# UNE COM

# Research and Scholarship Fall Forum

Girard Innovation Hall

October 13th, 2023

# UNE COM Research and Scholarship Fall Forum

Friday, October 13, 2023
Innovation Hall, UNE Portland Campus

12:00 p.m. **LUNCH**

1:00 p.m. **WELCOME REMARKS**

1:15 p.m. **POSTER PRESENTATIONS / JUDGING SESSION #1**

2:05 p.m. **BREAK**

2:15 p.m.

**Keynote Address**

**IS BRAIN INJURY A CHRONIC DISEASE? LESSONS FROM SPORT TO COMMUNITY**

**Ross D. Zafonte, D.O.**

*President, Spaulding Rehabilitation Hospital Chief, Physical Medicine and Rehabilitation Massachusetts General Hospital & Brigham and Women's Hospital, Earle P. and Ida S. Charlton Professor and Chairman, Department of Physical Medicine and Rehabilitation, Harvard Medical School.*

3:15 p.m. **POSTER PRESENTATIONS / JUDGING SESSION #2**

4:00 p.m. **BREAK – TEA/COFFEE**

4:15 p.m. **ORAL PRESENTATIONS**

**Student Doctor, Natalie Mistikawy, OMS-II**
*Basic Science: The Role of Lysosomal NUDT5 in the Pathogenesis of TFE3-Renal Cell Carcinoma*

**Student Doctor, Olivia Esteireiro, OMS-II**
*Original Research – Clinical: Use of Group Ketamine-Assisted Therapy for Promoting Treatment-Resistant Mental Health*

**Student Doctor, Emily Toy, OMS-III**
*Clinical Scholarship Case Study Oral Presentation: The Use of Blood Flow Restriction Therapy Post-Matrix Autologous Chondrocyte Implantation*

5:00 p.m. **AWARDS PRESENTATION**

*Please park in Bishop Street lot.*
*Shuttle will bring you to campus.*

UNE UNIVERSITY OF NEW ENGLAND
INNOVATION FOR A HEALTHIER PLANET

# First Poster Judging Session 1:15pm

| Poster # | Student Name | COM Affiliat | Title of Abstract | Mentor's Name |
|---|---|---|---|---|
| 1 | Benjamin Mugg | OMS 2 | Variable CGRP Expression May Explain Pain Differences Across Stages of Osteoarthritis | Tamara King PhD |
| 2 | Christopher Keck | OMS 1 | The Utility of BiTE Armed T Cells in Ovarian Cancer is Enhanced by Leverage of the PD-1/PDL-1 Axis with PD-1 Checkpoint Blockade, Engagement of Endogenous Immunity, and Epitope Spreading Responses | Dr. AJ Robert McGray PhD |
| 3 | Dengyumei Du | OMS 2 | Investigating the Differences in Nociception (Baseline Sensitivity) of Male and Female Drosophila melanogaster | Geoffrey Ganter PhD |
| 4 | Elizabeth Gagen | OMS 2 | Ageism's Association with Self-reported Health in Older Adults | Thomas Meuser PhD |
| 5 | Gabriel DeOliveira | OMS 2 | Transection of the Saphenous Nerve Results in Denervation of the Tibia with Modest Changes in Cortical Bone Mineral Density in Female Mice | Kathleen Becker, PhD |
| 6 | Grace Simonson | OMS 2 | Alleviating Worries of Dementia Among Older Adults Who Attend an Aging Brain Seminar | Dr. Susan Wehry, M.D. |
| 7 | Hannah Gallegos | OMS 2 | Pain Processing in Response to Noxious Cold Water Versus Noxious Electrical Stimulation | Katherine Rudolph, PT, PhD |
| 8 | Hari Nair | OMS 2 | How Does Hyperuricosuria Impact Kidney Stone Risk? | Dr. Dinesh Singh, MD |
| 9 | Hayley Gibson | OMS 3 | The Impact of Oral Contraceptive Pills on Concussion Recovery in Female College Athletes | Paul Berkner, DO |
| 10 | Hunter Scott | OMS 2 | Sex-dependent Differences in Synovial Nerve Growth Factor Levels Do Not Correspond to Differences in Joint Pain Between Male and Female Rats | Tamara King PhD |
| 11 | James Withers | OMS 3 | Psychiatric History and Post-Concussive Sleep Symptoms in Adolescent Athletes | Paul Berkner, DO |
| 12 | Jenson Kaithamattam | OMS 1 | Patient perspectives of a digital pill system to measure adherence to oral heart failure pharmacotherapy | Dr. Peter Chai |
| 13 | Jhanavi Kapadia | OMS 1 | Emergency Department Based Peer-Driven Interventions for Substance Use Disorders: A Scoping Review | Elizabeth Samuels, MD, MPH, MHS |
| 14 | Kaitlyn Belknap | OMS 2 | Fatty Acid Binding Proteins Influence on the Bone Marrow and Spleen Microenvironment In Vivo | Michaela Reagan, PhD |
| 15 | Maggie Loiselle | OMS 1 | Bacterial Metabolic Signaling Drives Neutrophil Responses in Infected Airways | Lael Yonker, MD |
| 16 | Mara Davoudi | OMS 2 | Investigating Primary Cilium-Mediated Modulation of Nociceptive Pathways | Kerry L Tucker, PhD |
| 17 | Natalie Mistikawy | OMS 2 | The Role of Lysosomal NUDT5 in the Pathogenesis of TFE3-Renal Cell Carcinoma | Harry Filippakis, Ph.D. |
| 18 | Neal Canastra | OMS 1 | Concurrent antidepressant use in patients undergoing sports meniscal surgery may confer greater risk of developing postoperative opioid use disorders. | Aristides I. Cruz, Jr., MD, MBA |
| 19 | Olivia Esteireiro | OMS 2 | Use of Group Ketamine-Assisted Therapy for Promoting Treatment-Resistant Mental Health | Selma Holden, MD, MPH, MS |
| 20 | Pantelis Antoniou | OMS 1 | Knowledge, Attitudes and Behaviours on Antimicrobial Resistance Across 14 Member States in the World Health Organization European Region: Results from a Cross-Sectional Survey | Ketevan Kandelaki, MD, MPH |
| 21 | Peter Giunta | OMS 2 | Lymph Node Metastases Develop Through a Wider Evolutionary Bottleneck Than Distant Metastases | Kamila Naxerova, PhD |
| 22 | Rachel Marino | OMS 1 | Thoracoabdominal Aortic Aneurysm Life-Threatening Events Following Endovascular Aortic Repair | Marc Schermerhorn, M.D. |
| 23 | Samantha Dunn | OMS 2 | Preliminary Results of P-RAD: A Randomized Phase II Study of Pre-operative Radiation Therapy with Immunotherapy and Chemotherapy for High-Risk Breast Cancer | Alice Ho, MD, MBA |
| 24 | Sarah Lafleur | OMS 2 | Investigating the Role of the Kynurenine Pathway in Macropinocytosis and Proliferation of TSC2-deficient Cells | Harry Filippakis PhD |
| 25 | Siddhant Sharma | OMS 3 | Bile Acids Partially Mediate the Bone Reduction and Marrow Adiposity Loss Caused by Vertical Sleeve Gastrectomy in Mice | Ziru Li PhD |
| 26 | Vasiliki Patsiogiannis | OMS 1 | Emergency Department in Home: A Novel Approach to Delivering Acute Care to Patients in the Home | Evan Berg, MD |
| 27 | Brittany Bertaux | OMS 2 | Current Status of HPV-targeted Therapies Development in Head and Neck Cancer | Jong Chul Park, MD |
| 28 | Caitlin Coates | OMS 2 | Self-management Interventions and Outcome Measures for Individuals with Chronic Traumatic Injury: A Scoping Review | Jeffery Schneider, MD |
| 29 | Delanie Kneeland | OMS 4 | Electromyocardial Manifestations in Left Ventricular Noncompaction Cardiomyopathy in the Pediatric Population with Crucial Diagnostic Considerations: A Systematic Review | Fitzsimons, PhD |
| 30 | Emily Toy | OMS 3 | The Use of Blood Flow Restriction Therapy Post-Matrix Autologous Chondrocyte Implantation | Danielle Buglione Bifolco, DPT |
| 31 | Jonathan Daniel | OMS 2 | Commotio Cordis in Sports | Geoffrey McCullen |
| 32 | Julia Balboni | OMS 2 | The Advantage of a Right-Side Anterior Retroperitoneal Approach for Primary Lumbar Spine Surgery | Dr. Brian Perri, D.O. |

# Poster Judging Session Two 3:15pm

| Poster # | Student Name | COM Affiliat | Title of Abstract | Mentor's Name |
|---|---|---|---|---|
| 33 | Ariana Pitaro | OMS 1 | Clinical Trial-Ready Patient Cohorts for Multiple System Atrophy: Coupling Biospecimen and Induced Pluripotent Stem Cells Banking to Longitudinal Deep-Phenotyping | Vikram Khurana, MD, PhD |
| 34 | Arsal Shah | OMS 2 | The Effect of High-Contact Sport Exposure on Baseline Neurocognitive Performance in High School Students | Paul Berkner, DO |
| 35 | Bridget Kelly | OMS 3 | Contemporary Treatment Paradigms Increase Survival in Pancreatic Cancer | Timothy L. Fitzgerald, MD |
| 36 | Casey McAndrews | OMS 2 | Improved Bone Morphology Following Six Months of Treatment with Canagliflozin in a Non-Diabetic Preclinical Model | Carolyn Chlebek, PhD |
| 37 | Chloe Aloimonos | OMS 2 | Changes of Lumbar Spinal Cord GFAP and CD137 Expression Following Sciatic Nerve Crush in Mice | Dr. Ling Cao MD, PhD |
| 38 | Courtney Christoforo | OMS 2 | The Effect of Extended Panel Molecular Testing on Treatment Decisions for Patients with Lung, Breast, Colon, and Prostate Cancer | Christian Thomas, MD |
| 39 | Devin Jozokos | OMS 2 | Youth Concussion Project: Highlighting the Importance of Concussion Education in School-Aged Children | Dr. Paul Berkner, D.O. |
| 40 | Elena Masters | OMS 2 | Herbal Supplements in Pregnancy: “Natural” Does Not Equal “Safe” | Andrea Bodine, MD |
| 41 | Erin Byrd | OMS 2 | An Evidence-Based Approach to Labeling Older Adult Health Status: Stable vs. Declining | Dr. Thomas Meuser, PhD |
| 42 | Hannah Gallegos | OMS 2 | Epidemiology and Outcomes of Traumatic Vascular Injury Repair by Trauma Surgeons and Vascular Surgeons in a Collaborative Model | Marco Sozzi, MD |
| 43 | Jeyrie Ramos Aponte | OMS 2 | Gastric X/A-Like Cells Mediate Effects of Gut-Bone Axis on Skeletal Homeostasis | Ziru Li, PhD |
| 44 | Jonathan Volpe | OMS 2 | Does Autonomic Drive Influence Pain Processing or the Response to Pain Treatment | Rudolph, Katherine, PT, PhD |
| 45 | Julia Baracewicz | OMS 1 | Tightness Shifts in the U.S. and China: Implications of Tightening or Loosening Norms during the Coronavirus Pandemic. | Quinnehtukqut McLamore, Ph.D. |
| 46 | Kamilla Beisenova | OMS 2 | Endocrine Catastrophes Supported by ECMO: A Case Series | Walter DeNino MD |
| 47 | Kieu-My Nguyen | OMS 4 | Impact of the Transition to Pass/Fail Scoring for COMLEX Level 1 and USMLE Step 1 on Osteopathic Medical Students at UNECOM | Cheryl Doane, DO; Carol Brenner, Ph |
| 48 | Laura Olivieri | OMS 4 | Evaluating Provider Needs: Developing a Comprehensive Assessment to Enhance Care for Individuals living with HIV/AIDS in Maine | Dr. Philip Day, PhD |
| 49 | Lee Esposito | OMS 4 | Minimally Invasive Lumbar Decompression (MILD) as a Treatment for Lumbar Spinal Stenosis | Dr. David Bozak, DO |
| 50 | Lindsey Gray | OMS 1 | Treg Depletion Syndrome: Skin Inflammation Unleashed by ADCC Depleting Biologics | Rachael Clark, MD, PhD |
| 51 | Madeleine Powers | OMS 2 | A Morphological Study of the Meniscus, Cartilage and Subchondral Bone Following Closed-Joint Traumatic Impact to Knee | Gerardo Narez, PhD |
| 52 | Madison Philhower | OMS 2 | Nerve Conduction Study in a Tat Induced HIV-associated Sensory Neuropathy Model | Ling Cao, MD/PhD |
| 53 | Maria Mazzu | OMS 3 | Development and Feasibility of the Comfort Measures Only Time out (CMOT) to Reduce Distress During Palliative Withdrawal of Mechanical Ventilation | Corey R Fehnel, MD, MPH |
| 54 | Max Russell | OMS 2 | Successful left ventricular assist device explantation due to myocardial recovery and driveline infection | Woolston, Sophie L., M.D. |
| 55 | Nathan Nuengchana | OMS 2 | Changes in Tollip Expression in the Development of HIV-Tat-associated Sensory Neuropathy | Ling Cao, M.D., Ph.D. |
| 56 | Neda Toutounchi Shabestari | OMS 3 | Management and Treatment of Patient with COVID-19 in Long Term Care | Jabbar Fazeli, MD |
| 57 | Pavania Elavalakanar | OMS 1 | G-CSF Administration is Associated with Worse Treatment Response and Survival after CAR T-Cell Therapy | Jon Arnason, MD |
| 58 | Rachelle Mendola | OMS 2 | Activity-dependent genetic labeling of corneal neurons in the spinal trigeminal nucleus and lateral parabrachial nucleus in response to corneal pain | Ian Meng, Phd |
| 59 | Samantha Scetta | OMS 2 | Review and Potential Clinical Validation of the Insignificance of Race in Prenatal Biochemical Screening for Fetal Anomalies | Dr. Ricky Grisson, MD, MPH |
| 60 | Simona Lysakova | OMS 1 | Psychosocial Function of Vitiligo Patients in the Face of Stigmatization: A Systematic Review | Tracey A. Revenson, PhD |
| 61 | Swapnika Mallipeddi | OMS 2 | Implementing Low-Barrier COVID-19 Testing Clinics for Vulnerable Populations in Partnership with Community Based Organizations | Kathleen Fairfield, MD |
| 62 | Tsunagu Ichikawa | OMS 2 | Irisin Enhances Osteocyte Mechanosensitivity to Fluid Shear Stress | Estell, Eben PhD |
| 63 | Anna Holcomb | OMS 3 | The Prozone Phenomenon: A Case Study Examining the Rare Syphilis Phenomenon | Mohamedazhar Gangat, MD |
| 64 | Gabrielle McGeorge | OMS 1 | Mice Deficient in PDE3A Develop Characteristic Findings of Nonalcoholic Steatohepatitis | Bernadette Chen, M.D. |

# Student Abstracts by Poster Number

**1.**

**Variable CGRP Expression May Explain Pain Differences Across Stages of Osteoarthritis**

Mugg, B OMS II, Scott, HT OMS II, Zuke, JT B.S., Caradonna, P B.S., King, T Ph.D.

University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction**: Osteoarthritis (OA) pain is often described as mid stage OA, characterized by increasingly predictable pain during everyday activities, such as climbing the stairs. Advanced OA pain is associated with development of persistent pain which often results in the avoidance of recreational and social activities. The underlying physiological mechanism behind transition between mid-stage and advanced OA pain remains unknown. Furthermore, it has been found that females have a higher prevalence of OA pain and report this pain as more severe. CGRP has been proposed to contribute to synovitis, and increased CGRP was observed in human patients with symptomatic knee joint OA. We used a rat model of OA pain to examine the hypothesis that sprouting of CGRP expressing nerve fibers innervating the knee joint will correspond with emergence of advanced OA in males and females.

**Methods**: Rats knee joint spaces were injected with saline (control) or with monosodium iodoacetate (MIA) to induce advanced or mid stage knee joint OA. In males, 80 mg/ml MIA induces advanced OA pain and 16 mg/ml MIA induces mid-stage OA pain. In females, 16 mg/ml MIA induces advanced OA pain. Two weeks post-knee joint injection, rats underwent tissue collection and knee joints were processed for immunohistochemical staining of CGRP. CGRP expressing nerve fiber endings within the medial connective tissue of the joint were imaged and analyzed using image J.

**Results**: In males, our preliminary data indicate a dose dependent increase in CGRP positive fiber length. When compared across sex, females had longer CGRP positive fiber lengths compared to males.

**Conclusions:** Preliminary results support the hypothesis that significant sprouting occurs in mid stage and advanced OA pain with the lowest sprouting seen in males treated with 16 mg/ml, representing mid stage osteoarthritis. Preliminary data suggests that CGRP expressing sensory nerve fiber endings undergo pathological sprouting within the knee joint corresponding to development of both mid-stage and advanced OA pain. Our preliminary data also indicate that females may have higher levels of CGRP positive joint innervation compared to males, even in the uninjured state.

Acknowledgements: The University of New England College of Osteopathic Medicine. This work has been supported by the Khan Student fellowship. All work was IACUC approved. Tissue processing was performed by the COBRE histology and imaging core.

**2.**

**The Utility of BiTE Armed T Cells in Ovarian Cancer is Enhanced by Leverage of Engagement of Endogenous Immunity, of the PD-1/PDL-1 Axis, and and Epitope Spreading Responses**

Keck[1,2], Christoher MSc OMS I, McGray[1], AJ Robert PhD, Chiello[1], Jessie.

Roswell Park Comprehensive Cancer Center, Department of Immunology, Buffalo, New York.
University of New England College of Osteopathic Medicine, Biddeford, Maine.

**Introduction:** Ovarian cancer is a challenging disease with a considerable mortality rate that is in part attributed to its often late-stage diagnosis. Despite the significant levels of tumor infiltrating lymphocytes (TILs) present in high grade serous ovarian tumors, immunotherapeutic treatments remain limited in efficacy. In many cases this can be attributed to the high proportion of non-tumor antigen specific, “bystander”, T cells in the TIL population. Utilizing subset of adoptive cell therapy (ACT) that includes the arming of T cells with Bispecific T Cell Engagers (BiTEs) it is possible to redirect bystander TILs against a target antigen. We hypothesize that there is substantial rationale for synergistic combination of BiTE armed T cell therapy with PD-1 checkpoint blockade to enhance tumor killing capabilities of these individual treatment modalities. Based on previous data, we also hypothesize epitope spreading responses may be a mechanism of endogenous immune cell engagement in BiTE armed
therapy and, thus, could be a viable point of leverage to improve the therapeutic efficacy and enhance durable tumor control.

**Methods:** Tumor cell killing efficacy of BiTE armed T cells in combination with PD-1 was measured in vitro using a serial co-culture models. Concurrently, changes in T cells exhaustion and killing were measured via flow cytometry and IFNγ and Granzyme B ELISA assays. Epitope spreading responses were assessed in vivo by the enhancement of OVA antigen specific CD8+ T cell population in tumor bearing mice. Interrogation epitope spreading mechanisms utilized tri-culture models with mature dendritic cells, followed by flow cytometry analysis of SIINFEKL (OVA) epitope presentation on MHC class II molecules.

**Results:** The addition of PD-1 blockade produces a statistically significant increase killing by BiTE armed T cells in vitro as the T cells approach exhaustion in serial co-culture. Concurrent analysis of the kinetic changes of T cell markers revealed significant differences in exhaustion and killing related marker (PD-1, CD107a, CD39, and CD3e) kinetics of BiTE armed T cell vs bystander T cells population. There is also demonstrated evidence of epitope spreading through the increased accumulation of OVA specific T cells in the TME of BiTE armed T cell treated mice as compared to unarmed T cell controls.

**Conclusions:** Significantly our results support utilization of PD-1 checkpoint blockade in combination with BiTE armed T cell therapy as a method to enhance therapeutic efficacy. These interrogations also begin to uncover specific underlying mechanisms related to T cell exhaustion, loss of effector function, and the durability of tumor killing responses by T cells, all of which could serve as points of therapeutic leverage in ovarian cancer treatment. We also demonstrate epitope spreading responses as powerful and exploitable point of leverage in BiTE armed T cell therapy.

**3.**

**Investigating the Differences in Nociception
(Baseline Sensitivity) of Male and Female *Drosophila melanogaster***

Du, D, OMS II, University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** Chronic pain treatment in the US relies on opioids, but their dependency poses risks of morbidity. Addressing the crisis requires innovative strategies like genetic pharmacology. Research shows women's higher susceptibility to chronic pain. Drosophila

melanogaster, mirroring human responses to noxious stimuli, is a model organism. The conserved nociception pathway in Drosophila offers insights into human processes. This study focuses on foundational pain sensitivity of male and female Drosophila in response to thermal stimuli. The main hypothesis is that feminizing male nociceptors causes hyposensitivity and masculinizing female nociceptors causes hypersensitivity[TD1].

**Method:** This investigation involved the manipulation of male and female primary nociceptors through RNA interference, utilizing the Gal-4 and UAS system to modify the sex determination splicing cascade. Activating the Transformer-female (Tra-F) gene is expected to feminize male nociceptors, while suppressing Tra-F is expected to masculinize female nociceptors. Individual flies were immobilized using a vacuum setup and exposed to an infrared laser directed at their thoracic region. Flies held cotton coated with sugar, enabling leg grasp. The time between laser stimulation onset and cotton release was recorded as indicative of the threshold behavioral pain response.

**Result:** The experimental groups, Tra-F and Tra-IR[TD2], demonstrated no significant differences in responsive percentages compared to the no-Gal4 normal control group, with p-values of 0.576 and 0.91 respectively. However, significant variations in responsiveness[TD3] were observed between the experimental groups and the no-UAS normal control, with p-values of 0.018 and 8.7e-10. Notably, significant differences were also evident between the two normal control groups (no-Gal4 and no-UAS)

**Conclusion:** Although both Tra-F and Tra-IR experimental groups exhibited significant differences in nociception sensitivity compared to the no-UAS control, no such distinctions were found when compared to the no-Gal4 control. Both groups demonstrated hypersensitivity to noxious stimuli, compared to no-UAS, contradicting the initial hypothesis. This outcome urges an exploration of the relationship between fly pigmentation and temperature shifts achieved during thermal stimulation. We may also explore the efficacy of adult fly sex determination cascade modifications, and extend the sex manipulation to other neurons in the pain circuit.

**Acknowledgements:** The study was conducted at the University of New England College of Osteopathic Medicine, with support from the Kahn Family Foundation. Gratitude is extended to the Ganter Laboratory, in the College of Arts and Sciences, for its valuable assistance.

**4.**

**Ageism's Association with Self-reported Health in Older Adults**

Gagen, E, OMS II[1], Meuser, TM, Ph.D.[2]
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]University of New England Center for Excellence in Aging and Health, Portland, Maine

**Introduction:** Victimization through ageism is a common occurrence in older adults that has associations with negative mental and physical health outcomes. There are many other factors, however, that also influence health outcomes, including demographics (e.g., advancing age is associated with poorer physical health), personality style (e.g., neuroticism is associated with poorer mental health), and loneliness – a risk factor for decline in both physical and mental health. The UNE Legacy Scholars Program (LSP) collects annual survey data on health and wellness from adults aged 55+ years primarily residing in Maine. It includes epidemiological surveys as well as additional questions regarding participants demographics and self-evaluation of their health. The purpose of this project was to determine if self-rated victimization through

ageism independently predicts poorer mental and physical health when controlling for other relevant factors.

**Methods:** Data from 230 participants were used in this project (76% female, mean age 74). Physical and mental health were measured through 2 approaches: The SF-12 questionnaire, a well validated epidemiological survey, and a composite scale created using multiple variables from the Legacy Scholars dataset. Hierarchical multiple regression was employed to determine the degree to which ageism-related victimization is independently predictive of the dependent variables when controlling for demographics, personality traits, and loneliness.

**Results:** Victimization through ageism was shown to be predictive of poorer self-rated mental and physical health when controlling for age, sex, personality traits, and loneliness. This was true in each approach to measurement of the dependent variables: established measure (SF-12) and composite from LSP variables. Ageism was more predictive of physical health than of mental health and was also more predictive when using the composite variables over the SF-12.

