



# Research Week 2020

## Abstract Book

OHSU Research Week is an annual university-wide event that celebrates research performed by students, faculty, postdocs, and staff across all schools, centers, institutes and education programs.

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# Research Week 2020

## Three-Year Experience of a Multidisciplinary Central Nervous System Clinic Model for Radiation Oncology and Neurosurgery (RADIANS) in a Community Hospital Setting

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### Keywords

central nervous system, multidisciplinary, neuro-oncology, neurosurgery, radiation therapy

### Abstract

#### Introduction

As academic centers partner and establish healthcare systems with community hospitals, delivery of subspecialty, multidisciplinary care in community hospital settings remains a challenge. Improving outcomes for central nervous system (CNS) disease is related to integrated care between neurosurgery (NS) and radiation oncology (RadOnc) specialties. Our multidisciplinary community hospital-based clinic, RADIANS, previously reported high patient approval for simultaneous evaluation with NS and RadOnc physicians. Three-year experience is now reported.

#### Methods

Prospectively collected clinical and demographic patient data over three years was conducted. Patient surveys were administered. Descriptive statistics reported as mean and percentages for patient characteristics, diagnosis, treatment and outcomes.

#### Results

Between August 2016 and August 2019, 101 patients were evaluated. Mean age was 61.2 years and mean distanced traveled was 54.9 miles (Range = 0.3 - 340). Patient Satisfaction Score was 4.79 (0-5 Scale, 5-very satisfied). Most common referral source was medical oncologists. Seventy-two patients had malignant CNS disease (brain mets 28; spine mets 27; both 6; primary brain 9; primary spine 2), 29 had benign CNS disease. Post-evaluation treatment: radiation therapy (RT) only (n=29), neurosurgery (NS) only (n=16), both RT and NS (n=22), and no RT/NS intervention (n=34). Fractionated stereotactic radiosurgery was most common RT delivered; craniotomy with tumor resection was most common NS

performed. Treatment outcomes: local control=61/67 (91%); radiation necrosis or radiation-induced myelitis=2/51 (3.9%).

## Conclusions

The RADIANS multidisciplinary community hospital-based CNS clinic model is first of its kind to be reported, continuing strong patient approval at extended follow-up. Data indicates the model serves as a regional referral center. Patients with varying degrees of co-morbidities, systemic disease status, and oncologic staging can be treated with evidence-based treatment modalities for complex CNS disease, yielding high rates of local control and low rates of grade 3 or 4 radiation-induced toxicity, while having access to ongoing clinical trials.



# Research Week 2020

## Alternative low stress diurethane dimethacrylate for BisGMA-free resin composites

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### Keywords

resin composites, polymerization stress, chemistry

### Abstract

#### Objective

The aim of this study is to test BisGMA-free systems using newly synthesized diurethane dimethacrylates (2EMATE-BDI) as the base monomers for resin composites.

#### Methods

2EMATE-BDI or TEGDMA were copolymerized with UDMA at 40/60 and 60/40 mass ratio. BisGMA-TEGDMA at 60/40 mass ratio served as control. 0.2wt% DMPA and 0.4wt% DPI-PF6 were used as initiators. Inorganic filler particles were incorporated at 70wt%. Photocuring procedures were accomplished with a mercury arc lamp (320-500nm, 800mW/cm<sup>2</sup>). Composites were tested for kinetics of polymerization, polymerization stress, 3-point bending test, water stability and *S. mutans* biofilm formation. Data were analysed with one-way ANOVA/Tukey's test and Student's T test (95%).

#### Results

In general, in comparison to BT, formulations containing 2EMATE-BDI showed significant reduction in R<sub>P</sub>MAX, and slight reduction in final DC. The polymerization stress for the 2EMATE-BDI-containing materials was 30% and 50% lower than BT and analog TEGDMA-containing formulations, respectively. This can be only partially explained by the lower conversion (less than 10% reduction). Flexural strength were similar for all groups after storage in water. The moduli of the 2EMATE-BDI-containing materials were equal or higher than the TEGDMA-containing materials. The incorporation of 60wt% 2EMATE-BDI increased the hydrophobicity in 38% in comparison to BT. Biofilm formation was similar among the tested groups, which may also indicate equivalent biocompatibility.

#### Conclusion

The stark reduction in polymerization stress associated to the marked hydrophobicity without compromising mechanical properties and handling characteristics validates the

use of the newly synthesized 2EMATE-BDI monomer as diluent for BisGMA-free dental resin composites.



# Research Week 2020

## Gaps in Emergency Department Care for Suicidal Refugees: A Conceptual Model and Case Example

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### Keywords

Refugee, Mental health, Suicidal ideation, Emergency department, Social determinants of health

### Abstract

#### Aims

Refugees are at increased risk of mental health challenges, encounter many social issues such as homelessness and food insecurity, and experience barriers to accessing culturally appropriate outpatient care. As such, many refugees who experience a mental health crisis present to emergency departments (EDs) to seek mental health care and support for physical needs.

To investigate gaps and barriers in care, this project integrates literature on ED treatment of suicidality and an applied case example of a homeless, US-settled Somali refugee with PTSD, polysubstance abuse, and chronic suicidal ideation seeking ED care.

#### Methods

We reviewed documentation of the patient's initial ED visit and any treatment occurring in the six months before and after the ED visit. We looked for documentation of enhanced suicide screening, safety planning, structured follow-up, and support of physical needs (e.g. housing).

We applied a patient-centered access to care model from the literature to characterize gaps and barriers in care. Determinants of access described in this model include availability and acceptability of care, characteristics of care settings and opportunities (e.g., outreach, coordination), and patient abilities (e.g. perception of care needs).

#### Conclusions

The present case demonstrated several areas for enhancing ED treatment of suicidal refugees. Although the patient engaged in many primary care, ED, and case management visits in the six months after their ED visit, appropriate follow-up mental health care for the patient's recurrent suicidal ideation was not documented.

Missed opportunities and barriers involved provider perceptions of patient needs, accommodation of the patient's abilities, and continuity of care. Each may have contributed to further delay and gaps in appropriate suicide preventive care limiting mitigation of suicide risk factors.

We provide recommendations for improving access to appropriate care given the unique barriers faced by refugees. Future research should solicit provider and patient perspectives to contextualize the care provided.



# Research Week 2020

## Bioactive Polymers for *S. mutans* Biofilm Inhibition

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### Keywords

Bioactive polymers, Dental materials, Biofilm, antifouling, *S. Mutans*.

### Abstract

The development of biofilms on dental restorations may lead to the formation of secondary caries. The purpose of this study was to determine the efficacy of bioactive small molecules (G43 & G43TEG) to disrupt/inhibit biofilm formation of bacterial species contributing to caries causing biofilm dysbiosis. G43 and G43TEG were synthesized and minimum inhibitory concentration (MIC) against *S. mutans* were established. The MIC was determined to be 25-50 $\mu$ M for both G43 and G43TEG a slight reduction of viable biofilm cells (Fig. 1) with a visual disruption of the biofilm. Polymerizations of dental resins were slightly affected by 4% G43 or G43TEG (Fig. 1), however cured  $\geq$ 70% DC for both cases. Analysis of leachates showed no detectible G43 or G43TEG (<11  $\mu$ M). This study demonstrated that bioactive molecules in the G43 family affect *S. mutans* biofilm viability (25-50  $\mu$ M). Further, G43 and G43TEG were tolerable for polymerization kinetics, retaining relatively high final DCs.





# Research Week 2020

## Why You Should Care About Where

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### Keywords

Geographic Information Systems (GIS); Social Determinants of Health (SDOH); Informatics; Data Analysis

### Abstract

What can we understand and predict about our health based on where we live, where we work, and where we've been?

In 1854, Dr. John Snow drew a map showing the relationship between the homes of people who had died from cholera and the location of the water pumps in the area. He mapped health information in order to understand the source of the outbreak, and used his map to show that cholera was caused by drinking contaminated water. Today we continue use location as a context to help us understand and interpret health data - to understand the effect of social determinants; to predict and monitor epidemics; to demonstrate the relationship between our environment and our health.

In 2015, NIH Director Francis Collins tweeted "If DNA is our biological blueprint, then ZNA (zip code at birth) is the blueprint for behavioral & psycho-social makeup." Indeed, zip code is a more powerful determinant of our lifespan than even our genetic code. Why is this? What are the factors involved? How should we make these insights actionable? What is reasonable to conclude about a patient's health based on the community in which they live (and what isn't)?



# Research Week 2020

## Functional Connectivity of Sensory Processing Disorders

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### Keywords

autism; sensory processing disorder; MRI

### Abstract

Approximately 95% of children with Autism Spectrum Disorder (ASD) report a sensory processing disorder, such as hypersensitivity to sound and touch. Recent work suggests that auditory hypersensitivity may be explained by connections between auditory cortices and the amygdala. Resting-state functional connectivity MRI will be used to examine these proposed connections in children with ASD and in Japanese macaques that display component behaviors of ASD. Using a novel machine learning approach, connectivity results between humans and macaques will be directly compared to ascertain whether the macaque model appropriately captures the sensory processing connectivity profile of children with ASD. Importantly, the macaque model uses maternal high-fat diet, a common prenatal risk factor of ASD, to generate symptoms of ASD in the offspring. Thus, if the machine learning comparison succeeds, it would additionally implicate maternal high-fat diet specifically in the development of sensory processing disorders in individuals with ASD.



# Research Week 2020

## Idiopathic Granulomatous Mastitis: the Role of Rheumatologists in Treating This Rare Cause of Breast Pain

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### Keywords

Idiopathic granulomatous mastitis, methotrexate, granuloma

### Abstract

#### Background/Purpose

Idiopathic granulomatous mastitis (IGM) is an inflammatory breast disease occurring primarily in young women (1, 2). The diagnosis of IGM is made by breast biopsy showing non-caseating granuloma after other causes of granulomatous mastitis have been excluded (1, 4). IGM is a poorly understood disease; there is no consensus regarding underlying cause, risk factors, and optimal treatment of this condition (3).

#### Methods

IGM patients were identified via the OHSU Cohort Discovery tool who carried a diagnosis of "granulomatous mastitis". 30 patients seen between 2007-2018 were identified. Retrospective chart review was used to verify that IGM diagnosis was accurate, collect data on baseline characteristics, clinical features and treatment course/outcomes. 2 patients were excluded (1 diagnosed with alternative condition and 1 without adequate follow-up).

#### Results

Of the 28 IGM patients, all were female, the mean age was 32, the majority (60.7%) were Hispanic. Mean follow-up was 27 months and 17% were treated by rheumatologists. 92.9% and 92% has history of pregnancy and breastfeeding, respectively. Four patients had inflammatory arthritis/artralgias and 5 had erythema nodosum. In 23 patients with adequate follow-up data, treatment groups were divided into surgery plus high dose steroids (n=3), high dose steroids (n=12), methotrexate (MTX) and high dose steroids (n=3) and other (n=5). 7 patients (30%) had disease relapse and 4 patients (17%) had persistent disease. The highest rates of relapse were in the steroids alone group (42%) and lowest rate of relapse was in the methotrexate group (0%). Overall, 83% of patients achieved a disease free remission with post-remission follow-up of over 1 year in 74%.

## Conclusions

This case series of 28 IGM patients suggests that MTX in combination with high dose steroids may successfully treat IGM, although larger prospective studies are needed. We also report a higher incidence of arthritis/arthralgia and erythema nodosum than previously described.



# Research Week 2020

## Effect of the Communication Matrix Community of Practice on Students' Expressive Communication Skills

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### Keywords

Developmental Disability, Intervention, Communication Development, Rehabilitation

### Abstract

#### Background

Developing Individualized Education Plans (IEPs) or Individualized Family Service Plans (IFSPs) for children with severe disabilities is challenging because many educational practitioners lack the background knowledge and skills to assess the communication needs of students and develop appropriate communication-related goals and objectives. One promising method for increasing educational professionals' knowledge and skills are communities of practice, which provide web-based learning and professional development opportunities. The purpose of this study was to examine whether using the online Communication Matrix Suite of tools (training webinar, assessment, custom report, and community) would result in higher quality expressive communication goals and significant growth in expressive communication skills.

#### Method

A quasi-experimental, one-group pre-test post-test design was used to examine the effects of the Communication Matrix Suite intervention. We examined changes in pre and post intervention measures of expressive communication using the Communication Matrix and IEP quality. 102 professional-student pairs were included in the study. The Communication Matrix Suite included a set of four online tools designed to support educational professionals in assessing the expressive communication skills of and selecting appropriate educational goals for students with complex communication needs.

#### Results

One-way repeated measures ANOVA were conducted to compare scores on the Communication Matrix Assessment pre and post-intervention and to compare the quality of IEP goals. Scores on the Communication Matrix Assessment were significantly higher following the intervention. There was no significant difference in IEP/IFSP quality.

#### Discussion

Comparison of the Communication Matrix Assessment scores of the students before and after their teachers and speech-language pathologists participated in the study indicated significant increases in expressive communication skills, but no difference in IFSP/IEP quality. Results provide initial evidence of the promise of the Communication Matrix Suite for increasing students' expressive communication skills.



# Research Week 2020

## The BRIDGE-C2 Center: A Learning Laboratory to Improve Cancer Screening and Prevention in Underserved Populations

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### Keywords

dissemination and implementation science; cancer prevention; health disparities

### Abstract

#### Description

The newly funded Building Research in Implementation and Dissemination to Close Gaps and Achieve Equity in Cancer Control (BRIDGE-C2) Center is one of three National Cancer Institute's Advanced Implementation Science Centers in Cancer Control. This innovative Center, based in the Department of Family Medicine at the Oregon Health & Science University and partnered with OCHIN, Inc., will provide a regional resource for dissemination and implementation (D&I) science. The BRIDGE-C2 Center's overarching goal is to advance D&I science to improve cancer screening and prevention in underserved populations.

#### Objectives

Community health centers (CHCs) provide excellent care to over 28 million people, but like many primary care practices serving populations impacted by health disparities, they face obstacles to delivering evidence-based cancer prevention to their patient populations. The BRIDGE-C2 Center will create tailored, focused approaches to support diverse practices' implementation of evidence-based interventions to close gaps in cancer prevention care.

#### Setting and Participants

The BRIDGE-C2 Center brings together primary care providers, health services researchers, implementation scientists, and cancer control experts. All CHC members of OCHIN share a linked electronic health record; these data will enable surveillance of cancer screening and prevention across the network. This electronic health record network includes >645 CHCs that serve nearly 3.6 million patients nationwide.

#### Methods

We will conduct pilot studies that develop and test strategies to improve implementation of evidence-based cancer prevention, rapidly scale up successful pilots into large-scale pragmatic trials, and disseminate our findings. The Center will also provide infrastructure for D&I scientists including robust and innovative laboratories for empirical work and new methods and measurements.

#### Discussion

The BRIDGE-C2 Center will create the organizational infrastructure, enhance methodology, and connect researchers with primary care teams in order to propel the D&I field forward while also improving cancer screening and prevention gaps in CHCs.





# Research Week 2020

## Characterizing Blood-Brain Sterol Pathways in Individuals with Deficient Sterol 27-Hydroxylase (CYP27A1) Enzyme Activity

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### Keywords

cerebrotendinous xanthomatosis (CTX), Blood-Brain Barrier, genetic disorders, cholesterol metabolism, sterol 27-hydroxylase

### Abstract

Aberrant cholesterol metabolism is thought to play an important role in brain pathophysiology for many neurodegenerative disorders. How sterol metabolism impacts cerebral accumulation of toxic sterol species is not fully characterized. The brain houses 20-25% of total body cholesterol in a de novo synthesized pool unable to traverse the BBB. Formation of 7 $\alpha$ -hydroxy-3-oxo-4-cholestenoic acid (7-HOCA) by the sterol 27-hydroxylase (CYP27A1) enzyme is one route of cerebral cholesterol removal, with flux of 7-HOCA demonstrated to occur across the BBB into the periphery. Deficient CYP27A1 activity is associated with cerebrotendinous xanthomatosis (CTX); a rare genetic disorder that can cause irreversible neurological decline associated with formation of cerebellar xanthomas, consisting mostly of cholesterol and a saturated analogue, cholestanol. Xanthomas can also form on tendons in CTX, including the Achilles tendon. In CTX a 7-HOCA precursor, 7 $\alpha$ -hydroxy-4-cholesten-3-one (7 $\alpha$ C4) is markedly elevated and can be converted to cholestanol, resulting in accumulation of this sterol. Peripheral 7 $\alpha$ C4 readily crosses the BBB, and elevated cerebral 7 $\alpha$ C4 is thought to contribute to cholestanol accumulation in the brain. In this study, sterols were measured in the blood and CSF of CTX patients and healthy controls. In addition, an atypical patient with putative CTX genotype and large tendon xanthomas, but with normal cholestanol and healthy brain function, was studied. 7 $\alpha$ C4 was elevated in CTX compared to control plasma, with an intermediate 7 $\alpha$ C4 level found in the atypical patient. 7-HOCA was <2mg/ml in CTX compared to 21-107ng/ml in control plasma, with 4ng/ml found in the atypical patient. 7-HOCA was not detectable in CTX CSF compared to 5652,920ng/ml in controls and 412ng/ml in the atypical patient. We hypothesize the atypical CTX case may be a result of residual CYP27A1 activity that allows adequate conversion of 7 $\alpha$ C4 to 7-HOCA to prevent cholestanol accumulation in the brain and periphery as normally occurs in CTX.



# Research Week 2020

## Acute Compartment Syndrome: Do we treat patients differently because of implicit bias?

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### Keywords

Compartment Syndrome Fasciotomy Implicit Bias

### Abstract

#### Purpose

Implicit bias is an unconscious assessment of others that may lead to unintended prejudice. Socioeconomic attributes often complicate the assessment and treatment of trauma patients, particularly in the management of acute compartment syndrome (ACS). Our aim is to evaluate for the presence of social implicit bias among orthopaedic surgeons who performed fasciotomies for ACS. We hypothesize that social implicit bias impacts time to fasciotomy in patients diagnosed with ACS secondary to lower extremity trauma.

#### Methods

A billing database was reviewed to include all lower extremity 4-compartment fasciotomies performed by orthopaedic surgeons between 2008 and 2018. Retrospective review of time to fasciotomy, demographics and implicit bias factors defined as positive urine drug screen, active intoxication, current or prior history of opioid or illicit drug use, homelessness, & lack of medical insurance were included. Patients were divided as "at risk" or "not at risk," based on having implicit bias factors. A t-test analyzed the two groups with respect to time to fasciotomy.

#### Results

A total of 93 patients were identified; 7 patients were excluded by history for non-traumatic mechanisms, leaving 86 patients for analysis. There were 59 patients (68.6%) that met "at risk" criteria. The mean time to fasciotomy was 12.2 hours (range 0.1 – 51.4 hrs, SD 11.4 hrs). There was no significant difference ( $p=.438$ ) in time to fasciotomy between the "at risk" (mean 12.1 hrs, range 0.1 – 51.4 hrs, SD 11.6 hrs) and "not at risk" groups (mean 12.4 hrs, range 1.5 – 45.2 hrs, SD 9.9 hrs).

#### Conclusion

Trauma patients "at risk" for social implicit bias had no significant difference in time to fasciotomy for ACS when treated by orthopedic surgeons. We plan to compare implicit bias in matched cohorts for those who received fasciotomies for possible ACS and those who did not receive fasciotomies.



# Research Week 2020

## Proximal Tubule Megalin Inhibition Prevents Acute Kidney Injury Due To Rhabdomyolysis in Mice

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### Keywords

Kidney injury, trauma, disaster, epithelial transport, myoglobin

### Abstract

#### Introduction

Destruction of skeletal muscle (rhabdomyolysis) releases myoglobin, causing rhabdomyolysis-induced acute renal injury (rhAKI). As rhAKI commonly occurs in austere environments such as earthquakes and armed conflict, supportive care is challenging. Specific therapy would be a significant advance. Since myoglobin is taken into renal tubular cells via the renal cortex-specific transporter megalin (LRP2), we hypothesized that interfering with megalin would ameliorate rhAKI.

#### Methods

We bred inducible, proximal tubule-specific megalin knockout mice (LRP2 fl/fl, Ndr1CreERT2, iMegKO). Glomerular filtration rate (GFR) was measured at baseline and 24 hours and urine was collected for 24 hours before and after experiments. Male mice received 8mL/kg 50% glycerol intramuscularly. 24h later, plasma and urine myoglobin, and myoglobin clearance were quantified. Kidney sections were imaged for pathology, injury markers (KIM-1 and caspase-3), and megalin and myoglobin. C57BL/6 mice then received cilastatin, a pharmacologic megalin inhibitor, or vehicle, simultaneously with glycerol injection, and were similarly evaluated.

