and TNFα was regulated by IL-17B, suggesting a regulatory mechanism of IL-9 in RA FLS. Further experiments are needed to explore the role of IL-9 in the interplay of proinflammatory cytokines in the synovium of RA patients that lead to perpetuation of this condition.

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Dimethyl Sulfoxide Inhibits Both MyD88 and TRIF Activation in the Cervical Epithelial Barrier

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OBJECTIVE: Preterm birth is believed to be a final common pathway of a multitude of instigating factors, and inflammation plays a significant role in prematurity. However, the precise mechanisms of preterm parturition remain unknown. These studies assess if the mechanism of inflammation with known toll-like receptor (TLR) agonists on cervical epithelial cells activate the MyD88 or TRIF pathway, and if these activated pathways can be mitigated with Dimethyl Sulfoxide (DMSO). The MyD88 is an adaptor protein for TLRs that complexes with other proteins to phosphorylate the inhibitory component of NF-κb, allowing its release and translocation into the nucleus. TLR4 can also cause nuclear translocation of NF-κb in an MyD88-independent manner via the TRIF pathway. The MyD88 and TRIF pathways ultimately result in increased cytokine production, particularly IL-6 and IFN-α, respectively.
STUDY DESIGN: For this study, we used immortalized ectocervical (ECTO) and endocervical (ENDO) cells. Both cell lines were plated at a concentration of 4.0 x 104 cells per well for 24 hours. Cells were treated with 10 ug/ml of lipopolysaccharide (LPS), a TLR4 agonist; 1 ug/ml of Poly (I:C), a TLR3 agonist; and 25 uM of CPG A, a TLR9 agonist. After 24 hours media was collected and the cytokines IL-6 and interferon alpha (IFN-α) were measured with an enzyme immunosorbent assay (ELISA). Additionally, both cell lines were pretreated with DMSO 22 hours and again one hour prior to TLR agonist treatment. Media was again collected and assessed for IL-6 and IFN-α.
RESULTS: Exposure to LPS and Poly (I:C) significantly increased IL-6 in both cell lines ($p<0.01$), and DMSO mitigated this increase in IL-6 ($p<0.01$). Neither LPS nor Poly (I:C) increased IFN-α in either ECTO or ENDO cells. CPG-A did not significantly increase IL-6 in either cell line, but did increase IFN-α concentrations for both ECTO and ENDO cells ($p<0.01$). DMSO inhibited the CPG-A induced increase in IFN-α ($p<0.01$).
CONCLUSION: These studies demonstrate that an inflammatory challenge with LPS or Poly (I:C) activates the MyD88 pathway increasing IL-6 concentrations. Additionally, CPG-A stimulated the TRIF pathway increasing IFN-α concentrations. These studies also showed DMSO inhibits both IL-6 and IFN-α levels in cervical epithelial cells, suggesting DMSO inhibits both MyD88 and TRIF inflammatory pathways and may be a potential therapeutic strategy to reduce prematurity.

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Magnesium Deficiency In Chronic Alcoholism

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Magnesium deficiency is common in chronic alcoholism. The mechanism of this deficiency is multifactorial and can result in a variety of clinical manifestations. This report will review the current understanding of the pathophysiology of magnesium deficiency and its clinical manifestations in the context of chronic alcoholism. We will also present a case report of an alcoholic patient who was found to have a severe magnesium deficiency while manifesting a spectrum of symptoms and clinical findings associated with hypomagnesemia.

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Estimated Cost Efficacy of US Food and Drug Administration Approved Treatments for Acne: Isotretinoin as First-line?

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Patients with acne are generally encouraged to attempt topical and oral therapies, often in a stepwise manner, before using isotretinoin. We sought to estimate the cost efficacy of US Food and Drug Administration (FDA) approved acne treatments to evaluate whether Isotretinoin would be a cost-effective first-line treatment. Medication costs were obtained from the National Average Drug Acquisition Cost (NADAC) database maintained by the US Centers for Medicare & Medicaid Services. Laboratory fees were obtained from the American Medical Association, and office visit fees are standard at our university. Cost calculations were standardized to seven months of treatment because this is endpoint when patients treated with isotretinoin will have achieved the upper end of their weight-based cumulative dose (range is 120-150mg/kg total body weight. Topical antibiotics contained the least costly FDA approved therapy for acne. Clindamycin Phosphate 1% (60 Pledgets) were $410.20 for the treatment period. Also inexpensive was the oral hormonal Spironolactone Tablet (25 mg) at $451.38. Oral antibiotics were not significantly more expensive with Minocycline Capsule (50 mg) at $509.37. The most expensive option was Isotreinoin. This category also had the widest range of cost, with the cheapest being $1,320.88 (45kg person taking Claravis, Myorisan, & Zenatane) to $11,680.21 (90kg person taking Absorica). In the patient with moderate to severe acne, isoretinoin can be the cost-effective first-line choice if the patient requires long term treatment. Our study provides meaningful cost efficacy data that may influence acne treatment selection.

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Investigating a new mechanism for CAR T cell imaging and elimination

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Introduction: Chimeric Antigen Receptor (CAR) T cells are a novel cancer immunotherapy which consist of an extracellular antigen binding domain which is composed of a monoclonal antibody-derived single chain variable fragment linked to intracellular CD3 and CD28 or 4-1BB for signal 1 and 2. CARs can also co-express other proteins for added function. To treat, patient T cells are transduced with the CAR vector and expanded ex vivo, and then cells are reintroduced to attack tumor cells. CAR T cells have shown clinical promise in treating CD19+ B-ALL, B Cell Maturation Antigen (BCMA+) multiple myeloma, and other contexts. However, patients receiving treatment can suffer from severe cytokine release syndrome after infusion, so CAR T cell-specific elimination is needed to reduce toxicities. We have identified a potential target (ELS16) for CAR T cell-specific elimination and in vivo imaging.