**Conclusion:** Since victimization through ageism independently predicts poorer self-rated mental and physical health, it appears to be an important screening metric for evaluating health in older adults. Age discrimination is not always obvious and someone having these experiences may not be aware of the impact it can have on their health. These results also emphasize the important role that ageism plays in healthcare. Many patients face age discrimination in healthcare which may compound the negative effect it has on their health.

**Acknowledgements:** The University of New England College of Osteopathic Medicine.

IRB approved, #0523-19

**5.**

**Transection of the Saphenous Nerve Results in Denervation of the Tibia with Modest Changes in Cortical Bone Mineral Density in Female Mice**

DeOliveira[1], G, OMS-II, Lizotte[1], T, Caradonna[2], P, Eaton[2], V, King[1,2], T, Ph.D., Becker[1], K, Ph.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]COBRE for the Study of Pain and Sensory Function, University of New England, Biddeford, ME

**Introduction**
Osteoporosis affects over 53 million adults in the United States and is a major risk factor for fractures, 10% of which involve the tibia and fibula. The nervous system has been identified as a regulator of bone mineral density (BMD), with sensory and sympathetic neurons upregulating bone formation and bone resorption, respectively. The impact of sensory denervation on bone and its impact on fracture risk have not been well established. Preliminary data from the Becker Lab has shown the saphenous nerve, a sensory nerve, as a primary source of tibial innervation coupled with L2 dorsal root ganglion (DRGs) in mice. We hypothesize that saphenous nerve injury will decrease tibial innervation, reduce BMD, and increase nerve injury signal, ATF3, in the L2 DRG.

**Methods**
The saphenous nerve was transected (SNT) or a tibial resiniferatoxin (RTX) injection was performed in 8-9 week-old C57Bl6/J mice. Innervation in the proximal tibial periosteum was

quantified 14 days post-SNT with immunohistochemistry to assess total (β3-tubulin), sensory (calcitonin gene-related peptide, CGRP), and sympathetic (tyrosine hydroxylase, TH) innervation. BMD and architecture were assessed by DEXA and microCT analysis (n=10-15/sex) 3 months post-SNT. ATF3 expression was assessed in the L2 DRG harvested 72-hours post-surgery and compared between RTX (n=2) and vehicle (n=5) injected mice.

**Results**
SNT resulted in a 45-55% decrease in β3-tubulin ($p=0.003$), CGRP ($p=0.007$), and TH ($p=0.049$) positive fibers in the tibia ipsilateral to SNT compared to contralateral control tibiae. No change was observed in cancellous bone ($p>0.6$) in the proximal tibia of SNT mice compared to sham control mice tibiae. However, cortical tissue mineral density was only reduced in female SNT mice ($p=0.012$). Finally, tibial injury with RTX increased ATF3 staining in the L2 DRG compared to vehicle injected mice.

**Conclusion**
These studies revealed the saphenous nerve as a source of sensory and sympathetic tibial innervation. Denervation of both fiber types resulted in a modest decrease of tibial cortical bone and no change in cancellous bone. This data indicates the saphenous nerve only minimally regulates BMD in adult mice. However, denervation may play a key role in fracture healing. Additionally, increased ATF3 staining in the L2 DRG of RTX mice displays sensitivity of the saphenous nerve in tibial injury. Further studies are needed to assess the effect this has on bone strength and fracture healing.

**Acknowledgement**
The University of New England (UNE) College of Osteopathic Medicine. A special thanks to the Becker lab for allowing me to contribute to their progress and supporting this work in advancing research into the relationship between bone health and the nervous system. Thank you to the UNE Histology and Imaging Core for training and use of equipment, which allowed this project to take place. This work has been supported by the Kahn Family Foundation Research Fellowship, a pilot grant from P30GM145497, and R16GM150784. Animal work was approved by the UNE IACUC committee (protocol #032521-007).

**6.**

Alleviating Worries of Dementia Among Older Adults Who Attend an Aging Brain Seminar
Simonson, G, OMS II, Wehry, S, M.D.
University of New England College of Osteopathic Medicine, Biddeford, Maine

Introduction: Research demonstrates the public lacks knowledge and holds a negative perception regarding dementia. This contributes to prevalent concerns regarding dementia in later years, which is now called dementia worry. Dementia worry negatively impacts cognitive ability in otherwise healthy older adults, but no successful or easily accessible programs to address these specific concerns have been identified. We hypothesized participation in an aging brain seminar would significantly alleviate dementia worry in older adults.

Methods: A qualitative pre-post survey research design was used. Attendees completed anonymous paper surveys immediately before and after the seminar which were later transcribed to Redcap. Both surveys included the 12-item Dementia Worry Scale - a validated set of Likert scales used in other studies to assess long-term dementia worry. Two additional Likert questions were added to the post-survey to determine the immediate effect on dementia worry and intent to adopt strategies learned from the seminar. The 45 minute in-person talk,

followed by a Q&A, covered normal and abnormal aging brain changes, and research based strategies for healthy brain aging. Attendees were recruited by AgingME through partnerships at community centers in Maine. Data was screened to exclude incomplete surveys, non-older adults, and participants with prior diagnoses of anxiety or dementia. Descriptive data analysis was run in Excel, and Mann-Whitney analysis was run in VassarStats.

Results: At the time of this abstract, 7 sessions were attended by 160 people; 94 pre- and 97 post-surveys were returned. After screening, viable data was obtained for 61 pre- and 61 post-surveys. 69% reported their dementia worry was somewhat or significantly improved; 68% reported they were very likely or definitely going to take action. Collectively, the Dementia Worry scale was reduced (median pre=19, median post=16, range=12 - 41), but results were insignificant (p=0.058).

Conclusion: The aging brain seminar was successful. It resulted in an immediate reduction of dementia worry and intent to change behavior, and it can be effectively delivered by a medical student. Further research is warranted to determine if the seminar has a long-term effect on dementia worry and sustained adoption of healthy behaviors.

Acknowledgments: The University of New England College of Osteopathic Medicine. This work has been supported by the Peter Morgane Student Research Fellowship (to GS), and the Health Resources & Services Administration, GWEP award #U1QHP33080-04-01 (to SW). IRB exemption was granted by the University of New England Office of Research Integrity (protocol #0523-08).

**7.**

## Alleviating Worries of Dementia Among Older Adults Who Attend an Aging Brain Seminar

Simonson, G, OMS II, Wehry, S, M.D.
University of New England College of Osteopathic Medicine, Biddeford, Maine

Introduction: Research demonstrates the public lacks knowledge and holds a negative perception regarding dementia. This contributes to prevalent concerns regarding dementia in later years, which is now called dementia worry. Dementia worry negatively impacts cognitive ability in otherwise healthy older adults, but no successful or easily accessible programs to address these specific concerns have been identified. We hypothesized participation in an aging brain seminar would significantly alleviate dementia worry in older adults.

Methods: A qualitative pre-post survey research design was used. Attendees completed anonymous paper surveys immediately before and after the seminar which were later transcribed to Redcap. Both surveys included the 12-item Dementia Worry Scale - a validated set of Likert scales used in other studies to assess long-term dementia worry. Two additional Likert questions were added to the post-survey to determine the immediate effect on dementia worry and intent to adopt strategies learned from the seminar. The 45 minute in-person talk, followed by a Q&A, covered normal and abnormal aging brain changes, and research based strategies for healthy brain aging. Attendees were recruited by AgingME through partnerships at community centers in Maine. Data was screened to exclude incomplete surveys, non-older adults, and

participants with prior diagnoses of anxiety or dementia. Descriptive data analysis was run in Excel, and Mann-Whitney analysis was run in VassarStats.

Results: At the time of this abstract, 7 sessions were attended by 160 people; 94 pre- and 97 post-surveys were returned. After screening, viable data was obtained for 61 pre- and 61 post-surveys. 69% reported their dementia worry was somewhat or significantly improved; 68% reported they were very likely or definitely going to take action. Collectively, the Dementia Worry scale was reduced (median pre=19, median post=16, range=12 - 41), but results were insignificant (p=0.058).

Conclusion: The aging brain seminar was successful. It resulted in an immediate reduction of dementia worry and intent to change behavior, and it can be effectively delivered by a medical student. Further research is warranted to determine if the seminar has a long-term effect on dementia worry and sustained adoption of healthy behaviors.

Acknowledgments: The University of New England College of Osteopathic Medicine. This work has been supported by the Peter Morgane Student Research Fellowship (to GS), and the Health Resources & Services Administration, GWEP award #U1QHP33080-04-01 (to SW). IRB exemption was granted by the University of New England Office of Research Integrity (protocol #0523-08).

**8.**

**How Does Hyperuricosuria Impact Kidney Stone Risk?**

Nair[1,2,3], H, OMS I; Ryan[2], T, B.S.; Motamedinia[2], P, M.D.; Montgomery[3], T, M.D.; Dahl[3], N, M.D. Ph.D.; Singh[2], D, M.D.
1University of New England College of Osteopathic Medicine, Biddeford, Maine
2Yale School of Medicine, Department of Urology
3Yale School of Medicine, Department of Internal Medicine, Section of Nephrology

**Background:** Nephrolithiasis presents a significant public health burden, with an estimated prevalence of 10% and recurrence rate of 50% within 10 years. A known risk factor for renal stones is hyperuricosuria, which may occur with excessive dietary intake of purine-rich foods, found in animal protein. It remains unclear whether hyperuricosuria presents a greater risk for calcium-based or uric acid (UA) kidney stones. In this study, we sought to better understand how UA excretion impacts kidney stone risk.

**Methods:** We retrieved demographic, clinical, and laboratory data from a retrospective database of kidney stone patients seen at Yale from 1994 to 2021. Patients were included in this study if they had a kidney stone analysis, 24-hour urine, and serum chemistry within 1 year of each other. Patients taking xanthine oxidase inhibitors were excluded from the study. We divided patients into groups based on kidney stone composition, defined as the primary component being >50% calcium oxalate, calcium phosphate, or UA. We evaluated multiple measures of UA metabolism, including serum UA, UA normalized to creatinine, UA clearance, and UA per volume glomerular filtration. Group differences were analyzed by chi-squared and Kruskal-Wallis tests via Prism GraphPad.

**Results:** Out of 10163 nephrolithiasis patients, 4294 had a kidney stone analysis, of which 844 met the inclusion criteria. We identified 619 calcium oxalate stone formers (COSFs), 145 Uric Acid Stone Formers (UASFs), and 80 calcium phosphate stone formers (CPSFs). UASFs were more likely to be male ($p<0.01$) and displayed significantly lower urine pH ($p<0.01$) and eGFR ($p<0.01$). UASFs exhibited greater serum UA ($p<0.01$) and lower urine UA normalized to creatinine. UASFs also showed lower UA clearance than COSFs ($p<0.01$), but greater UA per volume glomerular filtration ($p<0.01$). There were no significant differences between calcium-based stone formers and UASFs in terms of absolute UA excretion, fractional excretion of UA, and glomerular load of UA between all three groups.

**Conclusion:** Despite forming UA kidney stones, UASFs demonstrate lower UA excretion than calcium-based stone formers, suggesting that decreased pH and renal function may play a more significant role on UA stone formation. Treatment efforts for UA stones should focus on urine alkalinization and chronic kidney disease management. Future research could study whether xanthine oxidase inhibitors are more indicated in calcium stone formers.

**Acknowledgements:** Yale University, Department of Urology and Department of Internal Medicine, Section of Nephrology. This work was supported by the Peter Morgane Student Research Fellowship.
**IRB**: Institutional Review Board Approval was obtained in August 2018 at Yale University where this study was conducted.

**9.**

## The Impact of Oral Contraceptive Pills on Concussion Recovery in Female College Athletes

Gibson[1], H, OMS III, Stephenson[1,2], K, Ph.D., Berkner[1], P, D.O.
1-University of New England College of Osteopathic Medicine, Biddeford, Maine;
2- Harvard Medical School, Department of Physical Medicine and Rehabilitation, Boston, MA

### Introduction

The purpose of this study is to evaluate if female athletes' concussion recovery differs between those who take oral contraceptive pills (OCPs) and those who do not. Research has suggested there is a difference in concussion symptoms and recovery between males and females that is not well understood but may be attributed to hormonal cycling. OCPs reduce fluctuations in hormone levels during the menstrual cycle and may mitigate some of the sex differences reported in previous literature.

### Methods

This is a retrospective analysis of the Head Injury Tracking (HIT) platform, a registry of concussions reported in Division III college athletes. Health information (e.g., age, sex, last menstrual period (LMP), OCPs use, ADHD history, injury date, injury mechanism, evaluation date, Post-Concussion Symptom Scale responses, and return dates for school and sport) was recorded by athletic training staff at each school. Participants included females aged 18 to 24, with a LMP within 90 days of injury, evaluated within 14 days who returned to school and sport within 180 days of injury. Those with ADHD were excluded. Cases were grouped by OCP use. Independent sample T-tests were used to test for group differences in time to return to play, time to return to school, and symptom scores.

**Results**
The final sample included 249 athletes (OCP users *n= 161;* non-OCP users *n*=88). Athletes not taking OCPs returned to sports significantly slower after concussion (26.45 ± 32.07 days after injury) than their counterparts taking OCPs (19.92 days ± 20.01) (*t*=-1.98, *p*=.004, *d*=.24). They did not differ on days to return to school (*p*= 0.53) where athletes on OCPs returned to school on average 7.08 ± 8.11 days after injury compared with those not on OCPs who returned 7.42 ± 7.34 days after injury. Additionally, they did not differ in symptom scores (*p*= 0.62). Athletes on OCPs had an average symptom score of 18.81 ± 16.07 compared to 20.02 ± 15.55 in those not on OCPs.

**Conclusion**
This data suggests that athletes on OCPs return to sport sooner than those who are not; yet, there were no differences in return to school. It is possible that academic demands may contribute to this outcome. Despite the difference in return to sport timeline, there is no significant difference in symptom score. It is not possible to fully describe the impact of OCPs on concussion recovery and it is clear that more research is needed to understand concussion recovery, specifically in females.

**Acknowledgements**
The University of New England College of Osteopathic Medicine and The Maine Concussion Management Initiative. The University of New England IRB committee deemed this project Non-Human Subjects Research (project #20.02.20-023)

**10.**

**Sex-dependent Differences in Synovial Nerve Growth Factor Levels Do Not Correspond to Differences in Joint Pain Between Male and Female Rats**

Scott, HT, OMS-2, Mugg, B, OMS-2, Zuke, JT, B.S, King, T, Ph.D.
University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** Osteoarthritis (OA) pain is categorized as pain during joint use that dissipates during rest (mid-stage OA pain) or development of persistent pain that does not diminish with joint rest (advanced stage OA pain). Females have higher prevalence of pain and report more severe pain. Mechanisms underlying sex differences and transition from mid-stage to advanced OA pain are unknown. Nerve growth factor (NGF) expression in joint tissue and synovial fluid is proposed to promote OA pain through direct nociceptor sensitization and hyperalgesia, sprouting of sensory neurons in pathologic bones, and increased innervation. Our study compared NGF expression in the knee joint synovial fluid of male and female rats treated with 16 mg/mL monosodium iodoacetate (MIA), which induces mid-stage OA pain in males and advanced OA pain in females. We hypothesized that MIA treated female rats will show increased NGF expression in their synovial fluid compared to male rats.

**Methods:** Male and female Sprague Dawley rats received MIA injections of 16 mg/mL MIA. Two weeks later, weight asymmetry was used to verify MIA-induced knee joint pain and synovial fluid was collected. NGF levels were assessed using a commercially available ELISA kit. Statistical analyses were performed using analysis of variance (ANOVA).

**Results:** Intra-articular injection of 16 mg/mL MIA produced weight asymmetry within 14 days post-injection verifying knee joint pain. Preliminary data indicate that knee joint injection of 16 mg/mL MIA did not alter NGF levels within the synovial fluid of male or female rats compared to contralateral control joints.

**Conclusion:** MIA-induced weight asymmetry indicates induction of OA joint pain. Lack of differences in synovial NGF of MIA treated joints of male or female rats disproves our hypothesis. However, this is consistent with published and newly collected data within Dr. King's laboratory demonstrating that males and females treated with 16 mg/mL MIA display similar levels of joint pathology despite females developing advanced OA pain and males developing mid-stage OA pain.

**Acknowledgements:** The University of New England College of Osteopathic Medicine and the Department of Biomedical Sciences. A special thanks to the King Lab and the UNE COBRE Behavior Core for their support and previous efforts. This work was supported by the Peter Morgane Student Research Fellowship (to HS) and the Kahn Family Foundation (to BM). Animal work was approved by the UNE IACUC committee.

**11.**

**Title: Psychiatric History and Post-Concussive Sleep Symptoms in Adolescent Athletes**

Withers[1], J, MS-III, Mendola[2], R, MS-II, Stephenson[1,2,3], K, Ph.D., Berkner[1,2], P, D.O.

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Maine Concussion Management Initiative, Maine
[3]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Boston, Massachusetts

**Introduction:** Sleep disorders are common following a concussion and are associated with increased recovery time. Pre-existing depression is linked to an extended recovery time and elevated acute post-concussion symptoms, including sleep symptoms. The purpose of this study was to examine the impact of a history of psychiatric treatment (HxPsy) on post-concussive sleep symptom severity among adolescent athletes and to investigate sex differences in post-concussive sleep symptoms in adolescent athletes with a HxPsy.

**Methods:** A retrospective analysis of the Maine Concussion Management Initiative (MCMI) database was conducted to investigate the relationship between a HxPsy and post-concussion sleep symptoms in high school athletes (14-18 years) within 2 to 7 days of sustaining a concussion. The Post-Concussion Symptom Scale (PCSS) was completed by each athlete as part of their post-injury testing battery. The PCSS is scored on a Likert scale from 0 (none) to 6 (severe). Sleep-related items on the PCSS (which includes fatigue, trouble falling asleep, sleeping more than usual, sleeping less than expected, and drowsiness) were summed to create a sleep symptom score (0 to 30) where a higher score correlates increased sleep symptoms. The relationship between the sleep score and HxPsy was examined through an independent t-test. Sex differences were examined for those with a psychiatric history using a t-test. Statistical significance at $p \leq .05$.

**Results:** The final sample included 1146 adolescents ($M$=15.2 ±1.11 years old; 42% female), 110 with a psychiatric history, and 1036 without. Those who reported a HxPsy reported significantly more post-concussion sleep symptoms ($M$=6.00± 6.45) compared to those without

a HxPsy (*M*=3.48±4.56) (*t*(1144) = -5.27; *p*<.001; *d*=0.45). Females with a HxPsy (*n*=57; *M*=7.25 ±7.27) had significantly higher Sleep Symptom scores compared to their male (*n*=53; *M*=4.66 ±5.17) counterparts (*t*(108)= 2.13; *p* =.02; *d*=0.41).

**Conclusion:** This study provides evidence of a significant difference between those with and without a HxPsy on post-concussion sleep symptoms in adolescent athletes. It provides support for sex specific differences in post-concussion sleep symptoms in this population. This study adds to the existing literature on the importance of mental health screening in adolescent athletes with concussions and gives insight to which populations are more at risk of increased sleep symptoms post-concussion.

**12.**

Jenson J. Kaithamattam
University of New England College of Osteopathic Medicine
OMS-I
August 16, 2023

Title: Patient perspectives of a digital pill system to measure adherence to oral heart failure pharmacotherapy

Introduction/Background:
Heart failure (HF) affects 6.2 million Americans and is a leading cause of hospitalization. Despite effective pharmacologic options, adherence is suboptimal, resulting in disease progression. Digital pill systems (DPS) that use an ingestible radiofrequency emitter to measure medication ingestion may be a strategy to measure and respond to non-adherence.

Methods:
We conducted semi-structured qualitative interviews to explore facilitators and barriers associated with using the DPS to measure HF pharmacotherapy adherence among individuals admitted to the hospital with HF. Interviews covered baseline perceived adherence, introduced participants to the DPS and sought formative feedback and perceptions of the system. Debrief guides were reviewed with the study team and analyzed using a framework matrix.

Results:
Mean age of participants (N=20) was 68 years, predominantly female (N=11, 55%), white (N=13, 65%), and non-Hispanic (N=18, 90%). Most participants favored the use of DPS to measure HF pharmacotherapy adherence (N=12, 60%). Participants perceived the DPS as a helpful tool to self-monitor adherence and increase personal accountability. They also described interest in interacting with reminders associated with DPS adherence patterns. Only 30% of participants reported privacy concerns surrounding DPS.

Conclusion:
Individuals with heart failure perceived DPS as an acceptable and useful tool for measuring medication adherence.

**13.**

# Emergency Department Based Peer-Driven Interventions for Substance Use Disorders: A Scoping Review

Kapadia[1], JH, OMS-1, Naeem[2], AH, B.A., Zhang[2], R, B.S., Fan[2], M, B.S., Kirchwey[2], T, M.D., Lin[2], N, B.S., Becker[3], S, Ph.D., Samuels[4], EA, M.D., M.P.H., M.H.S

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Brown University Warren Alpert Medical School, Providence, Rhode Island
[3]Center for Dissemination and Implementation Science at Northwestern University Feinberg School of Medicine, Chicago, Illinois
[4]UCLA Department of Emergency Medicine, Los Angeles, California

**Introduction:** Increasingly, Emergency Departments (EDs) are implementing programs involving community health workers (CHWs) and peer recovery specialists (PRS) to engage individuals with substance use disorders (SUDs) and link patients to harm reduction services, addiction treatment, and social services. ED CHW and PRS programs are heterogenous, but there is a growing body of research evaluating the effectiveness of these programs. This scoping review aims to assess existing literature on CHW and PRS programs including program structure, services provided, and treatment outcomes.

**Methods:** We conducted a scoping review of ED-based CHW and PRS programs for patients with SUDs. Article searches were performed across databases such as PubMed, Embase, MedLine/OVID, and World of Science, in addition to grey literature sources. Article screening for eligibility was performed by two independent reviewers, with disagreements resolved by a third reviewer. Included articles underwent a thorough review, and data was extracted on intervention details and program outcomes.

**Results:** This review included sixty-five articles on thirty-seven distinct programs. Most programs (70.3%, 26/37) included peers on their intervention teams, while more than a third (35.1%, 13/37) utilized CHWs or health navigators. Less than half (40.5%, 15/37) of the programs provided services to patients with diverse SUDs, while 10.8% (4/37) exclusively focused on individuals with alcohol use disorder. Roughly half (48.6%, 18/37) centered on individuals with opioid use disorder. Just under half (45.9%, 17/37) extended services beyond ED involvement, encompassing inpatient care or community service navigation. Over a third (35.1%, 13/37) provided case management. All programs ensured referral to treatment. A little over a third (35.1%, 13/37) offered harm reduction services, with 21.6% (8/37) focusing on initiating buprenorphine treatment in the ED. About half (48.6%, 18/37) supplied services addressing health-related social needs. Most programs (70.2%, 26/37) assessed treatment engagement, with a significant proportion (80.8%, 21/26) reporting improved engagement among participants.

**Conclusion:** Programs involving ED-based CHWs and PRS vary in design and services provided. Evidence suggests that such programs potentially enhance treatment engagement. Further research is needed to evaluate effectiveness, identify components of successful programs, and promote the implementation of successful models.

**Acknowledgements:** This study was conducted at Brown University Warren Alpert Medical School. I want to thank my co-authors for their help and support in screening and reviewing articles. I also want to thank Dr. Samuels for her mentorship throughout this project. This study was partially supported by the COBRE on Opioids and Overdose (P20 GM125507) and the Centers for Disease Control and Prevention (R01CE003516).