#### Results

Tamoxifen treatment induced cre recombinase, causing deletion of megalin in the renal cortex of iMegKO mice but not cre- littermates (controls). After glycerol injection, controls demonstrated GFR  $22.4 \pm 0.3$  % of baseline, oliguria, and severe histologic injury. In iMegKO mice GFR was  $92.8 \pm 5.9$  % of baseline ( $p < 0.001$ ,  $n = 4-5$ ), and urine output was  $5.3 \pm 0.9$  mL/24h ( $p = 0.008$ ,  $n = 4-5$ ). In wild-type mice cilastatin preserved GFR ( $526 \pm 125$  vs.  $67 \pm 31$   $\mu$ L/min/100g,  $p = 0.03$ ,  $n = 4/gr$ ), urine output ( $1.8 \pm 0.3$  vs.  $0.4 \pm 0.1$ ,  $p = 0.01$ ,  $n = 4/gr$ ), and histology. KIM-1 and cleaved caspase-3 were reduced by megalin interference and cilastatin treatment. Pharmacologic or genetic interference with myoglobin increased

myoglobin clearance (5-16x) over controls and redistributed intrarenal myoglobin toward the cortex.

### Conclusion

Renal megalin deletion ameliorates rhAKI by increasing clearance of myoglobin. The FDA-approved megalin inhibitor cilastatin ameliorates rhAKI similarly. There is potential for rapid translation, enabling change in disaster and trauma medicine. Additional translational study is imperative.



# Research Week 2020

## Smart Predict: AAC app that integrates partner knowledge into word prediction

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### Keywords

AAC, Assistive Technology, Communication Disorders

### Abstract

#### BACKGROUND

Smart Predict is a mobile tablet-based dual-app system for augmentative and alternative communication (AAC) which permits vocabulary supplementation by partners to support communication by people with neurodevelopmental or neurodegenerative disease who use speech generating devices for expressive language. Partners augment word prediction capabilities while persons with complex communication needs control message construction.

#### PURPOSE

To evaluate Smart Predict to determine whether (1) partner engagement is increased during conversation; (2) message production is faster when the novel AAC app is used.

#### METHOD

Six literate adults who use AAC and three communication partners without disabilities participated in two single case alternating treatments research designs. Experiment I examined partner engagement; Experiment II examined efficiency. Each experiment included five data collection sessions with counterbalanced conditions. In the Smart Predict only condition, AAC users typed with the Smart Predict app alone. In the Smart Predict + partner app condition, partners used a separate tablet to add contextually relevant vocabulary to the user's app word prediction line.

#### RESULTS

##### Experiment I

Partner disengagement, measured by off-task behaviors observed, was greater in the Smart Predict only condition. Data visualization indicates no overlap in data between conditions; the supplemental vocabulary condition showing consistently increased partner engagement.

## Experiment II

AAC users demonstrated greater message efficiency, measured by characters/minute, in the Smart Predict + partner app condition. AAC user effort, measured by selections/character, was reduced in the Smart Predict + partner app condition in most sessions. In one instance, a unique phrase was not predictable, suggesting that vocabulary supplementation is not helpful if partners don't share familiar lexica.

## CONCLUSION

Under controlled conditions, Smart Predict + partner app increases partner engagement during conversations, increases message efficiency, and reduces effort. The contribution of supplemental vocabulary by knowledgeable partners enhances message generation. The concept of Smart Predict should be transferred to AAC technology.



# Research Week 2020

## Study Protocol for Using the International Prostate Symptom Score to Determine Patient Risk of Developing Post-Operative Urinary Complications After Elective Spine Surgery

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### Keywords

international prostate symptom score, post-operative urinary complications, lower urinary tract symptoms, spine surgery

### Abstract

#### Background

Little is known about how to predict a patient's risk of developing post-operative urinary complications (POUC) after elective spine surgery. The International Prostate Symptom Score (IPSS) is a validated survey that assesses lower urinary tract symptom (LUTS) severity, which could be used as a predictive tool for POUC.

#### Purpose

To determine whether the incidence of POUC in patients undergoing elective spine surgery increases with increasing severity of pre-operative LUTS as measured by the IPSS.

#### Study Design

Prospective cohort study.

#### Patient Sample

Adult patients who have a pre-operative visit for elective spine surgery at OHSU from July 2017 to June 2020 and a completed IPSS.

#### Methods

Electronic medical records will be reviewed to collect patient demographics, variables associated with POUC, and pre-operative IPSS. Patients will be divided into graded groups of LUTS severity according to IPSS using patients with no LUTS during the same time period as a control group. This data will be compared to the primary outcome measure of



POUC, which will be defined as any of the following events occurring during the time after surgery to discharge: the need for insertion of a Foley or straight catheter, an inability to void more than 8 hours after intra-operative Foley removal, an inability to void with a bladder scan of over 400 mL, presence of a urinary tract infection, and pharmacological treatment for urinary bother. Relative risk and chi-square calculations will be used to analyze group comparisons.

### Implications

If a predictive relationship between pre-operative moderate/severe LUTS and POUC occurrence is found, then this would suggest the utility of obtaining the IPSS before elective spine surgery. This would help identify patients who are at higher risk of developing such complications allowing pre-operative measures to be taken to determine if POUC occurrence can be reduced.



# Research Week 2020

## Fluid Creep in the PICU: Characterizing Fluid Administration Beyond Maintenance Fluids

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### Keywords

Fluid Management, Critical Care, Pediatrics, Clinical Practice, Fluid Overload

### Abstract

Critically ill children receive fluids for multiple reasons including resuscitation, nutrition, and medications. However, while it is well established that fluid overload is associated with negative outcomes in critical care, it is challenging for clinicians to consider all fluid sources and adjust accordingly. "Fluid creep" refers to insidious IV fluid intake (medications, flushes, etc.) in excess of standard predicted maintenance fluid requirements (MFR). This phenomenon has been previously described in burn patients and adults, but is less clear among pediatric patients. We aimed to quantify fluids administered to patients admitted to a quaternary Pediatric Intensive Care Unit (PICU) in comparison to predicted MFR in order to quantify the association between fluid creep (FC) and fluid overload.

Analysis included EHR-derived data from all PICU patients admitted between 2010-2019 and limited to the first 120 hours of PICU stay. Fluid volumes were indexed to patient weight and categorized by type. IV fluids were deemed "resuscitation" if administered at  $\geq 10\text{mL/kg/hr}$ . The Holliday-Segar method was used to estimate MFR. FC was defined as non-resuscitation IV fluid in excess of MFR. Fluid overload (FO) was defined as  $\geq 100\text{mL/kg}(10\%)$  in cumulative fluid balance. A logistic regression model was used to test for association between FC and FO.

The study included 14176 admissions by 10119 distinct patients (Table 1). Average daily fluid intake was  $97.9\text{mL/Kg}(SD=75)$  of which  $6.4\text{mL/Kg}(6.5\%)$  was resuscitation and  $36.0\text{mL/Kg}(37\%)$  was enteral. Average FC on Day 1 was  $23.4\text{mL/Kg}(SD=31)$ , and FC represented 21% of all fluid intake through Day 5. FO was present at some point in 16% of admissions. Day 1 FC (per mL/Kg) was associated with increased odds of FO (OR 0.0237, 95%CI 0.022-0.025,  $p<0.001$ ).

FC is a significant component of overall fluid intake and increased FC early in the PICU stay is associated with FO. Further analysis will evaluate potential confounding variables and clinical applications.



# Research Week 2020

## Vitalizing the Mission of Bridges Collaborative Care Clinic Through Employment of Hoshin Kanri and Quality Functional Deployment

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### Keywords

Strategic Planning, Student-Run Health Clinic, Underserved, Quality Improvement, Primary Care

### Abstract

The Bridges Collaborative Care Clinic (BCCC) is Oregon's first and only interdisciplinary, student-run clinic that provides free health and social services to underserved populations. Since its inception in 2016, the clinic has utilized a dynamic model of leadership with specific teams and responsibilities. This model worked effectively in early stages, however escalation of functional complexity led to lapses in communication, loss of information between teams, and an overall decline in efficiency and impact. Student volunteers and the BCCC Board of Directors recognized the need for change, and formed a strategic planning committee to guide improvement. The goal of the committee was to develop a framework for clinic expansion and specific strategies for accomplishing its mission. Community advisors with extensive experience in strategic planning, policy deployment, and business development served as advisors for the team. Team members performed community interviews and invited a diverse group of stakeholders to participate in four collaborative strategic planning meetings. The outcomes of the strategic planning effort include a prioritized list of patient (customer) needs, solutions to process and communication issues, and a timeline to guide the management of expansion projects with tasks and task managers. Solutions consisted of projects such as building referral networks, providing transportation to participants, creating a mental health program, and streamlining prescription delivery. Other solutions centered around internal development such as improving communication pathways and reorganization of the student leadership. The limited resources at the disposal of student-run health clinics create a natural obstacle for expansion, self-improvement, and program deployment. This project outlines the process, outcomes, and limitations faced by BCCC throughout its strategic planning process, which may be replicated or remodeled by other student-run clinics seeking improvement. It also serves to update the public on the current trajectory of Bridges Collaborative Care Clinic.



# Research Week 2020

## Report from the OHSU research trenches: A mixed-methods approach to understand how recruitment methods, culture and collaboration affects research study accrual

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### Keywords

recruitment; research studies; evaluation

### Abstract

This is a mixed-methods study aimed to understand the perceived effectiveness of research recruitment methods at OHSU, to establish best practices and measure outcomes longitudinally.

Clinical trial accrual data, a general survey of the research community and targeted interviews with research teams at OHSU were used to assess the study aims. Accrual data was obtained from the clinical trial management system, eCRIS, was analyzed using parameters from the NIH CTSA "Accrual Metric". The metric was calculated for clinical trials enrolling at OHSU during 2017. The survey, completed by 144 OHSU investigators, and research staff, asked about utilization and value of specific recruitment tools and methods. Interviews were conducted with 24 OHSU researcher staff members identified by the survey and over or under-enrolled accrual data, and inquired about recruitment facilitators and barriers.

According to survey respondents, the most frequently mentioned facilitator of recruitment was direct patient contact, either in the healthcare setting (58.4%) or through patient outreach (32%). Respondents also identified a lack of resources as a key barrier (21%) and a stated need (27%). Interview data expanded on these findings, as 23% of interviewees indicated a collaborative culture was key to recruitment success. A collaborative culture was defined by interviewees as including research integration into clinic, involved investigators, and cross-department referrals. Additionally, 20% of interviewees identified resources (i.e. funding, staff, time) as their greatest need. Notably, 13% of studies with an accrual ratio of "0" ("0" = no enrollment) had frequent staff turnover, thereby further highlighting the impact staffing levels has on recruitment.

This approach allowed for a uniquely targeted analysis of accrual facilitators and barriers. Additional investigation will focus on the impact of funding sources and departmental

factors on research recruitment at OHSU. Furthermore, best practices will be developed, as accrual is an essential element to research study success.



# Research Week 2020

## “Sobriety equals getting rid of Hepatitis C”- a qualitative study exploring the relationship between Substance Use Disorder and Hepatitis C among hospitalized patients

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### Keywords

Hepatitis C, Substance Use Disorder, Hospitalization,

### Abstract

#### Aim

Persons who use drugs (PWUD) commonly experience complex illnesses, psychosocial stressors, housing insecurity, and stigma, which may play a key role in their struggles with addiction. In a study of hospitalized PWUD with hepatitis C virus infection (HCV), participants described treating HCV as "part of recovery." These findings led us to explore patient perceptions of the relationship between substance use disorder (SUD) and readiness to engage with HCV curative treatment.

#### Methods

We audio recorded in-depth semi-structured individual interviews of 27 hospitalized adults with SUD and chronic HCV seen by an addiction consult service at an urban academic medical center between June and November 2019. We transcribed and dual coded interviews deductively and inductively at the semantic level then analyzed for themes using iterative categorization.

#### Results

Many patients described feeling that they should get their SUD treatment prior to HCV treatment in order to avoid possible reinfection. Patients newly engaged in SUD treatment during hospitalization felt that starting HCV treatment would serve as a "step towards recovery". They felt it would reinforce their motivation to continue SUD treatment. Among patients in recovery before hospitalization, many felt that HCV was a "symbol of using" in their "old life" and that HCV cure would allow them to "move forward." For them, having HCV directly challenged their identity as someone in recovery. Among patients with limited motivation to stop using, most were not interested in discussing HCV treatment during hospitalization.

## Conclusion

Counter to current national HCV eradication guideline recommendations, most hospitalized adults with SUD and HCV felt that addictions treatment should precede HCV treatment. Patients believed HCV cure could facilitate sobriety by "mentally putting drugs in the past" and was a future oriented action towards "better health." Discussing HCV treatment during hospitalization may be an opportunity to support people in their recovery journey.



# Research Week 2020

## The Importance of “Being There”: A Qualitative Study of What Veterans with Depression Want in Social Support

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### Keywords

social support, military veterans, suicide prevention, major depressive disorder

### Abstract

#### Background

Social connectedness exerts strong influences on health, including major depression and suicide. A major component of social connectedness is having individual relationships with close supports, romantic partners and other trusted members of one's social network.

#### Objective

The objective of this study was to understand how individuals' relationships with close supports might be leveraged to improve outcomes for primary care patients with depression and at risk for suicide.

#### Design

In this qualitative study, a semi-structured interview guide was used to probe patient experiences, views, and preferences related to social support.

#### Participants

We conducted interviews with 30 primary care patients at a Veterans Health Administration (VA) medical center who had symptoms of major depression and a close support.

#### Approach

Thematic analysis of qualitative interview data examined close supports' impact on patients. We iteratively developed a codebook, used output from codes to sort data into themes, and selected quotations that exemplified themes for inclusion in this manuscript.

#### Key Results



"Being there" as an important quality of close supports emerged as a key concept. "Being there" was defined in three ways: physical proximity, frequent or responsive contact, or perceived availability. Close supports who were effective at "being there" possessed skills in intuitively sensing the patient's emotional state and communicating indirectly about depression. Three major barriers to involving close supports in depression care were: concerns of overburdening the close support, a perception that awareness of the patient's depression would make the close support unnecessarily worried, and a desire and preference among patients to handle depression on their own.

## Conclusions

"Being there" represents a novel, patient-generated way to conceptualize and talk about social support. Suicide prevention initiatives such as population-level communication campaigns might be improved by incorporating language used by patients and addressing attitudinal barriers to allowing help and involvement close supports.



# Research Week 2020

## The association between cortisol and aggression in children with ADHD and emotional dysregulation: A proposal to analyze cross-sectional data from the MADDY study

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### Keywords

ADHD, CAM, integrative medicine, emotional dysregulation, aggression

### Abstract

#### Introduction

Attention-deficit hyperactivity disorder (ADHD) is a pervasive neurodevelopmental disorder characterized by symptoms of inattention and hyperactivity. In up to 50% of cases, children with ADHD have additional symptoms of emotional dysregulation including anger, irritability, or aggression. Aggression confers considerable additional risk for adverse health outcomes like illicit drug use and suicide. Aggression is associated with changes in cortisol, a steroid hormone involved in the stress response. The literature on the direction of the association is inconsistent and must be better characterized. Dysregulated cortisol may represent a treatment target in children with ADHD and symptoms of aggression.

**Objective.** We will assess the association between urinary cortisol and the severity of aggression in children who have ADHD plus symptoms of emotional dysregulation.

#### Methods

Data for this analysis are derived from the baseline assessment of a multi-site, randomized, controlled trial: The Micronutrients for ADHD in Youth (MADDY) Study. The study enrolled children aged 6-12 with a diagnosis of ADHD and symptoms of emotional dysregulation such as anger, irritability, or aggression. Using a cross-sectional study design, we will measure the association between urine cortisol levels and the severity and impairment of aggressive symptoms at baseline. Aggressive symptoms were measured using three subscales of the Child and Adolescent Symptom Inventory, Version-5 (CASI-5): Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), and peer conflict (PC) subscales. To test our hypotheses, we will use two methods: multivariable linear regression to model continuous outcomes (symptom severity) and logistic regression to

model binary outcomes (impaired; yes/no). Models will be adjusted for potential confounding variables.

## Results

The study is on-going.

## Conclusion

Our results will serve to better characterize the relationship between cortisol and aggressive behavior in children with ADHD. Further characterizing the pathophysiology of aggression in this population of children may refine treatment strategies and improve health outcomes across the lifespan.



# Research Week 2020

## Practice Gap in Atrial Fibrillation Oral Anticoagulation Prescribing at Emergency Department Home Discharge

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### Keywords

atrial fibrillation, emergency department, cardiology consult, anticoagulation

### Abstract

Current cardiology guidelines recommend oral anticoagulation (OAC) to reduce stroke risk in selected patients with atrial fibrillation (AF), but no formal AF OAC recommendations exist to guide emergency medicine (EM) clinicians in the acute care setting. We sought to characterize emergency department (ED) OAC prescribing practices after an ED AF diagnosis. This retrospective study included index visits for OAC-naïve patients  $\geq 18$  years old who were discharged home from the ED at an urban, academic tertiary hospital with a primary diagnosis of AF from 2012-2014. Five hypothesis-blinded chart reviewers abstracted data from patient problem lists and medical history in the electronic health record to assess stroke (CHA<sub>2</sub>DS<sub>2</sub>-VASc) and bleeding risk (HAS-BLED). The primary outcome was the provision of an OAC prescription at discharge in OAC-naïve patients with high stroke risk. Descriptive statistics and multivariable logistic regression assessed associations between OAC prescription and patient characteristics. We included 138 patient visits in our analysis, of whom 39.9% (n=55) were low stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc=0 in males and 1 in females), 15.9% (n=22) were intermediate-risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc=1 in males), and 44.2% (n=61) were high-risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc $\geq 2$ ). Of patients with high stroke risk and low-intermediate bleeding risk (n=57), 80.7% were not prescribed an OAC at discharge. Cardiology consultation and female sex, but not stroke risk (CHA<sub>2</sub>DS<sub>2</sub>-VASc score), were predictors of an ED provider prescribing an OAC to an OAC-naïve AF patient at ED discharge. The majority of OAC-eligible patients were discharged home without an OAC prescription. In OAC-naïve patients discharged home from the ED, cardiology consultation and sex were predictive of OAC prescription. Our findings suggest that access to expert opinion improves provider comfort with OAC prescribing and highlight the need for improved guidelines specific to ED-management of AF.



# Research Week 2020

## Outcomes for Geriatric Patients Evaluated in a Same-Day Multidisciplinary Central Nervous System Clinic for Radiation Oncology and Neurosurgery in a Community Hospital Setting

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### Keywords

multidisciplinary clinic, geriatric oncology, central nervous system disease, neurosurgery, radiation oncology

### Abstract

#### Background

The geriatric cancer population is rapidly increasing in the United States. Management of geriatric patients with central nervous system (CNS) disease requires a patient-centric, multidisciplinary approach together with meticulous assessment of their outcomes, as clinical studies guiding treatment recommendations are lacking in this patient population. We have previously reported the outcomes of our multidisciplinary community hospital-based CNS clinic, RADIANS, where both radiation oncology and neurosurgery specialists simultaneously evaluate patients in a same-day, single-setting clinic. We have sought to analyze the outcomes of the geriatric patient population of our RADIANS clinic.

#### Methods

We identified patients 65 years and older in our IRB-approved RADIANS Prospective Patient Registry for CNS Disease. Descriptive statistics were used to report patient characteristics, diagnoses, treatments and outcomes, and patient satisfaction scores.

#### Results

Between August 2016 and February 2020, 56 patients 65 years and older (mean age 74.6, range: 65-94; 32 women and 24 men) were evaluated in the RADIANS clinic. Mean distanced traveled by patients to clinic was 43.4 miles (med=8.3; range=0.6-341). Patient-reported Satisfaction Score was 4.81 (0-5 Scale, 5-very satisfied). The most common referral source was medical oncology. Forty-two patients had malignant CNS disease (brain mets-18; spine mets-12; both-4; primary brain-6; primary spine-2), 14 had benign CNS disease. Post-evaluation treatment: radiation therapy (RT) only (n=20), neurosurgery (NS) only (n=6), both RT and NS (n=14), and no RT/NS intervention (n=16). Fractionated

stereotactic radiosurgery was most common RT delivered; craniotomy with tumor resection was most common NS performed. Treatment outcomes: local tumor control=39/40 (97.5%); radiation necrosis/radiation-induced myelitis=0/34 (0.0%).

### Conclusions

This is the first report of outcomes in geriatric patients with CNS malignancies treated in a community hospital-based multidisciplinary clinic. We show excellent outcomes comparable to younger patients with CNS malignancies, as well as patient satisfaction and ability to travel great distances to receive multidisciplinary care.