Methods: BCMA-targeted (B24BBz) or CD19-targeted (1928z), exterior Gaussia Luciferase (xGluc), and ELS16 tricistronic vectors were cloned, transfected into RD and GalV9 retroviral vector packaging lines, and used to transduce T cells. CAR and ELS16 expression was confirmed by flow cytometry. xGLuc bioluminescence was evaluated with coelenterazine. A 99mTc-conjugated ELS16-substrate (sELS16) was used to evaluate ELS16 for imaging T cells. BCMA+ firefly luciferase+ OPM2 cells were injected into immunocompromised mice, visualized via bioluminescence with luciferin, and then treated with B24BBz CAR T cells or untransduced T cells. Tumor burden and CAR T cell persistence were analyzed via bioluminescence.

Results: xGLuc-B24BBz-ELS16 and xGLuc-1928z-ELS16 tricistonic CAR constructs were cloned and confirmed via DNA sequencing. CAR T cells were generated with transduction efficiencies of 28.6% and 27.07% for the BCMA and CD19 CARs, respectively. The xGLuc was validated in vitro with positive linear relationships between CAR+ cell number and bioluminescence intensity ($R2 = 0.9823$ and $R2 = 0.984$, respectively). GalV9 cells expressing xGLuc-1928z-ELS16 showed a 5-fold greater radioactive signal when incubated with 99mTc-sELS16 compared to cells saturated with 100x excess of unconjugated sELS16 prior to incubation with the 99mTc-sELS16. CAR+ T cells eliminated OPM2 cells in vivo evidenced by a reduction in tumor burden and persistence of CAR T cells compared to untransduced T cells.

Conclusions: Tricistronic CAR T cells can be visualized via bioluminescence and show specific radioactive signal in response to a 99mTc-ELS16. BCMA-targeted CAR T cells eliminate OPM2 cells and persist in vivo. Further studies will compare the functionality of B24BBz CAR T cells to other CAR T cells and will further evaluate ELS16 for in vitro and in vivo imaging and elimination.

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Assessing Hydroxyurea Therapy in Pediatric Sickle Cell Disease: A Review at CCMC

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Introduction: In Connecticut, hundreds of children with Sickle Cell Disease (SCD) face debilitating pain crises that require hospital admissions and chronic narcotic therapy resulting in many challenges at home and school, as well as affecting their physical and behavioral development. Despite this burden, the FDA has not approved any drugs to treat pediatric SCD. The NIH and HHS recommend that all pediatric patients with SCD are offered Hydroxyurea (HU), an antineoplastic drug used in myeloproliferative disorders and adult SCD. However, barriers including toxicity, inadequacies of HbF monitoring and patient nonadherence have resulted in widespread variation in HU use. In a retrospective chart review of HU treatment at CCMC we investigated, 1) whether MCV could predict patient adherence and therapeutic outcomes and 2) whether certain characteristics predisposed patients to developing toxicity.
Methods: Inclusion criteria was 2-fold: SCD pediatric patients seen for at least 3 months prior to the start of HU and SCD pediatric patients on HU for a minimum of 3 months. Therapeutic markers were collected from every outpatient, ED visit or first day of direct hospital admission and averaged annually for HU vs. baseline comparisons. Criteria for an unstable dose was incidence of thrombocytopenia or neutropenia on HU. Criteria for nonadherence was clinical admission as documented in patient chart. Paired t-test provided baseline v. on-HU comparisons, unpaired t-test provided between group comparisons and therapeutic correlations were analyzed by Pearson correlation coefficient.
Results: 33 patients were adherent, 23 were non-adherent. Average MCV increase for adherent group was 11.1 and 4.4 for non-adherent group ($p=0.00005$). For adherent group, magnitude of increase in MCV was inversely correlated with negative therapeutic outcomes, pain crises ($r=-0.4$), hospitalizations ($r=-0.4$) and transfusions ($r=-0.4$). The adherent group also had a statistically significant increase in weight (GC %) from baseline of +6.7 ($p=0.03$). Average MCV change was a better predictor of adherence than average HbF change ($p=0.00005$ vs. $p=0.01$) which may be due to increased data for MCV, 87.8% of visits had MCV while 36.3% of visits had HbF. 49 patients were on a stable dose of HU, 7 patients were on an unstable dose. Average age was the only difference between groups ($p=0.01$), stable dose averaged 8.1 years, unstable dose averaged 2.6 years, the RRR of neutropenia if on HU and under 4 y/o was 12.7.
Conclusion: Our data shows that MCV increase can predict patient adherence to HU and has strong correlations with positive therapeutic effects. Considering the current variations in HU therapy, we suggest that MCV be used as an accessible marker to help streamline and optimize care.