**14.**

## Fatty Acid Binding Proteins Influence on the Bone Marrow and Spleen Microenvironment In Vivo

Belknap[1], K, M.S., OMS II, Campbell[2], H, M.S., Ryzhov[2], S, Ph.D., Reagan[2], MR, Ph.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]MaineHealth Institute for Research, Scarborough, Maine

Multiple Myeloma (MM) is a hematological malignancy derived from the monoclonal expansion of plasma-B cells in the bone marrow. Each year, approximately 32,000 people are diagnosed with MM and 13,000 patients succumb to the disease. Increased fatty acid binding protein four (FABP4) expression is correlated with the accumulation of adipose tissue and an increased risk in developing MM. Similarly, fatty acid binding protein five (FABP5) is associated with negative outcomes for MM patients. Our lab is exploring the roles of endogenous FABPs of the host microenvironment on tumor outcomes using an FABP4/5 global knockout mouse, which has never been described before. Before inoculating these mice with cancer, we aimed to determine if there were any baseline differences between these and the WT control mice. We analyzed the microenvironment of the bone marrow and spleens of FABP4/5 heterozygous mice via flow cytometry to identify different cell populations. I initiated and performed optimization for all antibody selection, staining, cell identification, and analysis of this work. The flow cytometry markers we have used so far are: B220, CD11b, CD11c, CD19, CD38, CD3e, CD4, CD45, CD73, CD8, F4/80, IgD, IgM, Ly6C, Ly6G, and MHC II. Our work established the necessary protocols for the mouse genotyping, cell flow cytometric analysis, and breeding that will be necessary for the next steps of this work. We also optimized the methods for viable cell isolation from mouse bone marrows and spleen. Although there were no significant findings at this time, we are currently performing data analysis via FlowJo software and hope to have results analyzed to present in our poster. Future studies will elucidate further the roles of FABP4/5 from non-cancerous cells in multiple myeloma, and we will explore if changes in immune or other cells in the bone marrow of the FABP4/5 mice affect the growth or survival of myeloma cell lines injected into live murine models.

Acknowledgements: The University of New England College of Osteopathic Medicine and the MaineHealth Institute for Research. A special thank you to the Ryzhov lab for their support and guidance in receptor identification and signaling. This work has been supported by the Peter Morgane Fellowship (to KB). Animal work was approved by the MaineHealth Institute for Research IACUC committee (protocol # 2111).

**15.**

## Bacterial Metabolic Signaling Drives Neutrophil Responses in Infected Airways

Loiselle[1,2,3], M, OMS I, Liberati Moore[2,3], N, Ph.D., Deiss-Yehiely[4,5] E, Ph.D., Boribong[2,3], BP, Ph.D., Ausubel[6], F, Ph.D., Hurley[2,3], BP, Ph.D., Drenkard[2,3], E, Ph.D., Yonker[2,3,7], LM, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Massachusetts General Hospital, Mucosal Immunology and Biology Research Center, Boston, Massachusetts
[3]Massachusetts General Hospital, Department of Pediatrics, Boston, Massachusetts
[4]Massachusetts Institute of Technology, Department of Materials Science and Engineering, Cambridge, Massachusetts
[5]Massachusetts Institute of Technology, Koch Institute for Integrative Cancer Research, Cambridge, Massachusetts
[6]Massachusetts General Hospital, Department of Molecular Biology, Boston, Massachusetts
[7]Massachusetts General Hospital, Cystic Fibrosis Center, Boston, Massachusetts

**Introduction:** *Pseudomonas aeruginosa* is an opportunistic bacterial pathogen that infects the lungs of individuals with cystic fibrosis. Infection triggers neutrophil-mediated inflammation that can severely damage the airway, driving morbidity and mortality. Due to the rise in antibiotic resistant *P. aeruginosa* strains, there is an increased need for novel therapeutic strategies. Thus, we screened for bacterial components that contribute to neutrophil-mediated airway inflammation with a goal of identifying therapeutic targets. We hypothesized that bacterial factors elicit epithelial-secreted neutrophil chemoattractants in infected airways.

**Methods:** A *P. aeruginosa* strain PA14 non-redundant transposon insertion mutant library was screened to identify genes involved in bacterial-induced neutrophil migration. To determine the effect of bacterial mutations on the induction of neutrophil migration, lung epithelial cells grown on the apical side of transwell filters were infected with individual mutants. Neutrophils were then added to the basolateral side of the transwell and the number of neutrophils that migrated to the apical side was measured. Motility, adhesion, and neutrophil chemotaxis assays were then carried out on the identified mutants.

**Results:** Mutant PA14 23790::MAR2xT7 with a transposon insertion in the *leuB* gene was one of several mutants that showed a significant reduction in neutrophil migration compared to wild-type, which was three standard deviations below the mean of all mutants examined. Increasing doses of infection did not rescue this defect. An in-frame deletion mutation in the *leuB* gene (PA14Δ*leuB*) that we constructed exhibited a similar reduction in neutrophil migration. Interestingly, neutrophil migration was restored when exogenous leucine, the biosynthetic product of the *leuABCD* operon, was added during transmigration assays. PA14Δ*leuB* displayed normal levels of motility, adhesion, and direct neutrophil chemotaxis to bacterial suspensions. However, there was a significant reduction in neutrophil chemotaxis to the supernatant containing epithelial and bacterial secreted products that was collected after PA14Δ*leuB* infection compared to wild-type.

**Conclusion:** These findings suggest that *leuB* plays an important role in the bacterial-epithelial interaction that elicits the neutrophil response to *P. aeruginosa* airway infection. However, future research is necessary to further elucidate the role of *leuB* and identify therapeutic targets.

**Acknowledgements:** This work was conducted in the Mucosal Immunology and Biology Research Center at Massachusetts General Hospital and was supported by grants from the Cystic Fibrosis Foundation (YONKER18Q0, YONKER20A0-KB) and NIH/NHLBI (5K08HL143183). Blood sample collection from human subjects was approved by the Mass General Brigham IRB committee (protocol # MGB 2011P000620).

**16.**

## Investigating Primary Cilium-Mediated Modulation of Nociceptive Pathways

Davoudi, M S, OMS-II[1,2], Jordan, E E, D3[2,3], Tucker, K L, Ph. D[1,2].

[1]University of New England, College of Osteopathic Medicine
[2]Center for Excellence in the Neurosciences, Biddeford, Maine
[3]University of New England, College of Dental Medicine, Portland, Maine

**Introduction:** The primary cilium is a non-motile organelle protruding from the cell body of most vertebrate cell types. Primary cilia facilitate fundamental cell-signaling processes that are vital for organogenesis. In humans, cilium dysregulation during gestation and in postnatal life results in a group of medical syndromes termed “ciliopathies”. Ongoing studies have identified a role for primary cilia in the modulation of nociception in paclitaxel (Taxol)-induced peripheral neuropathy. Taxol is used to treat many types of cancers and often results in adverse side effects, including pain, tingling, and numbness. Primary cilia mediate cell signaling through transport of molecules bidirectionally along their microtubule-based axoneme, termed intraflagellar transport (IFT). *Ift88* is a gene critical to proper development and function of the primary cilium, whose elimination results in loss of ciliary signaling in the target tissue. To determine the role of primary cilia in nociception, we have utilized a conditional knockout of *Ift88* and hypothesize that this will result in the absence of primary cilia on dorsal root ganglia (DRG) neurons. To visualize the neuronal cilia, we are pursuing an *in vitro* approach using acutely-dissociated DRG neurons.

**Methods:** The mutant mouse strain used in this experiment contains an Advillin:Cre recombinase gene, which is expressed in DRG neurons, and is homozygous for the $Ift88^{flox}$ allele. Tamoxifen-inducible CRE recognizes the floxed sequences flanking the *Ift88* gene, resulting in deletion of the floxed *Ift88* sequence, thereby eliminating the function of the primary cilium in the murine sensory neurons. Retrieval of DRG neurons was performed by transcardial perfusion with laminectomy and DRG removal. The DRGs were enzymatically digested to liberate the neurons and cultured for three days, allowing for axon network formation. Subsequently, paraformaldehyde fixation and immunofluorescence staining for primary cilia were performed, and images were obtained with confocal microscopy for morphological characterization.

**Results:** Associated cultures of DRG neurons elaborate robust primary cilia within 3 days of plating. After one week of tamoxifen-induced CRE expression, we expect to see loss of the primary cilia.

**Conclusion:** Once primary cilia loss through this technique is validated, additional behavioral studies investigating the response to noxious stimuli (e.g., mechanical, heat, inflammatory) shall be conducted.

**Acknowledgements:** The University of New England College of Osteopathic Medicine.
This study was funded by National Institutes of Health (NIH) grant 1R21NS130249-01 (KLT)

**17.**

## The Role of Lysosomal NUDT5 in the Pathogenesis of TFE3-Renal Cell Carcinoma

Mistikawy[1], N, OMS II, McGrath-Conwell[1], A, Henske[2], EP, M.D., Filippakis[1], H, Ph.D.

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Division of Pulmonary and Critical Care, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts

**Introduction**: Translocation renal cell carcinoma (tRCC) is a rare and morphologically distinct subtype of RCC that affects all ages. In tRCC, gene fusion events between TFE3 and other genes, including PRCC, drive oncogenesis. TFE3, a microphthalmia transcription factor, controls autophagy and lysosome biosynthesis, for which little is known in tRCC. This research aims to understand how TFE3 gene fusions drive tRCC tumorigenesis with the goal of identifying novel therapeutic targets. Our preliminary studies revealed that Nudix Hydrolase 5 (NUDT5) is unexpectedly localized in the lysosomes of TFE3-PRCC cells, but not in normal TFE3-expressing cells. We hypothesize that tRCC drives NUDT5 lysosomal translocation to confer a metabolic advantage and support TFE3-dependent tumorigenesis.

**Methods**: We performed Liquid Chromatography/Mass Spectrometry (LC/MS) of lysosomal and cytoplasmic fractions from HEK293T cells with or without TFE3 fusion gene activation. Lysosomal localization of the most enriched proteins was confirmed using immunofluorescence (IF) and quantitative real-time PCR (qRT-PCR). In parallel, we used flow cytometry to quantify the lysosomal function and number in cells with or without TFE3-PRCC activation. Furthermore, steady state metabolomic analysis was performed in the lysosomes and cytoplasm of cells with TFE3-PRCC activation and compared to cells with physiological TFE3 expression.

**Results:** Aberrant TFE3 activation increased lysosomal function by 50% ($p<0.001$) and lysosomal numbers by 20% ($p<0.01$), compared to normal TFE3-expressing cells. IF experiments revealed nuclear localization of TFE3, suggesting TFE3 activation drives lysosomal biogenesis and function. Next, proteomics revealed NUDT5 as a significantly enriched protein in the lysosomes of TFE3-PRCC cells, compared to cytoplasmic fractions. Finally, metabolomics revealed that TFE3-PRCC cells have elevated lysosomal glutathione metabolism.

**Conclusion**: Our data supports our hypothesis that TFE3-PRCC activation leads to increased lysosomal biogenesis and altered metabolism. The unexpected localization of NUDT5 within TFE3-PRCC lysosomes suggests that it plays a role in lysosomal processing of glutathione. We are currently investigating the role of NUDT5 in potentiating lysosomal metabolism and viability of tRCC cells. By investigating the increased lysosomal metabolism of tRCC cells, we aim to establish its connection to tRCC tumorigenesis and potentially identify a new therapeutic target.

**Acknowledgements:** This study was initiated at Brigham and Women's Hospital and is ongoing at University of New England, College of Osteopathic Medicine. This work was partially supported by the Department of Defense Kidney Cancer Research Program (to HF).

**18.**

**Title:** *Concurrent antidepressant use in patients undergoing sports meniscal surgery may confer greater risk of developing postoperative opioid use disorders.*

Zhu[1], A, MS III, Canastra[3], N, OMS I, Owens[1,2], B, MD., Cruz[1,2], A, MD., MBA.

[1] Brown University Department of Pediatric Orthopedics Surgery, Providence, Rhode Island
[2] University Orthopedics Inc, Providence, Rhode Island
[3] University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** Developing opioid use disorder (OUD) has been recognized as a possible adverse outcome following common orthopedic procedures. Preoperative opioid use is associated with a higher risk of developing OUD. Less is known about whether preoperative antidepressant use/prescriptions may also confer a risk for developing a subsequent opioid use disorder following common orthopedic surgeries. This study sought to examine the risk of developing OUD following meniscal surgery after prior exposure to antidepressant prescriptions.

**Methods:** The Rhode Island All Payers Claims Database (APCD) contains all healthcare insurance payment information for all people with health insurance in Rhode Island. Patients in the APCD who underwent meniscal surgery between 2011 and 2020 were identified using the Current Procedure Terminology (CPT) codes 29880, 29881, 29882, and 29883. Patients with opioid prescriptions within one month after surgery were identified with national drug codes and included in the final analysis. Patients with a prior opioid use disorder (OUD), as identified by ICD-9 and ICD-10 codes, were excluded. Multivariable logistic regression was used to determine how patient characteristics influenced the development of an OUD within one year of opioid prescription following meniscus repair.

**Results:** A total of 5,534 patients were identified with 35 (0.6%) of these patients diagnosed with an OUD within one year of surgery. Multivariable logistic regression showed that patients with Medicaid (OR 6.41, 95% CI: 2.93 to 14.02, $p<0.001$) and with a prescription for antidepressants prior to surgery (OR 3.48, 95% CI: 1.48 to 8.17, $p=0.004$) had increased odds of having a subsequent OUD diagnosis. Interestingly, opioid use prior to surgery did not significantly increase odds of subsequent OUD diagnosis when controlling for prior antidepressant use (OR 2.11, 95% CI: 0.92 to 4.84, $p=0.079$).

**Conclusions:** Prior exposure to antidepressant medications/prescriptions is a greater risk factor than prior exposure to opioid medication for developing OUD in patients undergoing meniscal surgery. It is important for healthcare providers to assess patients' prior antidepressant use when prescribing post-op opioid medication after meniscal surgery to decrease the potential risk of opioid dependence.

**Acknowledgments:** University Orthopedics Inc, and the Department of Pediatric Orthopedic Surgery at Brown University.

**19.**

## Use of Group Ketamine-Assisted Therapy for Promoting Treatment-Resistant Mental Health

Esteireiro[1], O, B.S., OMS-II, Holden[1,2], S, M.D., M.P.H., M.S.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Riverbird Clinic, Portland, Maine

**Introduction:** The current effectiveness of individualized treatment for those with depression, anxiety, and post-traumatic stress often isn't as robust as needed, causing dissatisfaction for healthcare providers and ongoing suffering for patients. Ketamine is an alternative with a robust safety profile and low cost and, as such, is at the forefront of psychedelic-assisted psychotherapy. Practitioners of ketamine-assisted therapy (KAT) combine medically-supervised ketamine use with interactive therapeutic sessions, which has been proven to help patients with treatment-resistant mental health disorders. In many indigenous cultures, healing occurred in a communal setting through ceremonial expanded states of consciousness. Aspects of community healing are implemented in group medical visit models, which also has known effectiveness. There is currently no data on the combination of KAT being used in a group model for treatment-resistant depression, anxiety, or post-traumatic stress. This pilot study aims to explore the effectiveness of group KAT for patients with these conditions by tracking changes in self-reported symptoms of depression, anxiety, post-traumatic stress, and self-compassion through validated questionnaires.

**Methods:** Five cohorts of five patients each underwent a six-week experience that included three group KAT sessions. Individually-dosed ketamine was given with the support of a therapist and physician team, followed by group integration sessions and a home-therapy program. To assess its impact, the clinic administered baseline questionnaires, then re-administered PHQ9, GAD7, PCL7, and the 26-point Self-Compassion Scale after course completion.

**Results:** Follow-up results were available from 18 of the 25 participants. Non-parametric comparisons of baseline to post-treatment measures demonstrate significant decreases in PHQ9 ($p=.001$), GAD7 ($p=.006$), and PCL7 ($p<.0001$) scores.

**Conclusion:** Preliminary results show promising effectiveness for group ketamine-assisted therapy to address treatment-resistant mental health disorders, particularly for symptoms associated with anxiety, depression, and trauma. Qualitative and longitudinal follow-up results could explore the possibility of durable symptom relief and emergent themes. By acknowledging the ceremonial forms of healing and nudging psychedelic therapy towards its traditional community-based roots, an inclusive environment of cultural psychiatry may be possible.

**Acknowledgements:** The Riverbird Clinic and University of New England College of Osteopathic Medicine. Special thanks to the Peter Morgane Research Fellowship, awarded to OE, for funding and supporting this work. This study was granted IRB exemption by the University of New England Office of Research Integrity (IRB #0123-05).

**20.**

**Abstract Category:** Original Research

## Knowledge, Attitudes and Behaviours on Antimicrobial Resistance Across 14 Member

**States in the World Health Organization European Region: Results from a Cross-Sectional Survey**

Singh-Phulgenda[1]*, S, Ph.D., Antoniou[2]*, P, M.P.H., OMS I, Lo Fo Wong[3], D, Ph.D., Iwamoto[3], K, M.Sc., Kandelaki[3], K, M.D., M.P.H.

[1]Infectious Diseases Data Observatory (IDDO), University of Oxford, Oxford, United Kingdom
[2] Consultant for WHO Regional Office for Europe, Copenhagen, Denmark from February to May 2023
[3] WHO Regional Office for Europe, Copenhagen, Denmark
* Authors contributed equally

**Introduction**
Antimicrobial resistance (AMR) is a major global public health threat requiring urgent action. Regional data on knowledge, attitudes and behaviours among the general public regarding antibiotic use and AMR is limited for countries not participating in Eurobarometer surveys conducted by the European Commission.

**Methods**
A multicentric, cross-sectional survey of the general public was conducted in the capital cities of 14 Member States of the WHO European Region. A validated questionnaire from the AMR Eurobarometer survey was used to collect data on antibiotic use and knowledge, access to antibiotics, and understanding of policy responses through face-to-face exit interviews.

**Results**
Out of 8221 respondents from 14 Member States, 50% took antibiotics in the past 12 months and the majority (53%) obtained their most recent course from a medical practitioner. The most reported reasons for taking antibiotics orally in the past 12 months were cold (24%), sore throat (21%), cough (18%), and flu (16%). Overall, 84% of participants showed a lack of knowledge about appropriate antibiotic use. However, only 37% of respondents reported receiving any information in the past year about the importance of avoiding unnecessary antibiotic use. Doctors were the most cited (50%) and most trusted (80%) source of information. Among respondents who experienced COVID-19, 28% took antibiotics with a prescription, while 8% took antibiotics without a prescription.

**Conclusion**
This study highlights gaps in knowledge and understanding of appropriate antibiotic use, indicates a need for more awareness campaigns and educational initiatives, and suggests a crucial role for doctors in this process. The findings also emphasize the role of the general population in combating AMR. The data serve as baseline information for future evaluations and interventions in the Region.

**Funding**
This study was funded by grants provided by the Ministries of Health of Germany and the Kingdom of the Netherlands, which had no role in data collection, analysis, or interpretation of data. The Control of Antimicrobial Resistance Programme, under the Division of Country Health Programmes of the World Health Organization Regional Office of Europe, was the recipient of these grants and coordinated the development of this survey.

**Ethics Approval**
The study was exempted from review of the WHO Ethics Review Committee (Protocol Number ERC.0003790). Participants were informed about the objective, outcomes and any associated risks of the study and were only included for interviews if they provided consent.

**Acknowledgements**
The authors would like to give special thanks to the participating Member States (Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, Moldova, Tajikistan, Türkiye, Uzbekistan) for facilitating the data collection and providing their contributions to this survey.

**21.**

## Lymph Node Metastases Develop Through a Wider Evolutionary Bottleneck Than Distant Metastases

Giunta[1], P, OMS-II, Reiter[2,3,4], JG, PhD, Hung[5,6], WT, PhD, Lee[5,6], I, PhD, Nagpal[2,7], S, PhD, Degner[5,6], S, MS, Liu[5,6], G, M.D., Wassenaar[5,6,8], E, MD, Jeck[9,10], WR, PhD, Taylor[9,10], MS, PhD, Farahani[9,10], A, PhD, Marble[9,10], SD, PhD, Knott[11], S, PhD, Kranenburg[12], O, PhD, Lennerz[9,10], JK, MD, Naxerova[5,6], K, PhD

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine, USA
[2] Canary Center for Cancer Early Detection, Department of Radiology, Stanford University School of Medicine, Palo Alto, CA, USA
[3] Stanford Cancer Institute, Stanford University School of Medicine, Palo Alto, CA, USA
[4] Department of Biomedical Data Science, Stanford University School of Medicine, Palo Alto, CA, USA
[5] Center for Systems Biology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[6] Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[7] Center for Applied Mathematics, Cornell University, Ithaca, NY, USA
[8] Department of Surgery, St Antonius Hospital, Nieuwegein, the Netherlands
[9] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[10] Center for Integrated Diagnostics, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[11] Department of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, CA, USA
[12] Division of Cancer and Imaging, University Medical Center Utrecht, Utrecht, the Netherlands

**Introduction:** Cancer typically develops over many years before rising to clinical attention. This means that primary tumors contain substantial intratumor heterogeneity and represent a rich reservoir of genetic diversity. Heterogeneity found within metastases (intra-metastatic) as well as between distinct metastatic lesions (inter-metastatic) is considerably less understood. This genetic diversity contains information about cancer progression at sites of metastasis. Our research explored inter- and intra-lesion heterogeneity at lymph node and distant metastases in colorectal cancer. We hypothesized that levels of heterogeneity would differ between lymph node and distant metastases.

**Methods:** We analyzed a published collection of human colorectal cancer phylogenies, focusing on patients with paired primary tumor and metastasis samples. We examined the proportion of

metastatic samples that formed monophyletic or polyphyletic clades in phylogenetic trees of patient tumor samples. We developed a mathematical framework to quantify the likelihood that monophyletic groups would arise by chance for a given phylogeny. We calculated a root diversity score (RDS) as the probability that metastases form a common clade in a tree with a certain number of samples. We validated our data with an independent cohort of 20 patients with samples from a resected primary colon cancer and at least one lymph node and distant metastasis. We isolated DNA from these samples, and genotyped them using hypermutable polyguanine tracts, that act as a molecular fingerprint from which we constructed robust phylogenetic trees.

**Results:** In the published dataset, we found that 67% of distant metastases formed monophyletic clades, whereas only 10% of lymph node metastases formed distinct clades. We found that the root diversity scores for distant metastases were significantly lower compared to lymph node metastases. In our independent cohort, we again found that root diversity scores were significantly lower in distant metastases than in lymph node metastases from the same patient.

**Conclusions:** Our results demonstrate that lymph node and distant metastases have different levels of genetic diversity. They suggest that lymph node metastases are polyphyletic, polyclonal, and develop through a wider evolutionary bottleneck than distant metastases. This indicates that the two sites are subjected to different levels of selection and may form through distinct evolutionary mechanisms.

**Acknowledgements:** This work was supported by grants from the NIH (R37CA225655), AACR (561314) and NHLBI (P01HL142494) to K.N. and from NCI (R00CA22999102) to J.G.R. We thank S. Bian, F. Tang and W. Fu for sharing with us the frequencies of CRC01 subclones across different anatomic sites.

**22.**

### Thoracoabdominal Aortic Aneurysm Life-Threatening Events Following Endovascular Aortic Repair

Marino, R, M.S., OMS I, University of New England College of Osteopathic Medicine, Biddeford, Maine

**Background:** This study aimed to evaluate the perioperative morbidity and mortality related to endovascular abdominal aortic aneurysm repair (EVAR), complex EVAR, and thoracic endovascular aortic repair (TEVAR), and the details of these procedures to mitigate future risks. We characterized the odds of adverse outcomes and complications including death from the Society for Vascular Surgery's Vascular Quality Initiative (VQI) registry. There was a gap in research evaluating the association of life-altering events with endovascular repair, procedural factors, and comorbid conditions. The primary outcome of the study was post-operative thoracoabdominal aneurysm life-altering events (TALE). TALE was defined as a composite endpoint of postoperative death, permanent postoperative dialysis, permanent postoperative paralysis, and/or postoperative stroke. Secondary outcomes included identifying comorbid and procedural characteristics associated with post-operative TALE. Evaluation of TALE is useful in assessing the preoperative risk used to counsel patients on these risks.

**Methods:** We performed a retrospective cohort study of patients who underwent EVAR, complex EVAR, or TEVAR using data from the VQI. We collected data on baseline

demographics, smoking status, race/ethnicity, comorbid conditions, and procedural details. The primary outcome was post-operative TALE. Secondary outcomes included identifying anatomic and procedural characteristics associated with post-operative TALE.

**Results:** We identified all patients who underwent, complex EVAR, and in the VQI. The rates of perioperative mortality were greatest in TEVAR patients. Stroke occurred in at the highest rate in TEVAR patients. Permanent dialysis was observed at equal rates in both complex EVAR and TEVAR patients. Chronic kidney disease and cerebrovascular disease were associated with higher odds of TALE. The use of left upper extremity adjuvant access was associated with higher odds of TALE in complex EVAR patients and the use of multiple adjuvant access sites was associated with higher odds of TALE for TEVAR patients.