# Research Week 2020

## Burnout Is Real!: Implementing a Wellness Group Model for Research Staff

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### Keywords

Burnout, wellness, health, research

### Abstract

#### Purpose

Despite many scholarly strides made towards understanding suicidal ideation and suicidal self-directed violence, little research has been done on how this work affects research staff interacting or interfacing with at-risk participants. Burnout, compassion fatigue, and vicarious trauma affect the well-being of healthcare and research staff across mental health and healthcare fields. While the hardships of studying difficult topics go unseen, and untreated, research staff are at risk of increased mental health distress and turnover. In this presentation, we will review a model intended to increase wellness and coping among study staff working in difficult research topics such as suicide, high mortality and chronic illness, and death.

#### Objectives

1) Introduce relevant literature regarding work-related stress in suicide-prevention; 2) Describe unique and shared challenges across different research and healthcare roles; 3) Present several strategies currently being implemented to inform tailored stress management programming.

#### Description

Investigators at the VAPORHCS developed an intervention model, a staff wellness group, to bolster coping and support among research staff who are at risk of burnout, vicarious trauma, and compassion fatigue. The model aims to 1) incorporate safety procedures into study protocols, 2) brief all staff on safety procedures, 3) conduct staff wellness groups, and 4) debrief with facilitators of the wellness groups. For this presentation, we will largely focus on conducting a staff wellness group and report our own experiences participating in a group. Jason Chen, PhD will present on the development and application of a model for wellness among research staff. Kyla Tompkins, MA will review applied experience of implementing burnout prevention strategies as a non-clinician/research staff person.



# Research Week 2020

## Creating a sustainable immunization program for the underserved.

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### Keywords

Underserved, Vaccine

### Abstract

#### Background

Bridges Collaborative Care Clinic (BCCC) is Oregon's first multi-institutional and multi-disciplinary student-run free clinic. BCCC's mission is to engage vulnerable populations by providing low-barrier, participant-centered care and services in the Portland metro area through an interprofessional, student-led clinic. As an interprofessional collaboration, BCCC engages students from public health, medicine, nursing, pharmacy, dentistry, physician assistant, and social work programs.

#### Methods

An immunization program created collaboratively between medical, dental, nursing, and pharmacy students was designed to integrate interprofessional students in community-based infectious disease prevention. This project follows the Oregon State House Bill 2220 that adds the prescription and administration of vaccines into a dentist's scope of practice.

Community partners included Oregon Health Authority (OHA) and Transition Projects, Inc. (TPI). TPI provides housing and social services to individuals experiencing homelessness in the Portland metro area.

#### Results

Number of students from each program

Number of vaccines provided

#### Discussion

This illustrates how the different health professions educational programs contribute to an interprofessional clinic and public health interventions



Importance of early educational experiences in response to changes in healthcare professions' scope of practice.



# Research Week 2020

## The Impact of Deceased Donor Management on Donor Heart Utilization and Recipient Graft Survival

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### Keywords

organ procurement, heart transplantation, critical care, brain death, thyroid hormone

### Abstract

#### Introduction

Current risk-adjusted models used to predict donor heart utilization and cardiac graft survival from organ donors after brain death (DBDs) do not include donor critical care data. We sought to identify novel independent predictors of donor heart utilization and cardiac graft survival to better understand the relationship between donor management and transplant outcomes.

#### Methods

This was a prospective observational study of DBDs managed from 2008 to 2013 by 10 organ procurement organizations. Demographic data, critical care parameters, and treatments were recorded at three standardized time points during donor management. The primary outcome measures were donor heart utilization and cardiac graft survival.

#### Results

From 3,433 DBDs, 1,134 (33%) hearts were transplanted and 969 (85%) cardiac grafts survived after  $684 \pm 392$  days of follow-up. After multivariable analysis, independent positive predictors of donor heart utilization included standard criteria donor status (OR = 3.93), male sex (OR = 1.68), ejection fraction > 50% (OR = 1.64), and  $\text{PaO}_2:\text{FiO}_2 > 300$  (OR = 1.31). Independent negative predictors of donor heart utilization included donor age (OR = 0.94), body mass index > 30 kg/m<sup>2</sup> (OR = 0.78), serum creatinine (OR = 0.83), and use of thyroid hormone (OR = 0.78). For cardiac graft survival, after controlling for known recipient risk factors, thyroid hormone dose was the only independent predictor (OR = 1.04 per  $\mu\text{g}/\text{hr}$ ).

#### Conclusion

Modifiable critical care parameters and treatments predict donor heart utilization and cardiac graft survival. Thyroid hormone was identified as a negative predictor of donor heart utilization yet a positive predictor of cardiac graft survival, warranting a randomized clinical trial of thyroid hormone in DBDs to determine the impact on both donor heart utilization and cardiac graft survival.



# Research Week 2020

## Is worker safety, patient safety?

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### Keywords

Social Network Analysis, Safety Climate, Worker Safety, Patient Safety

### Abstract

#### Introduction

Patient and worker safety relies on leadership, safety culture and teamwork to be effective, yet are often administratively "siloe" leading to interference that often sacrifices one area at the expense of the other. To demonstrate that from workers' viewpoint, worker and patient safety are intertwined, our study mapped advice networks of patient safety and worker safety using Social Network Analysis (SNA) among healthcare workers.

#### Methods

Cross-sectional survey administered through email among Registered Nurses (RNs) and Certified Nursing Assistants (CNAs) (n=54, 75.3% response rate) of a critical access hospital in rural Oregon. Participants nominated from a roster as many co-workers they would ask advice about 1) safe patient handling and 2) general patient safety. Networks were mapped through SNA and analyzed through quadratic assignment procedure (QAP).

#### Results

Each participant nominated an average of 11 (SD  $\pm$ 13.1) peers for safe patient handling advice and 9 (SD  $\pm$ 7.3) for patient safety. The correlation between co-worker nominations for worker and patient safety was .51 ( $p < 0.001$ ). Half as many peers nominated for safe patient handling advice were also nominated for patient safety.

#### Discussion

Significant overlap between patient and worker safety networks suggests that from workers' viewpoint, their safety is interconnected with patient safety. Further, safety networks are not domain specific, building on similar safety climate findings across an organization and by unit. Limitations of sample size make determining causality not feasible.

#### Conclusion

Organizations should consider how to integrate patient and worker safety since they require similar resources and often intersect.



# Research Week 2020

## Psychiatric and medical profiles of autistic adults in the SPARK cohort

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### Keywords

autism; psychiatric disorder; adult; medical disorder; cohort

### Abstract

This study examined lifetime medical and psychiatric morbidity reported by caregivers of 2,917 autistic adults participating in the US research cohort SPARK. Participants were 78.4% male, 47.3% had intellectual disability, and 32.1% had persistent language impairments. Childhood language disorders (59.7%), speech/articulation problems (32.8%), sleep (39.4%) and eating problems (29.4%), motor delays (22.8%) and history of seizure (15.5%) were the most frequently reported clinical features. Over two thirds (67.2%) had been diagnosed with at least one psychiatric disorder (anxiety disorders: 41.1%; ADHD: 38.7%). Compared to verbally fluent participants, those with language impairments had lower frequencies of almost all psychiatric disorders. Female sex and older age were associated with higher medical and psychiatric morbidity.



# Research Week 2020

## Predicting Adolescent Binge Drinking from Brain Networks at Rest

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### Keywords

adolescence, alcohol, resting-state fMRI, graph theory

### Abstract

Patterns of alcohol consumption during adolescence differ from those observed during adulthood; namely, adolescents are more likely to consume alcohol less frequently, but in larger quantities per occasion, when compared to adults. Importantly, this binge-pattern of drinking carries substantial risks for adverse outcomes, including involvement in motor vehicle accidents, alcohol poisoning, and sexual victimization. Although prior work has examined neural correlates of emergent alcohol use among adolescent populations, the present study takes a novel, data-driven approach by incorporating graph theory metrics of resting-state functional connectivity with predictive modeling via machine learning. To identify risk factors for future binge drinking, a subset of participants were selected from an ongoing prospective longitudinal study (National Consortium on Alcohol and Neurodevelopment in Adolescence). All participants were alcohol-naïve at baseline ( $n=150$ ), but 51% ( $n=77$ ) emerged into binge drinking over the course of four years of follow-up assessments (transitioners), while the rest remained abstinent from alcohol use (controls). Resting-state fMRI data were pre-processed and parcellated using a functional atlas to construct weighted, undirected adjacency matrices, then thresholded to retain the top 15% of edge weights. Graph analyses were performed using the Brain Connectivity Toolbox implemented in MATLAB (Rubinov & Sporns, 2010). Network parameters of interest were entered into a supervised random forest (RF) algorithm to distinguish the two groups of participants, as well as to identify the most important input features for classification. The RF model had an overall accuracy of 60%, with 70% sensitivity and 50% specificity. Notably, several characteristics of the frontoparietal network were important for this classification task, including average clustering coefficient, characteristic path length, and betweenness centrality. These metrics help to establish functional "hubs" in the network, and suggest that differential functioning of brain regions relevant for executive control may underlie a predisposition for future binge drinking.



# Research Week 2020

## Characterizing Language Atypicalities in Autism Spectrum Disorder

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### Keywords

ADHD, Autism, Language Assessment, Pragmatics, Social Skills

### Abstract

#### Background

Communication development is measured in terms of linguistic content and social interaction. Group differences in these areas may support diagnostic differentiation between neurodevelopmental disorders. We compared structural and pragmatic aspects of language in Autism Spectrum Disorder (ASD), typical development (TD) and Attention Deficit Hyperactivity Disorder (ADHD).

#### Methods

174 children were recruited for an fMRI study: 101 with ASD (mean age:11.3 years; 85 males), 28 with TD (mean age:11.6 years; 12 males), and 45 with ADHD (mean age 11.5 years; 31 males). Cognitive scores were significantly lower for the ASD group compared to TD and ADHD (98.8 vs 113.4 and 111.6,  $p < .001$ ). Parents completed the Children's Communication Checklist-2nd Edition (CCC-2) resulting in total, structural, and pragmatic scores. ANOVA and ANCOVA were used to compare the clinical groups.

#### Results

Nine ANOVA models revealed significant ( $p < .001$ ) between-group differences. Games-Howell post-hoc tests revealed that children with ASD scored significantly lower on all CCC-2 scores than children with ADHD and TD. Effects sizes were larger for pragmatic ( $\eta^2: .56-.65$ ) than structural ( $\eta^2: .20-.47$ ) scores. With the exception of two structural scales, the ADHD group scored significantly lower than TD and their scores fell between the ASD and TD groups. Covarying FSIQ reduced the size of CCC-2 differences across groups only minimally. When structural scaled scores were covaried alongside FSIQ, pragmatic scaled scores remained strongly different across diagnostic groups, with a very large effect size for the composite score ( $\eta^2: .49$ ).

#### Conclusion



Results suggest that differences in pragmatic language are robust predictors of ADHD and ASD diagnoses even after accounting for cognition and structural language differences. Easy to administer parent questionnaires may support clinicians in considering an ASD diagnosis when ADHD is a contributing factor. Future work will further characterize language in ASD and apply natural language processing methods to improve this type of measurement.



# Research Week 2020

## Context and quality: A mixed-methods study of physical therapy managers' use of information systems to oversee clinical quality

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### Keywords

Technology acceptance, Quality, Physical Therapy, Organizational Behavior

### Abstract

Complex organizational problems require systematic approaches to understand root causes and effectively intervene. Quantitative approaches allow researchers to understand how factors impact organizational operations. However, qualitative approaches allow researchers to understand why certain factors exist and how those factors affect employees and other stakeholders. When healthcare stakeholders interact with information systems, a complex sociotechnical ecosystem is created. Thus, a mixed-methods approach is often necessary to understand the various stakeholders' perspectives and the poorly-understood interactions between various workflows and systems.

This study used physical therapy managers' adoption of clinical information systems to oversee clinical quality as a use case for a proposed mixed-methods research design to explore sociotechnical systems. Utilizing team-based Rapid Qualitative Inquiry, researchers explored the various aspects of the role of manager as an overseer of clinical quality and their use of information systems. From that phase of the research, the team identified several themes. Three of these themes were drawn forward to the next phase of the study.

In the quantitative phase of the research, questions were created to represent the factors identified in the qualitative phase. These questions were added to a previously developed survey representing the Unified Theory of Acceptance and Use of Technology (UTAUT). Utilizing structural equation modeling, the team preliminarily established psychometrics for survey questions. Next, they explored causal relationships between the various factors in an attempt to explain managers' intention to use their respective information systems to manage clinical quality.

Several qualitative themes coalesced into an over-arching framework describing the competitors for managers; attention and a framework describing the influencers of managers' use of technology. The final UTAUT model explained 64.9% of the variance in managers' intention to use their information systems. This study presents an efficient model for studying complex sociotechnical ecosystems.



# Research Week 2020

## Implementation and Evaluation of Student-Driven Addiction Medicine Curricula

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### Keywords

education, addiction, substance use disorders, undergraduate medical education

### Abstract

In 2017, 21 million individuals in the United States suffered from a substance use disorder (SUD) involving alcohol or drugs. This is a public health crisis and the American health professional workforce is unprepared to care for patients with SUDs. This problem is due, in part, to the lack of addiction medicine education that healthcare providers receive in school. On average, medical schools offer 12 hours of exposure to this material over four years. We intend to describe best practices for the development and implementation of student-initiated course material in both elective and required curricula. Previous studies have shown that brief educational interventions that teach students crucial addiction medicine concepts can have a lasting impact on the addiction practice of future physicians.

To address the lack of addiction medicine education in medical school, students at Oregon Health & Science University (OHSU), University of California - San Francisco (UCSF), and University of Washington (UW) created and implemented addiction medicine curricula. We hypothesize that the implementation of student-led addiction content for undergraduate medical learners will be both feasible and acceptable. This will be done through enrollment and attendance and assessing changes in student self-assessment of SUD knowledge and attitudes. This will hopefully elucidate the role of student-led curricular development in addressing public health crises.



# Research Week 2020

## Large Neutral Amino Acid Supplementation Improves Clinical Efficacy of Usual Care in Adult PKU

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### Keywords

Phenylketonuria, Inherited Metabolic Diseases, Medical Nutrition Therapy, Medical Foods, Orphan Products

### Abstract

#### Introduction

PKU requires lifelong management, but the childhood PKU diet does not accommodate for post-adolescent patient variations, including: (1) the diet's effect on blood phenylalanine (Phe) concentrations, and (2) the therapeutic benefits of prescribed blood Phe targets. Most adult patients discontinue the inflexible diet, and are exposed to PKU's adverse effects. Research supports large neutral amino acids (LNAAs) as potential alternative strategy; we propose an additive LNAA strategy.

#### Objective

We aim to evaluate the clinical efficacy of a combined treatment strategy: usual care (the PKU diet) with LNAA supplementation.

#### Methods

An N-of-1 RCT was used to compare control and combined treatments: usual care (A) and usual care +LNAAs (B). A priori design randomly alternated 3 pairs of ~8-week treatment periods (ABBAAB). The adult subject historically experienced persistent symptoms, despite achieving prescribed blood Phe control (above U.S. target but within European guidelines). A run-in period established baseline measures and LNAA dose responsiveness (0.22g/kg PheBLOC™). Neuropsychological and biological treatment responses were assessed using the PKU-QoL Questionnaire, blood Phe, and Phe:Tyr ratio. Treatment comparisons utilized mean values across repeating periods.

#### Results

PKU-QoL scores supported clinical superiority for usual care +LNAAs, as (1) symptom frequencies fell to zero and (2) negative dietary impact scores decreased. Blood analysis showed marked Phe:Tyr decrease (A=14.1; B=3.1), but no significant change in Phe levels

(B= -14.9%). Due to symptom resurgence following the withdrawal of usual care +LNAA, we made an ethical decision to end the experiment after two cycles (ABBA).

## Conclusions

In this single-subject investigation, usual care +LNAA corresponded with improved symptoms, without blood Phe changes. Moreover, the PKU biomarker Phe:Tyr significantly responded to the combined treatment and better correlated with symptom changes. These findings suggest clinical efficacy, and repeated investigation, with additional subjects, is needed to establish the potential benefits of additive LNAA strategies for adult PKU management.



# Research Week 2020

## The Effect of an Educational Seminar on Medical Director and First Responder Attitudes Surrounding the Practice of Hands-on Defibrillation

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### Keywords

hands-on defibrillation, CPR, safety, attitudes

### Abstract

#### Introduction

Hands-on defibrillation (HOD) is the practice of providing uninterrupted chest compression during the delivery of defibrillator shocks. The practice of HOD may be safer than traditionally thought and improve outcomes by minimizing interruptions to compressions, but adopting such a change in long-established protocols would require healthcare provider buy in. This research project investigates the attitudes of first responders and medical directors on the matter.

#### Methods

This was a survey-based study conducted during the 2019 Oregon Statewide EMS Conference and 2019 National Association of EMS Physician Medical Directors Oregon Forum. Participants were asked to complete a paper survey regarding HOD before and after attending an educational seminar. The educational seminar presented a summary of a comprehensive literature review on HOD. Survey data was analyzed by a statistician using SPSS to perform Wilcoxon signed ranks tests and Mann-Whitney U tests.

#### Results

A total of 43 participants responded to the survey including MD/DO (16), Firefighter-Paramedic/EMT (12), and Paramedic/EMT (15). Within this population there were EMS Medical Directors (17) and Fire Chiefs (6). Survey data revealed statistically significant changes in participant attitudes regarding the safety of HOD ( $p < 0.001$ ) and willingness to personally perform HOD ( $p < 0.001$ ). Regarding bias, 81% of participants thought the information session provided a balanced perspective on the risks and benefits of HOD, 17% were neutral, and 2% disagreed. After the educational seminar, 94% of medical director respondents thought that it was safe to perform HOD with insulating gloves. Among participants, 76% reported that the educational seminar influenced their attitudes.

## Conclusions

Providing first responders and medical directors with evidence-based data on HOD influenced their attitudes and led to increased willingness to personally perform HOD.



# Research Week 2020

## Equivalency of Automated vs Conventional Language Assessment in Children with and without Neurodevelopmental disorders

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### Keywords

Autism, ADHD, Language Disorder in children

### Abstract

#### Background

Language assessment for children has predominately utilized face-to-face testing methods (i.e., conventional administration); however, automated administration could increase clinician efficiency, access to services, standardization of administration, and perhaps child interest (Laborda, 2007; Noland, 2017). Though automated assessment may have advantages, this new method of assessment has limited evidence for score equivalence (Carson, Gillon & Boustead, 2011). In this project, we evaluate the equivalence of scores across conditions for four expressive subtests of a modified common language assessment: Expressive Vocabulary (EV), Recalling Sentences (RS), Word Structure (WS), and Formulated Sentences (FS).

#### Methods

77 children with Autism Spectrum Disorder (ASD), Attention-Deficit Hyperactivity Disorder (ADHD) and Developmental Language Disorder (DLD), and Typical Development represent the subset of participants who received both automatic and conventional administrations in a larger study designed to develop automated test scoring using speech recognition. Participants were randomly assigned to balanced conditions (automatic or conventional), and tests were administered four-six weeks apart.

#### Results

Data entry is ongoing; preliminary analyses are from 41 participants (average age 7.1 years (sd=1.1); 63% male, 75% Caucasian) with ASD (10), ADHD (10), DLD (5) and TD (16). Pearson's product-moment correlations were run to assess relationships between raw scores on four conventionally or automatically administered expressive language tasks. Preliminary analyses showed the relationship to be linear with both variables on each task normally distributed, as assessed by Shapiro-Wilk's test ( $p > .05$ ), and there were no outliers. There were statistically significant, strong correlations between visit one and



visit two raw scores,  $r(39) = .97$  (RS),  $.88$  (EV)  $.92$  (WS),  $.90$  (FS),  $p < .0005$  for all correlations.

### Conclusions

Initial results are promising support for reliability of testing in automatic conditions. Additional analyses will be completed prior to Research Week 2020 and will include the rest of the subject pool and further analysis of condition effects.



# Research Week 2020

## Design and Implementation of a High School Curriculum Campaign for the Detection and Prevention of Melanoma

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### Keywords

Melanoma

### Abstract

#### Background

Oregon has one of the highest incidence rates of melanoma in the country. Despite the preventable nature of melanoma, there is no formal statewide, high school-based educational curriculum to teach high school students about the disease. Early intervention may be key to detecting and reducing melanoma.

#### Design

As part of the War on Melanoma campaign, the Department of Dermatology faculty and medical students at Oregon Health and Sciences University created a 50-minute active learning lesson plan that is being taught to high school students in the state of Oregon. The curriculum addresses four learning objectives that align with the Oregon Health Education Performance Indicators using a 5E lesson plan model (engage, explore, explain, elaborate, and evaluate).