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The Effect of CDK5 Inhibitors on Vesicular Transport and Metastasis of Breast Cancer Cells

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Breast cancer is the leading cause of cancer in women, with invasive ductal carcinoma (IDC) making up more than 80% of all diagnosed breast cancers (1). Ductal carcinoma in situ (DCIS) is a noninvasive neoplasm that precedes IDC, with a breach in the basement membrane causing the neoplasm to turn from the noninvasive to invasive form. This metastasis through the basement membrane and surrounding extracellular matrix is accomplished with invadopodia, or actin-rich protrusions on the cell membrane. Alone, invadopodia precursors are short lived (≤ 10 min), but are stabilized by the TKS5 scaffolding protein, which create more active and longer lasting (≥ 60 min) invadopodia (2). Additionally, membrane-anchored metalloproteinases (specifically MT1-MMP) are also concentrated at the surface of invadopodia, and help break down the ECM and facilitate invasion. To reach the surface of invadopodia, both TKS5 and MT1-MMPs are packaged into late-endosomes and transported on microtubules, where kinesin motors move the endosomes towards invadopodia and dock them to the cell surface. Meanwhile, dynein motors detach the endosomes from the surface and move them away from invadopodia (2,3). Dynein is inhibited by CDK5 (3). This study investigated whether inhibiting CDK5, and thereby promoting dynein action, would decrease the concentration of TKS5 and/or MT1-MMPs at invadopodia, thereby reducing invasion. Invasive MDA-MB-231 human ductal carcinoma cells were treated with 10 μM of either Roscovitine or Purvalanol A – both CDK5 inhibitors (4,5). Fluorescent staining revealed a significant decrease in TKS5 at invadopodia with Roscovitine, but not Purvalanol A. MT1-MMPmcherry endosomes were tracked in real time, with data showing no change in MT1-MMP endosome location with either drug. These results suggest that, at the given dose, Roscovitine may allow increased dynein action at TKS5 endosomes. This would result in TKS5 endosomes moving away from invadopodia, making the invasive structures less stable. This study has revealed the potential of using Roscovitine to decrease the amount of invadopodia in IDC, and encouraged future research to examine Roscovitine as a means to decrease invasion.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Dermatologic Conditions in a Shelter-Based Homeless Population: Lessons Learned from a UCONN Medical Student-Run Dermatology Clinic

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Background: Among the homeless, dermatologic conditions are very common due to the exposure of skin to environmental elements and often inadequate clothing and hygiene. In an effort to reduce barriers to care and increase convenience for these underserved patients, the UConn South Park Dermatology Clinic in Hartord, CT was founded by medical students in 2008.
Objective: The goals of our study were (1) To assess the frequency of dermatologic conditions occurring in a shelter-based homeless population from August 2008 to February 2016; (2) Understand patient demographic characteristics of age, gender, race, and season of treatment and (3) Determine the suspected skin malignancy rate in this population.
Methods: We completed a retrospective chart review of patients seen at the free dermatology clinic. Two hundred and seventy-three patient paper charts from 45 clinics were reviewed and demographics, diagnoses, and treatment data were recorded.
Results: Overall, 273 patients, between the ages of 1-67 (average 37), were seen for dermatologic concerns. Demographically, 54% were male and 46% were female with 30% identifying as African American/Black, 29% Hispanic, and 25% Caucasian (16% did not disclose). More than 85 separate dermatologic conditions were recorded with 26% of patients presenting with more than 1 complaint. The top ten diagnoses (per total # of patients) over 8 years were: acne (18.7%), atopic dermatitis (10.6%), tinea pedis (9.2%), xerosis (8.1%), folliculitis (5.1%) and with less than 5% frequency: post-inflammatory hyperpigmentation, seborrheic dermatitis, tinea infections (body and head), psoriasis, and verruca vulgaris. Additionally, the rate of malignancy per total patients seen was 2.6% with 7 patients presenting with lesions suspicious for basal cell carcinoma (2), melanoma (3), and dysplastic nevus (2). Diagnosis trends were also analyzed based on gender, race, age, and season.
Conclusions: Although unexpected, our most common diagnosis at the clinic was acne with approximately 1 in 5 patients presenting with this condition. Some of our findings mirror frequencies of dermatologic conditions identified in sheltered homeless populations in previous studies. Differences seen may be attributed to geographic and demographic variability. The suspected malignancy rate, which has been rarely studied, is of particular interest due to this population's risk for chronic sun exposure, lack of consistent sunscreen use, and poor access to dermatologic screening. Additionally, our most common diagnoses will advise decisions about medication and treatment supplies ordered for future clinics.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Characterization of Immune Cell Composition within the Tumor Microenvironment of Colorectal Cancer in Smoking and Aspirin Taking Patients