**Conclusion:** TALE was observed in 10% of TEVAR, 6.8% of complex EVAR, and 1.4% of EVAR patients. Factors commonly associated with TALE include symptomatic repair, more proximal landing zone, use of adjuvant access for complex EVAR and TEVAR, and wider aortic diameter. While TALE was observed after all repair types, higher rates were observed in patients who underwent complex EVAR and TEVAR.

**Acknowledgement:** Boston University Graduate Medical Sciences and the Beth Israel Deaconess Medical Center Department of Vascular Surgery.

**23.**

**Title:** Preliminary Results of P-RAD: A Randomized Phase II Study of Pre-operative Radiation Therapy with Immunotherapy and Chemotherapy for High-Risk Breast Cancer

**Authors:** Dunn, SA, OMS-II[1], Spring, L, M.D. [2], Keenan, J, B.S. [2], Gupta, G, M.D., PhD. [3]

[1]*University of New England College of Osteopathic Medicine, Biddeford ME*
[2]*Massachusetts General Hospital, Boston MA*
[3]*UNC Lineberger Comprehensive Cancer Center, Chapel Hill NC*

**Introduction:** Breast cancer (BC) is the second leading cause of cancer deaths in women worldwide. There is a rapidly growing body of evidence indicating that patients with certain high-risk BC subtypes may benefit from combination neoadjuvant immunotherapy and chemotherapy. However, 33% of patients on this regimen do not achieve a pathological complete response (pCR) to treatment and have a higher risk of recurrence. Preclinical studies indicate that adding radiation therapy(RT) results in synergistic immunogenicity and improves treatment responses. Herein we report the preliminary findings of a phase II randomized study evaluating the safety and efficacy of preoperative RT boost to the primary tumor in combination with neoadjuvant pembrolizumab and standard-of-care(SOC) neoadjuvant chemotherapy.

**Methods:** A total of 128 participants with high-risk BC will be enrolled and randomized to receive no, low, or high dose pre-operative RT in combination with pembrolizumab and neoadjuvant chemotherapy. Eligibility criteria includes patients who have biopsy-proven, lymph node(LN)-positive BC that is either triple negative(TNBC, defined as ER< 10%, PR< 10%, and HER2-negative) or high-risk hormone-receptor-positive

(HR+)/HER2- (grade III or with high-risk genomic assay score). Patients will receive preoperative RT to the breast(0Gy, 9Gy or 24Gy in 3 daily fractions) with pembrolizumab(400mg q3wk), followed by SOC neoadjuvant chemotherapy, and breast and LN surgery. Correlatives will be collected at baseline and throughout treatment and will include blood, tumor biopsies and surveys assessing quality of life, patient-reported symptoms, and financial burden. Patients will receive SOC adjuvant RT and systemic therapy and will be followed 2 years post-surgery to assess safety and durability of responses.

**Results**: To date, 46 participants have enrolled (28 TNBC and 18 HR+/HER2-), 12 of whom have completed treatment. 83%(10/12) achieved pCR in the breast and LN, with 2 patients achieving pCR in the LNs alone. Reported adverse effects are consistent with known safety profiles of each agent. Analyses of surveys and specimen biomarkers are ongoing.

**Conclusions:** Initial treatment and safety outcomes are encouraging, surpassing historical pCR rates(65%). If successful, this study will provide a new, patient-oriented therapeutic strategy for patients with high-risk BC and provide critically needed patient-reported outcomes and biomarker data for immunotherapy-driven BC treatment.

**Acknowledgements:** The University of New England College of Osteopathic Medicine and the Duke University Medical Center. A special thanks to the research teams at UNC Lineberger Comprehensive Cancer Center, the Massachusetts General Hospital, and Duke University Medical Center for contributing to this successful multicenter clinical trial. This work has been supported by Merck, Inc, the Breast Cancer Research Foundation, the Translational Breast Cancer Research Consortium, and the Peter Morgane Student Research Fellowship. This study was performed under Duke Health Institutional Review Board approval (Protocol #Pro00109284).

**24.**

## Investigating the Role of the Kynurenine Pathway in Macropinocytosis and Proliferation of TSC2-deficient Cells

Lafleur[1]* S, OMS II, Cox[1]* W, OMS II, McGrath-Conwell[1] A, Henske[2] EP, M.D., Filippakis[1] H, Ph.D.

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Division of Pulmonary and Critical Care, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts

* Authors contributed equally

**Introduction**: Tuberous Sclerosis Complex (TSC) is a multi-system genetic disorder that manifests as nodules and cysts; termed Lymphangioleiomyomatosis (LAM) in the lungs and angiomyolipoma in the kidneys. Normally, TSC1 and TSC2 genes inhibit the mechanistic target of Rapamycin (mTORC1), a major driver of cell metabolism and proliferation. Mutations in

these genes results in mTORC1 upregulation, causing over-proliferation and malignancy. TSC2-deficient (TSC2-dc) cells have elevated levels of macropinocytosis (MPC), a nutrient uptake mechanism. Targeting extracellular nutrient uptake via MPC could be a therapeutic approach for TSC and LAM. We aim to uncover the signaling mechanisms employed by TSC2-dc to promote MPC and proliferation, to discover a novel therapeutic target for TSC and LAM. We hypothesize that the kynurenine (Kyn) pathway is essential to MPC and the survival of TSC2-dc.

**Methods:** To study the role of essential amino acids in TSC pathogenesis, we performed quantitative real-time PCR to assess the expression of Kyn pathway genes in TSC2-dc and TSC2-ec. Immunofluorescence followed by confocal microscopy was performed to analyze the impact of tryptophan (Trp) uptake on MPC and subsequent AhR activation. MPC and proliferation of TSC2-dc and TSC2-ec was also assessed upon treatment with Kyn pathway inhibitors at 24, 48, 72, and 144 hrs.

**Results:** In TSC2-dc, nuclear AhR localization was observed, which was reversed upon Rapamycin treatment (20 nM, 24 hrs). *Ahr* mRNA levels in TSC2-dc cells was 50-fold greater than in TSC2-ec ($p<0.0001$). Expression of AhR-target genes *Tdo2* and *Ido1* cells was increased in TSC2-dc by 45-fold and 7-fold, respectively, compared to TSC2-ec ($p<0.01$). Inhibition of IDO1 (LM10; 10uM) or TDO2 (Linrodostat; 10uM) selectively decreased cell proliferation by 50% (*48hrs, $p<0.1$ and $p<0.0001$*). Interestingly, inhibition of AhR also lowered cell proliferation by 50% ($p<0.05$). Importantly, decreased MPC (*dextran-FITC*) was observed upon inhibition of the Ahr/Tdo2/Ido1-axis.

**Conclusion:** Collectively, our data suggests that the Kyn pathway plays a role in MPC and is necessary for the survival of TSC2-dc. This was evidenced by decreased proliferation in TSC2-dc when the *Ahr*/*Tdo2*/*Ido1*-axis was inhibited. Furthermore, treatment with Rapamycin decreased *Ahr* levels suggesting that Kyn pathway is regulated by an mTORC1-dependent mechanism. Overall, our results endorsed candidacy of the Kyn pathway as a novel therapeutic target in TSC.

**Acknowledgements:** This study was initiated at Brigham and Women's Hospital and is ongoing at the University of New England College of Osteopathic Medicine. This work was supported by the Peter Morgane Student Research Fellowship (to SL) and by The LAM Foundation (to HF).

**25.**

### Bile Acids Partially Mediate the Bone Reduction and Marrow Adiposity Loss Caused by Vertical Sleeve Gastrectomy in Mice

Sharma[1,3], S, OMSIII, Bozadjieva Kramer[2], N, P.h.D., Li[1], Z, P.h.D.

1. MaineHealth Institute for Research, Scarborough, Maine.
2. Department of Surgery, University of Michigan, Ann Arbor, Michigan.
3. University of New England College of Osteopathic Medicine, Biddeford, Maine.

**Background:** The incidence of obesity has increased to over a third of the U.S. population and bariatric surgery serves as a crucial treatment option for many patients. In the US, 256,000 bariatric procedures were performed in 2019 with vertical sleeve gastrectomy (VSG) being the most popular. VSG removes 80% of the stomach along with its great curvature, but this comes

with risk. Changes in enterohepatic circulation of bile acids mediate part of the metabolic effects of VSG. Prior research shows that bile acid increases after VSG and correlates with more bone loss. Since apical sodium-dependent bile acid transporter (ASBT) plays a key role in bile acid reabsorption in the ilium, we sought to determine whether ASBT could serve to reduce bone and marrow adiposity following VSG.

**Methods:** Male C57BL/6J mice at 4 months of age were fed with high fat diet for 8 weeks to induce obesity. Mice were divided into three groups, including sham, VSG, and VSG plus an ASBT inhibitor with mice randomly assigned to each group. The inhibitor was given at a dose of 20 mg/kg (formulated in the HFD) for 10 weeks. We collected bone tissues at 12 weeks post-surgery and used for micro-CT, paraffin-sectioned H&E staining and osmium staining.

**Results:** VSG significantly improved glucose tolerance and reduced body weight in obese mice but also showed a significant decrease in trabecular bone volume fraction (Tb. BV/ TV), trabecular bone mineral density (Tb. BMD), and trabecular connective density (Conn. Dens). Addition of the ASBT inhibitor provided a slight improvement of trabecular bone loss without statistical differences. In comparison, cortical bone also showed a decrease in cortical thickness (Ct. Th), bone area fraction (Ct. BA/TA), and bone mineral density (Ct. BMD). ASBT inhibitor significantly increased Ct. BA/TA and decreased cortical porosity compared with the VSG group. Lastly, histological analysis and osmium staining showed loss of adiposity in both proximal and distal tibia post-VSG, while ASBT inhibitor tended to prevent bone marrow adipose loss.

**Conclusion:** Based on the results above, we can conclude that the bone loss seen after VSG is partially mediated by bile acid resorption. More research is warranted to determine if circulating bile acids can act as a biomarker to identify patients that are at high risk for osteoporosis following bariatric surgery. Understanding this relationship would allow physicians to optimize treatment strategies for higher risk patients.

**Acknowlegments:** The MaineHealth Institute for Research. A special thank you to the Li lab for their support in this project, their funding, as well as their approved IACUC protocol.

**26.**

## Emergency Department in Home: A Novel Approach to Delivering Acute Care to Patients in the Home

McGrath[1], M, M.D., M.H.C.D.S., Patsiogiannis[1], V, M.P.H., C.P.H., OMS I, Estrella[1], D, M.P.H., Zambrano[2], J, M.D., M.H.S., Dvorkis[2], Y, M.S., Ekstrom[2], T, Berg[1], E, M.D.
[1]Research and Clinical Product Development, Medically Home Group Inc., 500 Harrison Ave, Boston, MA
[2]Atrius Health Center for Quality and Implementation Research, 133 Brookline Ave, Boston, MA

### Introduction

Emergency Departments (EDs) in the United States are experiencing historic overcrowding leading to delays in care, staff burnout and poor patient experience. Primary care practices struggle to triage and manage patients seeking acute care. Emergency Department in Home (EDiH) was created to rapidly deliver acute episodic care to patients at home as an alternative.

## Methods
EDiH operates in three phases: patient intake, care delivery, and care transition. Eligible patients are triaged by virtual nurses and cared for by in-home mobile integrated health clinicians within two hours of referral with medical direction from a virtual emergency medicine physician. Patients receive ED-level services at home including labs, imaging, and medications. Adult patients considered for the program reside in Massachusetts, have primary care managed by Atrius Health, and require an evaluation for acute symptoms.

## Results
EDiH delivered acute episodic care to 3,666 patients from January 1, 2021, to December 31, 2022. Patient average age was 79; 68% of patients were female and 29% male. Patient race/ethnicity include 77.6% white, 7.3% Black or African American, 1.9% Asian, 1.6% Hispanic or Latino, and 0.2% American Indian or Alaska Native. Chief complaints include dizziness, fever, shortness of breath, Covid-19, urinary tract infections and falls. After the EDiH encounter 3,056 of 3,666 (83.4%) of patients remained at home; 610 (16.6%) were escalated to a hospital ED; 510 (83.6%) of patients that were escalated to an ED, were admitted to the hospital. Of 3,056 patients who remained at home, 380 (12.4%) patients had an ED visit within 7-days of their EDiH visit; of the 380 patients who had an ED visit within 7-days, 325 (85.5%) were admitted to a hospital.

## Conclusion
EDiH is a feasible and safe program that delivers ED-level care to adults with acute symptoms, as an alternative to traditional facility ED care. This innovative model has the potential to reduce crowding in hospital EDs, reduce facility utilization, and improve patient experiences in acute care.

**Acknowledgments:** Our team gives special thanks to Gregory Snyder, Bruce Leff, Brian Klein, and Christina Olsen for their thoughtful consultation through this research. No external funding was received for this feasibility study. An ethics committee for the Atrius Health Quality and Implementation Research IRB reviewed the study and determined the exemption status for Human Subjects Research.

**27.**

### Current Status of HPV-targeted Therapies Development in Head and Neck Cancer

Bertaux[1], B, OMS II, Park[2], J, M.D., Park[2], S, M.D., Park[3], JC, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Seoul National University College of Medicine, Seoul, Korea
[3]Massachusetts General Hospital, Department of Head and Neck Cancer, Boston, Massachusetts

**Introduction:** While the incidence of smoking-related head and neck squamous cell carcinoma (HNSCC) has been declining, that of human papillomavirus (HPV)-mediated HNSCC has rapidly increased in the past decades worldwide. Despite rapid advances in therapeutics for solid tumors with novel immunotherapy and targeted therapeutic agents, no breakthroughs have

yet been made in the treatment of advanced HPV+ HNSCCs. This review aims to summarize the concepts and designs, early trial results, and future directions of various HPV-targeted experimental therapeutics for HPV-mediated head and neck squamous cell carcinoma (HPV+ HNSCC).

**Methods:** A systemic literature search of PubMed was conducted for HPV-targeted therapeutics. For clinical trial data, publications, major oncology conference abstracts, and the National Institutes of Health Clinical Trials Registry (ClinicalTrials.gov) information were reviewed. This review focused on the ones that are in the clinical stage and currently in active ongoing evaluation.

**Results:** Diverse approaches are being actively explored to target HPV+ HNSCC including therapeutic vaccines of various modalities, HPV-specific immune cell activating agents, and adaptive cellular therapeutics. All of these novel agents utilize immune-based mechanisms and target constitutively expressed oncogenic HPV E6 and/or E7 viral proteins. Most therapeutics demonstrated excellent safety, but single-agent activities are observed only in a few. Many are being tested in combination with immune checkpoint inhibitors.

**Conclusion:** Our review summarized various novel HPV-targeted therapeutics that are in the clinical phase for HPV+ HNSCC. Early-phase trial data suggest the feasibility and promising efficacy. Further strategies including selecting the optimal combination and understanding and overcoming resistant mechanisms are warranted for successful development.

**Acknowledgements:** Massachusetts General Hospital, Department of Head and Neck Cancer

**28.**

## Self-management Interventions and Outcome Measures for Individuals with Chronic Traumatic Injury: A Scoping Review

Coates[1], C, M.S., MSII, Velasquez[2], M, M.D., Shepler[2], LJ, M.P.H, Kazis[2,3,4], LE, Sc.D, Schneider[2,4,5], Jeffery, M.D.

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Department of Physical Medicine and Rehabilitation, Harvard Medical School, Spaulding Rehabilitation Hospital, Charlestown, Massachusetts
[3]Boston University School of Public Health, Boston, Massachusetts
[4]Rehabilitation Outcomes Center at Spaulding, Boston, Massachusetts,
[5]Department of Physical Medicine and Rehabilitation, Massachusetts General Hospital, Boston, Massachusetts

**Introduction:** Self-management education programs have been utilized in the treatment of chronic disease to empower and educate patients so that they may be better equipped to manage their treatment intervention options, increase motivation to work through disease related challenges, and to feel more confident about their treatment related decisions. Understanding how these programs impact the long-term treatment of chronic disease has been of significant importance in formulating more comprehensive care for chronic disease patients. Treatment of chronic traumatic injury could greatly improve if this understanding was implemented in the chronic traumatic injury patient population. Currently, there is room for a greater understanding

of what information has been published in the literature for self-management education programs for patients with chronic traumatic injury. As such, a scoping review to identify self-management interventions and related outcomes is being conducted. Additionally, we plan to identify existing gaps in knowledge related to self-management interventions.

**Methods:** Preferred Reporting Items for Systematic reviews and Meta-analyses guidelines were used to conduct a comprehensive search of peer-reviewed literature for articles from 2013-2023 using keywords relating to 'self-management' and 'chronic traumatic injury' in the following databases: PubMed (MEDLINE), Embase, Scopus, and ScienceDirect. Article inclusion criteria included: papers written in English, participants over the age of 18 years old, studies focusing on the physical traumatic injury population. This scoping review is inclusive of studies focusing on participants of all races, genders, educational status, and employment status with no limitations to socioeconomic or demographic backgrounds.

**Results:** At the current stage of this review, we have identified approximately 5 studies that fit the inclusion criteria from 598 results across 3 databases.

**Conclusion:** We have found limited research studies published solely on the chronic traumatic injury population. The results of this scoping review will identify gaps in the literature on those with traumatic injuries.

**Acknowledgements:** The authors would like to thank Cindy Stewart who is a research and teaching librarian with the University of New England.

**Funding:** NIDILRR#90DPBU0008

**29.**

## Electromyocardial Manifestations in Left Ventricular Noncompaction Cardiomyopathy in the Pediatric Population: A Systematic Review

Delanie M. Kneeland,[1,] OMSIV, Lindsey A. Fitzsimons,[1,] Ph.D., Gracie Hannigan,[1] OMSIV, Lyman Wu,[2] D.O., Kerry L. Tucker[1,] Ph.D.

[1]Department of Biomedical Sciences, College of Osteopathic Medicine, University of New England, Biddeford, Maine, [2]Albany Medical Center, Albany, New York

**Objective:** Left ventricular noncompaction cardiomyopathy (LVNC) is a structural heart defect that is considered a cause of sudden cardiac death because of severe systolic dysfunction and fatal arrhythmias. LVNC is increasingly acknowledged as a unique cardiomyopathy and has thus also recently increased in the occurrence of diagnosis. The purpose of this retrospective analysis is to dissect the empirical and medical data from 82 pediatric LVNC patients[KS4] to determine if common electromyocardial patterns are observed with respect to LVNC.

**Methods:** Qualitative analyses were performed to characterize individual arrhythmias, and summative analysis and interpretation of electrocardiogram (ECG) evaluations was gathered for the entire cohort. Articles were retrieved from the EMBASE database in the English language, totaling 4,475 articles related to LVNC between 1990 to October of 2021. The age of subjects included a range from pre-natal to 18 years of age. Each study that passed the inclusion criteria

was extensively reviewed for qualitative and quantitative ECG data respectively. 354 articles were included for full text evaluation and, ultimately, 62 articles that had legible ECG data met final inclusion criteria and were extracted and evaluated.

**Results:** Systematic review of LVNC cases and ECG presentation revealed waveforms consistent with re-entry patterns and atrioventricular node blocks, across the scope of sex and pediatric age subgroups, including a high incidence of the Wolff-Parkinson-White pattern, that are consistent with structural disruption originating within the left ventricle electrical system itself. Additional histological examination of pediatric endomyocardial biopsy tissue from LVNC patients and controls revealed pronounced abnormalities in the overall expression and patterning of N-cadherin and Connexin-43 proteins in addition to general cardiomyocyte structure and organization.

**Conclusions:** Taken together, results from this systematic review of ECG analysis and histological examination of cardiomyocyte structure reinforce the clinical and etiologic significance of pediatric LVNC. While LVNC in pediatric populations may not always present as acute clinical cases, further investigation into the electrophysiology and molecular phenotype of the disease supports the need for further evaluation and risk stratification for patients with suspected LVNC and/or ventricular arrhythmia.

**Acknowledgement**: A special thank you for the support of Tucker lab colleagues in the pursuit of primary cilia that initiated this review. The authors gratefully acknowledge the Saving tiny Hearts Society, whose generous financial support allowed this study to be performed.

**30.**

## The Use of Blood Flow Restriction Therapy Post-Matrix Autologous Chondrocyte Implantation

Toy[1], E, OMS III, Buglione Bifolco[2], D, DPT
[1] University of New England College of Osteopathic Medicine, Biddeford, Maine
[2] St. Charles Rehabilitation, Centereach, New York

**Introduction:** First performed in the U.S. in 2017, Matrix-induced autologous chondrocyte implantation (MACI) is used for the repair of symptomatic cartilage damage of the adult knee. As the cells adhere and begin to proliferate, it is important strengthen the quadriceps muscle without overloading the joint. Our patient presented with 41% quadriceps weakness at 4 months post-op and was subsequently evaluated for Blood Flow Restriction (BFR) Therapy.

**Case:** A 20-year-old female with a past medical history significant for a right tibial plateau fracture presented with chronic right knee pain that had been worsening for 2 years. Non-contrast MRI showed a defect of articular cartilage along the median eminence of the patella. Thus, a MACI was performed. Standard physical therapy began 14 days post-op. The patient attended physical therapy three times a week, however, she continued to experience significant quadriceps weakness. At 4 months post-op, the patient was referred to St. Charles Rehabilitation for BFR. The restriction was set to 80%, meaning blood could still come into muscle via arteries, but 80% of it was blocked from leaving through the veins. As blood comes into the muscle, the cells swell leading to muscle growth. In addition, the restriction allows the muscle to experience oxygen

depletion more quickly. With less oxygen, the body creates lactic acid to stimulate muscle hypertrophy. Common adverse effects of BFR include numbness, dizziness, subcutaneous hemorrhage, and, in severe cases, rhabdomyolysis. Our patient did not experience any of the aforementioned adverse effects and by 9 months post-op, the patient had more than doubled her quadriceps strength as measured by a dynamometer. At 85% quadriceps strength, the patient discontinued BFR and began a run-progression on an AlterG treadmill. By 11 months post-op, the patient was discharged from physical therapy. At 21 months post-op, the patient underwent repeat MRI of the right knee, which demonstrated sequelae of prior chondrocyte-based cartilage repair over the patellar apex inferiorly, with good fill by somewhat hyperintense repair tissue.

**Discussion:** Now in its sixth year of practice, the MACI procedure is still relatively new and as such, the rehabilitation protocol continues to evolve. This case supports the value and safety of BFR in recovery from MACI treatment. With BFR, the use of less weight protects the proliferating cartilage cells while still allowing for muscle strengthening.

**31.**

## Commotio Cordis in Sports

Beisenova, K, OMS II, Daniel, J, OMS II, Nuengchana, N, OMS II, Mast, P, OMS II, McCullen, G, M.D.

University of New England College of Osteopathic Medicine

### Introduction

Commotio cordis (CC) occurs as a result of a blunt impact to the chest that leads to arrhythmias and progresses into cardiac arrest[1]. This phenomenon is witnessed in sports commonly involving thrown objects such as in baseball, hockey, and lacrosse. For this reason, the victims are typically young and otherwise healthy individuals. Using public and open source information, this case report will explore a recent case involving professional football player, Damar Hamlin, while attempting to shed more light onto Commotio Cordis, its causes and treatment, and its relation to sports.

### Case Presentation

Damar Hamlin is a 24 year old football player for the Buffalo Bills. On January 2, 2023, Damar Hamlin collapsed immediately after rising off the ground following a routine tackle. Although he is an athlete in considerably the highest level of fitness, he experienced cardiac arrest. Due to the immediate availability of the field first responders and their quick administration of CPR, they were able to achieve return of spontaneous circulation (ROSC) on the field itself. On April 18th, 2023 Damar Hamlin was cleared to resume all football related activities

### Clinial Impacts/Relevance

Commotio cordis is the second leading cause of sudden cardiac death in athletes[2]. CC research is essential in advancing our knowledge of this potentially fatal condition, with the goal of reducing the incidence of CC and enhancing the overall safety and well being of individuals

participating in sports. Additionally, it is a more significant problem in child athletes than adult professional athletes, highlighting the importance of CC research for schools and local sports teams as their youth community is affected the most.