#### Measures

As of February 2020, twelve schools received curricula materials and will teach the curricula by the end of the 2019-2020 school year to an estimated 1,500 students across Oregon. Pre- and post-intervention surveys will obtain demographic information, assess student attitudes towards tanning beds and sunscreen use, and test knowledge acquisition based on the four learning objectives addressed by the War on Melanoma curriculum. Following the initial pilot in twelve schools, an interim analysis will be performed and the curriculum will be modified based on survey data and school feedback.

#### Analysis of Surveys

The effect of classroom lessons on responses to attitude, knowledge, and confidence questions will be evaluated by scoring separate composite scores pre- and post- class lesson. Linear mixed effects models will be used to examine changes in scores using educators as random effects to account for the intra-class clustering of students in schools.



# Research Week 2020

## To Screen or Not to Screen?: A Case Example of a High-Risk Suicide Attempt Survivor Presenting to the Emergency Department

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### Keywords

Suicide, screening, emergency department, case example

### Abstract

#### Aims

As many as 1 in 10 individuals who die by suicide were seen in an Emergency Department (ED) within the prior two months. Consequently, there has been a national push in recent years for universal screening for suicidal ideation (SI) in all EDs. However, few hospitals have adopted or enforced this guideline, despite research showing that it can double detection of SI and related behaviors. The goal of this project is to investigate the conditions under which screening occurs with a patient at high risk for suicide using a case example of a patient who presents to the ED with injuries caused by a suicide attempt (SA).

#### Methods

To investigate the gaps in care for this patient, we conducted a chart review of the ED visit and any visits in the year surrounding it. Additionally, we reviewed the guidelines for suicide screening at the hospital, state, and national level. We then used the Swiss Cheese Model to characterize the gaps in care. To supplement this case example, we conducted a literature review of suicide screening in EDs, suicide risk factors, and factors influencing acquired capability for suicide.

#### Results

In a review of notes in a one-year period, it was documented that this patient had multiple risk factors (chronic homelessness, veteran status, lack of social support, and past SA). We found that there were multiple missed opportunities for risk assessment and treatment for SI. During their ED visit, there were gaps in care at the organizational, supervisor, and at the caregiver/pre-condition levels.

#### Conclusions

This case study illustrates areas for improvement in suicide risk assessment in the ED and community care. A lack of guidance, various patient risk factors, and insufficient chart review led to gaps in care for a homeless patient seeking help from the ED.



# Research Week 2020

## Impact of Testosterone Therapy on Respiratory Support for Voice in Transgender and Gender Diverse Individuals

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### Keywords

Transgender, Respiration, Voice, Testosterone

### Abstract

#### Background

Testosterone therapy is considered standard of care medical treatment for transgender and gender diverse individuals assigned female at birth. The impact of gender affirming testosterone therapy on respiratory muscle strength has not yet been studied, nor have respiratory norms for transgender and gender diverse individuals undergoing this therapy been established. In considering voice for this population, establishing respiratory norms would aid the accuracy of pulmonary function testing for individuals who have undergone testosterone therapy and provide data to the limited pool of evidence on the vocal effects of testosterone therapy.

#### Purpose

The purpose of this pilot study was to explore the effect of testosterone therapy as part of medical treatment to align gender identity, on respiration and voice production, highlighting the need for larger studies to establish norms and better inform patients on possible respiratory changes post-treatment.

#### Methods

The primary outcomes of interest were respiratory volume and strength, reflected by measures of forced vital capacity (FVC), maximum inspiratory pressure (MIP), and maximum expiratory pressure (MEP). Because established respiratory norms are adjusted for biological sex, we compared participant data to published cisgender female and male norms. Twenty-four non-smoking transgender and gender diverse individuals, assigned female at birth participated in this study. Participants were aged 18-65 and on testosterone therapy consistently for at least the past year.

#### Results/Conclusion

We hypothesized that FVC, MIP and MEP may be increased by testosterone, closer aligning to cisgender male norms as compared to cisgender female norms. Results and conclusions will be presented.



# Research Week 2020

## The Role of Iron Repletion in Adult Iron Deficiency Anemia and Other Diseases

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### Keywords

Iron, anemia, hemorrhage

### Abstract

Iron deficiency anemia (IDA) is the most prevalent and treatable form of anemia worldwide. The clinical management of patients with IDA requires a comprehensive understanding of the many etiologies that can lead to iron deficiency including pregnancy, blood loss, renal disease, heavy menstrual bleeding, inflammatory bowel disease, bariatric surgery, or extremely rare genetic disorders. The treatment landscape for many causes of IDA is currently shifting towards more abundant use of intravenous (IV) iron due to its effectiveness and improved formulations that decrease the likelihood of adverse effects. IV iron has found applications beyond treatment of IDA and there is accruing data about its efficacy in patients with heart failure, restless leg syndrome, fatigue, and prevention of acute mountain sickness. This review provides a framework to diagnose, manage, and treat patients presenting with IDA and discusses other conditions that benefit from iron supplementation.





# Research Week 2020

## Risk of suicidal self-directed violence among survivors of head and neck cancer: A retrospective cohort analysis

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### Keywords

head and neck cancer survivors, suicide prevention

### Abstract

#### Purpose

Among a national cohort of Veteran head and neck cancer survivors (HNCS), we examined the associations between chronic pain, pre-cancer mental health and substance use disorder (SUD) diagnoses, and engagement in mental health services with risk of suicidal self-directed violence (SSDV).

#### Methods

We identified Veterans with a head and neck cancer diagnosis (stage I-IVB) who were treated in VA between 2012-2018. We extracted clinical information pre-and post-cancer diagnosis from VA Corporate Data Warehouse. We obtained data about SSDV events, which included both suicide attempts and death by suicide, from the validated Suicide Prevention Applications Network. Three adjusted logistic regression models determined associations between post-cancer chronic pain, pre-cancer mental health or SUD diagnoses, number of post-cancer mental health treatment encounters and any SSDV event (including death by suicide) controlling for cancer stage and treatment.

#### Results

Our cohort included 10,622 Veterans, comprised of 95% males with a mean age of 65 (SD=10.7). Sixty-five percent (n=6,936) had a documented mental health or SUD diagnosis during the observation period. Thirty-six percent (n=3,771) experienced chronic pain post-cancer. One hundred and fifty (1.4%) Veterans had at least one documented suicide related event, this included suicidal ideation (n=42,0.4%) or SSDV (n=80,1.0%; n=17, 0.2% of whom died by suicide). Chronic pain (OR=2.00, 95% CI=1.30,3.01), presence of pre-cancer mental health or SUD diagnoses (OR=2.90, 95% CI=1.78, 4.83), and number of post-

cancer diagnosis mental health and SUD treatment encounters (OR=1.01, 95% CI=1.00,1.01) were all significantly associated with SSDV.

## Conclusions

Among HNCS, risk factors for SSDV include chronic pain, pre-cancer mental health or SUD diagnoses, and mental health and treatment encounters following a cancer diagnosis. Our findings suggest an opportunity for HNCS who experience chronic pain or are already engaged in mental health services to undergo more robust suicide screening assessments and suicide prevention interventions.



# Research Week 2020

## Fast, multiplexed superresolution imaging of HER2 signaling in breast cancer with DNA-PAINT-ERS

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### Keywords

microscopy, imaging, her2, cancer

### Abstract

Super resolution microscopy (SRM) comprises various single-molecule localization techniques that can generate images at the 20 nm scale. In recent years, SRM based on DNA point accumulation in nanoscale topology (DNA-PAINT) has become increasingly useful for biological imaging for its robust capability for multiplexing. However, the practical use of DNA-PAINT has been limited by slow imaging speed. Here, we introduce DNA-PAINT-ERS, a set of strategies that can be easily integrated into current workflows for both accelerated DNA-PAINT and improved image quality.

In DNA-PAINT, single-molecule localization events arise from reversible hybridization between a docking strand (DS) oligo immobilized on an antibody and a complementary fluorophore-conjugated imager strand (IS) oligo diffusing in solution. We found that commonly used DS-IS pairs exhibited slow binding and unbinding kinetics and proposed a set of new strategies, collectively termed E-R-S (hence the term DNA-PAINT-ERS), that significantly improves the imaging speed of DNA-PAINT. We demonstrate the general applicability of DNA-PAINT-ERS for multiplexed SRM in merely 2-5 minutes per target using previously validated oligonucleotide constructs. Additionally, we showed that DNA-PAINT-ERS significantly improved the quality of the resulting images over current DNA-PAINT.

These advances have allowed us to use DNA-PAINT-ERS for the imaging of HER2 signaling in breast cancer. HER2 is a member of the epidermal growth factor (EGF) receptor family, and HER2 gene amplification and/or protein over-expression is commonly associated with human malignancies such as breast cancer. Using multicolor SRM based on DNA-PAINT-ERS, we can now image many different targets involved in the nanoscopic organization and signaling of HER2. The imaging results start to suggest a new mechanism that could lead to persistent HER2 signaling upon HER2-targeted therapy, thus contributing to therapeutic resistance.



# Research Week 2020

## Immediate and delayed recall measures in cochlear implant recipients: relationships with speech perception

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### Keywords

cochlear implants, CVLT-3, recall, cognition, speech perception

### Abstract

#### OBJECTIVES

Examine the relationship between immediate and delayed recall on the California Verbal Learning Test, Third Edition (CVLT-3) in adult cochlear implant (CI) recipients as it relates to list learning. Then, assess relationships between immediate & delayed recall and speech perception in this population.

#### METHODS

18 post-lingually deafened CI recipients participated in this study. Participants completed the CVLT-3, providing measures of immediate and delayed recall. Immediate recall measures consisted of 5 learning trials in succession after hearing a list of the same 16 words each time. Delayed recall measures consisted of both cued and non-cued recall with short and long-delay periods. Speech perception was assessed using the AzBio sentences with CI recipients in their best-aided condition.

#### RESULTS

Significant relationships between immediate and delayed recall were observed. The relationships between long-delay free recall and immediate recall measures grew stronger with each trial performed. Word acquisition across all 5 trials was also associated with long-delay free recall. Immediate and delayed recall measures significantly correlated with speech perception.

#### CONCLUSIONS

There was a strong relationship between immediate and delayed recall that progressed through all 5 trials. In addition to immediate and delayed recall measures, the improvement in word acquisition across all trials may prove useful to further understand

the variability associated with cochlear implant recipients' speech perception performance.



# Research Week 2020

## Deciphering atypical ubiquitin signals using pathogen-derived E3 ligases

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### Keywords

ubiquitin, E3 ligase, fluorescence, protein, bacteria

### Abstract

Ubiquitin is a small 8 kDa protein that is appended onto lysine residues of proteins as a post-translational modification, and functions in regulating diverse cellular processes. Through its own lysine residues or its N-terminus, ubiquitin can be joined into one of eight distinct polymeric chains using multiple ubiquitin monomers. Extensive research has led to an understanding of the cellular functions for some of the eight chains, but the biology of the remaining chains remain mysterious. Ubiquitin chains are generated by the incredibly diverse E3 ubiquitin ligating enzymes, each of which contain some level of specificity for a particular ubiquitin chain. One obstacle impairing the study for some of the mysterious chains is the lack of a known eukaryotic E3 ligase that generates the chain preferentially. Fortunately, many pathogenic bacteria have convergently evolved E3 ligases to co-opt the ubiquitin system of eukaryotic hosts to aid in establishing infection, enabling an alternative approach to study ubiquitin chain ligation. Here, we use protein mutagenesis techniques on E3 ligases from enterohemorrhagic *Escherichia coli*, *Salmonella Typhimurium*, and other pathogenic bacteria to explore the structural determinants of the mysterious Lys6-linked ubiquitin chains. Further, we report and utilize a novel E3 ligase with strong preference for Lys6-linked chain ligation, greater than that of any E3 ligase to our knowledge. Dysregulation of the ubiquitin cycle is implicated in numerous cancers, neurodegenerative diseases and autoimmune disorders, and by exploring the elusive Lys6-linked ubiquitin chain, our work expands the toolbox for decoding the ubiquitin system and its contributions to human health.



# Research Week 2020

## A Case Control Study using Pedal Acceleration Time as a Predictor of Limb Salvage in Patients Undergoing Revascularization Procedures

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### Keywords

Revascularization,

### Abstract

#### Background

The most accepted evaluators of lower limb arterial perfusion are arterial duplex ultrasound (DUS), ankle-brachial indices (ABIs), and toe-brachial indices (TBIs). In patients with diabetes or renal failure, ABI and TBIs can be unreliable due to medial wall calcification. DUS Interrogation of the pedal arterial arch is newly proposed method to measure limb perfusion. A previous study has shown a strong correlation ( $R^2 = 0.88$ ) between the Pedal Acceleration Time (PAT) and ABI in patients with no documented diabetes or renal failure. This study seeks to apply PAT as a predictor of the probability of limb salvage in patients with chronic limb-threatening ischemia (CLTI).

#### Methods

Patients undergoing revascularization procedures were studied ( $n=73$ ), 14 of these patients required higher level limb amputation. DUS was used to interrogate the pedal arch before and after the procedure and measured PAT in milliseconds (ms). PAT along with comorbidities, demographics, and presence of wound infection were compared to limb amputation events. A multivariate logistic regression model was used to determine the most significant predictors of limb amputation.

#### Results

Initial analysis showed differences (salvage vs amputation) in PAT after procedure (141 ms vs 213 ms,  $p<0.0001$ ), proportion of patients with wound infections (0.17 vs 0.5,  $p=0.009$ ), and proportion of patients with chronic kidney disease (CKD) (0.17 vs 0.57,  $p=0.006$ ). PAT along with presence of infection were found to be the two best predictors of the probability of limb amputation in the multivariate logistic regression ( $p=0.017$  and 0.033 respectively, pseudo  $R^2 = 0.82$ ).

## Conclusions

PAT continues to show promise in its efficacy as an indicator of vascular health in patients with CLTI. The results show that the PAT after the revascularization procedure and presence of infection are strong predictors of the necessity of amputation.





# Research Week 2020

## Barriers to eye care among participants of a mobile eye clinic

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### Keywords

eye care access

### Abstract

Barriers to health care access present critical challenges to improving eye health that are dynamic and complex, yet few studies have been able to quantitatively measure the impact of these barriers. This study aims to determine the association between initial barriers to seeking care and time since last eye exam (TLEE) utilizing a mobile screening clinic that provides comprehensive eye exams in Oregon.

### Approach

Participants (N=1699) from screenings conducted between 2014 and 2016 completed a demographic and subjective visual acuity questionnaire, and received a comprehensive dilated eye exam. Data regarding demographic information, subjective visual acuity, and measured visual acuity were analyzed with respect to TLEE and compared to the American Academy of Ophthalmology recommendations for preventive eye health exams.

### Results

A large percentage of Hispanic (34.9%,) and uninsured (28.6%) participants had no previous eye exam. Although 96.4% of Caucasians had a previous eye exam, 40.2% have not had an eye exam in 4 or more years. Diabetic participants had eye exams less frequently than the annual screenings recommended by the American Academy of Ophthalmology.

### Conclusions

Our results indicate that barriers to eye care must be assessed to gain an accurate understanding of the challenges that specific subpopulations face in accessing preventive care. Furthermore, it is especially important to improve eye care access for diabetic individuals to detect and treat diabetic retinopathy in a timely manner.



# Research Week 2020

## MEG as a predictor of the epileptogenic zone in patients being evaluated for epilepsy surgery

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### Keywords

MEG, Magnetoencephalography, epilepsy

### Abstract

#### Background

Magnetoencephalography (MEG) measures cortically-generated magnetic fields and creates a map of current dipoles that is overlaid on Magnetic Resonance Imaging (MRI) images of the brain in order to predict the epileptogenic zone. It is a part of the armamentarium of diagnostic tests available in the presurgical workup in patients with pharmaco-resistant focal epilepsy. Its efficacy and reliability in providing results concordant with other diagnostic studies and identifying additional epileptogenic foci is well-described in the literature. OHSU does not currently possess MEG as a diagnostic tool, requiring patients recommended for MEG evaluation to travel to out-of-state medical centers, often at significant personal cost.

#### Objective

To determine whether the spatial distribution of spike sources determined by MEG provides reliable information compared to intracranial electroencephalography (EEG) for planning surgery and predicting outcomes in patients with medically refractory epilepsy at OHSU.

#### Methods

8 adult patients with medically refractory epilepsy treated at OHSU who had undergone MEG were retrospectively identified and included in this analysis. The results from MEG were compared to intracranial EEG (iEEG) results to determine if MEG studies predicted the seizure onset zone, which was subsequently confirmed with iEEG studies conducted for surgical planning.

#### Results

MEG predicted epileptogenic foci in 6 of 8 patients evaluated. 1 patient did not undergo iEEG due to lack of definitive localization from various noninvasive imaging studies

(including MEG). 1 additional patient did not have any detectable epileptiform activity during MEG.

#### Conclusion

MEG is a useful, non-invasive imaging modality that has potential to aid in localization of epileptogenic foci. This case series presents MEG's efficacy in aiding the localization of epileptogenic foci in a limited cohort of patients. Utilization of MEG technology increases OHSU's diagnostic capabilities and has the potential to improve chances of definitive epilepsy therapy.



# Research Week 2020

## Critical moments: how veterans with a recent suicide attempt describe their thoughts and feelings before attempting suicide

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### Keywords

self-concept, self-compassion, suicide, suicidal ideation

### Abstract

#### Objective

Few studies have asked veterans about their lived experiences with suicidal thoughts and little is known about the thoughts and feelings that arise leading up to a suicide attempt. This study aimed to understand how veterans describe their thoughts and feelings just prior to attempting suicide and explored what may support recovery.

#### Methods

This was a national qualitative study of 50 (25 women, 25 men) United States (U.S.) Veterans who made a recent suicide attempt (prior 6 months). Participants were treatment-seeking patients at Veterans Affairs medical centers, recruited through their clinician. A modified grounded theory approach was used to conduct the semi-structured interviews, covering topics of military history, suicidal thoughts and attempts, and healthcare and recovery experiences.

#### Results

When asked about thoughts leading up to their most recent suicide attempt, veterans reported experiencing negative thoughts about how they viewed themselves, how others perceived them, and not living up to their ideal selves. We conceptualized veterans' negative beliefs and perceptions of self as negative self-concept. Veterans experiencing negative self-concept identified feelings of perceived failure, lack of achievement, and low self-esteem. When asked what would help or has helped in their recovery from suicide attempts, veterans expressed a desire to learn more about themselves and to feel like their thoughts, behaviors, and feelings were acceptable. We conceptualized this as a desire for increased self-compassion, which is the practice of kindness and understanding towards oneself in times of stress and acceptance of failure and imperfections as a shared human experience.

## Conclusions

These findings suggest an increased need to address negative self-concept among patients at risk for suicide, which may include examining the effectiveness of interventions focusing on teaching and practicing self-compassion skills in reducing suicidal behaviors.



# Research Week 2020

## Pheochromocytoma And Its Modern Clinical Phenotype: A Single Center Retrospective Review

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### Keywords

Adrenal Cancer, Pheochromocytoma, Incidental Masses

### Abstract

#### Objective

To describe the presentation and biochemical properties of pheochromocytomas (PCCs) as a function of size and cause for workup, including those symptomatic with hypertension or paroxysmal episodes, with known genetic predisposition (GP), or with an incidental mass (IM) on imaging.

#### Design

Single-center retrospective study of surgical resections for suspected PCC between 1998 and 2018.

#### Results

Fifty-eight patients underwent surgery for suspected PCC. Of those, forty-four patients (75.9%) had 50 masses confirmed as PCC on pathology. The most common cause for workup in all patients undergoing surgery for suspected PCC was IM (38.6%), followed by symptoms (34.1%), and lastly GP (27.3%). The median PCC size on imaging was 3.35 cm (range, 0.1 cm to 12.2 cm). The median tumor size was greatest in patients worked up for symptoms, followed by IM and GP patients (4.1 vs 3.4 vs 2.25 cm, respectively  $p = 0.176$ ). Unenhanced CT attenuation values were available for 20 PCCs with a median value of 36 Hounsfield Units (range 17 to 85). Symptom burden was greater in patients with masses  $>4$ cm who reported significantly more symptoms than patients with masses  $\leq 4$ cm (3.2 vs 1.52 symptoms reported, respectively  $p = 0.005$ ). Bilateral disease was more common in GP than symptomatic or IM patients (41.7% vs 13.3 vs 5.8%, respectively  $p = 0.040$ ). Biochemical testing was available for 39 patients with PCC; all but one patient had evidence of biochemical activity. Total urine metanephrines were elevated in masses  $>4$ cm vs. those  $\leq 4$ cm (7681 vs. 3339 mcg,  $p = 0.108$ ).