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Colorectal Cancer (CRC) is one of the most common cancers in the United States. It is the second most common cancer in women and the third most common cancer in men. It is also the second leading cause of cancer-related death among both men and women. Several recent studies have suggested the use of chemopreventative agents to lower the risk of developing CRC. One such class of agents are nonsteroidal anti-inflammatory drugs (NSAIDs). Daily aspirin specifically has been shown to lower rate of colorectal cancer up to 30%. There are, however, other factors that may both increase the risk of the development of CRC as well as interfere with the efficacy of aspirin as a preventative agent. One very common risk factors associated with CRC is smoking. Smoking could induce a polyp rate up to 70% higher than normal. Currently the proposed chemoprotective mechanism is based on its effect on the production of PGE2 and β-catenin which is a promoter of the inflammatory pathway and upregulates oncogenes such as c-myc, respectively. The increased in polyp formation in smoking is also believed to be related to an increased in inflammation as well as inflammatory markers, it should thus be in direct opposition to the effects of aspirin. However, when smokers who take aspirin still have a polyp incidence rate around 70%, paradoxically suggesting that aspirin has no protective effect on polyp development in smokers. In this study we look specifically at the rate of proliferation in normal crypts as well as from aberrant focal crypts (ACF) from samples taken by polypectomy. Using samples matched for obesity, age, gender, and race from 16 subjects we compare the effects of aspirin on nonsmokers and current smokers. We compared the rates of total proliferation in both ACF and normal crypts as well as differences in the rates of proliferation in normal tissue and ACF tissue. Using Ki-67 stained sections, we found that aspirin use showed nonsignificant decreased rates of proliferation in both normal and ACF sections in both smokers and nonsmokers, indicating a protective role of aspirin in regards to proliferation alone. However there may be other factors that have been implicated in the development of CRC such as the degree of inflammation, the involvement of prosurvival pathways, or the presence of prometastatic factors such as MMP-9. Future studies should aim to confirm the findings and investigate the contribution of alternative pathways.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Social Factors Influencing Family Planning Knowledge, Attitudes, and Practices in the Ngäbe Population in Bocas del Toro, Panama

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Introduction: According to Panama's 2009 National Sexual and Reproductive Health Survey, only 19% of indigenous women in Panama use modern family planning (FP) methods. The Ngäbe represent 62% of the indigenous population, but there has been limited research on their use of FP.
Methodology: 14 Ngäbe communities in Bocas del Toro served by Floating Doctors, a 501-C3, non-profit organization delivering health care to the remote coastal communities of Central America,were surveyed. Women between the ages of 18 and 50, who had >2 children were invited to be interviewed about FP knowledge, attitudes, and practices.
Results: A total of 148 women were enrolled, mean age 32.18 (SD=8), and mean number of pregnancies 4.9 (SD=2.5). On average, first sexual encounter occurred at age 14.7 (SD=1.9), with first pregnancy occurring at age 16.3 (SD=2.5), and mean spacing between first and second pregnancy was 2.8 years (SD=2.1). Only 7% of women could not name any family planning method. Women reported ideal age to begin having children as 21.5 (SD=4), and reported ideal birth spacing as 4.8 years (SD=2.4). 78% did not want to have more children but only 32% were currently using FP. 40% of women currently not using FP had used a form of FP in the past. 41% of women had ever used any FP methods. Respondents with unmet need for FP reported concerns about side effects (48%) and lack of access (32%) as main barriers to using FP. Women practicing indigenous religions were less likely than all other religious groups to use FP ($X2=19.0$, $p<0.001$). FP use was higher for women who received information on FP during prenatal visits ($X2=8.5$, $p=.003$), from health care providers ($X2=7.5$, $p=.006$), and who talked with a health care provider about FP during the last year ($X2=4.8$, $p=.029$). There was no significant association between age, location, education level, marital status, number of pregnancies, and FP use.
Conclusions:
Ngäbe women believe it is important to delay first birth, increase birth spacing, and have fewer children. This would improve women and child health outcomes. However, misconceptions about FP and concerns about side effects are widespread and deter FP use. Receiving accurate FP information from health care providers increases use. Qualitative research is needed to more fully understand how indigenous beliefs and traditional practices influence FP use.

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Distribution of Lipid 654 Diastereomers in *Porphyromonas gingivalis* Isolates

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Objectives: *Porphyromonas gingivalis*, a periodontal pathogen, produces a novel serine lipid class termed Lipid 654 that engages Toll-Like Receptor 2 (TLR2). This serine lipid class contains two fatty acids, one that is ester linked and the other is amide linked. Recent evidence showed that Lipid 654 class is de-esterified by the mammalian enzyme phospholipase A2. This enzyme is known to hydrolyze arachidonic acid from mammalian phospholipids and its expression is increased in chronic inflammation. However, PLA2 hydrolyzes only a portion of Lipid 654 isolated from *P. gingivalis.* Because PLA2 is known to enantioselective in hydrolyzing phospholipids, the purpose of this investigation was to determine whether Lipid 654 from *P. gingivalis* is composed of a mixture of R and S chiral forms as a potential explanation of partial Lipid 654 hydrolysis by PLA2.

Methods: Five isolates of *P. gingivalis* where grown in broth culture, verified by 16S ribotyping, and total lipids extracted. The total lipid extracts of each isolate were fractionated using semipreparative normal phase HPLC with neutral solvent. Fractions were then evaluated by mass spectrometry (MS) for fractions containing Lipid 654. These fractions were pooled, refractionated using an acidic solvent and fractions containing Lipid 654 were pooled and dried. Each Lipid 654 isolate was then fractionated using a LUX cellulose 4 chiral column in order to separate R from S Lipid 654 isoforms. The retention of R and S isoforms of Lipid 654 was confirmed using synthetic R and S standards of Lipid 654.

Results: This investigation demonstrated that all *P. gingivalis* isolates synthesize Lipid 654 predominantly in the R chiral form. Additional work using LC-multiple reaction monitoring-mass spectrometry confirmed that Lipid 654 prepared from these *P. gingivalis* isolates exists in the R isoform. Synthetic racemic Lipid 654 was subjected to PLA2 hydrolysis and using the same LC –mass spectrometric analysis confirmed that only the R isoform is hydrolyzed by PLA2.

Conclusions: Because Lipid 654 is recovered primarily as the R isoform from *P. gingivalis,* the partial hydrolysis of Lipid 654 by PLA2 cannot be explained by the presence of a mixture of Lipid 654 isoforms. Only the R isoform of Lipid 654 is hydrolyzed by PLA2.