## Discussion

Multiple studies point to the upstroke of the T wave to be the vulnerable window during which impact leads to initiation of ventricular fibrillation and consequently CC[3]. A hard object and a speed of 25-50mph are shown to cause most CC cases. On site emergency care should include trained personnel with set protocols to recognize and treat CC, immediate use of an AED and expedited defibrillation with a shockable rhythm. In-hospital care should focus on stabilizing the electrical activity of the heart and checking for myocardial injury, as well as other concurrent injuries from the impact. Prevention should include educating athletes and coaches about impact to the chest during sports play, as well as screening children for underlying pathologies.

**32.**

## The Advantage of a Right-Side Anterior Retroperitoneal Approach for Primary Lumbar Spine Surgery

Balboni[1], J, OMS II, Perri[2], B, D.O., Wong[2], A, M.D., Rao[2], R, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]DOCS Health, Los Angeles, California

**Introduction**: Lumbar total disc replacement has become increasingly common in the treatment of chronic low back pain. However, combined spinal pathologies can compromise the longevity of surgical interventions, often making necessary future revision surgeries. When reoperation follows the same trajectory as the primary surgery, prior surgical scarring can increase the risk of vascular or visceral complications. Despite this, a repeat left-side approach is commonly performed. To better safeguard against undue risk and minimize iatrogenic injury, this study explores an alternative approach to spinal reoperation.

**Methods**: This study includes two patients who underwent primary lumbar total disc replacement surgery at the L4-5 level. The first was a 30-year-old male who presented with severe low back pain and radiculopathy determined to be the result of degenerative disc disease. Despite attempts to alleviate symptoms with non-surgical interventions, the patient remained unresponsive to nonsteroidal anti-inflammatory drugs, corticosteroids, and physical therapy. The second patient was a 59-year-old male with a right L5 vertebral fracture. Following review of the preoperative MRI, the surgeon elected to use right-sided approach due to the location of the injury.

**Results**: When performed jointly by a vascular and spine surgeon team, a right-sided retroperitoneal exposure can be safely executed during the primary surgery without heightened risk of surgical complications. In both cases, the peritoneum, ureter, and iliac vessels were void of any iatrogenic injury. Blood loss averaged 100mL in each case and oxygen saturation remained uninterrupted. In the post-operative course, there were no reports of retroperitoneal hematoma, retrograde ejaculation, or deep vein thrombosis. Neither patient sustained intraoperative vascular injury requiring primary repair with suturing and both were discharged the following day.

**Conclusion**: This study identified a right-side retroperitoneal exposure of the anterior lumbar spine as a clinically relevant and feasible strategy in primary lumbar total disc replacement surgery to preserve the left-side retroperitoneal plane should reoperation become necessary in the future. By employing pre-operative planning to anticipate future patient needs, this approach allows the surgeon to navigate the disc space in the absence of prior abdominal scarring, better facilitating removal and reimplantation of the new prosthesis.

**Acknowledgement:** This study was funded in its entirety by DOCS Health. The authors declare that they have no known competing financial interests that could have appeared to influence the work reported in this paper. This study proceeded under local institutional review board approval and with informed consent from all human subjects. IRB Protocol Number 20215180.

**33.**

**Abstract Category:** Original Research

## Clinical Trial-Ready Patient Cohorts for Multiple System Atrophy: Coupling Biospecimen and Induced Pluripotent Stem Cells Banking to Longitudinal Deep-Phenotyping

Ndayisaba[1,2]*, A, M.D., Pitaro[1]*, A, OMS I, Willett[1]*, A, M.S., Jones[1], K, M.S., Melo de Gusmao[1], C, M.D., Olsen[1], A, M.D., Ph.D., Kim[3], J, M.D., Rissanen[1], E. M.D., Woods[4], J, M.D., Srinivasan[1], S, M.D., Ph.D., Nagy[1], A, M.S., Nagy[1], A, M.D., Mesidor[1], M, Cicero[1], S, Patel[4], V, M.D., Oakley[5], D, M.D., Tuncali[1], I, M.S., Taglieri-Noble[1], K, D.P.T., Clark[1], E, Paulson[1], J, M.D., Krolewski[1], R, M.D., Ph. D., Ho[1], G, M.D., Ph.D., Hung[1,6], A, M.D., Ph.D., Wills[6], A, M.D., Hayes[1], M, M.D., Macmore[6], J, Warren[7], L, Ph.D., Bower[8], P, Langer[8], C, Kellerman[8], L, Ph.D., Humphreys[9], C, M.D., Glanz[1], B, Ph.D., Dielubanza[10], E, M.D., Frosch[5], M, M.D., Ph.D., Freeman[11], R, M.D., Gibbons[11], C, M.D., Stefanova[2], N, M.D., Ph.D., Chitnis[1], T, M.D., Weiner[1], H, M.D., Scherzer[1], C, M.D., Scholz[12,13], S, M.D., Ph.D., Vuzman[14,15], D, Ph.D., Cox[1], L, Ph.D., Wenning[2], G, M.D., Ph.D., Schmahmann[6], J, M.D., Gupta[7], A, M.D., Novak[1], P, M.D., Ph.D., Young[3], G, M.D., Feany[4], M, M.D., Ph.D., Singhal[1], T, M.D., and Khurana[1], V, M.D., Ph.D.

[1] Brigham and Women's Hospital and Harvard Medical School, Department of Neurology, Boston, Massachusetts 02115
[2] Medical University of Innsbruck, Anichstraße 35, 6020, Division of Clinical Neurobiology, Department of Neurology, Innsbruck, Austria
[3] Brigham and Women's Hospital and Harvard Medical School, Department of Radiology, Boston, Massachusetts 02115
[4] Brigham and Women's Hospital and Harvard Medical School, Department of Pathology, Boston, Massachusetts 02115
[5] Massachusetts General Hospital and Harvard Medical School, Department of Pathology, Boston, Massachusetts 02114
[6] Massachusetts General Hospital and Harvard Medical School, Department of Neurology, Boston, Massachusetts 02114
[7]Cellular Reprogramming, Inc., Pasadena, California, USA.

[8]The Multiple System Atrophy Coalition, Inc., 7918 Jones Branch Drive, Suite 300, McLean, Virginia 22102
[9]Department of Pulmonary, Sleep and Critical Care Medicine, Salem Hospital, Mass General Brigham, Salem, Massachusetts 01970
[10] Brigham and Women's Hospital and Harvard Medical School, Department of Urology, Boston Massachusetts 02115
[11] Beth Israel Deaconess Medical Center and Harvard Medical School, Department of Neurology, Boston, Massachusetts 02115
[12] National Institute of Neurological Disorders and Stroke, Laboratory of Neurogenetics, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland 20892
[13] Johns Hopkins University Medical Center, Department of Neurology, Baltimore, Maryland 21287, USA
[14] Harvard Medical School, Department of Biomedical Informatics, Boston, Massachusetts
[15] Brigham and Women's Hospital, Division of Genetics, Department of Medicine, Boston, Massachusetts, 02115, USA.
* Authors contributed equally

## Introduction

Multiple system atrophy (MSA) is a fatal neurodegenerative disease of unknown etiology characterized by widespread aggregation of the protein alpha-synuclein in neurons and glia. Its orphan status, biological relationship to Parkinson's disease (PD), and rapid progression have sparked interest in drug development. One significant obstacle to therapeutics is disease heterogeneity. Here, we share our process of developing a clinical trial-ready cohort of MSA patients (69 patients in 2 years) within an outpatient setting and recruiting 20 of these patients into a longitudinal "n-of-few" clinical trial paradigm.

## Methods

First, we deeply phenotype our patients with clinical scales (UMSARS, BARS, MoCA, NMSS, and UPSIT) and tests designed to establish early differential diagnosis (including volumetric MRI, FDG-PET, MIBG scan, polysomnography, genetic testing, autonomic function tests, skin biopsy) or disease activity (PBR06-TSPO). Second, we longitudinally collect biospecimens (blood, CSF, stool) and clinical, biometric, and imaging data to generate antecedent disease-progression scores. Third, in our Mass General Brigham (MGB) SCiN study (stem cells in neurodegeneration), we generate induced pluripotent stem cell (iPSC) models, matched to biospecimens, including postmortem brain.

## Results

Over 5 years, of 406 patients with parkinsonism-ataxia spectrum disorders considered from MGB, we classified 127 with MSA at differing levels of certainty based on clinical consensus criteria that rely on the clinical history and examination. Of these 127, 69 "active" patients have been followed since 2019, when we developed our concept of a longitudinally tracked clinical-trial cohort. Skin biopsies obtained for fibroblast generation have yielded 38 iPSC lines derived from MSA patients and relevant disease controls

(spinocerebellar ataxia and PD, including alpha-synuclein triplication cases), 22 matched to whole-genome sequenced postmortem brain.

## Conclusion

IPSC models may facilitate matching patients to appropriate therapies, particularly in heterogeneous diseases for which patient-specific biology may elude animal models. We anticipate that deeply phenotyped and genotyped patient cohorts matched to cellular models will increase the likelihood of success in clinical trials for MSA.

## Ethics Approval

The study was exempted from review of the Mass General Brigham Institutional Review Board (Protocol #2020P003415, #2021P001091, and #2009P002373).


## Acknowledgements

Research was conducted at Brigham and Women's Hospital in Boston, MA. Essential grant funding was provided by the Brigham and Women's Hospital Research Institute (BRI) Director's Transformative Award, the Barbara Bloom Ranson Fund for Biomarker Discovery in MSA, and NIH grants 1P30AG062421-01 and 1R01NS109209-01A1. Additional funding sources include grants from the Parkinson's Foundation, National Ataxia Foundation, Sanofi-Genzyme, Novartis Pharmaceuticals the US Government Department of Defense, National Multiple Sclerosis Society, Nancy Davis Foundation's "Race to Erase MS" program, Harvard Neuro-Discovery Center, Ann Romney Center for Neurologic Diseases, and Water Cove Charitable Foundation.


**34.**

### The Effect of High-Contact Sport Exposure on Baseline Neurocognitive Performance in High School Students


Shah[1], A, OMS II, Stephenson[1-3], K, Ph.D., Berkner[1,2], P, D.O.
[1] University of New England College of Osteopathic Medicine, Biddeford, Maine
[2] Maine Concussion Management Initiative, Biddeford, Maine
[3] Harvard Medical School, Department of Physical Medicine and Rehabilitation, Boston, Massachusetts



**Background:** There is some speculation in the media regarding how participation in contact sports and subconcussive hits at the high school level could potentially decrease performance on baseline neurocognitive testing. The purpose of this study is to evaluate the effects of high-contact sports on neurocognitive performance during repeat baseline testing in high school males.

**Methods:** This is a retrospective analysis of a database of computerized neurocognitive testing called immediate post-concussion assessment and cognitive testing (ImPACT) from Maine high schools. Participants included male high school athletes (between ages of 14-18 years) in the New England Area between 2009 and 2019. Participants who were female, with prior concussions, with a history of brain surgery, a diagnosis of a learning disorder, and those who participated in sports that were not clearly high- or low-contact were excluded from this study. Constructs measured by ImPACT include verbal and visual memory, visual motor speed, reaction time, and concussion symptoms. These students took ImPACT as part of their typical

preseason evaluation twice, approximately 2 years apart. Participants who reported low-contact ($n$ = 366) and high-contact ($n$ = 2298) sports were analyzed as separate groups. Groups were compared using a multivariate analysis of variance (MANOVA), $p \leq .05$.

**Results:** The final sample included 2,664 participants for baseline test 1 (mean age = 14.4, SD = 0.60) and baseline test 2 (mean age = 16.24, SD = 0.64). The results of a MANOVA showed a main effect for group ($F(5, 2654) = 3.18$, $p = 0.007$), and a main effect for time ($F(5, 2654) = 2.57$, $p = 0.03$); however, the interaction between group and time was not significant ($F(5, 2654) = 0.182$, $p = 0.97$). There were statistically significant differences within groups over time for visual memory ($F(1, 2658) = 6.04$, $p = 0.01$) and visual motor speed ($F(1, 2658) = 6.31$, $p = 0.01$).

**Conclusion:** Although there were statistically significant differences in visual memory and visual motor speed, the differences between the group scores were not clinically significant. Since there is no interaction between the groups over time, this supports that there are no effects of participating in high-contact sports on computerized neurocognitive baseline testing that manifests in this age group of 14-18 years. Furthermore, it supports the idea that for this age group, participation in youth and high school-level contact sports is safe.

**Acknowledgment:** We gratefully acknowledge the Maine Concussion Management Initiative (MCMI) for supporting concussion testing for youth and clinician education in Maine. IRB (# 201406) for the ImPACT baseline testing registry was obtained, and held current, through Colby College.

**35.**

## Contemporary Treatment Paradigms Increase Survival in Pancreatic Cancer

Kelly, B, OMS III, Nicolais, Laura, M.D., Fitzgerald, Timothy L., M.D.
1University of New England College of Osteopathic Medicine, Biddeford, Maine
2Maine Medical Center, Department of Surgery, Portland, Maine

**Background:** Over the last decade, a paradigm shift has occurred in treating pancreatic cancer. In 2011, two landmark trials involving novel multiagent chemotherapy (MAC) regimens ushered in a new standard of care for both palliative and neoadjuvant treatment. However, the implication for survival at a population level remains unclear.

**Methods:** A retrospective study of the National Cancer Database from 2004-2019 was conducted. Patients from 2004-2010 were classified as Era 1, and those treated from 2011-2019 as Era 2. Data analyses were conducted in R.

**Results:** A total of 316,393 patients with pancreatic adenocarcinoma were identified, with 87,742 treated in Era 1 and 228,651 in Era 2. On multivariate analysis, socioeconomic, geographic, and treatment facility factors were associated with survival. These factors included private insurance, higher income, and receipt of treatment in the Northeast or at an academic medical center. Patients were further analyzed in 4 subgroups: Imminently resectable (AJCC T1), locally advanced, surgically resected, and stage IV. The trends above persisted across all subsets. In addition, rates of MAC administration significantly increased between Era 1 and Era 2 across all subsets. On multivariate analysis, survival increased in entire cohort and each subset

(Figure 1); surgical patients (18.7 vs. 24.6 months, HR 0.85, 95% CI 0.82-0.88, p<0.001), imminently resectable patients (12.2 vs. 14.8 months, HR 0.90, 95% CI 0.86-0.95, p<0.001), high risk patients (9.6 vs. 11.6 months, HR 0.82, 95% CI 0.79-0.85), p<0.001), and stage IV patients (3.5 vs. 3.9 months, HR 0.86, 95% CI 0.84-0.89, p<0.001). Regardless of the treatment year, surgery rates in imminently resectable patients were surprisingly low at ~ 50%. However, resection rates increased for patients with locally advanced tumors, 24.4 vs. 25.8 (p<0.001). For imminently resectable patients who underwent surgical resection, median survival increased from 22.7 to 26.6 months from Era 1 to Era 2 (HR 0.92, 95% CI 0.87-0.97, p=0.001). A similar increase in median survival was observed in high-risk surgical patients, rising from 18.0 to 22.8 months (HR 0.81, 95% CI 0.77-0.85, p<0.001).

**Conclusion:** Contemporary MAC treatment has improved survival for all patients with pancreatic cancer. Unfortunately, the underuse of surgery in early, resectable disease persists. Across all subset analyses, outcome inequalities in association with insurance status, location, and facility type.

**Acknowledgements**: This research study was conducted at Maine Medical Center in Portland, Maine. A special thank you to Dr. Timothy L. Fitzgerald for his mentorship and support.

**36.**

## Improved Bone Morphology Following Six Months of Treatment with Canagliflozin in a Non-Diabetic Preclinical Model

Chlebek[1], C, PhD, McAndrews[2], C, OMS II, Costa[2], S, M.S., MacFarlane[2], E, OMS III, Yakar[3], S, PhD, Rosen[1], CJ, M.D.
[1]Maine Health Institute for Research, Scarborough, Maine
[2]University of New England College of Osteopathic Medicine, Biddeford, Maine
[3]New York University College of Dentistry, New York, New York

**Introduction:** Canagliflozin (CANA) is a sodium-glucose transport protein 2 (SGLT2) inhibitor that is commonly used to treat type II diabetes. Recent evidence has shown that SGLT2 inhibitors also have cardioprotective effects, which has led to an increasing use of these agents in non-diabetic patients. CANA treatment in diabetic patients has been associated with increased bone fracture risk with differential effects on bone morphology in short- versus long-term treatment. Few studies have been conducted to analyze the effects of intermediate-term treatment with CANA in a non-diabetic model. We aim to characterize the effects of six months of CANA treatment on bone morphology in a non-diabetic mouse model.

**Methods:** Male and female C57Bl/6J mice aged three- or six-months received either control or canagliflozin-containing diet (180 ppm) for six months. Body mass, composition, and bone mineral density (BMD) were assessed monthly. At euthanasia, fasting blood glucose was recorded, and the right femur was collected for micro-computed tomography and dynamic histomorphometry.

**Results:** Six months of treatment with canagliflozin significantly lowered fasting blood glucose levels in all groups but did not alter body weight or composition. All CANA-treated mice had increased femoral cortical and trabecular thickness compared to their age- and sex-matched controls. Females treated with CANA showed increased cortical bone area while trabecular number and bone volume fraction were increased in males treated with CANA. Young CANA-treated mice showed increased femoral and areal BMD but not the adult CANA mice.

**Conclusion:** Intermediate-term treatment with CANA in non-diabetic mice resulted in improved trabecular and cortical bone morphology. We found both sex- and age-dependent effects of CANA treatment on bone morphology where females showed increased cortical bone structure while males showed more trabecular benefits. Younger mice exhibited improved bone morphology following treatment whereas adult mice did not. Previous studies have found that the SGLT2 is not expressed in bone tissue, suggesting that reduced serum blood glucose levels resulting from CANA treatment may be associated with improved bone morphology in non-diabetic preclinical models.

**Acknowledgements:** The Maine Health Institute for Research, the University of New England and the New York University College of Dentistry. Special thanks to the Yakar lab for their support in micro-computed tomography analysis. IACUC approval was granted by the Maine Health Institute for Research IACUC committee (protocol # 2209).

**37**.

### Changes of Lumbar Spinal Cord GFAP and CD137 Expression Following Sciatic Nerve Crush in Mice

Aloimonos, C, OMS II, Bean, EN, PhD, Cao, L, MD PhD

**Introduction:** CD137 ligand (CD137L) is a costimulatory molecule in regulating immune responses. Previously, our lab demonstrated a contributing role of CD137L in neuropathic pain. Intrathecal injection of the neutralizing antibody against CD137, receptor of CD137L, reduced sciatic nerve crush (SNC)-induced heat hypersensitivity. Preliminary study detected significant CD137 expression within astrocytes. To further delineate the role of CD137-CD137L pathway in neuropathic pain, we examined the expression of CD137 in the lumbar spinal cord dorsal horn following SNC in both CD137L KO and WT mice using immunohistochemistry (IHC). We hypothesized that CD137L KO mice would display a reduced expression of CD137 compared to WT mice following SNC.

**Methods:** C57BL/6 WT and B6.CD137L KO mice (8-10 weeks old) were subjected to SNC or sham surgery. L5 spinal cords were extracted at days 0 (naïve), 3, 7,14, 28, and 56 post-surgery and processed for IHC (2/sex/time/treatment/genotype). Tissue sections were co-stained for astrocytic marker glial fibrillary acidic protein (GFAP, 1:1500, Rat-anti-GFAP) and CD137 (1:1500, Rabbit-anti-CD137) with secondary antibodies, (1:500, Donkey-anti-Rat-Alexa Fluor488) and (1:1000, Goat-anti-Rab-Cy3) respectively. Contralateral and ipsilateral sides of spinal cord dorsal horn areas were imaged using a Keyence BZ-X710 microscope and analyzed using ImageJ. At least 3 sections per tissue were examined for the integrated density of fluorescence and the resulting average was used in data analysis. This study is on-going. A multivariate analysis of variance (MANOVA) was run with available data using IBM SPSS on the

average GFAP and CD137 integrated densities with sex, day, genotype, treatment, and their interactions as factors.

**Results:** For GFAP expression, MANOVA indicated significant main effects of Day and Sex, and significant interactions between Day and Sex, Day and Genotype, and Sex and Genotype. For CD137, significant interactions between Day and Sex, Day and Treatment, Sex and Genotype, and Genotype and Treatment were detected. MANOVA and appropriate post-hoc analyses will be performed once data collection is completed. Astrocyte-specific CD137 expression will also be further examined.

**Conclusions:** Lumbar spinal cord expression of CD137 and GFAP appear to be modified by surgery, time, sex, and genotype. Identifying the CD137 expression pattern will help us to further understand the involvement of CD13 in neuropathic pain development.

**Acknowledgements:** COBRE Histology and Imaging Core (NIH/NIGMS P20GM103643 (Meng)). IACUC Protocol # is 110722-018.

**38.**

## The Effect of Extended Panel Molecular Testing on Treatment Decisions for Patients with Lung, Breast, Colon, and Prostate Cancer

Christoforo[1], C, OMS II, Williams[2], P, Pesco[3], J, OMS III, Thomas[4], CA, M.D.
[1] University of New England College of Osteopathic Medicine, Biddeford, Maine [2]New England Cancer Specialists, Department of Oncology, Scarborough, Maine, [3] University of New England College of Osteopathic Medicine, Biddeford, Maine, [4]New England Cancer Specialists, Department of Oncology, Scarborough, Maine

**Introduction:** Extended Panel Molecular Testing (EPMT) is increasingly utilized for patients with advanced malignancies, especially when standard treatments are no longer effective. We aimed to determine the impact of EPMT results on the treatment of patients with metastatic breast, colon, lung, and prostate cancer by assessing the number and potential actionability of EPMT and their effect on patients' treatment selection. We also examined EPMT test utilization (tissue versus circulating tumor DNA testing).

**Methods:** Between 2016 and 2023, 2,136 patients with stage IV lung, breast, colon, and prostate cancer were analyzed at New England Cancer Specialists with the following criteria: EPMT result available (Y/N), EPMT result (tier I-III), Therapy directed by EPMT (Y/N), and reasons why EPMT-directed therapy was not initiated. The type of testing, solid tumor or liquid tumor testing was recorded in an Excel data file.

**Results:** We evaluated 941 tests between 2016 and 2023, (544 lung, 147 breast, 124 colon, and 126 prostate cancer). Of the completed tests, 65% of breast cancer (n=94), 64.7% of lung cancer (n= 352), 66% of colon cancer (n=82), and 37% of prostate cancer (n=47) yielded actionable mutations. Targeted therapy received: 107 lung cancer patients (30%), 31 breast cancer patients (33%), 2 colon cancer patients (2%), and 4 prostate cancer patients (8.5%). Reasons to not receive EPMT-directed therapy: standard of care therapy (38%), clinical trial (9%), poor performance status (15%), patient refusal (2%). Over the study period, a steady

increase in the amount of EPMT performed as well as an increase in the utilization of circulating tumor DNA testing was observed.

**Conclusions:** EPMT is increasingly utilized and has led to an increase in treatment choices for patients with malignancies, especially due to an increased number of circulating tumor DNA testing. For patients with actionable results who did not receive targeted therapy, a variety of reasons were identified that prevented initiation of targeted therapies. We hypothesize that the number of molecular tests being conducted will continue to increase over time, thus increasing potential treatment options for patients with malignancies for whom standard of care treatment is no longer effective.

**Acknowledgements:** This work was supported by a grant to CC from the Department of Clinical Research, New England Center of Cancer Specialists

**39.**

## Youth Concussion Project: Highlighting the Importance of Concussion Education in School-Aged Children

Jozokos[1], D, OMS II, Brustman[1], K, OMS II, Mendola[1], R, OMS II, Gremillion[1], M, OMS II, Pepling[1], J, OMS II, Stephenson[1-3], K, Ph.D., Berkner[1-2], P, D.O.

[1]University of New England, College of Osteopathic Medicine, Biddeford, Maine
[2]Maine Concussion Management Initiative, Biddeford, Maine
[3]Harvard Medical School, Department of Physical Medicine and Rehabilitation Boston, Massachusetts

**Introduction:** Previous literature has shown that children overall lack knowledge about concussions. The Maine Concussion Management Initiative (MCMI) has developed an interactive education session to teach school-aged children how to recognize, respond, and recover from concussions. The purpose of this study is to investigate school-aged children's baseline knowledge of concussions and the effectiveness of an interactive education model on improving concussion knowledge.