#### Conclusion

Incidental adrenal masses are the most common cause of workup for PCC. Tumor size and number of symptoms reported were greatest in patients worked up for symptoms suspicious of PCC. Biochemical testing was positive in all but one PCC patient and larger masses correlated with higher total urine metanephrines.



# Research Week 2020

## A novel approach for melanoma circulating tumor cell isolation from patient whole blood

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### Keywords

CTCs, Single-cell, Transcriptomics, Immunotherapy, Melanoma

### Abstract

The current standard for investigating melanoma, solid tumor biopsy, is a costly and inefficient means of extracting information about disease progression through repeat tumor biopsies. Alternatively, circulating tumor cells (CTCs, cells that have broken away from the primary tumor or metastatic sites) can be extracted from the blood in a liquid biopsy using a minimally invasive blood draw. We hypothesize that analyzing these CTCs both genetically and epigenetically may divulge important insights into melanoma progression, evolution, and response to treatment. The purpose of this study is to develop improved methods for CTC isolation. Here, we demonstrate a novel workflow for isolating melanoma CTCs. We successfully validate this approach by isolating and sequence verifying single A375 melanoma cells enriched from whole blood. Previous strategies for CTC isolation have been problematic; microfluidic approaches to CTC isolation may miss CTCs of aberrant morphology, while other antibody-based CTC isolation strategies are limited by using only a small number of antibodies to label their cells. Our approach does not rely upon cell morphology, and takes advantage of a large cocktail of antibodies tailored specifically for melanoma CTCs to overcome these limitations. Future studies include single cell RNA sequencing to make mechanistic insights into melanoma evolution over the course of immune checkpoint blockade (ICB) therapy targeting the PD-1 axis.





# Research Week 2020

## Defining Stress among Oregon Corrections Professionals

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### Keywords

stress, occupational stress, corrections

### Abstract

Corrections professionals experience some of the highest levels of chronic stress compared to other occupations. This leads to poor mental and physical health, increased mortality, negative job performance, and increased economic costs, such as work-related injuries, sick leave, worker's compensation claims and disability. Improving health and safety among this occupation requires identifying the factors contributing to stress and the associated economic impact. We assessed corrections professionals (n=296) working at six different Oregon Department of Corrections facilities near the Portland-area of varying security levels. Participants completed a cross-sectional survey, including demographics, work history and validated stress and occupational constructs. The outcome of perceived stress was measured by the Perceived Stress Scale (PSS-4 Short Form; Cohen, Kamarack & Mermelstein, 1983). Using a mixed linear effects regression model, we found that perceived stress increases with increased work-related stress ( $p=0.02$ ), work hours ( $p=0.03$ ), operational stressors ( $p=0.002$ ), and procedural injustice ( $p=0.03$ ) and decreases with more time employed at current facility ( $p=0.06$ ), improved job satisfaction ( $p<0.001$ ), and among married or partnered individuals ( $p=0.05$ ). Further, perceived stress increases the odds of missed workdays due to work-related injuries (OR=1.18, 95% CI 1.05, 1.33;  $p=0.01$ ). However, there is no association with perceived stress and worker's compensation claims (OR=1.04, 95% CI 0.88, 1.23;  $p=0.61$ ). Identifying these predictors of stress and related adverse effects can inform the development of policy changes to improve working conditions, mental well-being, physical health, job performance, and economic outcomes within corrections.



# Research Week 2020

## Is home exercise for dizziness after mild traumatic brain injury enough? Could wearable sensors help?

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### Keywords

Vestibular, rehabilitation, mTBI, sensor, technology

### Abstract

#### Purpose

Vestibular rehabilitation (VR) is used to treat dizziness after mild traumatic brain injury (mTBI) and relies on patients to independently perform a prescribed home exercise program (HEP). Barriers to this approach include impaired cervical proprioception that may impact ability to position the head and trunk and self-limiting movements to avoid symptoms. Wearable sensors may aid clinical assessment and performance monitoring, improving rehabilitation efficacy during HEP. The purpose of this study is to determine if 1) wearable sensor technology is a reliable measure for performance of VR exercises and 2) there are differences in exercise performance between controls and mTBI.

#### Subjects

Twenty-three participants with mTBI (18F/5M, 35.4 [12.7] yo; 44.1 (22.5) days post injury) and 16 controls (9F/7M, 28.7 [5.1] yo) have enrolled.

#### Methods

Participants wore two wearable sensors (Opal V2, APDM) on their head and trunk while four common vestibular exercises were performed. Exercises were performed on three separate days; including two bouts of horizontal and vertical head turns. Outcomes measures included sensor-based range of motion (ROM) and angular velocity. SPSS v22 was used to calculate intraclass correlation coefficients (ICC) for reliability and independent-samples t-tests compared between group baseline performances.

#### Results

Reliability measures were good-excellent; ICCs 0.689–0.976 for ROM and 0.822–0.957 for angular velocity. The largest group differences were seen in angular velocity of head movements during gait: horizontal (mTBI: 263.5°/s ± 74.3; control: 377.8°/s ± 81.7; p = 0.001) and vertical (mTBI: 178.9°/s ± 65.5; control: 265.2°/s ± 69.7; p = 0.001).

## Conclusions

Wearable sensor characterization of a vestibular HEP revealed good reliability for both head ROM and angular velocity during exercises indicating they could be useful for tracking progress. Preliminary analyses suggest that people with mTBI moved their heads slower compared to control subjects. Wearable sensors could guide physical therapy, improving HEP efficacy and compliance.



# Research Week 2020

## Varying long-term liver involvement in patients with Alagille syndrome in a single center study

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### Keywords

Alagille, liver disease, liver transplant

### Abstract

#### Background

Alagille syndrome (ALGS) is a multisystem disorder due to mutations in the JAG1 or NOTCH2 genes with variable phenotype penetrance. Liver disease in ALGS can change in severity, with some patients eventually requiring a liver transplant (LT). We present a case series of the varying long-term hepatic involvement of eight patients.

#### Methods

A chart review was performed and laboratory values and ALGS features were obtained. Descriptive statistics were used to summarize the clinical elements and severity of liver disease.

#### Results

The average age of ALGS diagnosis was 18 months. Of the eight patients, three had severe liver disease with one having a biliary diversion, one with an ileal exclusion, and two having had liver transplants. The five patients with mild liver disease have liver enzymes and bilirubin ranging from normal to stable elevation.

Table 1. Liver function over time.

Average values

Values at time of ALGS diagnosis (n=8)

Current values for patients with mild liver disease (n=5)

Current values for patients with severe liver disease (n=3)\*

ALT (U/L)

172.8

177

AST (U/L)

180

115

169

Total Bilirubin (mg/dL)

7.9

0.7

8

GGT (U/L)

970\*\*

327\*\*\*

304

Platelets (K/cu mm)

437

262

203

Current values at the time prior to LT if applicable

N=7

N=4

Conclusion

Liver disease in ALGS has a variable course and the severity at diagnosis does not necessarily predict progression to severe disease. Of our eight patients, the three with severe liver disease had elevated bilirubin, significant pruritus, and poor growth prior to transplant compared to those with mild disease. While routine monitoring of liver function and clinical features is important for all ALGS patients, the degree of cholestasis may suggest progression to severe liver disease and anticipate the need for transplantation.



# Research Week 2020

## Targeting nucleic acid sensors for cancer immunotherapy

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### Keywords

Nucleic Acid Sensors, RIG-I, CT26, IFN-I response

### Abstract

The RNA sensor RIG-I (retinoic-acid inducible gene 1), also known as DDX58, recognizes cytosolic short dsRNA and plays a major role in the antiviral response. RIG-I activation triggers the type I Interferon (IFN) response and the expression of pro-inflammatory cytokines. Activation of cytosolic nucleic acid sensors has been associated with the potentiation of a robust anti-tumor immune response. In the present study, we activated RIG-I using a 5' -triphosphorilated-hpRNA in CT26, a murine colorectal carcinoma cell line. After 24h, we observed 4,474 genes that were differentially expressed between RIG-I activated and control group. According to the functional enrichment analysis, these genes are involved in the antiviral and innate immune responses. Specifically, we found Mx1 as the most differentially expressed gene, among other interferon response genes such as Mx2, Cxcl10, Ifi44l and Oas1. In vivo, injection of RIG-I stimulated CT26 cells markedly decreased tumor growth compared to their non-stimulated counterparts. Consistently, tumor weight was also decreased in RIG-I stimulated group. RNA expression analysis from the RIG-I activated tumors showed significant upregulation of IFN-I response genes which was consistent with our in vitro results. Multicolor flow cytometry analysis showed increased frequencies of Natural Killer Cells (NKs) and Dendritic Cells (DCs). Interestingly, RIG activated tumors also elicited significantly less exhausted CD8+ cells. Overall, our data highlight a critical role of tumor cell RIG-I in shaping the tumor immune microenvironment. Importantly, our work identifies several cellular and molecular immune correlates that can be exploited for combination therapies to enhance immune responses to tumors.



# Research Week 2020

## Understanding Barriers to Recruitment Among Patients with Lung Cancer into an Exercise Study

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### Keywords

Lung Cancer, Recruitment Methodology, Clinical Research, Exercise

### Abstract

#### Introduction

Exercise may mitigate functional decline among patients with cancer and the importance of partner support for engaging in healthy behaviors is increasingly being recognized. Clinical trials with dyads can explore this but can suffer from challenging recruitment. Understanding barriers to recruitment in exercise interventions among patients with lung cancer and their dyad partners is important when designing future studies.

#### Methods

In a clinical pilot trial of exercise in lung cancer dyads, we employed three recruitment strategies: in-person in lung cancer ambulatory clinics, cancer registry mailings, and posts on research study opportunities webpages. Our intervention required dyad attendance of twice weekly, in-person, one-hour yoga classes with a once weekly at-home practice for the first six weeks followed by six weeks of a once weekly in-person class with twice weekly at-home practices. Eligibility requirements: stage I-IV non-small cell lung cancer, physician clearance for exercise participation, and a partner willing to participate in classes and surveys.

#### Results

Clinic recruitment yielded 261 potentially eligible patients. 46 (18%) did not meet eligibility criteria and among those who declined to participate, 50 (19%) cited driving distance burden and 26 (10%) declined due to other reasons, primarily a lack of available partner. We mailed letters to 386 patients from the OHSU Cancer Registry, which yielded 3 eligible patients. No patients were recruited from the research study opportunities webpages. We enrolled 23/261 dyads (18%) into our study.

#### Discussion

Utilizing recruitment methods from two high-traffic lung cancer ambulatory clinics and posting study information on several research opportunity websites, our enrollment rate was only 18%. Due to the requirements of our study, and most eligible patients citing driving distance burden or lack of available partner as the main deterrent for participation, investment in home-based or telemedicine exercise trials, where support partners could join remotely, may increase study participation.





# Research Week 2020

## Mental Health of Families during Childhood Cancer Treatment and Survivorship

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### Keywords

pediatric oncology; mental health; health experiences

### Abstract

#### Background

There are few studies on the long-term psychological impact of caring for a child who underwent treatment and survived cancer. While young survivors of childhood cancer report a need for psychological support during and after treatment, little is known about this experience from the caretaker's perspective.

#### Methods

Parents of childhood cancer survivors participated in semi-structured, qualitative interviews conducted by researchers trained in the 'Database of Individual Patient Experiences' (DIPEX) methodology. Interviews focused on identifying topics most important to patients and families throughout the process of cancer diagnosis, treatment, and survivorship. 29 interviews were completed thus far. Using NVivo, interview transcripts were dual-coded and analyzed using the constant comparison method to identify both common and divergent themes. Identified themes were deliberated until consensus was reached.

#### Results

In preliminary analysis of the initial 22 interviews, the following themes emerged: (1) need for mental health support for families during and after cancer treatment; (2) difficulty asking for and accessing psychological help while in caretaker role; and (3) recognition and diagnosis of posttraumatic stress disorder after treatment. Prevalent barriers identified by participants to mental health access included feeling overwhelmed by cancer diagnosis and treatment, fear of acknowledging cancer diagnosis, and an intense focus centered around caring for their children and not themselves. Multiple participants suggested providing mental health counselors to caretakers during and after treatment as part of standard practice.

#### Conclusions

Despite the success of completing treatment and surviving cancer, many caretakers of childhood cancer survivors reported symptoms of depression and anxiety surrounding the profound impact of cancer on their lives. Solutions should focus on implementing emotional support interventions for families during and after cancer treatment as standard care. There is a need to improve psychological interventions for family members during and after the traumatic experience of caring for a child with cancer.



# Research Week 2020

## Evaluation of Inter-Sample Variability in Anomalous Ideation Scale IRT Parameter Estimates

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### Keywords

Psychometrics, Item Response Theory, Latent Traits, Anomalous Ideation

### Abstract

Previous research has shown that belief in conspiracy theories and paranormal phenomena is related to attitudes about controversial scientific topics (e.g., climate change, vaccines, and genetically modified food) as well as levels of general (mis)trust in science. However, there has been relatively little literature comprehensively evaluating the reliability of the measurement tools used to assess paranormal and conspiracist beliefs. It is important to ensure the psychometric properties of these measures so that future research can use the scales with appropriate confidence. In this study, we adopt an Item Response Theory (IRT) framework to assess item and scale functioning and compare parameter estimates across three large, independent general population samples. Several methods are used to assess the variability in scale functioning across samples. We discuss the implications of these results for the measurement of conspiracist and paranormal belief as well as for expectations about the stability of psychometric results in general.



# Research Week 2020

## Hospitalization among Persons who Use Drugs and Hepatitis C Treatment Trajectory – An Exploratory Qualitative Analysis

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### Keywords

Hepatitis C, Addiction, Substance use disorder, hospitalization

### Abstract

#### OBJECTIVES

Rates of hospitalizations due to complications from drug use and infections with hepatitis C virus (HCV) have increased amidst the ongoing substance use epidemic. Persons who use drugs (PWUD) face numerous barriers to initiating and completing HCV treatment. Since hospitalization is an opportunity to engage PWUD regarding substance use, we aimed to understand how hospitalization alters HCV treatment readiness and engagement.

#### METHODS

We conducted in-depth semi-structured individual interviews with hospitalized adult PWUD with HCV seen by an addiction consult service at an urban academic medical center from June to November 2019. We audio-recorded and transcribed interviews. Transcripts were coded in dyads deductively and inductively at the semantic level then analyzed for themes using iterative categorization.

#### RESULTS

Of 27 participants, average age was 41 (range 23-64) years; majority were Caucasian (85%), male gender (67%), and primarily used opioids (78%). Many patients felt over-burdened by acute illness, outpatient follow-up, homelessness, and other stressors. Mostly, these patients did not have the bandwidth for HCV during their current admission. However, some patients felt hospitalization was an opportune time, especially if experiencing prolonged length of stays, to learn more about HCV and to develop an HCV treatment plan. Finally, for a few highly-engaged patients with prior outpatient plans for HCV treatment initiation, acute illness disrupted their pre-hospitalization HCV treatment trajectory. Patients frequently described negative interactions with the healthcare system prior to current hospitalization which influenced their ongoing medical engagement. Most

patients felt hospital providers failed to discuss HCV and were dismayed at missed opportunities to assess HCV in a controlled setting.

## CONCLUSIONS

Hospitalization can be a strong motivator for some PWUD to prioritize HCV treatment, however others feel overwhelmed by acute medical issues and/or psychosocial stressors. Hospital providers should ask patients about HCV and address needs regarding HCV education and linkage to care.



# Research Week 2020

## Gigli saw olecranon osteotomy for distal humerus fractures: A cutting-edge technique

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### Keywords

humerus fracture, Olecranon osteotomy, Gigli saw

### Abstract

#### Purpose

Olecranon osteotomy is commonly performed for open reduction and internal fixation of intraarticular distal humerus fractures, as it affords direct visualization of the articular surface to achieve anatomic reduction. Historically, a chevron osteotomy with an oscillating saw has been utilized. Recently, however, using a Gigli saw to complete the olecranon osteotomy has been suggested as a more efficient technique. The purpose of this study was to compare complication rates of the chevron and Gigli saw osteotomy techniques.

#### Methods

A 7-year retrospective chart review of all patients at our academic level 1 trauma center with operatively treated AO/OTA type 13C distal humerus fractures undergoing olecranon osteotomy was performed (2012-19; n=48). The primary outcome measure was overall complication rate, which included infection, arthrofibrosis, nerve injury, and all-cause reoperation. Between group differences in complication rates were assessed using t-tests and chi-squared tests.

#### Results

23 patients (48%) received an olecranon osteotomy with the Gigli saw technique. An overall complication rate of 56% was observed with the chevron technique, compared to 30% with the Gigli saw technique. This difference was not statistically significant ( $p = 0.10$ ). However, patients with a chevron osteotomy were significantly more likely to develop arthrofibrosis ( $p = 0.03$ ) or a nerve injury ( $p = 0.02$ ).

#### Conclusion

Complications rates in the chevron and Gigli saw osteotomy groups were not statistically different. While fracture severity and reduction quality may impact complication rates,

the Gigli saw osteotomy technique does not appear to increase complication rates. This favorable safety profile, in combination with the speed and simplicity of the Gigli saw technique, warrants further study and consideration for utilization in clinical practice.



# Research Week 2020

## The Hegemonic Discourse on Care as Free and Female: Women's Agency in Unpaid Eldercare

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### Keywords

Feminist Poststructuralism, Theory Development, Family Caregiving, Eldercare

### Abstract

#### Aims and Methods

In the United States, over 20.5 million women provide unpaid care labor to an older adult. During the last year of life, over 75% of Medicare beneficiaries depend solely on the unpaid labor of their daughters and female spouses to meet daily care needs. Significant inequities exist in the impact of unpaid eldercare on the health of U.S. adults, with women consistently experiencing more negative outcomes based on myriad metrics. In order to understand and oppose the structural forces underlying these inequities, we have developed a feminist poststructuralist theory of agency for women providing unpaid eldercare. Our theory development process included reviewing existing literature, identifying dominant and subjugated discourses, defining core concepts, and illustrating these concepts with exemplars.

#### Description of Theory

The two central feminist poststructuralist concepts we leverage are the discursive, intersectional construction of identity and the relational nature of agency. These conceptions form sharp contrasts with dominant biological identity essentialism and conceptions of agency as synonymous with autonomy. While individual women's agency may be constrained by the hegemonic discourse on eldercare as freely given and naturally female, relational agency to oppose external and internalized oppression can be mobilized through the emancipation of subjugated discourses.

#### Conclusions and Implications for Healthcare

Lack of choice, structurally enforced sublimation of needs and selfhood, entrapment, and captivity abound in marginalized women's narratives of providing unpaid care labor to older adults. Women survivors of childhood maltreatment may be especially vulnerable to constraints of relational agency and re-traumatization in the context of familial eldercare. The disproportionate deleterious impact of providing unpaid care on the health and well-being of women with such experiences must be acknowledged and addressed. We plan to use our feminist poststructuralist theory of agency to revolutionize



nursing discourse on unpaid eldercare, directing research and practice to empower women carers.



# Research Week 2020

## A single-center comparison of thymoglobulin, basiliximab, and alemtuzumab induction therapy in simultaneous pancreas-kidney transplant patients

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### Keywords

SPK transplant, abdominal organ transplant, diabetes

### Abstract

#### Background

There are few studies that compare the safety of multiple induction therapies in simultaneous pancreas-kidney transplant (SPKT) patients. The purpose of this study is to compare basiliximab, thymoglobulin (ATG), and alemtuzumab according to HLA matching to assess allograft survival, rejection rate, and post-operative complications.

#### Methods

A retrospective chart review of 59 performed SPKTs recipients between 2006 and 2018 was conducted. Recipients [Male/Female 1.95:1, mean age: 42.9 years, range 26-61 years, mean BMI 26.0 ±3.1, mean duration of dialysis: 20.4±23.9 months] received induction with basiliximab (n=31; 20 mg on the day of surgery followed by the same dose POD-4) if they had zero or one HLA-DR mismatch, and received either alemtuzumab (n=14; 0.5 mg/kg, max of 30 mg once on the day of surgery) or ATG (n=14, 1.5mg/kg for 4 days starting at the day of surgery) if they had two HLA-DR mismatches. Maintenance immunosuppressive therapy for all subjects in the study was the same.