Future directions: Future work will be directed toward understanding the partial hydrolysis of Lipid 654 by PLA2.

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Optimizing the Effectiveness of an Ocular History Questionnaire in School Aged Children

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Introduction: The American Academy of Pediatrics (AAP) recommends visual acuity screening (VAS) at ages 6, 8, 10, 12, and 15 and use of their ocular history questionnaire (OHQ) at non-screening ages. This project sought to explore the agreement between specific questions of the OHQ and the VAS in English-speaking families and augment the currently recommended OHQ to optimize sensitivity and PPV. The setting of our research was the Community Health Center at Connecticut Children's, which serves a very low income population with a 24% prevalence of decreased visual acuity.

Methods: The currently recommended OHQ was administered to patient families at Community Health Center at Connecticut Children's Hartford, CT between 11/2015 and 7/2016. OHQ were collected from patients ages 6-18 who were receiving Well Child Visits in order to ensure that they would receive a VAS that day. Patients who either had or wore glasses were excluded, as well as those that did not list English as their preferred language. VAS results were retrieved from the electronic health record.

Results: Of the sample size of 164 patients, 60% were male, 61% Hispanic, 85% Husky/Medicaid and the average age was 121.7 months. A smaller sample of n=18 revealed an average time of completing the survey of 1:35. The OHQ had a 64% sensitivity and a 21% positive predictive value. The OHQ and VAS results were not significantly correlated (p=0.0636).

Each question in the OHQ was individually analyzed in terms of sensitivity, positive predictive value and Fisher's exact test to find correlation between the question result and the vision screen result. By ranking these results and then removing questions that failed due to more "I don't know" answers than true failing answers, three questions (7,14,16) were consistently the best and were used to make a new, shorter OHQ.

Of the 24 shorter OHQ completed, 52% were female, 68% Hispanic, 92% Husky/Medicaid and the average age was 146.8 months. A smaller sample of n=21 revealed an average time of completing the survey of 0:54. The shorter OHQ had a 100% sensitivity and 25% positive predictive value (PPV). The OHQ and VAS results were significantly correlated (p=0.0194).

Discussion: By individually evaluating the currently recommended questions in the OHQ, a more effective OHQ was created. The modified OHQ took 43% less time to complete and had a sensitivity of 100%. While only 22% of the families reported that they were Spanish speaking on their electronic health record, 68% of patients were Hispanic which brings into question how many families are not literate in English. The major weakness of this study was excluding Spanish speaking population when more than half of the patients in the study were Hispanic.

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Cone Beam CT is Superior at Diagnosing Maxillary Sinus Pathology

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Objective

Approximately 40 million cases of sinusitis are reported in the United States each year. According to the center for disease control, patients get radiographs of the jaws with panoramic imaging that includes the maxillary sinuses more often than any other part of the body. While panoramic radiographs show sinus pathology to a certain extent, they do not depict the entire sinus in detail. The objective of this study was to compare the diagnostic ability of panoramic imaging and a cone beam CT (CBCT) that provides three dimensional information of the imaged area with a reasonably low radiation dose.

Methods

A total of 32 maxillary sinuses from 16 dry skulls were used to simulate a variety of maxillary sinus pathologies**.** Mucous retention cysts and mucous thickening were randomly simulated on the floor, medial wall, lateral wall and roof of the sinus by using dental inlay wax. Some of the simulations were done more anteriorly in the sinus and some were randomly simulated on the posterior aspect. A preoperative panoramic radiograph and a CBCT was done for all the skulls. A post-operative Panoramic and CBCT were done after the sinus pathology was simulated. The images were evaluated to compare the diagnostic

Results

Interim data analyses showed that mucus retention cysts and marked mucosal thickening, specifically in the anterior plane were detectable equally on both modalities. Panoramic radiographs could not show simulated pathology on the medial wall, lateral wall and the roof of the sinus. CBCT was able to detect the simulated pathology at all locations.

Conclusions

Cone Beam CT is superior at diagnosing sinus pathology when compared to panoramic imaging.

Support

This research was supported by the UConn School of Dental Medicine Summer Research Fellowship.

CBCT Analysis of Impacted Incisors: Bone and Root Parameter Differences

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Objectives: To assess differences in alveolar bone and root parameters in subjects with unilateral impacted maxillary central incisors by cone-beam computed tomography in comparison with the contralateral, normally erupted maxillary central incisor.

Methods: A total of 22 subjects were included in the study; 14 with an impacted left central incisor and 8 with an impacted right central incisor. Alveolar bone width was measured at 2mm, 6mm, and 10mm apical to the alveolar crest to assess potential differences in bone width due to lack of eruption of the incisor. Also measured was the distance from the bony palate to the incisal edge of the impacted incisor, and incisal edge to the incisal edge of the normally impacted incisor to determine the severity of impaction of the sample group from a vertical perspective.

Results: There was a significant difference between the alveolar bone width at 6mm ($p < 0.001$) and 10mm ($p = 0.002$) apical to the alveolar crest of the impacted side [6mm: 11.61mm ± 2.67, 10mm: 12.44mm ± 3.23] and the non-impacted side [6mm: 9.09mm ± 1.77, 10mm: 10.31mm ± 2.68]. Length and morphology of the root was also evaluated. There was a significant reduction in root length ($p < 0.001$) of the impacted incisor compared to the normal incisor. Seven of the 22 impacted incisors were also found to have root dilaceration. The average distance from the palate to incisal edge was 15.77mm ± 6.96 and from incisal edge to occlusal edge was 14.25mm ± 5.42.