**Methods**: Participants (7-11 years old) engaged in an education session that included a lecture and concussion simulation activities using concussion goggles. A pre-test of ten true or false questions was administered before the lecture and then again immediately after. Data was collected by counting and recording the number of correct responses per question indicated by participants raising their hands. The percentages of correct answers at pre- and post-test were calculated per group by taking the total number of correct answers, dividing it by the total number of possible points, and then multiplying by one hundred. The percent correct for pre- and post-test timepoints were compared. During the first data collection, question 4 for group 1 ($n$=11 females) and question 6 for group 3 ($n$=21 females) from the pre- and post-test were not included in the final analysis due to an error in test administration.

**Results:** Both males (n=73) and females (n=83) showed improved knowledge and understanding of concussions at the post-test time point. Females improved from 74.8% (597/798) at pre-test to 91.1% (727/798) at post-test and exhibited a test score increase by 16.3%, which is greater compared to male participants. Males improved from 76.7% (560/730) at pre-test to 86.7% (633/730) at post-test and had a 10.0% score increase.

**Conclusion:** This data shows improved knowledge of concussions and endorses the utility of an interactive concussion curriculum for school-aged children. This program has the ability to increase recognition and awareness of concussions in children, potentially resulting in higher instances of injury reporting and better management of the injury.

**Acknowledgement**: The University of New England College of Osteopathic Medicine for supporting this research. IRB for this project was obtained through UNE (#0222-09-02).

**40.**

**Herbal Supplements in Pregnancy: "Natural" Does Not Equal "Safe"**

Masters[1], EM, OMS II, Seehusen[1], CN, OMS III, Bodine[2], A, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Berkshire Medical Center, Pittsfield, Massachusetts

**Introduction**: The use of herbal supplements has grown in popularity with increased access to online storefronts promoting these products as a "natural" way of alleviating pregnancy symptoms. Despite a lack of evidence regarding herbal supplement use during pregnancy, patients continue to seek these products due to the belief that the natural label correlates with safety. The goals of our study were to examine the prevalence of seven herbal supplements used and the pregnancy outcomes.

**Methods**: In our retrospective study, an online, anonymous, voluntary, qualitative survey was sent to eligible, English speaking, patients, aged 18-50, identified via Berkshire Medical Center's EMR using all ICD10 codes for pregnancy during the year of 2022 The survey captured demographics, herbal supplement(s) (ginger, licorice, chamomile, almond oil, peppermint oil, raspberry leaf, and fenugreek) used during pregnancy[AB5], the frequency of use, and pregnancy outcomes (delivery gestational age and method, birth defects, hypertensive disorders). Data was quantified using percentages.

**Results:** The patient list consisted of 1357 emails, 41 were undeliverable, leaving 1316 sent, of which 120 (9%) responses were received. Majority of respondents were Caucasian (84.2%), aged 18-35 (72.5%), with a bachelor's degree (35.8%). At least 1 of 7 herbal supplements were used by 52 (43.3%) respondents. Ginger was used by 31 (59.6%), 5-7 d/wk, primarily in the 1$^{st}$ trimester (73.3%). Licorice was used by 3 (5.9%), 1-2 d/wk, varied distribution. Chamomile was used by 16 (31.7%), 1-2 d/wk, with uncertain timing (62.5%). Almond oil was not used. Peppermint oil was used by 3 (5.9%), 2-7 d/wk, primarily in the 1$^{st}$ [AB6]trimester (66.7%). Raspberry leaf was used by 35 (68.6%), 2-7 d/wk, primarily in the 3$^{rd}$ trimester (94.3%). Fenugreek was used by 2 (3.9%), 1-4 d/wk, in the 3$^{rd}$ trimester (100%). Majority of respondents delivered at term 97 (83.7%), vaginally 84 (71.8%). No birth defects were reported. Hypertensive disorders were reported in 31 (26.5%) with 18 (15.4%) having gestational hypertension, 11 (9.4%) pre-eclampsia, and 2. (1.7%) eclampsia.

**Conclusions:** Raspberry leaf, ginger, and chamomile were the most used herbal supplements in our study. The majority of the pregnancies delivered at term, vaginally, without birth defects. Hypertensive disorders were higher than the national average of 18%. The preliminary data raises awareness of the need for obstetric providers to discuss herbal supplements[AB7].

**Acknowledgement:** The University of New England College of Osteopathic Medicine and Berkshire Medical Center. This work was supported by the Peter Morgane Student Research Fellowship (to EMM). Berkshire Medical Center IRB exemption was granted (#2023-003) University of New England IRB exemption was granted. (# 0323-24)

**41.**

**An Evidence-Based Approach to Labeling Older Adult Health Status: Stable vs. Declining**

Byrd, EM, OMS II, Meuser, TM, PhD
University of New England (UNE) College of Osteopathic Medicine, Biddeford, Maine

**Introduction**: At the University of New England, the Legacy Scholars program has been collecting self-reported data for several years from Maine residents over the age of 55. This dataset was used to identify evidence-based candidates to classify older adult health status as either stable or declining. There's considerable and growing interest in the impacts of environmental factors on health in advancing age. Changes in metabolism, body composition, and other factors can make older adults more susceptible to environmental influences. One that is particularly relevant in Maine is exposure to contaminants in well water, arsenic in particular. It has been estimated that over 50% of Maine's wells contain potentially harmful levels of arsenic that require active filtering. The present project was undertaken in support of research on well water safety and health for older Mainers, co-led by investigators at UNE and MDIBL. An evidence-based, binary variable was needed for certain analyses. The purpose of this project was to develop such a variable.

**Methods**: Using SPSS software, the Legacy Scholars dataset (n = 663) was reviewed to identify many candidate variables that would reflect a change in health status over time by running a statistical frequency. A literature review was also conducted to support each of these variables. We systematically chose 12 items to serve as covariables in our project - perceived functional health (6 items) and perceived cognitive health (6 items). Each of these items were coded into a new binary variable that categorized each respondent as either a 0 (no change overtime) or 1 (change overtime). These binary variables were then summed together to represent our final binary variable needed for analysis.

**Results**: The final binary variable (i.e., stable 0; declining 1) was derived based on the mean and standard deviation (SD). One SD above the mean was defined as the cut point for declining health. Respondents that scored between 0 - 4 were coded as 0; 5+ as 1.

**Conclusion**: This final binary variable represents older adult health status and categorizes respondents to the Legacy Scholars annual survey as either having stable or declining health. This information will be utilized in the future to establish a causative relationship between contaminant exposure in Maine, such as arsenic, and a declining health trajectory. Preliminary findings will be featured in the poster presentation.

**Acknowledgement**: The University of New England College of Osteopathic Medicine. A special thanks to Dr. Jane Disney, MDI Biological Laboratory, for her support in water contamination research. This work has been supported by the Carmen Pettapiece Student Research Fellowship (to EB). IRB approval was granted by the University of New England (protocol # 1122-04).

**42.**

## Epidemiology and Outcomes of Traumatic Vascular Injury Repair by Trauma Surgeons and Vascular Surgeons in a Collaborative Model

Gallagher1, S, M.D., M.B.A., Sozzi1 M, M.D., Gallegos1, H, B.S., Ugarte1, C, M.D., Park1, S, M.D., Schellenberg1, M, M.D., M.P.H., Matsushima1, K, M.D., Magee2, G, M.D., Inaba1, K, M.D., Martin1, M, M.D.
1Division of Trauma and Acute Care Surgery, Department of Surgery, Los Angeles County + University of Southern California Medical Center, Los Angeles, California
2Division of Vascular Surgery, Department of Surgery, Los Angeles County + University of Southern California Medical Center, Los Angeles, California

**Background:** Management roles for peripheral vascular injuries (PVI) are a source of ongoing debate given the concern for the loss of vascular skills among general and trauma surgeons. We sought to analyze outcomes of PVI managed by trauma surgeons (TS) or vascular surgeons (VS).

**Methods:** This is a retrospective study of a single, level 1 trauma center. Trauma patients with PVI who underwent repair from 2010 to 2021 were included. Patients were separated into groups by the surgical specialty (TS or VS) undertaking the first intervention of the injured vessel.

**Results:** A total of 194 patients were included, with 101 (52%) PVI managed by TS and 93 (48%) by VS. The TS group had more penetrating injuries (84% vs 63%, $p < 0.01$), were more often hypotensive (17% vs 6%, $p = 0.01$), and had a higher median Injury Severity Score (ISS) (10 vs 9, $p < 0.001$). Time from arrival to OR was lower in the TS group (77 vs 257 mins, $p < 0.01$), with no difference in rates of preoperative imaging. The TS group performed damage control surgery (DCS) more frequently (21% vs 1.1%, $p < 0.01$). There was no difference in reintervention rates between the two groups after excluding patients that required reintervention for definitive repair after DCS (13% vs 9%, $p = 0.34$). Mortality was 8% in the TS group and 1% in the VS group ($p = 0.02$) with no deaths related to the PVI repair in either group. There was no difference in PVI repair complication rates between the two groups (18% vs 13%; $p = 0.36$).

**Conclusions:** In our collaborative model at a high-volume trauma center, a wide variety of PVI are surgically managed by TS with VS immediately available for consultation or for definitive repair of more complex vascular injuries. TS performed more DCS on higher acuity patients. No difference in vascular-related complications was detected between groups.

**Acknowledgement:** Los Angeles County + University of Southern California Medical Center Department of Trauma and Acute Care Surgery and Department of Vascular Surgery. IRB approval was granted by the University of Southern California IRB Committee.

**43.**

**Gastric X/A-Like Cells Mediate Effects of Gut-Bone Axis on Skeletal Homeostasis**

Ramos Aponte[1,2], J, OMS-II, Picoli[2], C, Ph.D., Li[2], Z, Ph.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Center for Molecular Medicine, MaineHealth Institute for Research, Scarborough, Maine

**Introduction**: Bariatric surgery is the most effective way to reduce body weight and improve glucose metabolism, however, it has the downside of causing bone loss and increasing the risk of fractures, significantly impacting the quality of life. While changes in gut hormones and microbiota have been proposed as possible mechanisms driving bariatric surgery caused bone loss, the contribution of the major surgical site (the stomach) has been largely overlooked. The stomach contains various enteroendocrine cells, with X/A-like cells comprising ~20% of the population. These cells produce ghrelin and contribute to glucose homeostasis and lipid deposition. Additionally, ghrelin has been found to promote bone formation, and its circulating concentrations decrease significantly after bariatric surgery in both humans and rodents. Therefore, we propose that X/A-like cell-derived gastric hormones, such as ghrelin, might mediate the effects of gut-bone axis on skeletal homeostasis. We hypothesize that gastric X/A-like cell-derived secretory factors contribute to skeletal homeostasis.

**Methods:** To investigate this hypothesis, we developed an inducible X/A-like cell depletion mouse model by crossing ghrelin (*Ghrl*)-Cre mice with diphtheria toxin receptor (DTR) mice (*Ghrl*-DTR). This model allows us to deplete X/A-like cells by administering diphtheria toxin (DT). Male or female *Ghrl*-Cre+/DTR- and *Ghrl*-Cre+/DTR+ mice were treated with DT (100 ng/mice; twice a day; i.p.) for 7 days when they were 12 weeks old. Changes in body weight, body composition, glucose metabolism and skeletal parameters were evaluated 4 weeks after DT treatment.

**Results:** Our immunofluorescent data from the stomach demonstrated a 75 to 80% reduction of X/A-like cells after DT treatment. Correspondingly, circulating ghrelin concentrations decreased following DT injections. Interestingly, X/A-like cell depletion improved glucose metabolism without affecting mouse body weight or fat mass. However, the lack of gastric X/A-like cells resulted in decreased trabecular bone mineral density and trabecular bone number in male mice, with a tendency to reduce trabecular bone volume fraction. Nevertheless, cortical bone parameters were not impacted in either male or female *Ghrl*-DTR mice following DT treatment.

**Conclusions:** In summary, the depletion of gastric X/A-like cells improves glucose metabolism and impairs skeletal homeostasis.

**Acknowledgments**: This research was conducted at the Center for Molecular Medicine, MaineHealth Institute for Research. A special thanks to the Li Lab for their support. This work was supported by the Peter Morgane Fellowship and NIH 1P20GM121301. Animal work was approved by MaineHealth IACUC committee (protocol #2207).

**44.**

**Does Autonomic Drive Influence Pain Processing or the Response to Pain Treatment**

Volpe, J OMSII[1], Gallegos, H OMSII[1], Rudolph, KS. PT, PhD[2]
[1]University of New England, College of Osteopathic Medicine, Biddeford, ME,
[2]University of New England, Westbrook College of Health Professions, Department of Physical Therapy, Portland, ME

**Background:** The nervous system modulates pain by increasing pain, measured by heat temporal summation (HTS) and decreasing pain (pain inhibition), measured by pressure pain thresholds (PPT) during conditioned pain modulation (CPM). HTS and CPM are types of quantitative sensory tests (QST) that have been used to predict patient outcomes, however the jury is still out as to their use clinically. One reason for this may be the failure to account for the autonomic nervous system in regulating pain. Heart rate variability (HRV) is a proxy for autonomic drive. The aims of this study are to:

1. Assess differences in pain inhibition and pain facilitation resulting from exposure to two different painful conditioning stimuli (cold water hand immersion and noxious electrical stimulation (NXES)
2. Determine the relationship between the autonomic drive and pain modulation during NXES as measured by QST.

This presentation will report the results thus far for Aim 2.

**Methods:** Healthy participants (6♂, 4♀) ages 19-27 have been tested. Participants were familiarized with painful tests, then underwent PPT and HTS tests before and after (1) 2-min cold water hand immersion (COLD) and (2) 20-min treatment of NXES (at intensity=50/100 pain rating). The conditions were separated by 1-hour. Ten minutes of resting ECG data were collected. R-waves were identified and the inter-beat intervals (IBI) were calculated (Visual3D). The continuous IBI signal was used to assess HRV in the time and frequency ($f$) domains (Kubios HRV Standard v3.5.0). Differences in PPT and HTS by condition were assessed Paired t-tests and repeated measures ANOVAs were used to assess differences in PPT and HTS before and after each condition. Pearson correlation coefficients were used to explore relationships between variables.

**Results:** The NXES treatment elicited pain inhibition as indicated by higher PPT ($p=.037$) and reduced pain facilitation as indicate by lower HTS ($p=.004$). Seven participants had higher PPTs after NXES and were classified as responders (R). In the Rs low $f$ HRV correlated negatively with reduced HTS after NXES ($r=-.673$, $p=.097$) and high $f$ correlated positively with increased PPT after NXES ($r=.697$, $p=.094$), although neither reached the level of statistical significance at $p=.05$.

**Conclusions**: There appears to be a trend toward a relationship between pain modulation variables and autonomic drive. Further study of this aim is needed, with more participants before definitive conclusions can be made.

**Acknowledgment:** University of New England College of Osteopathic Medicine, Westbrook College of Health Professions and Department of Physical Therapy. This work has been supported by a Peter Morgane Student Research Fellowship (to JV).

**45.**

## Tightness Shifts in the U.S. and China: Implications of Tightening or Loosening Norms during the Coronavirus Pandemic

McLamore[1,27], Q, Ph.D., & Syropoulos[1,28], S, Ph.D., Li[4], M, Ph.D., Mentrup[4], E.F, Ph.D., Leidner[1], B, Ph.D., Hirschberger[2], G, Ph.D., van Bezouw[6], M, Ph.D., Rovenpor[26], D, Ph.D., Paladino[24], M.P, Ph.D., Baumert[4,25], A, Ph.D., Bilewicz[5], M, Ph.D., Bilgen[20], A, Ph.D., Chatard[7], A, Ph.D., Chekroun[8], P, Ph.D., Chinchilla[10], J, M.S., Choi[9], H.S, Ph.D., Euh[23], H, Ph.D., Gomez[10], A, Ph.D., Kardos[11], P, Ph.D., Khoo[12], Y.H, Ph.D., Légal[8], J.B, Ph.D., Loughnan[13], S, Ph.D., Mari[14], S, Ph.D., Tan-Mansukhani[15], R, Ph.D., Muldoon[16], O, Ph.D., Noor[17], M, Ph.D., Petrović[18], N, Ph.D., Selvanathan[19], H.M, Ph.D., Uluğ[20], Ö.M, Ph.D., Wohl[21], M.J, Ph.D., Yeung[22], W.L.V, Ph.D., Young[1], K, Ph.D., Zein[3], R.A, M.S., Mohammad[1], T, B.S., Tamkin[1], J, B.S., Ngyuen[1], L.H, B.S., Baracewicz[1], J, OMS I
[1]University of Massachusetts, Amherst, USA
[2]Interdisciplinary Center, Herzliya, Israel
[3]Universitas Airlangga, Indonesia
[4]Max Planck Institute for Research on Collective Goods, Germany
[5]University of Warsaw, Poland
[6]Universiteit van Amsterdam, the Netherlands
[7]Université de Poitiers, France
[8]Université Paris Nanterre, France
[9]Sungkyunkwan University, Republic of Korea
[10]Universidad Nacional de Educación a Distancia, Spain
[11]Bloomfield College, USA
[12]University of Malaya, Malaysia
[13]University of Edinburgh, UK
[14]University of Milano-Bicocca, Italy
[15]De La Salle University, Philippines
[16]University of Limerick, Republic of Ireland
[17]Keele University, UK
[18]University of Belgrade, Serbia
[19]University of Queensland, Australia
[20]Univeristy of Sussex, UK
[21]Carleton University, Canada
[22]Lingnan University, Hong Kong, China
[23]Univeristy of Minnesota, USA
[24]Univerity of Trento, Italy
[25]Univeristy of Wuppertal, Germany
[26]Univeristy of East Anglia, UK
[27]University of Missouri at Columbia, USA
[28]Boston College, USA

**Introduction:** Emergent research identifies cultural tightness-looseness as a crucial factor for understanding outcome differences during the coronavirus pandemic. Because *perceived* tightness-looseness can be measured as an individual-level

difference and it can shift during large-scale crises, we investigated whether such shifts occurred early in the pandemic in both China (a tight nation) and the U.S. (a loose nation) across three cohorts. These patterns extend advice that governments can increase compliance and trust by "tightening." Here, we utilized cross-sectional samples to detect shifts in perceived tightness-looseness from China (a strict lockdown) and the U.S. (a lax lockdown) during the early pandemic. We hypothesized that tightness might increase further in response to the crisis in China, whereas the U.S. might loosen further. We further investigated if these shifts help explain individual differences in compliance as well as institutional trust, a critical factor for pandemic outcomes.

**Methods:** These data were drawn from a larger project designed to investigate the roles of culture and trust in the pandemic. Participants in both countries were recruited using CloudResearch Panel Services. We selected three cohorts of unique participants from China and the U.S. in 2020 (1: May 4$^{th}$-21$^{st}$, 2: June 15$^{th}$-June 23$^{rd}$; 3: July 20$^{th}$-July 28$^{th}$). We used three invariant items for tightness-looseness, four items for COVID-19 compliance, and four items for institutional trust for information about the coronavirus.

**Results:** Perceived tightness and trust in scientific/government information was significantly higher among Chinese participants than among American participants. Among Chinese participants, trust in government information about the coronavirus increased over time. The pattern was inverted among Americans. Among Chinese participants, compliance increased indirectly through increased perceptions of tightness. Among Americans, compliance indirectly decreased through a reduction in perceived tightness.

**Conclusion:** We found that China was viewed as even tighter during the initial stages of the pandemic, and this links to greater compliance with Covid-19 measures and institutional trust. However, we found the inverse patterns among Americans. Our results suggest that tightness-looseness can adapt to changing social norms during crises. They further suggest that the approach to crises by national leadership affects the directionality of the change.

**Acknowledgements:** The authors are grateful to the NSF for funding this research (RAPID Grant # 2028922). A special thanks for Quinnehtukqut McLamore and Stylianos Syropoulos for joint first-authorship from the University of Massachusetts Amherst.

**46.**

**Endocrine Catastrophes Supported by ECMO: A Case Series**

Beisenova[1], K, OMSII, Jara[2], C, Caldwell[2], M, M.D., MacGillivray[2], D, M.D., DeNino[2], W, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, ME
[2]Maine Medical Center, Portland, ME

**Background:** The purpose of this study was to report the use of extracorporeal membrane oxygenation (ECMO) to support 4 patients who presented with cardiac collapse or multisystem organ failure (MSOF) due to endocrine disorders such as thyroid storm, pheochromocytoma, functioning extra-adrenal paraganglioma causing eosinophilic myocarditis, and MSOF that

developed after total thyroidectomy and neck dissection. 3 patients were on VA ECMO, 1 on VV ECMO.

**Methods:** All patients were treated on an inpatient basis between 2019 and 2021 at Maine Medical Center, Portland, ME. The main outcome measure was the clinical outcome for patients on ECMO for treatment of cardiogenic shock or respiratory failure due to catastrophic endocrine disorders.

**Results:** Patient 1, a 33 yo male was placed on ECMO for cardiovascular support after MSOF due to thyroid storm. The patient's thyroid storm and hyperthyroidism were medically controlled. The patient had definitive treatment of his hyperthyroid with total thyroidectomy. Patient 2, a 33 yo female was placed on ECMO following severe heart failure, LVEF 15%, due to eosinophilic myocarditis. Work-up discovered a functional extra-adrenal paraganglioma. The patient was treated with alpha-blockade, had recovery of LV function and had resection of the extra-adrenal paraganglioma. Patient 3, a 44 yo female was placed on ECMO after she developed a sepsis syndrome that progressed to ARDS and severe hypoxia after having a total thyroidectomy and neck dissection for thyroid cancer. Patient 4, a 59 yo female was placed on ECMO as a resuscitation effort after cardiac arrest. The patient was diagnosed with a pheochromocytoma and alpha-blockade was initiated. The patient went on to have laparoscopic adrenalectomy. All patients spent less than 7 days on ECMO spending 0-8 days in the hospital prior to ECMO initiation. ECMO initiation provided stabilization, medical treatment of the endocrine catastrophe, and eventual surgical treatment. Consequently, all 4 patients showed a positive response and clinical improvement, with sufficient cardiac and end organ recovery to be weaned off ECMO and be discharged home.

**Conclusions:** Use of ECMO to support patients with endocrine catastrophe is safe and effective in the setting of an experienced ECMO Center. Endocrine disorders should be considered as a cause for cardiogenic shock. Multidisciplinary collaboration between the ECMO and Endocrine (Surgical and Medical) teams is essential.

**Acknowledgement:** The University of New England College of Osteopathic Medicine and Maine Medical Center. IRB exemption was granted on March 20, 2023 by The MaineHealth Institutional Review Board.

**47.**

## Impact of the Transition to Pass/Fail Scoring for COMLEX Level 1 and USMLE Step 1 on Osteopathic Medical Students at UNECOM

Nguyen[1], K, OMS IV, Gomes Aversa[1], M, OMS IV, Gibson[1], H, OMS III, Brenner[2], C, PhD, Doane[3], C, DO
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]University of New England College of Osteopathic Medicine, Department of Research and Scholarship, Biddeford, Maine
[3]University of New England College of Osteopathic Medicine, Department of Primary Care, Biddeford, Maine

**Introduction:** Osteopathic (DO) medical students take the Comprehensive Osteopathic Medical Licensing Examination (COMLEX) for full medical licensure. In contrast, allopathic (MD)

medical students take the United States Medical Licensing Examination (USMLE); DO students may also take this exam. In 2022, COMLEX Level 1 and USMLE Step 1 scoring changed from a numerical score, to pass or fail (P/F). The Class of 2023 was the last cohort to receive a numeral score. This research seeks to understand the impact of P/F scoring on University of New England College of Osteopathic Medicine (UNECOM) students' decisions regarding taking USMLE.
**Methods:** This is a quantitative and qualitative mixed research study conducted via an anonymous survey on REDCap. Two separate surveys were sent; one to the Class of 2024 ('24) and another to the Class of 2023 ('23) at UNECOM. Survey questions were designed by the authors and asked if students took both licensing boards and their reasoning for the decision. Data analysis was performed using a Chi-Squared test.
**Results:** When comparing '23 and '24, 88% of students in '23 took both USMLE and COMLEX compared to 63% in '24 (p=0.002). In '23, 91% of students who paid for USMLE took the exam, compared to 74% in '24 (p=0.027). In '24, 23% of students said the switch to P/F affected their decision. Of those students, 2 took USMLE and 16 did not (p=3.1E-7). In '23, 70% of students signed up for both to keep options open compared to 72% in '24. In '23, 67% of students wanted to pursue a competitive specialty compared to 50% of students in '24. Of students who did not take USMLE, 2 in '23 attributed mental health or burnout issues, compared to 21 in '24. In '23, 1 student attributed not wanting a competitive specialty compared to 8 students in '24. In '23, 1 student did not USMLE due to failing practice tests compared to 7 students in '24.
**Conclusion:** The P/F change in scoring of COMLEX and USMLE had an impact on UNECOM students' decision to take both exams. After the switch, fewer students took both exams, and more chose to forgo USMLE after registering. The top reason for making these decisions was mental health and burnout. The switch to P/F impacted students who did not take both, but did not impact students who chose to take USMLE. There is a shift in attitudes amongst UNECOM students towards taking USMLE that needs to be further characterized as the impact of the P/F switch on residency applications is better understood in upcoming years.