#### Results

At 12-months follow-up, acute rejection rate (kidney or pancreas) was significantly higher in patients on ATG (85.7%) as compared to basiliximab (58.1%) and alemtuzumab (50%) (p=0.28). While all-cause graft failure was significantly lower in patients treated with ATG (14.3%) as compared to basiliximab (20%), alemtuzumab (21.4%) (p=0.003), there was no significant difference in immunological graft failure in the three groups (ATG 7.1%, alemtuzumab 7.1%, and basiliximab 9.7%, p=0.898). There was no difference in rates of CMV or BK virus infection, respectively, in the treatment groups (ATG 42.9% and 35.7%, basiliximab 48.4% and 22.6%, or alemtuzumab 42.9% and 21.4%, respectively p>0.5). There was no difference in post-induction cancer incidence in the treatment groups (ATG 14.3%, basiliximab 9.7%, or alemtuzumab 21.4%, p=0.56).

## Conclusions

Overall, use of Basiliximab in 0-1 HLA-DR MM and alemtuzumab and thymoglobulin in 2 HLA MM were comparable without significant difference in outcomes.



# Research Week 2020

## From "Eat Your Young" to "Grow Your Own:" Exploring Civility in Clinical Simulation for Nursing

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### Keywords

simulation, nursing, civility

### Abstract

Nursing school is the entry point for foundational knowledge and practice of nursing skills; it is also where learners acculturate to the nursing profession before licensure. Clinical simulation offers unique experiential learning within nursing curricula for learners to translate knowledge to practice, discover conceptual relationships, and collaborate with peers and faculty.

Nursing, however, has experienced historic challenges with incivility in education and practice and recent research studies have explored civility and incivility, collegiality, bullying, lateral/horizontal violence, and micro-aggressions in classroom, clinical learning, and nursing practice settings, including research of civility behaviors among and between students and faculty members.

A topic that has yet to be explored is understanding of civil behaviors among nursing simulation educators who design and deliver experiences for pre-licensure nurse learners. Nurse simulation educators may develop their simulation expertise through graduate nursing education and simulation certificate programs, professional development workshops, and/or from presentations at conferences. However, the vast majority learn the modality through informal on-the-job training on their own or from instructor peers – if they receive faculty development at all. Educators therefore often rely on their own professional and curricular experiences to inform their simulation practice. Civil practice is rarely a formal component of any formal or hidden nursing curricula.

In this descriptive discussion, I will highlight key literature on civility themes in nursing education and practice, summarize recent research about civility in practice related to patient outcomes, and advocate for further research into civility in nursing simulation education to inform faculty development solutions that foster positive outcomes for learners upstream and may lead to positive patient outcomes downstream.



# Research Week 2020

## Diagnostic Utility of Molecular and Flow Cytometric Findings in T-cell Large Granular Lymphocytic Leukemia

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### Keywords

T-cell large granular lymphocytic leukemia, chronic lymphoproliferative disorders, hematopathology, T-cell receptor

### Abstract

#### Background

T-cell large granular lymphocytic leukemia (T-LGLL) is a rare chronic lymphoproliferative disorder of mature cytotoxic T-cells. Accurate diagnosis relies on the integration of morphologic, immunophenotypic, molecular, and clinicopathologic findings. This study examined the frequency of abnormal findings in cases with clinical or hematopathologic suspicion for T-LGLL to investigate the relative importance of each diagnostic entity.

#### Design

Retrospective review of cases with clinical or hematopathologic suspicion for T-LGLL with concurrent flow cytometry, next-generation sequencing of STAT3/STAT5B, and T-cell receptor gene rearrangement (TCR) at a single academic institution from 2017-2019. Clinicopathologic information was abstracted from the chart.

#### Results

Of the 145 patients with clinicopathologic suspicion for T-LGLL, the 26 patients diagnosed with T-LGLL presented with: monoclonality by TCR gene rearrangement, genetic mutations, immunophenotypic aberrancy in T-cells, and at least one cytopenia. Compared to negative cases, monoclonality by TCR gene rearrangement in the T-LGLL population was statistically significant ( $p=0.001$ ). 43% of T-LGLL patients presented with STAT3 mutations and 5% presented with STAT5B mutations; whereas 11% of negative cases presented with STAT3 mutations and 3% presented with STAT5B mutations. 56% of patients with both T-LGLL and STAT3 mutations presented with co-mutations. 69% of T-LGLL cases had immunophenotypic aberrancy in T-cells, most commonly dim CD5, and 38% had restricted KIR expression. 64% of T-LGLL patients presented with at least one cytopenia, most commonly anemia, and 38% had a pre-existing autoimmune condition.

## Conclusion

The most commonly observed abnormalities in T-LGLL cases were monoclonal TCR gene rearrangements and immunophenotypic aberrancy by flow cytometry. STAT3/STAT5B and other mutations occurred at similar frequencies in patients with T-LGLL and those without. Diagnosis of T-LGLL requires integration of morphologic, immunophenotypic, and molecular findings and cannot rely on the presence of specific mutations. Additionally, in this clinicopathologic context, monoclonal TCR rearrangements are sensitive, but not specific, for a diagnosis of T-LGLL.



# Research Week 2020

## Increasing Self-Efficacy and Body Appreciation in Collegiate Athletes as Part of a Cooking Education Intervention

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### Keywords

Sports nutrition, body appreciation, self-efficacy, cooking, nutrition education

### Abstract

#### Purpose

Collegiate athletes often consume inadequate diets and have a high prevalence of disordered eating behaviors and body dissatisfaction. To improve dietary intake, previous research suggests that the use of a cooking and nutrition curriculum may support nutrition knowledge and self-efficacy. While these studies have provided insight into the relationship between nutrition education and confidence in cooking skills, incorporating a body appreciation component to the curriculum may support optimal health, athletic performance, and overall well-being. The purpose of this study was to assess the effectiveness of a nutrition and cooking education curriculum in improving self-efficacy and body appreciation in collegiate athletes.

#### Methods

A four-week nutrition education and cooking curriculum was developed and implemented in college athletes. A mixed methods approach was used to assess the effectiveness of the intervention. Quantitative data was collected at baseline and completion of the intervention to assess changes in self-efficacy and body appreciation. Qualitative data was collected at completion of the intervention to assess feasibility of the intervention.

#### Results

Ten athletes participated in the intervention. Quantitative results indicated significant improvements in self-efficacy ( $P=.003$ ) and no change in body appreciation ( $P=.28$ ). Qualitative data confirmed quantitative findings suggesting improvements in nutrition knowledge and self-efficacy in meal preparation.

#### Conclusions

Our findings indicate that the implementation of a cooking and nutrition education curriculum is indeed feasible and significantly increases self-efficacy in cooking and meal preparation as well as increases nutrition knowledge among collegiate athletes.





# Research Week 2020

## A Systematic Review of Tuberosity Healing and Outcomes following Reverse Shoulder Arthroplasty for Fracture According to Humeral Inclination of the Prosthesis

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### Keywords

proximal humerus fracture; reverse shoulder arthroplasty; systematic review; meta-analysis; tuberosity healing

### Abstract

#### Background

Proximal humerus fractures are common in the elderly population and are often treated with reverse shoulder arthroplasty (RSA). The purpose of this systematic review was to compare tuberosity healing and functional outcomes in patients undergoing RSA with humeral inclinations of 135°, 145°, and 155°.

#### Methods

A systematic review was performed of RSA for proximal humerus fracture using Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) guidelines. Radiographic and functional outcome data was extracted to evaluate tuberosity healing according to humeral inclination. Analysis was also performed of healed vs non-healed tuberosities.

#### Results

A total of 873 patients in 21 studies were included in the analysis. The mean age was 77.5 (range of 58-97) years and the mean follow up was 26.2 months. Tuberosity healing was 83% in the 135° compared to 69% in the 145° and 66% in the 155° groups ( $p=.030$ ). Postoperative abduction was highest in the 155° group ( $p<.001$ ). No significant difference was found in forward flexion, external rotation, or postoperative Constant score between groups. Patients with tuberosity healing demonstrated 18° higher forward flexion ( $p=.008$ ) and 16° greater external rotation ( $p<.001$ ) compared to those with unhealed tuberosities.

#### Conclusion

RSA for fracture with 135° humeral inclination is associated with higher tuberosity healing rates compared to 145° or 155°. Postoperative abduction is highest with a 155° implant, but there is no difference in in postoperative forward flexion, external rotation, or Constant score according to humeral inclination. Patients with healed tuberosities have superior postoperative forward flexion and external rotation compared to those with unhealed tuberosities.



# Research Week 2020

## Exploring Oregon Kindergarten Assessment Scores: Can we identify and learn from schools beating the odds?

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### Keywords

School Readiness, positive deviance, Oregon Kindergarten Assessment

### Abstract

School Readiness (SR) is an important predictor of child health and academic success; however, low-income children enter kindergarten with lower SR than their more affluent peers. In 2018, over half of all Oregon kindergartners were living in poverty and performed below the state average on the Oregon Kindergarten Assessment (OKA).

Positive deviance (PD) is an approach that highlights uncommon practices that reduce risk in low-resource communities. We used a PD approach to analyze data from the 2018-2019 OKA to identify positive deviants, defined as schools serving a large percentage of low-income children who are excelling on the OKA.

Publicly-available 2018-2019 OKA data was used to identify "high-poverty" schools, defined as schools serving greater than 75% economically disadvantaged students (n=212 schools). High-poverty schools were ranked by average Approach to Learning (AL) score. The AL segment of the OKA is an observational assessment, referring to tasks such as following directions. Positive deviants were defined as high-poverty schools with AL scores in the top centile (n=21 schools).

In the 2018-2019 school year, 41,005 children entered kindergarten in Oregon and 704 schools reported AL scores. The weighted mean AL score among all schools was 3.6 (1.8-4.6, SD=0.3). Schools serving less than 25% economically disadvantaged (ED) children (n=88) had a weighted mean score of 3.7 (3.0-4.4, SD=0.3); schools serving greater than 75% ED children (n=212) had a weighted mean score of 3.5 (2.2-4.5, SD=0.3); PD schools (n=21) had a weighted mean score of 4.1 (4.0-4.5, SD=0.1).

Previous analyses have already shown gaps in SR between higher and lower income communities. Utilizing a PD approach, we identified 21 high-poverty schools that are beating the odds on the OKA. Ongoing research includes school locality, school type (public vs charter), and school size, as well as community descriptors and resource accessibility such as libraries or HeadStart programs.



# Research Week 2020

## Does the type of congenital heart disease affect neurodevelopmental results?

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### Keywords

Neurodevelopment, Pediatrics, Congenital Heart Disease

### Abstract

Congenital heart disease patients have a higher rate of developmental disorders and cognitive delay.

A retrospective review was performed on CHD patients requiring cardiac surgery within the first year of life at Doernbecher Children's Hospital from 1/1/13-12/31/18. A surgical database collected patients' variables, including CHD, prenatal diagnosis, birth weight, gestational age, ND evaluation referral and results, and Early Intervention referral. Scaled Bayley scores were compared with  $\leq 4$  considered significantly delayed, 5-6 delayed, 7 low average, 8-12 average, 13 high average, and  $\geq 14$  superior.

Out of 151 patients, 64 (42.4%) were referred to ND services, and 60 (39.7%) patients accessed ND services, at a median age of 8.4 months. Patients with a longer length of hospital stay were more likely to undergo ND evaluation (22 vs 15 days,  $p=0.02$ ). Hypoplastic left heart syndrome and hypoplastic right heart syndrome patients had the longest median length of stay at the hospital at 29 and 21 days, respectively. Of patients who accessed ND services, 40 (66.7%) were referred to EI. HRHS patients scored the lowest on scaled cognitive Bayley scores with a median score of 7 ( $p=.0095$ ). HLHS and HRHS patients scored the lowest on gross motor skills, at medians of 3 and 5 respectively ( $p=0.001$ ). TOF and HLHS patients had the largest percentage of follow-up after their initial visits (71.4% and 69.2%).

Only 42.4% of CHD patients were referred to ND services, despite known risks. Excluding single ventricle patients, there was not an association between type of CHD and ND outcomes. While most patients with CHD had low to average scores on ND testing, single ventricle patients scored particularly low in cognitive and gross motor function. More than half of the patients who received initial testing followed-up with additional appointments in all CHD categories, demonstrating the importance of initial ND evaluation.



# Research Week 2020

## Effect of Patient Education on Healthcare Utilization and Satisfaction Following Peripheral Nerve Block for Ambulatory Surgery

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### Keywords

Pain management, regional anesthesia, patient education

### Abstract

#### Introduction

Postoperative pain poses a significant challenge for patients undergoing ambulatory orthopedic surgery with 30% of patients reporting moderate to severe pain. Regional anesthesia, including single shot peripheral nerve blocks (SS PNB) and continuous catheter peripheral nerve blocks (CC PNB), can reduce postoperative pain. PNBs pose challenges including higher rates of unplanned healthcare utilization postoperatively. It was hypothesized that enhanced patient education could decrease healthcare utilization and improve pain management satisfaction.

#### Materials and Methods

This is an interim analysis of a single center, prospective, usual care control, non-randomized cohort study. The usual care cohort received bedside teaching for SS PNB and a slideshow for CC PNB. All patients in the intervention cohort received a comprehensive mixed media education with handouts and videos. Primary outcomes included healthcare utilization and patient satisfaction, assessed by phone call.

#### Results

Healthcare utilization rate is similar between the usual care (15.5%) and intervention cohort (15.0%), but fewer subjects with SS PNB required healthcare resources after intervention (8.1% vs. 3.8%). More subjects in the usual care cohort sought medical attention multiple times compared to the intervention cohort (41.0% vs. 13.3%). In the usual care cohort 88.5% were satisfied with pain management vs. 91.0% in the intervention cohort. In the usual care cohort 90.1% were satisfied with the education provided vs. 95.0% in the intervention cohort.

#### Discussion

There are similar rates of healthcare utilization in the usual care and intervention cohorts. However, the proportion of subjects utilizing healthcare resources multiple times and the rates of healthcare utilization in those receiving SS PNB suggest a trend toward decreased utilization after implementation of a mixed media approach. Any form of educational material may be beneficial over bedside teaching alone. There is a trend toward improved satisfaction in postoperative pain management and education provided after a mixed media education implementation.



# Research Week 2020

## Investigating the Therapeutic Potential of Molecularly Targeted Therapy in Pediatric Spindle Cell Rhabdomyosarcoma

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### Keywords

Spindle Cell Rhabdomyosarcoma

### Abstract

Sarcoma is a cancer arising in the bone, connective, or soft-tissue and occurs at any age. Among these, spindle cell rhabdomyosarcoma (SCR) is a rare, aggressive skeletal muscle subtype predominately noted in children. Patients with SCR have poor outcomes despite intensive chemotherapy and radiation treatments, which emphasizes the need to understand tumor biology and identify molecularly targetable treatment options. Previous retrospective genomic studies uncovered recurrent MYOD1 and PIK3CA mutations in a cohort of SCR patients. However, there are limited human or murine SCR cell lines and animal models to test the efficacy of targeted agents. Recently, we generated a patient-derived SCR model cell line (SARC001) from a patient at Doernbecher Children's Hospital. Next-generation sequencing confirmed that SARC001 retains genomics aberrations found in the original tumor, including known mutations in MYOD1 and PTEN as well as novel mutations in PI3KCA and GNAS. Currently, the role of GNAS mutations in SCR and the efficacy of PI3KCA/mTOR inhibitors is unknown. Thus, this cell line represents an opportunity to functionally test the oncogenic potential of these novel mutations and the utility of targetable treatments. Using SARC001, the objectives are to test drug effects based on molecular aberrations and profile the pathogenic contributions of novel PI3KCA and GNAs mutations. The results show that among dual mTOR/PIK3CA, PIK3CA, mTOR, MEK inhibitors, and traditional chemotherapeutic agents, a dual mTOR/PIK3CA inhibitor, LY3023414, significantly inhibited SARC001 cell viability. Concomitantly, downstream effectors in the PIK3CA/AKT pathway, pS6 and p70S6K were significantly downregulated after LY3023414 and rapamycin treatments. Ongoing studies include investigating tumorigenicity and inhibitor-responses of SARC001 in vivo. Our results demonstrate the importance of patient-derived models, particularly in rare cancers such as SCR, for assessing preclinical efficacy of molecularly-targeted treatments. These studies are required to gain an understanding of tumor biology and inform future treatment options for improving patient outcomes.



# Research Week 2020

## Motor And Cognitive Developmental Scores In Offspring Of Pregnant Smokers At 12 Months Of Age

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### Keywords

vitamin C, smoking, childhood neurodevelopment

### Abstract

#### Background

It is estimated that more than 50% of smokers who become pregnant will continue to smoke despite the Surgeon General's warning. In some studies, prenatal smoke exposure has been associated with decreased cognitive, motor, and behavioral function in the offspring.

#### Objective

We conducted the current analysis to determine whether the neurodevelopmental scores collected by domain on the Ages and Stages Questionnaire (ASQ) scores at 12 months of age differed between offspring of prospectively identified pregnant smokers versus nonsmokers.

#### Design/Methods

The validated ASQ-3 was obtained at 12 months of age for offspring delivered to pregnant smokers randomized to vitamin C versus placebo during pregnancy and offspring of pregnant nonsmokers also studied prospectively. Z-scores for each ASQ domain were calculated using the normative data obtained from the ASQ-3 user's guide. The raw scores and Z-scores per domain were compared between groups using the Wilcoxon signed rank test.

#### Results

ASQ results were obtained in 204 offspring of smokers and 32 of nonsmokers. The demographics of the two groups were: Smokers: 19% non-white, 87% government assisted or self-paid/none insurance status, 54%  $\leq$  high school education, 8 cigarettes/day at randomization into the study at  $< 23$  weeks of gestation. Nonsmokers: 6.3% non-white; 6.3% government insurance; 6.3%  $\leq$  high school education. The offspring of smokers had significantly lower scores in the problem solving (Z score of -0.04 in smokers versus 0.32 in



nonsmokers) and personal social (Z score of 0.04 in smokers versus 0.45 in nonsmokers) domains.

### Conclusions

This data suggests a potential difference in problem solving and personal social domains in offspring of smokers versus nonsmokers. However, we are limited by our sample size to be able to adjust for other important covariates. Further study with longer follow-up and more detailed neurodevelopmental testing is needed.



# Research Week 2020

## Challenges to Health Care Access Despite Health Insurance: Lessons from a Community Health Fair

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### Keywords

Health Fair, Health Insurance, Health Care Access, Underserved, Social Determinants of Health

### Abstract

The annual Health Care Equity Fair (HCEF) is a community health fair hosted in Portland, Oregon that provides free health services to underserved communities. During the 2018 fair, 77 attendees completed a Health Risk Assessment Questionnaire (HRAQ), of which 81.9% reported having high school education or higher, 80.5% having health insurance, 16.9% having current employment, and 37.7% having stable housing. Our data suggests that even those with housing, health insurance, employment, and education still require additional health services, with 31.2% of attendees citing medical costs as the most common barrier to achieving adequate healthcare. This suggests that health insurance coverage does not always lead to sufficient health access, with underinsurance being a significant problem.



# Research Week 2020

## Differentially expressed plasma proteins in pityriasis rubra pilaris patients treated with ixekizumab

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### Keywords

PRP, cytokines

### Abstract

Pityriasis Rubra Pilaris (PRP) is a rare and debilitating cutaneous disease characterized by widespread red scaly plaques, follicular papules, and palmoplantar keratoderma. The pathogenesis of PRP is poorly understood, although overexpression of Th17 cytokines have been reported suggesting an inflammatory pathogenesis that may share features with psoriasis. In this study, we used OLINK proximity extension assay technology to quantitate 92 plasma inflammatory proteins of 11 PRP patients treated with ixekizumab (NCT03485976). Samples were obtained at baseline (week-0) and the final study visit (week-24). Comparisons of plasma protein concentrations were made between pretreatment and posttreatment samples and between responders (as defined by a  $\geq 50\%$  improvement in Psoriasis Area and Severity Index [PASI50]) and nonresponders. P-values were adjusted for multiple hypotheses. Of the 92 proteins analyzed, we identified a paradoxical 5.7-fold upregulation of IL-17A at week-24 compared to baseline ( $p < 0.000001$ ), in contrast to previous reports of decreased plasma IL-17A gene expression in patients treated with ixekizumab for psoriasis. When stratified by treatment response status, responders had significantly lower levels of IL-17 and TNF family cytokines, including IL-17C ( $p < 0.0001$ ) and TNF ( $p = 0.001$ ), at week-24 compared to nonresponders, suggesting that additional inhibition of the Th17 axis may be required to treat recalcitrant cases of PRP. This observation was supported clinically by a nonresponder patient who had treatment success with an increased dose of ixekizumab after trial completion. To our knowledge, this is the first quantitative protein analysis of PRP. These findings support prior studies implicating dysregulation of the Th17 axis in PRP and may help elucidate relevant pathways to target and better treat PRP. Further research is warranted to compare samples to a control population, and to compare these systemic biomarkers to local changes in skin samples.