Conclusions: Alveolar bone width at 6mm and 10mm apical to the alveolar crest on the side of the impacted maxillary central incisor was found to be greater than the normally erupted side. Root length of the impacted incisors was less than the normally erupted incisor, but there was no association with root resorption of adjacent teeth.

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The Lower the Better: Systolic Hypertension is Associated with Diastolic Dysfunction

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Background and Objective: Heart failure (HF), or impairment of the left ventricle to fill with or eject blood, afflicts an estimated 5.1 million Americans (1). HF is subdivided into heart failure with preserved ejection fraction (HFpEF), characterized by diastolic dysfunction, and heart failure with reduced ejection fraction (HFrEF) characterized by systolic dysfunction. While the mortality rate for HFrEF has dropped precipitously with the advent of new therapies, treatment options for HFpEF have not had parallel success. Although hypertension is considered to be one of the risk factors associated with the development of HFpEF, the exact role of elevated blood pressure remains unclear. The recent SPRINT trial concluded that intensive treatment of hypertension (systolic blood pressure (SBP) maintained <120 mmHg), compared with standard treatment (SBP maintained <140 mmHg), significantly reduced the incidence of heart failure within the study population. However, the trial was not designed to further characterize the incidence between HFrEF and HFpEF (2). Based on these results, our study sought to determine if the degree of blood pressure reduction was an important determinant of diastolic dysfunction.

Methods: Following IRB approval, medical records of patients presenting for dyspnea between 1/1/15-9/30/15 were reviewed. Patients with ejection fraction <50%, age <50 years old, or significant valvular or kidney disease were excluded. Blood pressure measurements, number and type of antihypertensive medications, and echocardiographic parameters of diastolic dysfunction were retrospectively collected. Subjects were divided into hypertensive (SBP >130 mmHg) and normotensive (SBP<130 mmHg) groups. Differences between the two groups were assessed by Student's t test for continuous variables, with an alpha level of $p < 0.05$.

Results: 370 records were initially screened, and 152 qualified for the study. 74 patients were matched into the hypertensive group and 78 into the normotensive group. The mean SBP was significantly higher in the hypertensive group compared with that in the normotensive group (143 vs 119 mmHg, $p<0.01$). Tissue Doppler evaluation of E wave ($p=0.018$), A wave ($p=0.01$), medial E' ($p=0.013$), lateral E' ($p=0.004$), medial E/E' ($p=0.006$), and lateral E/E' ($p=0.001$) revealed statistically significant diastolic abnormalities in the hypertensive group compared to the normotensive group.

Conclusion: Systolic hypertension is an important determinant of diastolic dysfunction. Intensive blood pressure control may serve as a therapeutic strategy against the progression of diastolic dysfunction.

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Educating Healthcare Professionals About Endocrine Disrupting Chemicals in Consumer Products

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Healthcare professional education of environmental health, including endocrine disrupting chemicals (EDCs), is minimal despite the significant amount of scientific evidence suggesting the association between EDCs and negative health effects in humans (1,2,3,4). EDCs are ubiquitously detected in consumer products, foods, beverages, personal care products, and household cleaning products and nearly all of the general U.S. population is exposed to EDCs (5). Infants and children, who are in critical periods of development are particularly vulnerable to the effects of EDCs exposures and primary healthcare professionals serve as important resources in communicating the potential dangers of EDCs exposures. Our specific aims are to: 1) develop EPA/ATSDR-sponsored training for healthcare professionals regarding the health effects associated with EDCs in consumer products; 2) demonstrate an improvement in the learner's knowledge following completion of each learning module. We searched PubMed for English-language, peer-reviewed publications for studies in which estimated or measured prenatal or childhood EDC exposures were associated with health effects. In addition, we included peer-reviewed fact sheets and professional health provider societies' statements regarding EDCs. We summarized the epidemiological evidence about the potential health effects of five EDCs commonly found in consumer products–bisphenol A, triclosan, phthalates, parabens, and polybrominated diphenyl ethers–and developed three peer-reviewed learning modules in collaboration with Pediatric Environmental Health Specialty Units (PEHSU). The modules summarize the potential effects of EDCs on child development and health and educate healthcare professionals with strategies to counsel patients about exposures. Our next steps are to assess the efficacy of each learning module using pre-tests and post-tests to gauge knowledge gained following each module.

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

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Introduction. Many patients in sub-Saharan Africa suffer from dyspepsia [1]. It is controversial how often Helicobacter pylori is the cause, and would thus merit treatment with combined antibiotic therapy. However, untreated H. pylori infection can lead to chronic gastritis, gastric MALT lymphoma, peptic ulcer disease, and gastric carcinoma [2]. Testing for H. pylori is expensive and thus accurate diagnosis based on history would be invaluable in developing countries. This study attempts to identify the prevalence of H. pylori in Kisoro, Uganda, assess the utility of symptoms as a diagnostic test, and identify risk factors for infection.

Methods. Patients in the outpatient clinic at St. Francis Mutolere Hospital in Kisoro, Uganda were tested for H. pylori antigen in the stool and antibody in the blood. Each patient was also administered an IRB-approved survey that assessed demographics, exposure risk factors and symptoms of dyspepsia. 155 patients were enrolled (101 females, 54 males). Statistical analysis was performed using SPSS v.22.