**UNE IRB Project Number: 1122-10**

**48.**

## Evaluating Provider Needs: Developing a Comprehensive Assessment to Enhance Care for Individuals living with HIV/AIDS in Maine

Olivieri[1], L, OMS IV, Day[2], P, PhD
[1] University of New England College of Osteopathic Medicine, Biddeford, Maine
[2] UMass Chan Medical School, Department of Family Medicine and Community Health, Worcester, Massachusetts

**Introduction**: The New England AIDS Education and Training Center (NEAETC) is an organization that provides HIV/AIDS education, resources, assistance and consultation to health care professionals and the community throughout Maine, Connecticut, Massachusetts, New Hampshire, Rhode Island and Vermont. Annually, this organization surveys health care providers in these states following educational trainings to determine needs for additional resources and educations in their area. Of those surveyed in the 2022, only 9% (n=29) of respondents worked in Maine. Due to Maine's rural geography, in contrast with other states in the region, the requirements of providers will differ from those practicing in more urban states. With over 1,600

individuals living with HIV and AIDS in Maine, there is a need for providers to be up to date on best practices to provide comprehensive care to this population.

**Objective:** Develop a needs assessment survey that will connect with more providers in Maine, who may have not accessed or responded to earlier assessments, and respond to remote specific needs in this area by delivering targeted training, protocols and other resources through NEAETC.

**Technical Approach:** The needs assessment was developed by analyzing past NEAETC needs assessments and Maine-specific needs assessment to identify recurrent patterns pertaining to the requirements of both providers and patients. The survey will assess provider needs across the domains of clinical care guidelines, comorbidities of HIV, prevention strategies, social determinants of health and interpersonal and practiced-based methods in reducing stigma and creating a welcoming practice.

**Further Actions:** The completed survey will be distributed to healthcare providers in various regions of Maine. The goal is to collect information from both rural and urban providers to ensure an accurate representation. Following survey data collection, the NEAETC will provide training opportunities and resources to match provider needs.

**Acknowledgements:** The University of New England College of Osteopathic Medicine, the UMass Chan Medical School and the New England AIDS Education and Training Center. A special thanks to Maine healthcare providers, Tiffany Townsend and Ardyce Peters.

**49.**

**Minimally Invasive Lumbar Decompression (MILD) as a Treatment for Lumbar Spinal Stenosis: A Case Report**

Esposito, L, OMS IV, Kelly, R, D.O., Bozak, D, D.O., Bruce, L, PA-C
University of New England College of Osteopathic Medicine, Biddeford, Maine
Pennsylvania Pain and Spine Institute, Chalfont, Pennsylvania

**Introduction:** Low back pain associated with tingling and numbness may be the result of a spinal nerve or cord compression. Degeneration can narrow the central canal and lateral recesses of the spine, resulting in impingement. Central canal stenosis leads to a phenomenon called neurogenic claudication. According to this principle, spinal extension narrows the central canal, while flexion maintains patency. Patients express leg pain that worsens after long walks and find relief in spinal flexion, known as the shopping cart sign. Minimally Invasive Lumbar Decompression (MILD) opens the central canal and defers the need for surgery. Our patient presented to the clinic for low back pain with evidence of lumbar central canal stenosis and received MILD therapy for relief of symptoms.

**Case:** A 76-year-old female presented to PA Pain and Spine Institute for low back pain associated with tingling and numbness. Symptoms worsened if she stood for more than five minutes and was dependent on a cane for ambulation. ADLs became progressively difficult, and she noticed a significant functional decline. Physical examination revealed limited motion of the lumbar spine in all planes, and she maintained a flexed posture. MRI identified bilateral lumbar facet arthropathy, ligamentum flavum hypertrophy, and severe central canal stenosis at L4/L5. Based on the symptoms at presentation and the imagining obtained, she was determined to be a candidate for MILD. At her one-month postoperative visit, she no longer used a cane and

walked for longer periods without experiencing discomfort. Extension of the lumbar spine did not reproduce symptoms she was previously experiencing. Her clinical improvement demonstrates an overall positive effect on her functional outcome.

**Discussion:** The pathology of both central and lateral spinal stenosis is similar. Osteophytes, facet arthropathy, and ligamentum flavum hypertrophy contribute to the narrowing of either recess; however, their treatment options vary. MILD is indicated for central stenosis and involves debulking stenotic areas. This patient had evidence of central canal narrowing and suffered functional impairment, making her a prime candidate for MILD. This procedure offers lasting relief while delaying the need for a more invasive procedure, such as a laminectomy which carries a higher cost, bleeding risk, and risk of infection. MILD is performed in an outpatient setting, is cost-effective, and carries a low complication risk.

**50.**

**Treg Depletion Syndrome: Skin Inflammation Unleashed by ADCC Depleting Biologics**

Gray[1,2], L, OMS I, Larocca[2,3], C, M.D., Merola[2,4], J, M.D., Kupper[2,3], T, M.D., Teague[2], J, Ph.D., Gehad[2] A, Ph.D., Gerard[2], N, M.S., LeBeouf[2,3], N, M.D., Clark[2], R, M.D., Ph.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Brigham and Women's Hospital, Department of Dermatology, Boston, Massachusetts
[3]Dana Farber Cancer Institute, Center for Cutaneous Oncology, Boston, Massachusetts
[4]Brigham and Women's Hospital, Department of Rheumatology, Boston, Massachusetts

**Introduction:** T cell depleting antibodies used for the treatment of cutaneous T cell lymphoma, such as alemtuzumab (αCD52), utilize an IgG1 constant region and deplete T cells via antibody dependent cellular cytotoxicity (ADCC), which requires accessory cells that are rare in skin. These therapies deplete T cells in blood and purge recirculating T cells from skin, but do not deplete skin resident memory T cells (T RM). We observed new onset eczematous dermatitis in a subset of alemtuzumab treated leukemic CTCL (L-CTCL) patients that was associated with an 89% depletion of FOXP3 + Tregs from skin, suggesting Treg are a recirculating cell type. Studies in healthy human skin confirmed 72% of cutaneous Tregs were recirculating, compared to 19% of proinflammatory/conventional CD4 + T cells. We now report an L-CTCL patient who developed erythrodermic psoriasis following treatment with alemtuzumab and we hypothesize that the depletion of recirculating T cells in the skin allowed for the unmasking of psoriasis in this patient.

**Methods:** DNA extraction from blood and skin was performed and sent to Adaptive Biotech for TCR sequencing to analyze T cell populations before and after treatment. Gene expression analysis performed by Nanostring was used to further evaluate L-CTCL-associated and psoriasis-associated gene expression before and after treatment with alemtuzumab. Sections from FFPE samples were used in immunostaining to quantify the presence of regulatory T cells in the pre- and post-alemtuzumab skin samples.

**Results:** TCR sequencing found clearance of the malignant T cell clone from blood and skin and a new polyclonal expansion of resident memory T cells that were present before treatment. Gene expression profiling of skin biopsies demonstrated reduced expression of L-CTCL associated genes (CCR4, CCL5, CX3CR1, CD70) and increased psoriasis associated genes (IL-17A, IL-1B,

CXCL1,5,9) after alemtuzumab treatment. Multiplex immunostaining demonstrated an 89% depletion of Treg from skin after treatment and the presence of expanded CD8 + CD103 + T RM and IL-17A producing cells in the epidermis.

**Conclusion:** Depleting monoclonal antibodies can be effective therapies for L-CTCL but those that deplete by ADCC can induce inflammatory dermatoses by depleting recirculating Treg from skin. Depleting biologic medications intended for the treatment of skin limited CTCL should be formulated using constant regions that do not depend on ADCC for T cell depletion.

**Acknowledgements:** This work was conducted at Brigham and Women's Hospital in the Department of Dermatology and has been supported by the NIH/NCI (U01 CA253190-02). IRB approval was granted by an external IRB (DFCI Protocol Number: 02-016).

**51.**

## A Morphological Study of the Meniscus, Cartilage and Subchondral Bone Following Closed-Joint Traumatic Impact to Knee

Powers[1], M, OMS II, Haut Donahue[2], T, Ph.D., Narez[1], G, Ph.D., Dejardin[3], L, D.V.M., Wei[4], F, PhD, Haut, R, PhD
[1]Department of Biomedical Engineering, University of Massachusetts Amherst, Amherst, MA,
[2]Department of Biomedical Engineering, University of Memphis, Memphis, TN,
[3]Department of Small Animal Clinical Sciences, Michigan State University, East Lansing, MI,
[4]Orthopaedic Biomechanics Laboratories, College of Osteopathic Medicine, Michigan State University, East Lansing, MI

**Introduction**: Following traumatic damage to the anterior cruciate ligament (ACL) and meniscus, 78–83% of patients will develop post-traumatic osteoarthritis (PTOA) at a faster rate compared to controls, regardless of treatment modality (surgical or conservative interventions). Knee PTOA is a debilitating disease that affects all tissues within the joint. Due to the complex sequalae of tissue interactions, few studies have examined this interplay. This study documents the degree of damage to the menisci, cartilage, and subchondral bone in a closed-joint impact injury animal model with surgical ACL reconstruction and analyses whether injury to the meniscus compromises the underlying cartilage and the subchondral bone.

**Methods**: This study utilized a closed impact injury animal model that ruptured the ACL and caused partial damage to the medial meniscus. Then the knee joints underwent ACL reconstruction along with a partial or full medial meniscectomy. Morphological analyses were then performed on the menisci, cartilage, and subchondral bone at 1-, 3- and 6-months post injury.

**Results**: The morphological scores of the medial and lateral menisci worsened with time, as did the tibial plateau and femoral condyle articular cartilage scores. Medial meniscal damage was significantly correlated to the degeneration of the medial tibial subchondral bone at 1 month ($p$ = 0.01), and to the medial tibial cartilage at 3 months ($p$ = 0.04). Only one significant correlation was observed in the lateral hemijoint in respect to the lateral tibial cartilage lateral tibial subchondral bone at 6 months ($p$ = 0.05).

**Conclusion**: Early meniscal damage in the medial hemijoint resulted in subsequent damage to the medial cartilage and underlying tibial subchondral bone; this damage also likely affected the

lateral hemijoint. Degenerative changes in the medial meniscus, femoral and tibial articular cartilages, and subchondral bone were correlated to better understand tissue interactions following injury. The data supports an alternative course of treatment for acute medial meniscus injury that avoids full or partial meniscectomy, since the approach may be the primary cause of degenerative changes in the underlying cartilage and subchondral bone. In an effort to mitigate the risk of further iatrogenic injury, this study serves to inform a new approach to the treatment of meniscal injuries.

Acknowledgements: University of Massachusetts Amherst Biomedical Engineering Department and our collaborators at Michigan State University. I would like to acknowledge Dr. Tammy Haut Donahue and Dr. Gerardo Narez for their guidance and the opportunity to work on this project. Research reported in this publication was supported by the U.S. Department of Defense under Grant Numbers W81XWH-16-1-0734 and W81XWH-16-1-0735.

IACUC: All animal procedures for this study were approved by the Institutional Animal Care and Use Committee at Michigan State University (IACUC #05/16-073–00 and #PROTO201900255)

**52.**

## Nerve Conduction Study in a Tat Induced HIV-associated Sensory Neuropathy Model

Philhower, M, OMS III, Cao, L, M.D., Ph.D.
University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** HIV-associated sensory neuropathy (HIV-SN) continues to be one of the most common neurological complications in HIV patients despite combined antiretroviral treatment. Patients living with HIV-SN commonly report symptoms of pain, numbness, and paresthesia. It has been proposed that the interaction of the HIV viral protein, transactivator of transcription (Tat), and nervous system could potentiate neuronal damage leading to the symptoms of HIV-SN. In our preliminary time-course experiment assessing sciatic nerve conduction properties in the doxycycline-inducible Tat transgenic mouse model (iTat Tg mice), we observed an increase in maximum amplitude of compound muscle action potential (CMAP) in males but not in females following Tat induction. A larger scale study was planned, and we hypothesized that the maximum amplitude of the CMAP recorded along the sciatic nerve will increase in male iTAT Tg mice following Tat induction compared to female iTat Tg mice and non-induced iTat Tg mice.
**Methods:** Adult iTat Tg mice (3-4 months old) were used in this study. Expression of HIV Tat1-86 (strain HIV-1 HXB2) was induced by daily intraperitoneal injections of doxycycline hyclate (DOX) for 14 days (day 0-13) (5 males and 5 females). As controls, iTat Tg mice were injected, daily for 14 days, with pH-matched PBS only (pH =3.0) (5 males and 4 females). Nerve conduction studies were performed on days -7, -3, 3, 7, 10, 14, 17, 21, 28, and 35. The latency, maximum amplitude, and duration of the CMAP were measured along the sciatic nerve using the UltraPro$^{TM}$ S100 Neurodiagnostic System. Hind paw grip strength was measured concurrently to verify behavioral changes of Tat-induced neuropathy.

**Results:** Unlike what we observed in the preliminary study, Tat induced a significant reduction of the percent change in maximal amplitude in male but not female iTat Tg mice at days 3 and 7. Similar to our previous study, Tat did not induce significant changes in other nerve conduction related parameters.
**Conclusion:** The induction of Tat in iTat Tg mice did produce a time and sex-dependent effect on the maximal amplitude. However, the direction of change warrants further investigation, which will help us understand the relationship between sciatic nerve physiological changes and the observed HIV-SN-like behavioral responses.
**Acknowledgement:** This work has been supported by the University of New England College of Osteopathic Medicine Peter Morgane Student Research fellowship with funding from the Khan Family Foundation (to MP). We would like to thank Dr. Eliz Bean from the Cao Lab for her technical assistance. Animal work was approved by the IACUC (protocol # 0311521-004).

**53.**

Development and Feasibility of the Comfort Measures Only Time out (CMOT) to Reduce Distress During Palliative Withdrawal of Mechanical Ventilation

Mazzu[1,3], MA, OMS II, Fischer[3], AG, B.A., Campbell[2], M, R.N., Ph.D., Schwartzstein[3,4], R, M.D., White[5], DB, M.D., Mitchell[3,4,6], SL, M.D., M.P.H., Fehnel[3,4,6], CR, M.D., M.P.H.
[1]University of New England School of Medicine, Biddeford, ME
[2]Wayne State College of Nursing, Detroit, MI
[3]Beth Israel Deaconess Medical Center, Boston, MA
[4]Harvard Medical School, Boston, MA
[5]University of Pittsburgh School of Medicine, Pittsburg, PA
[6]Hebrew Senior Life, Marcus Institute for Aging Research, Boston, MA

**Objective:** To develop and examine the feasibility of Comfort Measures Only Time out (CMOT) procedure to reduce distress during palliative withdrawal of mechanical ventilation (WMV) among patients at end of life in intensive care units (ICU).

**Methods:** Procedural time outs and checklists are evidence-based processes commonly used in the ICU setting. The CMOT checklist intervention was guided by published literature, findings from a large prospective observational study of WMV (OBSERVE-WMV), and a panel of experts in palliative care, nursing, geriatrics, critical care, neurocritical care. Clinicians are being recruited in medical or neuroscience ICUs and trained on how to identify eligible patients and complete the intervention through participation in either live seminar or online training software. Outcomes assessing feasibility of the CMOT, such as acceptability, usefulness, and recommendation for future use will be collected via survey from ICU clinician participants. Secondary outcomes to be collected include rate of patient distress during WMV.

**Results:** A published systematic review found that there are significant gaps in evidence for the process of palliative WMV. The OBSERVE-WMV study identified modifiable care processes in patients undergoing withdrawal of mechanical ventilation at end of life, and risk factors associated with post WMV distress including morbid obesity, deeper stages of coma, and pre-extubation distress. The above was leveraged in the creation of a CMOT training set for clinicians with the goal being that the CMOT checklist and time out intervention be completed

prior to palliative WMV. Iterative development and reaction panels among experts have resulted in a finalized CMOT checklist for pilot testing among ICU clinicians.

**Conclusion:** Evidence gaps in the process of palliative WMV may be addressed by the CMOT intervention. Study launch with clinician training sessions for the CMOT has commenced and will be followed by pilot testing among 46-patients to establish feasibility. Following further refinement, future multicenter testing of the CMOT will test its association with reduction in rate of distress at end of life.

**Acknowledgment:** Hebrew Senior Life Marcus Institute for Aging Research and Beth Israel Deaconess Medical Center. IRB approval #2023P000160. This work has been supported by the Peter Morgane Student Research Fellowship (to MM). Study grants are reported from NINR 5R01NR015768 (MC), NIH-NHLBI K24HL148314 (DBW), NIA K23AG066929 and NIH-NIA R03AG060186 (CRF), and NIA U54AG063546, NIH R01 AG058539, NIH 2R37AG032982, and NIH NR016865 (SLM).

**54.**

## Successful Left Ventricular Assist Device Explantation due to Myocardial Recovery and Driveline Infection

Russell[1], JM, OMS-II, Coffin[2], ST, M.D., DeNino[3], WF, M.D., Woolston[4], SL, M.D.
[1]University of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Maine Medical Center Division of Cardiovascular Disease, Portland, Maine
[3]Maine Medical Center Division of Cardiac Surgery, Portland, Maine
[4]Maine Medical Center Division of Infectious Disease, Portland, Maine

**Introduction:** For patients with ventricular assist devices (VADs), infectious complications are frequent causes of increased morbidity and mortality. Once hardy organisms colonize prosthetic devices like VADs, they are difficult to eradicate without explantation. In most patients with chronic VAD driveline infections who are eligible for transplant, cure of infection occurs upon device removal at the time of transplantation. LVAD explant outside of transplantation is not typically entertained as a treatment of infection, given the associated risks.

**Case:** A 35-year-old male with history of chronic systolic heart failure underwent VAD implantation in 2018. At the time of implantation, the VAD was intended as a bridge to heart transplant contingent on tobacco cessation. Unfortunately, the patient was unable to cease smoking and thus was ineligible for transplant. In 2020, the patient developed a superficial driveline infection with methicillin-susceptible *Staphylococcus aureus* (MSSA), which was suppressed with oral antibiotics. In 2021, he re-presented with new onset driveline discharge, culture then demonstrated *Citerobacter freundii*. Simultaneously, the patient experienced significant recovery in cardiac function, able to resume jogging up to seven miles per day. In October 2022, the patient presented with driveline discharge, culture identified *Pseudomonas aeruginosa*. He was treated with ciprofloxacin PO for 10 days. At end of therapy, culture demonstrated a now drug-resistant *Pseudomonas*. Infectious Disease consultants were concerned about the

ability of this organism to develop antibiotic resistance while on antibiotic therapy, especially in the context of being ineligible for transplantation. With concern that increased antibiotic pressure would only cause further resistance, his VAD was explanted in November of 2022. The patient was discharged on post-op day six. A six-week course of IV meropenem was completed via PICC line at home, and he was prescribed ciprofloxacin for antibiotic suppression. To date, the patient has had an excellent outcome. Several months post-explant, the patient has demonstrated consistent cardiac recovery and remains infection-free.

**Discussion:** This patient's experience illustrates the importance of multidisciplinary VAD teams that include a strong presence of infectious disease specialists, and in extreme circumstances, the use of VAD explantation without transplantation to cure drug resistant infection.

**55.**

## Changes in Tollip Expression in the Development of HIV-Tat-associated Sensory Neuropathy

Nuengchana, N, OMS II, Bean, N. E, PhD, Cao, L, M.D., Ph.D.
University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** HIV-associated sensory neuropathy (HIV-SN) is the most common form of neuropathy associated with HIV infection. Tat, trans-activator of transcription, is a regulator actively related to HIV infection. Prior studies with doxycycline-inducible Tat transgenic (iTat) mice revealed Tat's contribution to HIV-SN. NanoString® RNA analysis of iTat lumbar spinal cords (LSC) suggested the role of Toll-like receptor (TLR) pathway in HIV-SN. Specifically, a transient upregulation of Tollip, a key TLR pathway regulator, was verified via quantitative RT-PCR. Thus, we examined LSC Tollip expression in iTat mice via immunohistochemistry (IHC) and expected to see a tat-induced, time-dependent change in Tollip protein expression.

**Methods:** Tat expression was induced in adult iTat mice (2-4 months old) by daily intraperitoneal injections of 100 µg/kg Doxycycline Hyclate from days 0-13. LSC were collected at days 0 (naïve), 3, 7, 14, 28, and 35 post Tat induction (3/sex/time) and were processed for IHC. PBS (pH=3) controls (3/sex) were included at day 14. Earlier test showed that Tollip+ cells were mostly tyrosine hydroxylase (TH)+. IHC was conducted using primary antibodies (Abs): rabbit anti-Tollip (Proteintech 11315-1-AP, 1:1000) and goat anti-TH (Thermo OST00324W, 1:750), and respective secondary Abs: donkey anti-rabbit Alexa Fluor 488 (Jackson ImmunoResearch 711-545-152, 1:1000) and donkey anti-goat Alexa Fluor 568 (Invitrogen A11057, 1:1000). Then, images were taken with a Keyence BZ-X710 microscope and analyzed with ImageJ. All images were scored on a scale of 1-5 based on the staining and sectioning quality. Images scored <3 were excluded. Tollip+ cells were counted in left- and right-side anatomically-defined circular regions encompassing spinal cord laminae 6-10. Tollip+ cell density (cell number/$mm^2$) was calculated and used in the data analysis with IBM SPSS Statistics.

**Results:** The study is ongoing and full analysis will be done later with completed data. An initial ANOVA analysis showed a significant main effect of time (p=0.004). Tollip+ cell density began to increase at day 14, peaked at day 21, and returned to day 0 levels at day 28. This is consistent with the Tollip RNA expression that peaked at day 7. There was also a potential main effect of sex (p=0.08).

**Conclusion:** Changes in LSC Tollip expression is likely to be time and sex dependent. Exploration of the role of Tollip and downstream signaling molecules may help identify treatments for HIV-SN.

**Acknowledgements:** COBRE Histology and Imaging Core (NIH/NIGMS P20GM103643 (Meng)).

IACUC #: 031521-004

**56.**

**Management and Treatment of Patient with COVID-19 in Long Term Care**

Fazeli[1], J, M.D., Toutounchi Shabestari[2], N, OMS III, Sprague[3], R, OMS III,
[1]Maine Geriatrics, Geriatric Medicine, Biddeford, Maine,
[2]University of New England College of Osteopathic Medicine, Biddeford, Maine
[3]University of New England College of Osteopathic Medicine, Biddeford, Maine

**Background:** Older people and individuals with pre-existing conditions - characteristics that describe most residents of long-term care facilities (LTCFs) - are at a higher risk for severe disease or death. Despite this, the standard of care for COVID-19 for residents in LTCFs has not been fully developed. The goal of our research project is to design a COVID protocol for the older adult population. Our aims are to 1.) Determine the change in mortality of residents who were infected with COVID-19 before and after COVID-19 vaccines became available; 2.) Determine how common symptoms and treatments correspond with patient outcomes.

**Methods:** This study is a retrospective chart review using data from 120 residents who had COVID-19 between March 2020 to July 2022 from 4 LTCFs throughout Southern Maine. We made three scoring systems, with 0 being the lowest and 4 being the highest score. One was a comorbidity scoring, which added 1 point for obesity, hypertension, diabetes, and COPD. Another was a symptom based COVID severity score, which added 1 point for hypoxia, cough, congestion, fever, and weakness. Last was a treatment based COVID severity score, which added 1 point for dexamethasone, antibodies, IV fluids, and oxygen. We used these scores along with vaccine, recovery, and mortality data and evaluated these residents on Excel.