# Research Week 2020

## INFLUENCE OF CAREGIVER WEIGHT-LOSS PROGRAM ON CHILDREN'S PHYSICAL ACTIVITY

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### Keywords

physical activity, sedentary, children, dyad

### Abstract

#### Purpose

To assess the influences of change in moderate-to-vigorous physical activity (MVPA) /sedentary time (ST) of caregivers participating in a commercial weight-loss program (CWLP) on their children's change in MVPA/ST.

#### Background

While research shows that caregiver participation in CWLP can help reduce their weight-related outcomes, the secondary effects on a child's weight-related behaviors from caregiver participation in a CWLP are less known.

#### Methods

Data from 29 caregivers (20 parents and 9 grandparents) and their children/grandchildren were collected during an 8-week participation period. MVPA/ST data were collected using accelerometers, and BMI data were calculated from measured height and weight at beginning and end. Multivariate linear regression assessed the associations of changes in caregiver's percent of time spent in MVPA/ST and changes in their child's percent of time spent in MVPA/ST, controlling for child's sex and age. Beta coefficients ( $\beta$ ) with 95% confidence intervals (CI) were reported.

#### Results

For caregivers that decreased BMI over 8-weeks, changes in time spent in MVPA was strongly associated with the change in children's time spent in MVPA compared to caregivers who maintained/increased BMI ( $\beta=2.61$  [95% CI: 0.45, 4.77] and  $\beta=0.24$  [-2.16, 2.64], respectively;  $R^2=0.37$ ). Similarly, changes in caregivers' time spent in ST was strongly associated with changes in children's time spent in ST compared to caregivers who maintained/increased BMI ( $\beta=2.42$  [1.02, 3.81] and  $\beta=0.35$  [-0.45, 1.14], respectively;  $R^2=0.63$ ).

## Conclusion

Our findings reinforce encouraging caregivers to enroll in a CWLP may not only improve their weight-related behaviors, but also weight-related health in their children, including MVPA/ST.



# Research Week 2020

## Location-specific differentiation potential of clonal articular cartilage progenitor cells

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### Keywords

Articular Cartilage, Chondrogenesis, Tissue Engineering

### Abstract

#### Introduction

Articular cartilage has a very poor regeneration potential following injury, and former dogma held that it contains no progenitor cells. However, in recent years, articular cartilage progenitor (ACP) cells, which have the ability to produce stable articular cartilage *in vitro*, have been isolated and cloned from the tissue. However, we have found a subset of ACPs that undergo hypertrophic chondrogenesis, indicative of an endochondral chondrocyte phenotype. This study aimed to understand where this subset of ACPs reside in the tissue.

#### Methods

ACPs were isolated from different zones of normal human articular cartilage and single cell clones were stimulated to undergo chondrogenesis *in vitro* in 3D pellet culture for 14 days.

#### Results

At day zero, SOX9 and COL10A1 gene expression, measured by qPCR, were significantly higher in deep zone ACP pellets while no significant differences ( $p > 0.05$ ) for Col1A1, Col2A1, MMP13, ACAN, and PRG4 were observed. At 14 days, total glycosaminoglycan (GAG, a measure of proteoglycan production) content of pellets was significantly greater ( $p < 0.05$ ) from superficial zone ACP clones compared with their deep zone counterparts. Hydroxyproline levels, a surrogate marker of total collagen content, was also significantly increased ( $p < 0.05$ ) in superficial versus deep clones. We observed no significant difference ( $p > 0.05$ ) in DNA content/pellet at 14 days.

#### Discussion

These data suggest that there are distinct populations of chondrocyte progenitors residing in different zones of human articular cartilage. ACPs collected from the superficial zone produce more matrix, as indicated by significantly increased proteoglycan and collagen

production in 3D cultures. Significantly, collagen X gene levels were higher in the deep zone clones, indicating this is the origin of clones with an endochondral versus stable chondrocyte phenotype. These different clones provide a resource to investigate epigenetic and genetic factors that control endochondral versus stable chondrocyte chondrogenesis.



# Research Week 2020

## Characterization of single-domain antibodies against Zika virus structural and non-structural proteins

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### Keywords

Zika virus

### Abstract

The flavivirus Zika virus (ZIKV) has extensive human health impact yet lacks vaccines and antiviral treatments in part due to gaps in understanding of its infectious cycle. To gain further insight into the infectious cycle without complete ablation of host or viral proteins we designed alpaca derived variable-heavy-chain antibody fragments (VHHs) against ZIKV. VHHs are encoded on a single gene, can be expressed in mammalian cells, and bind cognates in cytoplasm. Therefore, an entire alpaca VHH repertoire can be screened for ZIKV inhibitory function intracellularly. To obtain a library with ZIKV activity, we first immunized alpacas with whole inactivated ZIKV virions alongside recombinant ZIKV structural and non-structural proteins. We then isolated a library of VHH genes representative of the alpaca's immune repertoire from the peripheral blood. Currently we are isolating VHHs capable of disrupting ZIKV infection through two complementary screens: 1) Phage display and iterative panning against ZIKV antigens and 2) lethal ZIKV challenge of VHH expressing stable cell lines. From phage display we have evidence of individual VHHs with structural protein (capsid and envelope) and non-structural protein (NS5, NS3) binding activity. We expect to isolate VHHs capable of disrupting viral entry, genome replication, and assembly. We will then use inhibitory VHHs alongside mutated ZIKV proteins to better characterize functions and binding partners of ZIKV proteins during viral replication. An example is the unknown role of ZIKV capsid protein on host lipid manipulation.





# Research Week 2020

## Does Surgical Delay Impact Blood Loss During Acetabular Fracture Surgery?

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### Keywords

Surgical Delay, Acetabular Fractures, Trauma, Blood Loss

### Abstract

#### Purpose

The dogma in acetabular fracture care is that delaying surgery allows for intrapelvic clotting. Existing literature insufficiency utilizes surgeon reported blood loss (BL) as a variable. The purpose of this study is to use a novel, quantitative, formula-based approach to determine the impact of surgical delay on intraoperative BL during acetabular surgery.

#### Methods

Adult patients presenting to our Level 1 trauma facility receiving unilateral acetabular ORIF were reviewed (2008-18, n=372) for surgical details, pre- and postoperative hematocrit, and intraoperative transfusions. Intraoperative BL was estimated using adaptations of the Gross and Nadler Formulas:

$$\text{Blood loss} = \text{BV} \times ((\text{Hct0} - \text{HctF} + \text{Units Transfused} \times 1.9) / \text{HctAVG})$$

$$\text{Blood volume(Male)} = 0.3669 \times \text{H}^3 + 0.03219 \times \text{W} + 0.6041$$

$$\text{Blood volume(female)} = 0.3561 \times \text{H}^3 + 0.03308 \times \text{W} + 0.1833$$

Univariate and stepwise multivariate linear regression was used to determine the association between hospital day and calculated BL.

#### Results

Of 349 eligible patients (94%), 67% (233/349) sustained associated patterns of acetabular fractures. There was a statistically significant association between the hospital day of surgery and calculated BL (-400mL, SE 0.02, p=0.002), translating to 40 +/- 20 mL less BL per day. Using a maximally selected rank statistic, the optimal cut-point for early vs delayed surgery was set at 1 day. Early surgery was associated with an increase in 403 mL

of BL relative to delayed surgery ( $p=0.0002$ ) and specifically,  $50 \pm 13$  mL less BL per day ( $p<0.0001$ ).

#### Conclusion

Formula-derived values for intraoperative blood loss rather than surgeon opinion indeed appears to decrease with surgical delay. It indeed may be beneficial to delay surgery for specific, fragile patients.



# Research Week 2020

## Public Perception of Predictive Cancer Genetic Testing and Research in Oregon

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### Keywords

Qualitative, focus groups, marketing, outreach, recruitment, disparity, rural, heritable, pathogenic variants, genetic testing

### Abstract

Nationwide efforts are engaging communities in large genetic studies to better estimate the population-wide prevalence of some heritable cancers that have medical recommendations, however, effective communication about benefits and risks of both personal genetic testing and participation in bio-repositories remains challenging in some communities. To successfully engage an Oregon population in longitudinal research that includes predictive genetic testing for pathogenic or likely pathogenic variants associated with an increased risk for cancer, researchers conducted 35 focus groups with 203 adults (two of which were held in Spanish) in 24 of Oregon's 36 counties to better understand knowledge and attitudes related to genetic testing and willingness to participate in longitudinal genetic research. While participants at most focus group sites (33 of 35) described "concerns about outcomes" as barriers to predictive genetic testing, the desire to learn about health risks in oneself to inform personal or family medical decisions buffered fears for many participants, with 33 of the 35 sites citing "families" (e.g., children, close relatives, extended family members) as key motivators for participation in genetic research. Participants, particularly in rural areas, highlighted critical factors for research recruitment, such as trust, personal interaction, public education about genetic research, and clear communication about study goals and processes. Our statewide findings reflect that public interest in predictive cancer genetic testing and cancer genetic research can surpass lack of knowledge of the complex topics, particularly when benefits for self and family are emphasized and when study considerations are well articulated.



# Research Week 2020

## Mass and Structural Selective Ion Soft\_Landing for Separation, Collection and Characterization of Amyloid-Beta Peptide Structures and their Role in Alzheimer Disease

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### Keywords

Alzheimer, Soft-Landing of Biomolecules, Analytical Technologies

### Abstract

Advancements in ion mobility technology, particularly Structures for Lossless Ion Manipulations (SLIM), have enabled the detailed characterization of heterogeneity of biomolecular structures in a sample. SLIM enables the resolution of subtle variations of molecular structures (e.g. separation of conformations, isotopes, double bond positions, stereoisomers, isotopologues, isotopomers, etc.) which could be markers for diseases. SLIM also enables IMS separations with high resolution, high throughput, high ion utilization efficiency. In this work, we will present SLIM technology and its game-changing ability to perform analytical separations with unprecedented utility and precision. Particularly we will present the development of IMS technology that utilizes the sample nearly 100% of the time (as against traditional IMS which uses sample about 1% of the time owing to the pulsed nature of IMS). Further, we will present the ability to use such high ion utilization IMS separator in conjunction with high structural resolution and mass spectrometry to perform structure and mass selective soft-landing of biomolecular species.

The ability to collect material with structural and mass selectivity using SLIM enables in building materials of biomolecules to test hypotheses about their functionality in disease inception and progression. One potential model system we intend to study is the effect of conformations of amyloid-beta peptides in the kinetics of aggregation of beta-sheets, which are considered the leading cause for neuro-degenerative Alzheimer's disease. We propose to collect individual structures of A $\beta$  peptides using our mass and size selection capability while maintaining their functionality, reintroduce the selective structures into the solution phase and study how the kinetics of aggregation occurs in-vitro. This will potentially provide an understanding of the specific A $\beta$  structures' role in aggregation and thus providing opportunities for early disease detection and interventions. A similar approach can be extended to other disease models where molecular structures play a role in disease prognosis.



# Research Week 2020

## Extreme diabetic neglect is no worse than poor diabetic control in lower extremity fracture patients

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### Keywords

Orthopedic Surgery, Diabetes, Hemoglobin A1C, Fracture

### Abstract

#### Purpose

Patients with poor diabetic control who sustain lower extremity fractures present a challenge due to a high risk of complications; we believe but do not know whether worse control accentuates the consequences. We aimed to study post-operative risk profile as a function of diabetes control in patients with lower extremity fractures and predicted that as diabetic control proceeded towards extreme neglect, we would see a commensurate rise in major complications.

#### Methods

All patients presenting to our Level 1 academic trauma facility (2013-18) with Hgb A1C values  $>7$  & operatively treated lower extremity fractures were reviewed, yielding 121 unique patients. Reviewed data include: age, BMI, comorbidities, injury details, surgical fixation, A1C & major complications. We accepted maximum A1C values for the entire year before the traumatic event to best reflect the degree of diabetic neglect. Major complications included loss of reduction, nonunion, infection, and need for salvage procedure.

#### Results

94 patients had sufficient data for analysis; 63% had A1C values  $>8$  & 24% exceeded 10. 30% sustained a major complication. A1C distribution did not differ between patients with & without complications (Mann-Whitney U test,  $p = 0.53$ ). A receiver operating characteristic curve was calculated with cutpoints at A1C integers of 6-17+ (Figure 1). The area under the curve was 0.53 (95% CI: 0.40-0.66), indicating that higher A1C values are no better than chance at identifying patients with major complications.

#### Conclusion

Extreme diabetic neglect did not predict higher major complication rates after lower extremity fracture fixation. This suggests that surgical options should not be withheld for patients with high A1C, and that open surgery should not be automatically eliminated as an option in patients with disaster level diabetes.



# Research Week 2020

## Executive Function in Infants and Toddlers born Low Birth Weight (LBW) and Preterm: A Longitudinal Study

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### Keywords

Executive Function, Infant and Toddlers, Brain Development, Assessment

### Abstract

The goal of this study was to extrapolate early indicators of executive function (EF) from traditional infant/toddler assessments for purposes of early identification. Infants born LBW (N=99) were assessed across three age periods (6 corrected-age in months, 18 corrected age in months, and 3 years). The control group (full-term), N=41) were assessed during these same intervals. Children were administered the Bayley Scales of Infant and Toddler development (BSID-III), the Dimensions of Mastery Questionnaire (DMQ-18), and the Behavior Rating Scale of Executive Function (BRIEF-P) at age 3 years. results at age 3 showed that children in the full-term group scored statistically significantly higher on the BSID-III on all scaled and composite scores. Using multivariate analysis, we found significant differences on BSID III scaled subtests based on change scores between 6 and 18 months, and between 18 months and 3 years, children who were full-term showed significantly larger, positive average difference scores, compared to the LBW group. LBW difference scores on the motor composite and fine motor showed a negative difference, meaning the average scores decreased. Ef components extracted from the infant assessments were also significant. AT 6 months, full-term children demonstrated more attention to tasks, At 18 months, full-term children demonstrated the ability to inhibit behaviors more than their LBW and preterm peers. At age 3 years, full-term children showed higher scores in attention, working memory, and plan/organize. Key outcomes include: Early indicators of EF were identified across three age periods. Change scores indicated that children who were LBW and preterm lost skills at 22 age periods (18 months and 3 years).



# Research Week 2020

## Struggling to Connect: Barriers and Facilitators for Community Engagement Among Recently Psychiatrically Hospitalized Veterans

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### Keywords

Suicide, Community, Veterans

### Abstract

Military veterans continue to demonstrate elevated rates of death by suicide compared with the general population. In particular, veterans with a recent psychiatric hospitalization have a proximal increase in suicide risk within the first three months after discharge from acute care. Bolstering protective factors, such as social connectedness, may help decrease these risk factors and therefore suicide risk. Veterans however generally report low social connectedness and thus may have limited supportive others available following hospitalization. The goal of the current project is to develop a conceptual model of the community engagement experience among recently psychiatrically hospitalized veterans utilizing a qualitative research approach to inform future interventions.

Recently psychiatrically hospitalized veterans (N = 20) were recruited from an inpatient psychiatric unit at a large, urban, Western, Veterans Health Administration Medical Center. We designed our study using a modified Grounded Theory approach to collect qualitative data. We interviewed veterans within one week of their discharge and one month afterwards using semi-structured interviews to capture a broader range of experiences. We created analytic memos for each interview to identify initial patterns and to inform the development of our coding manual. All patterns identified within our data were confirmed through independent, inter-rater reliability coding and synthesized into a conceptual model of community engagement.

Veterans reported experiencing an overall lack of social connectedness with limited engagement in meaningful activities. We identified several patterns related to challenges (e.g. logistics), needs (e.g. tailoring activities to a specific veteran), and areas for intervention (e.g. strategies for self-disclosure) with respect to increasing community engagement following psychiatric hospitalization. Overall, our findings suggest the need for a multicomponent program to facilitate veteran community engagement that includes specific strategies to support veteran, community, and clinical stakeholders.





# Research Week 2020

## Development of OHSU's mobile application RespectForAll

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### Keywords

application, mobile, community, education, resources

### Abstract

#### Background

In April 2018, Oregon Health & Science University (OHSU) received a grant from the Oregon Department of Justice to fund initiatives that increase support and resources for people who experience sexual misconduct (harassment and gender-based violence) and discrimination. This funding included the development of a mobile application for the OHSU community.

#### Objective

Our objective was to develop a mobile application that provides useful, trauma-informed, user-specific resources and information related to incidents (sexual misconduct and discrimination) experienced by any OHSU community member and provide information on a user's responsibility to report incidents on campus.

#### Methods

We created application logic for students, faculty, and employees to identify pertinent information and resources for themselves and when helping others. We conducted semi-structured interviews with campus stakeholders to identify key application information. Several rounds of internal and external testing, semi-structured interviews, and application previews with students, faculty, and staff informed changes made to the flow, design, content, and overall interpretation. Users will have access to community resources within their zip code through the integration of 211info.org.

#### Results

An external consultant (AC) completed seven semi-structured interviews with three faculty, two staff, and two students using the web or mobile versions. The interviews were recorded and notes were drafted. Additionally, we demonstrated the app to groups of stakeholders (AAEO, Student Health and Wellness, Graduate Students). The following

themes emerged from the interviews and stakeholder demonstrations: questions about data storage, privacy and safety, use of plain language, and dissemination strategies. The mobile (Apple and Android) and web versions of the application are now available to use ([www.ohsurespectforall.com](http://www.ohsurespectforall.com)).



# Research Week 2020

## Behind the responses to Fall Prevention Motivational Interviewing: Patient perceptions about fall risks, fall prevention strategies, and self-identity

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### Keywords

Fall Prevention, Behavior Change

### Abstract

#### Background

Older adults are often reluctant to engage in fall prevention activities.

#### Objectives

Understand how older adults respond to fall prevention and identify attributes that affect their responses to fall prevention.

#### Methods

Qualitative content analysis of the brief Fall Prevention Motivational Interviews (FPMI) that were delivered in a clinical trial to older adult inpatients in a VA hospital.

#### Results

Thirty patients (mean age 72.3; standard deviation = 5.7; 93.3% male) participated in the FPMI. Participants showed various responses to fall prevention from acceptance and engagement to ambivalence to denial or giving-up. Three attributes affecting how they respond to fall prevention were: (a) their perception of fall risks, (b) their perception about fall prevention strategies, and (c) self-identity. If participants perceived that their fall risks were temporary or modifiable, they were more likely to engage in and accept fall prevention activities. If participants perceived that their fall risks were rather permanent or unmodifiable, they seemed to have difficulty accepting fall prevention or gave up from engaging in fall prevention. Participants were more willing to adopt fall prevention strategies that involve minor adjustments or that were not too obvious but expressed more resistance to adopting strategies that required major adjustment or more obvious. Finally, their response accepting or not accepting fall prevention was influenced by their perception whether the fall risks and fall prevention strategies are acceptable as their self-identity.

## Conclusion

These findings underscore the importance of understanding older adults' perceptions about fall prevention and their self-identity to better facilitate individualized approaches to engage patients in fall prevention.



# Research Week 2020

## Hold My Beer: Intoxication past the legal limit does not drive differences in acetabular fracture pattern

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### Keywords

Acetabulum, Fractures, Trauma

### Abstract

#### Purpose

Trauma patients frequently have social challenges, among them alcohol intoxication, at the time of their injury. The fracture literature does not contain any thorough analyses of injury and fracture characteristics of the intoxicated. We took shots at characterizing the fracture patterns and injury characteristics evident in intoxicated patients with acetabular fractures compared to sober peers.

#### Methods

All patients receiving unilateral acetabular fixation presenting at our Level 1 trauma facility with measured admission BAL were examined (2008-18; n=371). Charts were reviewed for demographic and injury data, including blood alcohol level (BAL) upon admission. Injury radiographs were interpreted by a fellowship trained traumatologist to classify fracture patterns utilizing the Judet & Letournel system. Intoxication status (defined as BAL >0.08) and fracture patterns were analyzed using descriptive statistics, such as contingency tables, and unpaired T-tests.

#### Results

39 patients (10.5%) were intoxicated above the legal limit upon admission with acetabular fractures. This group was younger (41 yrs v 51 yrs,  $p<0.01$ ), included more smokers (71 v 37%,  $p<0.01$ ), and experienced high energy mechanisms (e.g. motor vehicle collisions, 67% vs 49%,  $p<0.01$ ). There was no significant difference between elementary and associated patterns in the sober vs intoxicated groups (38% elementary vs 33%,  $p=0.63$ ). Additionally, there was no difference in reoperation rates at one year.

#### Conclusion

Intoxicated patients are more likely to be young smokers who are involved in high energy mechanisms than patients who abstain. There are no clear fracture patterns associated with patients who could not pass a legal sobriety test.