Results. The prevalence of current H. pylori infection based on positive antigen tests was 5.2% (8/151) and the lifetime prevalence based on positive antibody tests was 41.9% (65/155). The rates of gastrointestinal disorders based on the Rome III criteria [3] were as follows: functional dyspepsia 67.7%, epigastric pain syndrome 7.7%, and post-prandial distress syndrome 42.6%. Out of the patients who had a positive antigen test (8), exactly half did not meet the qualifications for any of the functional GI disorders, suggesting that symptoms alone may not be able to predict H. pylori infection (sensitivity 50%, specificity 30%, PPV 3.85%, NPV 91.49%). Antigen positivity was associated with a lack of clean drinking water ($p<0.1$) and significantly correlated with crowding (>3 people in the household) ($p<.05$). A low socioeconomic status was not linked to antigen positivity. However, there was a strong correlation of having a family member with ulcers and testing positive for the antibody ($p<.01$), suggesting that familial clustering may play a role in H. pylori acquisition. Antibody positivity was also correlated with lack of soap ($p<0.1$) and the symptom of early satiation ($p<.05$).

Conclusions. There is a high prevalence of both functional dyspepsia and H. pylori in Kisoro, Uganda. Symptoms of dyspepsia alone may not be sensitive enough to diagnose infection with H. pylori. However, symptoms in combination with the patient's living conditions and a family history of ulcers may help to lead physicians to a diagnosis when testing is not available.

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The Role Of CD169+ Splenic Macrophages During Systemic Listeria Monocytogenes Infection

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Introduction:The precise role of splenic CD169+ macrophages following bacterial infection is poorly characterized. Current paradigm indicates that CD8α+ dendritic cells are the "obligate cellular entry point" for Listeria monocytogenes (LM) in the spleen. However, research from the Khanna lab suggests that CD169+ macrophages are the initial host of LM. To show that the CD169+ macrophages are the early host of LM we used two-photon microscopy to perform dynamic real-time imaging following infection. Furthermore, we hypothesized that these macrophages play a subsequent role in activating the adaptive arm of the immune response and the formation of immunological memory.

Methods: For in-vivo imaging studies, wild type (WT) mice were infected with green fluorescent protein-expressing LM (LM-GFP) intravenously (iv). Fluorescent antibody specific for CD169 was also administered iv. Spleens were harvested and interactions between macrophages and LM were dynamically recorded.

For T cell studies, we used CD169-DTR (DTR) mice, which enabled the targeted depletion of CD169-expressing cells following treatment with diphtheria toxin (DT). We transferred OTI cells, specific for ovalbumin, into WT and DTR mice and immunized them with irradiated LM expressing ovalbumin (IRL-OVA). Blood was collected at various time points and analyzed using flow cytometry. At 30 days mice were challenged with a lethal dose of LM and bacterial burdens were quantified 24 hours post recall infection.

Results: Two-photon microscope videos revealed uptake of LM by CD169+ macrophages 90 minutes post infection. We also observed several CD169+ macrophages containing phagocytized LM-GFP. Flow cytometric analysis of T Cell activation following IRL immunization in the absence or presence of CD169+ macrophages did not show any obvious deficiency in the magnitude or phenotype of activated OTI CD8 T cells. However, bacterial titers at 24 hours post recall infection with a lethal dose of live LM 30 days post immunization revealed higher counts in the mice that were depleted of CD169+ macrophages before primary immunization.

Conclusion: Visualization of LM-GFP being captured by CD169+ splenic macrophages suggests that the current paradigm regarding CD8α+ dendritic cells as the obligate cellular entry point for bacterial agents in the spleen should be revised. The similarities in T cell activation early after immunization between WT and DTR mice suggest that other cell populations are activating CD8+ T cells in the absence of CD169+ macrophages. However, the increased bacterial titers after rechallenge suggests a role for the CD169+ macrophages in establishing functional immunologic memory.

Supported by: The UConn School of Medicine Summer Research Fellowship

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Subacromial Bursa vs Bone Marrow Stromal Cells for Cell-Based Tendon Repair

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Introduction: Surgical repair strategies for tendon-related injuries often lead to undesirable outcomes. Subacromial bursa is discarded as surgical waste during rotator cuff surgery; however, bursa cells may be a potent progenitor cell source to improve tendon repair. The objective of this study is to compare bursa-derived cells with the gold standard bone marrow stem cells (BMSC) to engraft into surrounding tendon and produce extracellular matrix. It is hypothesized that bursa cells will show greater engraftment and increased tendon healing compared to BMSC.

Methods: Subacromial bursa and BMSC from the humeral head were harvested from five donors (56.8 ± 5.5 y/o) during primary arthroscopic rotator cuff repair. Bursa was digested in collagenase and BMSC were concentrated in the Arthrex Angel system prior to plating. Cells were expanded to P1-P2 in a 5% O2 incubator and transfected with Ubiquitin-cherry lentivirus to label the cells. Cells were incorporated into fibrin gels and implanted into full-length, central-third patellar tendon defects of 70 NOD scid gamma mice (bursa in one limb and BMSC in other). 40 control mice received fibrin gel without cells in one limb and defect only in the other.