**Results:** By 4/30/2021, all 4 LTCFs had finished giving their residents the COVID vaccine and booster. Of the 39 residents who passed before 4/30/2021, 26 of the residents died due to COVID-19. Of the 18 residents that died after 4/30/21, all had COVID vaccine and booster, and all recovered from the initial infection, but died due to other diseases. Of the 51 residents who recovered and lived, they all received vaccines, and only 4 residents recovered and lived that refused the vaccine[TD8]. We have found that between death due to COVID vs. symptom-based COVID score in a logistic regression, there is a significant result (p-value: 0.002). While

the logistic regression of death due to COVID vs. treatment-based COVID score yields no significance (p-value: 0.101). We also found a strong linear relationship between symptom score and comorbidity score with an $r^2$ of 0.899.

**Conclusions:** This data shows the importance of vaccination in LTCFs. This data also suggests that the use of our comorbidity score and symptom-based COVID severity score can help better identify older residents who have a higher risk of mortality due to COVID-19.

**Acknowledgement**: The University of New England College of Osteopathic Medicine and Maine Geriatrics. A special thanks to Dr. Gugliucci for introductions and navigating UNE IRB. This work has been supported by the Peter Morgane Student Research Fellowship. IRB exemption was granted by the University of Southern Maine (protocol # 22-07-1887) and was acknowledge by University of New England (UNE IRB # 0922-03).

**57.**

## G-CSF Administration is Associated with Worse Treatment Response and Survival after CAR T-Cell Therapy

Elavalakanar[5], P, M.Sc., OMS I, Bindal[1], P, M.D., Trottier[3], C, M.D., Dodge[2,4], L, Logan[2], E, RN, Sermer[2], D, M.D., Leukam[2], M, M.D., Weinstock[2], M, M.D., Joyce[2], R, M.D., Liegel[2], J, M.D., Rosenblatt[2], J, M.D., Avigan[2], D, M.D., Alonso[2], C, M.D., Arnason[2], J, M.D.

1. Division of Hematology/Oncology, Department of Medicine, University of Massachusetts Medical Center, T.H. Chan School of Medicine
2. Division of Hematology/Oncology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts
3. Department of Medicine, Tufts Medical Center, Boston, Massachusetts
4. Harvard T.H. Chan School of Public Health, Boston, Massachusetts
5. University of New England College of Osteopathic Medicine, Biddeford, Maine

**Background:** Chimeric antigen receptor T (CAR T)-cell therapy has led to durable responses in many, but not all, patients with relapsed/refractory non-Hodgkin's lymphoma (NHL) and heavily treated multiple myeloma (MM). Correlative data has shown that the initial response phase is driven by CD8+ T-cells in patients post CAR T-cell therapy. Preclinical data has shown that G-CSF may directly reduce the effector function of CD8+ T cells. Studies on the prognostic impact of G-CSF post CAR T-cell therapy are limited. There are no consensus guidelines for prolonged cytopenia management using growth factor support post infusion. Here, we recorded the use of G-CSF in patients treated with CAR T- cell therapy and analyzed its potential impact on treatment response and survival.

**Methods:** This is a retrospective analysis of 80 consecutive adult patients with B cell NHL (n=60) or MM (n=20) treated with CAR T-cell therapy from 2016-2022 at our institution. Baseline characteristics, laboratory data, and G-CSF records (day +1 to +30) following CAR T-cell therapy were collected from medical records. We used a chi square test/Fisher's exact test to compare proportions between groups. We calculated unadjusted and adjusted hazard ratios

(HR) and 95% confidence intervals (CI) for overall survival (OS) and progression-free survival (PFS) and compared survival between the groups using the Mantel Cox log rank test.

**Results:** 26.2% of patients were neutropenic at time of CAR T-cell infusion, 76.2% developed neutropenia before day +30, and 68.7% of patients received G-CSF for management of neutropenia post infusion. G-CSF administration was associated with worse treatment response at day +30, with only 65.5% of patients in the G-CSF group attaining partial response or better, compared to 88% of patients in the non-G-CSF group. Patients who received G-CSF had significantly worse PFS (4.43 vs 63.1 months) and OS (13.7 vs 67.8 months) compared to patients not treated with G-CSF.

On multivariate analyses, differences in survival with G-CSF use persisted despite adjusting for prior lines of therapy, and underlying disease for PFS and OS. Both NHL and MM groups had significantly worse OS when compared to patients in the non-G-CSF group.

**Conclusion:** In this study, administration of G-CSF within 30 days of CAR T-cell therapy is associated with worse treatment response, PFS and OS irrespective of underlying disease or prior lines of therapy.

**Acknowledgement:** Beth Israel Deaconess Medical Center and its Hematology/Oncology Division. IRB exemption was granted by the Dana-Farber Harvard Cancer Center (DF/HCC) IRB committee (protocol 19-848).

**58.**

## Activity-dependent genetic labeling of corneal neurons in the spinal trigeminal nucleus and lateral parabrachial nucleus in response to corneal pain

Mendola, R, OMS II, Glory, C, B.S., Niyonkuru, K, B.S., Meng, I, Ph.D.
University of New England, College of Osteopathic Medicine, Department of Biomedical Sciences, Center for Excellence in the Neurosciences, Biddeford, Maine

**Introduction:** Dry eye disease is marked by symptoms such as discomfort, pain, and visual changes that may impact daily living. With pain being a significant symptom of this disease, it is paramount to elucidate the neural pathways activated by corneal pain and alterations induced by dry eye. The aim of this study was to genetically label activated neurons using the transgenic mouse line Fos-TRAP2 following corneal stimulation in control and dry eye animals.

**Methods:** Targeted recombination in activated populations (TRAP) mice were used to identify corneal stimulation-activated neurons. Male and female TRAP2 mice ($Fos^{2A\text{-}iCreER}$, Jackson Laboratory) were crossed with the CAG-Sun1/sfGFP reporter line to visualize neurons in the trigeminal nucleus caudalis (TNC) and the lateral parabrachial nucleus (LBPN) activated by corneal hypertonic saline application in control and lacrimal gland excision (LGE)-induced dry eye mice. 4OHT (75 mg/kg, i.p.) was injected

15 min prior to either corneal hypertonic saline (5M NaCl, 5 applications, once every 3 min), no stimulation (mock application of saline), or no treatment (remained in holding chamber after i.p. injection). LGE was performed 2-weeks prior to 4OHT treatment. Two weeks after 4OHT, all animals received corneal hypertonic saline and were perfused 90 min later. Immunohistochemistry for GFP and c-Fos protein was performed on free floating 50um sections.

**Results:** Hypertonic saline increased the number of Sun1-GFP and Fos-positive neurons in the TNC on the side ipsilateral to stimulation. Animals that did not receive corneal hypertonic saline after 4OHT demonstrated lower levels of Sun1-GFP expression, yet still had a significant number of Fos-positive neurons due to the application of hypertonic saline on the day of the perfusion. Quantification of Sun1-GFP and Fos-positive neurons in the LPBN is ongoing. Mice that received vehicle instead of 4OHT did not express Sun1-GFP.

**Conclusion:** These results support the use of this mouse line to identify neurons activated corneal stimulation. Future studies will isolate Sun1-GFP-positive cell nuclei and perform single nucleus RNA sequencing to identify expression patterns in corneal activated neurons and alterations following dry eye.

**Acknowledgements:** The University of New England College of Osteopathic Medicine. Special thanks to the Histology and Imaging Core and the Behavior Core for their help with this project. This work has been supported in part by the Kahn Family Foundation Fellowship (to RM) and the National Institutes of Health/National Eye Institute (U01EY034709). IACUC approval #052720-011.

**59.**

## Review and Potential Clinical Validation of the Insignificance of Race in Prenatal Biochemical Screening for Fetal Anomalies

Samantha Scetta, OMS II, University of New England, College of Osteopathic Medicine, Biddeford, Maine

Dr. Ricky Grisson, MD, MPH, Department of Pathology, Lifespan Academic Center, Providence, Rhode Island

**Background**: In maternal serum screening, several variables are considered critical for calculating fetal risk assessment for aneuploidy and open neural tube defects: Maternal age, history of insulin dependent diabetes, tobacco use, and race. The College of American Pathologists mandates the use of race as a correction factor for laboratories performing prenatal biochemical screens, resulting in an automatically corrected serum AFP level based upon patient race. Recognizing that race is a social construct, there is limited justification to include race as a parameter in prenatal screening. The purpose of this study is to validate the biochemical analyte screening performed on maternal patients.

**Methods**: This is a prospective cohort study of 95 pregnant patients receiving prenatal testing and obstetric care at Lifespan Academic Medical Center starting in Dec. 2022 to present. A convenient sample of remnant specimens collected for first and/or second trimester TORCH titers, cell free fetal DNA, and maternal serum screening for ONTDs were tested offline for prenatal serum analytes (hCG, PAPP-A, UE3, DIA). The medical record was then abstracted for pertinent clinical history. All first and second trimester ultrasounds, cell free fetal DNA, carrier screening tests, amniocentesis karyotypes and birth outcomes were assessed. The LMS Alpha Software Version 8 was used to calculate potential risk for fetal aneuploidy and ONTD. The risk assessment was then adjusted for gestational age, weight, and historical or medical statuses. The patient's risk calculation was then adjusted for each of four racial/ethnic designations– Black, White, Other, Overall.

**Results**: Between racial designations for trisomy 13 and trisomy 18, no discrepant results were observed. Two discrepant results were observed between Black/Other and White patient racial designations for ONTDs. One or two discrepancies were observed between Black, White, and Other patient racial designations for trisomy 21. Ultrasonographic markers for fetal aneuploidies were observed in 5 patients with low-risk prenatal biochemical screens.

**Conclusion**: We are awaiting birth outcomes to determine the appropriate conclusions as to whether race can be recommended for removal from the prenatal biochemical screens. In the chart review performed, it is so far demonstrated that prenatal screening is further complicated by including race in risk assessment, and that racial designation is not a useful parameter for birth outcomes.

**Acknowledgements**: Thank you to laboratory personnel at Newport Hospital and Rhode Island Hospital for coordinating analyte testing and remnant specimen processing for this ongoing Quality Improvement Study.

**60.**

**Psychosocial Function of Vitiligo Patients in the Face of Stigmatization: A Systematic Review**

Lysakova[1], S, OMS I, Stuhlmann[2, 3, 4], CFZ, M.S., Jordan[5], C, Ph.D., Revenson[2, 4] , TA, Ph.D.
[1] University of New England College of Osteopathic Medicine, Biddeford, Maine
[2] The Graduate Center, CUNY, New York, New York
[3] University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany
[4] Hunter College, City University of New York (CUNY), New York, New York
[5] William Paterson University of New Jersey, Wayne, New Jersey

**Objectives:** Vitiligo is a chronic skin disease characterized by the development of well-defined depigmented patches. Vitiligo is the most frequent cause of skin depigmentation, affecting 0.5-2% of people globally. People with vitiligo are five times more likely to display depressive symptoms than healthy controls, and one quarter of people with vitiligo have psychiatric comorbidity and poor quality of life (QoL). Frequent experiences of stigma may contribute to

these psychological outcomes. This systematic review (PROSPERO Pre-registration: CRD42021165956) examined the link between vitiligo-related stigma and quality of life.

**Methods:** Following PRISMA guidelines, a keyword search was conducted for peer-reviewed articles on skin disease, stigmatization, and psychosocial outcomes (e.g., coping, comorbidity, physical and mental health, social and sexual relationship functioning, and health behaviors) in PsycINFO, PubMed, and CINAHL databases. Studies were screened for eligibility by two independent researchers. Data were extracted for quantitative studies with samples of participants with vitiligo. Results were synthesized narratively.

**Results:** The initial search yielded 264 articles; after screening, 43 studies met inclusion criteria, of which eight quantitative studies with samples of vitiligo were identified. Five of the quantitative studies were conducted in Europe and the USA. Only three studies reported race, where 84% of the sample were white. Six studies used validated stigma measures, while the remaining used non-validated, author-created measures. Stigma experiences were common and often associated with behaviors to hide symptoms (e.g., cosmetic camouflage), greater distress, and lower QoL. Each of the studies reported significant associations between stigma and QoL, indicating that greater stigma was related to lower quality of life with a moderate to large effect (r's = -0.35 to -0.80).

**Conclusion:** Findings highlight the paucity of research on stigma among people with vitiligo, but overall suggests a significant effect on psychological well-being, specifically QoL. Race was often unreported despite evidence that the emotional burden of vitiligo is higher among patients with darker skin who have contrasting, more visible vitiligo areas. Further study of vitiligo-related stigma and its psychosocial implications is needed to guide multidisciplinary approaches to treatment interventions.

## 61.

## Implementing Low-Barrier COVID-19 Testing Clinics for Vulnerable Populations in Partnership with Community Based Organizations

Ngandu[1], D, I.M.G, Awale[1], S, B.S., Sclar[1], GD, Ph.D, Goldstein[2], J, M.P.H, Joshi[3], S, Nicoll[4], L, Ph.D, Volkers[5], A, Fernandes[5], C, Tucker[6], A, S.H.R.M.-C.S.P, Mudasigana[6], ML, Price[1], G, M.D., Ahmed[1], A, M.D., Mallipeddi[8], S, [OMS II], Hashmi[8], H, [OMS III], Vinton[2], L, M3], Parker[9], D, Jacobs[1], EA, M.D., Ph.D, & Fairfield[1], K, M.D., Dr.PH

[1]MaineHealth Institute for Research, Portland, ME
[2]Tufts University, School of Medicine, Boston, MA
[3]Princeton University, Princeton, NJ
[4]Portland Community Free Clinic, Portland, ME
[5]Preble Street, Portland, ME
[6]Greater Portland Health, Portland, ME
[8]University of New England College of Osteopathic Medicine, Biddeford, ME
[9]Bates College, Lewiston, ME

**ABSTRACT**

**Introduction:** The COVID-19 pandemic disproportionately affected people from vulnerable communities. There was a need to improve accessibility of COVID-19 testing and treatment to reduce spread of COVID-19. With national RADx-UP initiative funding, we created a partnership between an academic medical center and three community based organizations (CBOs) to offer low-barrier COVID-19 walk-up testing clinics to vulnerable populations in Portland, Maine.

**Methods:** We aimed to serve people who are unhoused, immigrants, and low-income and/or uninsured. The clinics were operated collaboratively by the study team and community partners: one CBO serving people who are unhoused, a Federally Qualified Health Center serving a large and diverse immigrant community, and a free clinic serving low-income/uninsured people. We offered COVID-19 rapid antigen tests. Clinic staff administered a brief survey on reason for testing and then instructed participants on how to self-swab. While staff processed the test, participants were asked to complete a voluntary patient survey. For positive cases, we offered eligible patients antiviral treatment within 24 hours. Clinic staff also completed observational field notes to capture aspects of clinic implementation.

**Results:** Between January 2022 and May 2023, we completed 246 tests, 17 of which were positive for COVID-19 (7%). Among the 246 tests, 240 clinic participants consented to the staff survey. People sought testing for a variety of reasons, including symptoms (60%), close contact exposure (29%), and/or need for a negative test result to access services (e.g. healthcare, shelter) or an activity (e.g. work, travel) (; 33%). Overall, people primarily tested due to symptoms with only 7% testing due to close contact exposure alone. Based on the patient survey findings, the clinics reached the intended vulnerable populations. Among the 130 clinic participants who consented to the patient survey, 39% were unhoused (43/110), 22% spoke a language other than English at home (23/105), 23% were uninsured (25/97), and 46% made less than $20,000 before taxes in 2019 (45/98). The field notes captured how this collaboration with community partners helped build trust.

**Conclusion:** Providing low-barrier testing clinics is instrumental to reducing the spread of COVID-19 and reducing disparities in antiviral treatment access. Partnering with trusted CBOs is an approach that may better facilitate testing among vulnerable populations.

**Acknowledgements:** This research was conducted by the MaineHealth Institute for Research in collaboration with Preble Street, the Portland Community Free Clinic, and Greater Portland Health. The study was funded by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number U54GM115516.

## 62.

### Irisin Enhances Osteocyte Mechanosensitivity to Fluid Shear Stress

Ichikawa[1,2], T, OMS II, Estell[2], E, Ph. D., Rosen[2], C, M.D.

[1]University of New England College of Osteopathic Medicine, Biddeford, Maine

[2]MaineHealth Institute for Research, Scarborough, Maine

**Introduction:** Irisin is a myokine released during exercise with complex effects on bone remodeling. This study investigates irisin's impact on osteocyte response to fluid shear, a physical stimulus generated during exercise.

**Methods:** OCY454 cells were cultured [2] for 48 hours in ibidi flow channels with or without 10 ng/mL of recombinant irisin [1] in MEMα. Intracellular calcium levels were tracked in real time with the fluorescent indicator Fluo4-AM under exposure to 1 minute of 1 Pa fluid shear in HBSS via syringe pump, after 1 minute of rest to establish baseline fluorescence. Relative calcium concentration was quantified as mean cellular fluorescence normalized to mean value during baseline, with a responding cell defined as greater than 1.2. In separate experiments, OCY454 cells irisin-preconditioned for 48 hours were cultured under exposure to 1 Pa fluid shear or in static conditions for 2 hours, and RNA was isolated from cell lysates to run qPCR on key osteocyte genes. Statistical significance of percentile response and mean peak magnitude/gene expression was determined using Chi-squared and Welch's t-test respectively.

**Results:** Irisin-preconditioned cells responded more significantly to fluid shear than controls, with significantly higher mean peak calcium levels. Irisin and fluid shear independently increased DMP1 expression, a marker of mature osteocytes, and their combined effect significantly surpassed controls and individual conditions. Irisin treatment significantly increased E11G38 expression, an osteocyte dendrite marker, in static and shear conditions, while fluid shear alone had no effect.

**Conclusion:** Irisin enhanced osteocyte fluid shear response, elevating percentage of responders and peak calcium levels. DMP1 expression indicated that like fluid shear, irisin signaling alone can stimulate key osteocyte genes. Amplified fluid shear response in irisin preconditioned cells suggests irisin's synergistic ability to further affect mechanosensitive gene expression. Stimulation of E11G38 by irisin alone indicates that irisin also has direct signaling effects on osteocyte function. Future work aims to elucidate calcium signaling mechanisms, and the influence of altered mechanosensitivity and irisin's other downstream effects on osteocyte function.

**References:** 1. Kim et al, Cell 2018. 2. Xu et al, J Orth Res 2019.

**Acknowledgements:** This work was performed at MaineHealth Institute for Research in the laboratory of Dr. Clifford Rosen. This work was supported in part by the Peter Morgane Research Fellowship, NIH/NIAMS K01AR081959.

## 63.

### The Prozone Phenomenon: A Case Study Examining the Rare Syphilis Phenomenon

Holcomb[1], A, OMS III, Azat[1], M, OMS IV, Lamboy[1], B, OMS IV, Lamboy[1], J, OMS IV, Gangat[2], M, MD.
[1]Univsersity of New England College of Osteopathic Medicine, Biddeford, Maine
[2]Northern Light Eastern Maine Medical Center, Bangor, Maine

**Introduction:** For patients undergoing syphilis testing, a diagnosis is made via serologic testing by utilizing both nontreponemal and treponemal tests. Active syphilis is excluded for patients with a negative initial nontreponemal test. However, patients that present with history and physical exam findings concerning for syphilis can present with a false negative test due to the "prozone effect." The prozone reaction, though rare overall, results in a false-negative test due to an overabundance of antibodies that interferes with the formation of antigen-antibody complexes.

**Case:** This case is about a 66-year-old female with five lifetime sexual partners who developed generalized pruritic body rash in the Summer of 2022 and bilateral conjunctival injection with suboptimal response to topical steroids in the Fall of 2022. The patient had been having health complications over the past year and a half. Beginning in August 2022, she started to have a diffuse, maculopapular, pruritic rash. She received various courses of steroids and the rash eventually resolved over 3-4 months. Not long after, the patient reported experiencing bilateral eye injection in the Fall of 2022 and she was diagnosed with "dry eyes." After some time with no improvement, she was referred to Ophthalmology and was diagnosed with uveitis. Her ophthalmologist ordered blood work, which in early 2023, revealed a positive RPR (rapid plasma reagin) with a titer level of 1:512, a positive Treponema pallidum IgG and IgM, and C-Reactive Protein of 9.8. Paradoxically, patient's repeat RPR was negative.

**Discussion:** In our case study, the patient's initial RPR and T pallidum IgG and IgM were positive. Based on the patient's symptoms, it was concerning for neurosyphilis which led to a lumbar puncture for analysis of the CSF. However, the patient had a repeat RPR which was negative. This sample was subsequently diluted leading to a positive titer. Thus, evidence of the prozone effect. This case report helps raise awareness of the difficulties of the diagnosis of syphilis and the prozone phenomenon, both of which lead to delays in treatment of syphilis which can be treated with a widely available, inexpensive drug, Penicillin G.

**64.**

**Mice Deficient in PDE3A Develop Characteristic Findings of Nonalcoholic Steatohepatitis**

McGeorge[2],G, OMS I, La Perle[1], K, M.D., Nelin[1], L, M.D., Liu[1], Y, P.H.D., Chen[1], B, M.D.

[1]Nationwide Children's Hospital, Department for Perinatal Research, Columbus, Ohio
[2] University of New England College of Osteopathic Medicine, Biddeford, Maine

**Introduction:** Nonalcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease in children. NAFLD comprises a spectrum of diseases, ranging from NAFL to the inflammatory subtype nonalcoholic steatohepatitis (NASH). We found that global phosphodiesterase 3A (PDE3A)-deficient mice are small, have histologic evidence of NASH with micro/macrovesicular changes, hepatocellular coagulation necrosis with inflammatory infiltrates, and fibrosis.

**Objective:** The present study was completed to explore molecular pathways involved in mediating NASH in PDE3A-deficient mice.

**Methods:** Male (M) and female (F) 5 wk-old C57bl/6J (WT) and *Pde3a*$^{-/-}$ (KO) mice with early and late progression of disease, defined by absence or presence of rectal prolapse, were sacrificed. Liver was weighed and protein harvested. PDE3A, PDE3B, FASN, SREB1c, DGAT-2, PDK1-4, and β-actin expression were quantified by Western blot (n=3 per group/gender).

**Results:** M+F KO liver/body weight % were smaller than WT (3.7 vs 4.1, $p<0.0001$). M+F KO livers had increased PDE3B protein levels vs WT ($p<0.001$ M, $p<0.02$ F). FASN was decreased ~2.5-fold in M+F KO vs WT livers ($p<0.05$), while SREB1c was not different. PDK1-4 were each increased in F KO vs WT livers ($p<0.04$) and PDK2-4 were increased in M KO vs WT livers ($p<0.05$). Later disease progression in KO livers showed greater PDK1 compared to either WT ($p<0.002$) or KO with early disease ($p<0.002$). DGAT-2 expression increased ~4.5-fold ($p<0.03$) in M and ~16.4-fold in F KO vs WT livers ($p<0.002$).

**Conclusion:** These data suggest that KO mice have elevated free fatty acids (FFA) contributing to NASH pathogenesis. Upregulated DGAT-2, which catalyzes the final step to convert FFA into triglycerides, suggests a compensatory mechanism to dispose of excess FFA. PDKs have been shown to be induced by high FFA, cellular stress, and starvation. These data suggest it is not a result of de novo lipogenesis based on absence of SREB1c and FASN induction in KO livers. PDKs are critical for the metabolic flexibility within the liver. By inhibiting PDH activity, PDK can switch energy metabolism from carbohydrate to lipid fuels. An increase in PDK expression directly affects available FFA in the body due to enhanced metabolic pathways such as β-oxidation. We speculate that PDE3A KO mice have elevated FFA that upregulate PDK to increase β-oxidation, thereby producing mitochondrial reactive oxygen and toxic lipid species to trigger the lipotoxicity seen in NASH.

**Acknowledgement:** Nationwide Children's Abigail Wexner Research Institute and a special thank you to my mentor Dr. Bernadette Chen. This work was funded by Nationwide Children's Hospital and the animal work was approved by the Nationwide Children's Hospital IACUC and laboratory safety committee under the approved IACUC protocol #AR0800038.