Analysis: Tendons were imaged at 1, 2, 5 and 8 weeks using two photon microscopy, a fluorescent 3D imaging technique. Imaged tendons were uploaded into OrientationJ plugin in Fiji. Regions of interest (ROI) were traced for the anterior bridge, struts, and defect space (Fig. 1A) across every slice along the defect length (Fig. 1B). In each ROI, red pixels divided by total pixels were quantified as the percent area of cell engraftment. The bridge ROI was cropped to a 100 um width (Fig. 1C) and quantified at every slice along the defect length (Fig. 1B). Average tendon bridge thickness was thus obtained.

Results: Bursa cells trended towards greater engraftment into the host tissue at all time points compared to BMSC. At 8 weeks, 82% of limbs implanted with bursa cells contained cells while only 50% of limbs implanted with BMSC contained cells. At each time point, implantation of human cells stimulated a greater response from the host cells as the healing bridge was significantly thicker in the cell groups than no-cell controls ($p < 0.05$) (Fig. 2).

Conclusions: Bursa and BMSC derived from human donors and implanted into a mouse patellar-tendon defect model increased tendon healing. Bursa cells also displayed improved survival and engraftment compared to BMSC. This suggests that bursa-derived cells may be a readily available and improved source for cell-assisted tendon repair.

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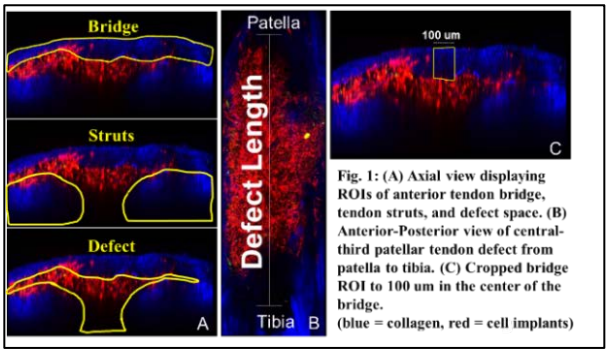

Fig. 1: (A) Axial view displaying ROIs of anterior tendon bridge, tendon struts, and defect space. (B) Anterior-Posterior view of central-third patellar tendon defect from patella to tibia. (C) Cropped bridge ROI to 100 um in the center of the bridge.
(blue = collagen, red = cell implants)

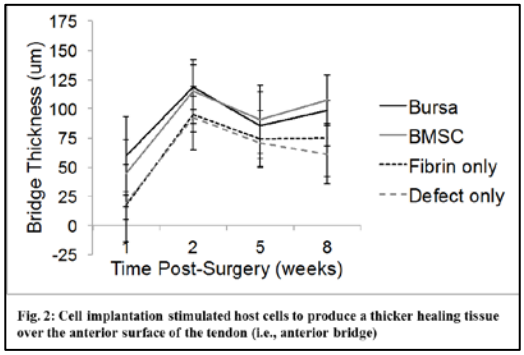

Fig. 2: Cell implantation stimulated host cells to produce a thicker healing tissue over the anterior surface of the tendon (i.e., anterior bridge)

Pap Smears in Peru: The Impact of Income and Education on Women's Attitudes

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Introduction: While the incidence of cervical cancer is 28.6 cases per 100,000 women across South America, the incidence in Peru is between 48.2 and 115.4 cases per 100,000 women (1). Furthermore, cervical cancer caused 12.3% of cancer deaths amongst Peruvian women in 2014 (2). An earlier study found setting up Pap smear clinics in rural locations made screening more accessible (3). This continuation study focuses on how income and education affect women's decision to have Pap smears and treatment if necessary.
Methods: Females aged 16-65 were recruited at rural health clinics outside Cusco. Women who had a Pap smear that day were eligible to complete a written survey. The survey included questions about demographics and attitudes toward Pap smears. Primary outcome variables included reasons for not having had prior Pap smears and whether Pap smears or returning for treatment are important. Variables were broken down into dichotomous categories for Chi-square analysis.
Results: A total of 697 women, mean age 36.44, (SD = 11.3) completed the survey. 17.36% of the participants had never had a Pap smear. Analysis showed that income affected whether or not women thought it was important to return for treatment ($p<.05$) but not whether Pap smears were important. Education level affected opinions on both returning for treatment ($p<.01$) and importance of Pap smears. ($p<.01$). There was no association between income or education and negative attitudes towards Pap smears being a reason for never having had one.
Conclusions: Education level, more than income itself, is an important factor in determining women's attitudes toward the importance of Pap smears and treatment. Education level affects whether a woman thinks Pap smears are important and whether it is important to return for treatment if necessary. Income level affects whether treatment, but not necessarily Pap smears, are important. Programs aimed at reducing the rate of cervical cancer through Pap smear utilization in Peru might also benefit from focusing on decreasing school dropout rates in these rural areas.

Supported by: The UConn School of Medicine Summer Research Fellowship

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1. Ferris, Daron G., MD, John Shapiro, MS, Christopher Fowler, BS, Carolyn Cutler, BA, and Jennifer Waller, PhD. "The Impact of Accessible Cervical Cancer Screening in Peru—The Día Del Mercado Project." Journal of Lower Genital Tract Disease 19.3 (2015): 229-33. Print.
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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.

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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.

OMICRON KAPPA UPSILON AWARDS: In recognition of excellence in the art, science, and literature of dentistry, Omicron Kappa Upsilon, the national dental honor society, presents $25 gift certificates to the UConn Health Co-Op to all students who have participated in Research Day activities.

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

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

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

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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.

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

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The Perl family for the Gustave Perl Memorial Award
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