Total

Elementary

Associated

Intoxicated

39

15 (38%)

24 (62%)

Sober

332

110 (33%)

222 (66%)



# Research Week 2020

## using conditional adversarial networks for intelligibility improvement for dysarthric speech and laryngectomees

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### Keywords

conditional adversarial nets, speech intelligibility

### Abstract

We explored voice conversion systems to improve speech intelligibility of 1) dysarthric speech and 2) laryngectomees.

In the first case, we explore the potential of conditional generative adversarial networks (cGANs) to learn the mapping from habitual speech to clear speech. We evaluated the performance of cGANs in three tasks: 1) speaker-dependent one-to-one mappings, 2) speaker-independent many-to-one mappings, and 3) speaker-independent many-to-many mappings. In the first task, cGANs outperformed a traditional deep learning (DNN) mapping in term of average keyword recall accuracy and the number of speakers with improved intelligibility. In the second task, we showed that without clear speech, we can significantly improve intelligibility of the habitual speech of one of three speakers. In the third task which is the most challenging one, we improved the keyword recall accuracy for two of three speakers.

In the second case, we aim to improve speech of laryngectomees in term of intelligibility and naturalness. We predict the voicing and voicing degree for laryngectomees from speech spectra using a deep neural network. We use a logarithmically falling synthetic F0 for statement phrases. Spectra are converted to synthetic target spectra using a cGAN.



# Research Week 2020

## Methamphetamines & acetabular reoperation rates: Poor outcomes from the front lines

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### Keywords

Orthopaedics, Methamphetamine, Complications, Reoperation, Surgery

### Abstract

#### Purpose

Per the US Census data, the West Coast houses the region with the highest amount of substance abuse admissions for methamphetamine. Methamphetamine abuse is associated with negative surgical outcomes, particularly regarding reoperation rates and survival probability. In this study we compare the acetabular reoperation rates after 1 year in meth abusers vs. non-users.

#### Methods

A retrospective chart review was performed looking at adult patients who presented to our Level 1 trauma center between 2008-2018 undergoing a unilateral traumatic acetabular ORIF. Inclusion required documentation of methamphetamine abuse via patient report or a positive urine toxicology screen. Uni- and multi-variate logistic regressions were used to determine the association between meth use and reoperation within one year, and further investigated using a Cox proportional hazards model.

#### Results

13% (36/268) of patients who experienced acetabular fractures abused meth. On average, meth abusers were 8 years younger and sustained higher rates of high-energy mechanisms; 66% were associated patterns. The unadjusted odds-ratio of one-year reoperation in patients who use meth was OR 2.63 ( $p=0.03$ ), rising to an adjusted OR of 3.13 ( $p=0.03$ , Fig 1). The unadjusted risk of reoperation for meth abusers was 17% at 90 days and 25% at 1 year.

#### Conclusion

Per our review and analysis, surgical fixation of acetabular fractures in methamphetamine abuser showed a 3-fold increase in adjusted odds ratio for 1-year reoperation rates. We recommend this data be used by surgeons going forward to help



with planning and discussion of how they can best approach operating on this high-risk population.



# Research Week 2020

## Is the Iliac Cortical Density Similarly Positioned in the Developing Pelvis?

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### Keywords

Pediatric, Pelvic-Ring-Fracture, Percutaneous-Iliosacral-Screw, Development, ICD

### Abstract

#### Purpose

Pelvic ring injuries in children at times require stabilization with percutaneous iliosacral (IS) screws. Iliac cortical density (ICD) is a critical fluoroscopic landmark in adults for safe placement of IS screws to avoid L5 neurovascular injury. It is unclear whether the classic ICD landmark is located similarly in the developing pelvis. The purpose of the study is to 1) evaluate if ICD is a useful fluoroscopic landmark in the pediatric population and 2) determine how ICD changes as the pelvis matures.

#### Methods

Consecutive pelvic CT scans in children aged 0-16 without pelvic ring injury were obtained at a single institution from 1/2017-6/2019. Patients with sacral dysmorphism, non-ambulatory status, or neuromuscular disorders were excluded. CT scans of 181 patients were reconstructed into lateral radiographs in order to measure the ratio of ICD height to S1 vertebral height at the anterior, midpoint, and posterior vertebral body.

#### Results

In all ages, ICD corresponded to sacral alar slope when correlated on CT. Mean height of S1 increased significantly with each age group for all locations ( $p < 0.001$ ), as well as the corresponding measure of ICD ( $p < 0.001$ ). There was a greater ratio of ICD overlap with the S1 body with each increasing age group. The mean anterior ICD to S1 height ratio was 22% in 0-2yr group compared to 55% in 15-16yr group ( $p < 0.001$ ). Excellent inter-rater (0.90) and intra-rater (0.89) correlation coefficients were observed among measurements.

#### Conclusion

ICD is a useful fluoroscopic landmark for safe IS screw placement in the non-dysmorphic pediatric pelvis. Overlap of ICD to S1 vertebral body increases significantly with age, subsequently increasing the safe zone for percutaneous IS screws. For very young patients

requiring IS screws, the margin for safe placement is lower when utilizing ICD as an intraoperative guide; therefore, navigation may be justified when placing IS screws in these children.



# Research Week 2020

## The development of initial nursing education in China: Scale, structure and distribution

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### Keywords

Nursing education, Scale, Structure, Distribution, Nursing shortage

### Abstract

#### Background

China is facing a nurse shortage. Strengthening the development of initial nursing education as the primary preparation for a robust nursing workforce must be addressed.

#### Objective

To describe the development of nursing education in mainland China and to analyze related issues.

#### Method

We analyzed the scale, structure and distribution of nursing education programs and recruitment from 2006 to 2017 in mainland China and compared them with the scale of the nursing workforce over the same time period.

#### Results

Initial nursing education in China has developed rapidly but geographic distribution is unbalanced, and the overall educational levels need to be upgraded. In 2017, the recruitment was 501,512 which consists of 50,590 (10.09%) in baccalaureate programs, 197,409 (39.36%) in advanced diploma programs and 253,513 (50.55%) in secondary diploma programs. The recruitment has stabilized at a more than 500,000 a year since 2009. The recruitment to secondary diploma programs continues to decline. Even with rapid growth, there are only 2.74 nurses per 1000 population in 2017. That same year, the recruitment of nursing students in each region per 1000 population was 0.26 (east), 0.40 (middle), 0.49 (west), and 0.34 (northeast), while the number of registered nurses per 1000 population had the opposite pattern (2.88 (east), 2.63 (middle), 2.69 (west) and 2.62 (northeast)).

#### Conclusions

Nursing education in China has developed rapidly but significant issues remain. We suggest monitoring the development of nursing education continuously, increasing recruitment to advanced diploma and baccalaureate programs to upgrade the overall initial education preparation of nurses, adopting multiple targeted strategies to promote the positive development of nursing education, balance the distribution of graduates, and improve recruitment and retention strategies to ease the nurse shortage throughout China.



# Research Week 2020

## Acetabular Fracture Pattern is Altered by Pre-injury Sacroiliac Joint Autofusion

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### Keywords

Acetabulum, sacroiliac joint autofusion, fracture pattern, high anterior column

### Abstract

#### Purpose

Acetabular fractures are complex injuries where force vector influences the resulting fracture pattern. There is an undescribed but anecdotally observed connection between preexisting autofused sacroiliac joints (aSIJ) and high anterior column (HAC) injuries. This study sought to characterize acetabular fracture patterns in patients with and without aSIJ.

#### Methods

All adult patients who received unilateral acetabular fixation at our Level 1 academic trauma facility (2008-18) were reviewed. Injury radiographs and CT scans were examined by a fellowship trained traumatologist to classify fracture patterns and identify preexisting aSIJ. Fracture types were subgrouped based on whether they had a HAC injury (includes: anterior column (AC), anterior column posterior hemitransverse (ACPH), or associated both column (ABC)). We performed a logistic regression to determine the association between aSIJ and HAC, adjusting for confounders using a forward stepwise regression model.

#### Results

61 of 371 patients (16%) had an aSIJ; this group was older (64 v 47yrs,  $p < 0.01$ ), male (95% v 71%,  $p < 0.01$ ), and had lower energy mechanisms (21% v 8%,  $p = 0.01$ ) and fewer smokers (19% v 45%,  $p < 0.01$ ). The most common fractures with aSIJ were AC (35%) and ABC (29%). aSIJ was associated with greater odds of a HAC injury (OR=4.97,  $p < 0.0001$ ). After adjusting for age, mechanism, injury severity, tobacco use, and sex, aSIJ remained associated with HAC fracture types (OR=2.74,  $p = 0.03$ ).

#### Conclusion

SIJ autofusion appears to affect the mode of failure in acetabular injuries; the rigid posterior ring may precipitate a HAC injury (ABC, AC, or ACPH). Surgeons should be aware of this phenomenon when classifying fractures and during preoperative planning.



# Research Week 2020

## Acetabular Surgery After-Hours: What could possibly go wrong?

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### Keywords

Orthopaedics, Trauma, fracture fixation

### Abstract

#### Purpose

Open orthopaedic trauma rooms have alleviated historical pressure to operate at odd hours but trauma centers remain busy; the effect of suboptimal conditions on outcomes of complex acetabular surgery is unknown. The purpose of this study was to investigate the association of surgical timing to medical and surgical complications after fixation.

#### Methods

Adult patients presenting to our Level 1 academic trauma facility (2008-18) receiving unilateral traumatic acetabular fixation were reviewed. "After hours" was defined a priori as surgeries where >50% of the surgical time was after 3pm to 7am, Monday-Friday & weekends, based on staffing patterns. Surgical complications (1 yr) included reoperations for infection, hardware failure, loss of reduction, posttraumatic arthrosis requiring arthroplasty, postoperative nerve palsy. Medical complications (30-days) included pneumonia, ileus, cardiac event, stroke, renal failure necessitating dialysis, death. Data was analyzed via contingency tables, uni and multivariate logistic regressions.

#### Results

167/370 operations (45%) occurred after hours by a priori definition. Overall complication rates: 12% medical; 15% surgical. No differences existed between medical (51% vs 46%) or surgical (46% vs 54%) complication rates between groups respectively. Sensitivity analysis of the break point did not reveal statistically significant differences. Few patients were operated on after 8pm, yet these patients had high combined complications exceeding 40%. This subgroup was too small to analyze independently.

#### Conclusion

Largely, surgical timing does not appear to influence complications in acetabular care. Granular examination of cases performed at the end of the day suggest high rates of



medical and surgical complications in a difficult to study sub-population. Surgeons should consider the dynamics at their own institution.



# Research Week 2020

## Assessment of beta-lactam allergies as rationale for receipt of vancomycin for surgical prophylaxis

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### Keywords

penicillin allergy, surgery, antibiotic stewardship

### Abstract

#### Background

Beta-lactam antibiotics are the drugs of choice for the majority of patients receiving antimicrobial prophylaxis in surgical procedures. Despite evidence showing low cross-reactivity between classes of beta-lactams, patients with reported allergies commonly receive vancomycin as an alternative to avoid allergic reaction. The objective of this study was to identify potentially inappropriate use of vancomycin surgical prophylaxis among patients with reported beta-lactam allergies.

#### Methods

Adult patients ( $\geq 18$  years) receiving vancomycin for surgical prophylaxis with a reported penicillin and/or cephalosporin allergy at our institution between August 2017 to July 2018 were evaluated for potential of penicillin allergy testing and/or receipt of standard prophylaxis. Surgery type and allergy history were extracted from the electronic medical record. Per our institution's penicillin-testing protocol, patients with IgE-mediated reactions  $< 10$  years ago were eligible for penicillin skin testing (PST), mild reactions or IgE-mediated reaction  $> 10$  years ago were eligible for direct oral amoxicillin challenge, and severe non-IgE mediated allergies were ineligible for penicillin allergy evaluation or beta-lactam prophylaxis.

#### Results

Among 830 patients who received vancomycin for surgical prophylaxis, 196 reported beta-lactam allergy and were included (155 with penicillin allergy alone; 21 with cephalosporin allergy; 20 with both cephalosporin and penicillin allergy). Approximately 40% of surgeries were orthopedic. Five patients were ineligible for beta-lactam prophylaxis. Per institutional protocol, 73 of 155 patients (48%) may have qualified for PST; 81 of 155 (52%) patients may have received a direct oral amoxicillin challenge. Only three patients with history of methicillin-resistant *Staphylococcus aureus* appropriately received additional prophylaxis with vancomycin and a beta-lactam.

## Conclusions

Patients with reported beta-lactam allergies often qualify for receipt of a recommended beta-lactam antibiotic. There exists an opportunity for improved beta-lactam allergy assessment as an antimicrobial stewardship intervention. Future studies should evaluate outcomes associated with beta-lactam allergy evaluation and delabeling in patients receiving surgical prophylaxis.



# Research Week 2020

## Discovering drug targets and virulence factors by mapping the lipid metabolism of the pathogenic fungus *Histoplasma capsulatum*

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### Keywords

Lipid metabolic map, drug target, virulence factor, fungal infection, multi-omics

### Abstract

Lipids are major components of biological membrane, energy storage molecules and cell signaling transducers. Therefore, not surprisingly, lipids play major function in host-pathogen interactions and are frequently targeted for drug development. Seeking to better understand the function of lipids in fungal pathogenesis and identify potential drug targets, we performed a comprehensive analysis of the *Histoplasma capsulatum* lipid metabolic pathway by integrating proteomic and lipidomic analyses. This analysis resulted in mapping of 5 major lipid metabolic pathways, 19 lipid subclasses and 371 individual lipid species. We demonstrate that the *H. capsulatum* fatty acid desaturation and sphingolipid metabolism diverge from *Saccharomyces cerevisiae* and human, being promising targets for drug development. Thiocarlide (inhibitor of fatty acid desaturases) and myriocin (inhibitor of the first step of sphingolipid biosynthesis) have minimum inhibitory concentrations of 12  $\mu\text{M}$  and 30 nM, respectively. The analysis also showed that *H. capsulatum* produces analogs of platelet-activating factor (PAF), a potent regulator of the human immune response. The structural information of the *H. capsulatum* PAF analogs was further validated by tandem mass spectrometry, ion mobility and liquid chromatographic analyses. We also demonstrated that the *H. capsulatum* PAF analogs induces platelet aggregation and the production of the cytokines interleukin-10 and tumor necrosis factor alpha. Overall, our approach led to the discovery of chemotherapy targets and the identification of an immunoregulatory bioactive lipid from *H. capsulatum*.



# Research Week 2020

## Definitive surgery? Risk factors for reoperation within 1 year after below knee amputation

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### Keywords

BKA, Amputation, Reoperation, Uncontrolled diabetes

### Abstract

#### PURPOSE

Below knee amputations (BKA) are a relatively common procedure in orthopedic patients with advanced pathology of the lower extremities due to infection, trauma, and neoplastic disease. Prior studies of outcomes following BKA have largely relied on the National Surgical Quality Improvement Program (NSQIP) database, whose 30-day postoperative window does not cover the entire at-risk period. The purpose of this study was to elucidate reoperation rates along a more clinically meaningful one-year timeline and identify risk factors for reoperation.

#### METHODS

We conducted a retrospective review of all BKAs performed by the orthopedic surgery service at our level 1 trauma center from 2008 to 2018. Patients were identified by CPT codes. Collected data included age, indication, BMI, diabetes, A1c, closure method, and substance use. Risk factors for reoperation were determined using multivariate logistic regression modeling. Survival data from time of surgery was plotted using Kaplan Meier curves.

#### RESULTS

Of 139 eligible patients, 52 (37%) underwent reoperation. The average time between surgery and reoperation was 93 days. Hemoglobin A1c was the only predictor variable identified after multiple logistic regression modeling (OR 1.07 per point,  $p=0.046$ ). Survival analysis showed that patients above a calculated A1c cutpoint of 8.1 had statistically significant greater probability of undergoing reoperation within 1 year, with fewer than 25% remaining.

#### CONCLUSION

Below knee amputation carries a high risk of reoperation within one year. Uncontrolled diabetes ( $A1c > 8.1$ ) is a major risk factor for reoperation within one year. This information

will be useful in counseling patients and setting expectations about outcomes following surgery.



# Research Week 2020

## The Quality of Self-retrieved YouTube Videos for Professional Medical Education: Qualitative and Semi-quantitative Review of the Literature

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### Keywords

Medical Education, YouTube, Literature Review

### Abstract

#### Purpose

Determine through a comprehensive review of available literature:

- 1) Is the quality of YouTube videos sufficient for professional medical education?
- 2) Are video characteristics or engagement metrics associated with quality?

#### Methods

The literature was searched for English-language studies on YouTube video quality for medical student and physician education. The primary outcome was scores on externally and internally developed quality rating tools for the assessment of video educational quality. Secondary outcomes included subjective global ratings of video fitness for medical student and physician education and the association of video characteristics (likes, views, search return order, author type) with the primary outcome.

#### Results

Following inclusion and exclusion, 32 studies were included in the final analysis; 3 studies utilized an externally validated rubric, 20 utilized an internally derived rubric, and 12 utilized a qualitative assessment of quality; several studies utilized more than one evaluation tool. Studies using externally validated rubrics had average scores of 1.32/4, 26/80, and 1.69/5 as assessed by GQS, Discern, and JAMA respectively. Studies using internally derived rubrics had a mean content score of 44% with a range of 10% to 71%. Studies using qualitative review found variable levels of accuracy, comprehensiveness, and usefulness. Video engagement metrics (likes, views, search return order) and author type were not shown to correlate with video content quality.

#### Conclusions

Lack of peer review, errors in presentation of medical topics, and suboptimal search algorithms render search results for medical content on YouTube inadequate for professional medical education. Video engagement metrics and author type are not reliable indicators of content quality. Learners may be unable to distinguish which videos are appropriate for professional medical education. The medical education community should consider peer review and other methods of quality ratings to help learner's identify appropriate video content for their professional education.





# Research Week 2020

## Effects of voluntary exercise on behavioral and cognitive performance in mice; a pilot study

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### Keywords

Running Wheel, cognition, learning, memory, mice

### Abstract

Alzheimer's disease (AD) is a neurological disorder that affects 44 million people worldwide and is the leading cause of dementia. It is characterized by memory loss, challenges with executive function, and difficulties learning and storing new information, among many other symptoms. Age is the most significant risk factor for AD, interacting with several genetic and environmental risk factors to contribute to disease manifestation. In addition to AD, age-related cognitive decline (ACD) and mild cognitive impairments (MCI) are of increasing concern with the increased longevity. There might be protective factors that can help mitigate the development of ACD, MCI, and AD. In this pilot study, we started to explore the effects of exercise as possible protective factor in human apoE mice. Voluntary wheel running, even in mild bouts, can improve cognition, memory, and executive function. This indicates that physical exercise may have some protective effect for ACD, MCI, and AD. Three-month-old male and female human apoE mice and 20-month-old wild type male mice underwent one week of home cage activity monitoring followed by a baseline analysis of muscle strength using the grip strength and wire hang tests. Subsequently, mice were provided access to running wheels for six weeks. Performance on the grip strength and wire hang tests were assessed again, followed by home cage activity monitoring for another week. Following this week of home activity testing, mice were tested for spatial and emotional learning and memory. Finally, the mice were perfused and their brains were harvested and preserved for immunohistochemical analyses. Preliminary results indicate that, as expected, wheel running improves some measures of cognition as well as general activity. A progress report on this pilot study will be presented during the Research Week. Funded partially by R21 AG065914 and RF1 AG059088.



# Research Week 2020

## Aversive learning in *C. elegans* upon *E. faecalis* infection

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### Keywords

Avoidance behavior, Host-pathogen interactions, Learning, *C. elegans*

### Abstract

*Caenorhabditis elegans*, a natural bacterivore, has proven to be a fruitful model organism for studying host-pathogen interactions, feeding behaviors, and learning. Previous studies have shown that the opportunistic human pathogen *Enterococcus faecalis* is a *C. elegans* pathogen, able to form a persistent, lethal infection in the intestine following ingestion. In addition to mounting a molecular immune response upon infection, *C. elegans* has developed avoidance strategies to escape harmful bacteria, homologous to danger avoidance seen in nearly all animals. Here, we describe both the molecular immune response and, for the first time, the behavioral response of *C. elegans* to *E. faecalis*. Immune signaling pathways come online quickly upon ingestion of *E. faecalis*. In addition, a fast form of aversive learning takes place along multiple sensory modalities in order to allow the animal to escape and avoid lethal patches of bacteria. Using the powerful genetic toolset available in *C. elegans*, along with simple behavioral analyses, we have been able to begin elucidating the neuronal and molecular pathways governing this aversive learning.



# Research Week 2020

## DNA Methylation Correlates with Network Surface Area in Discordant ADHD Twins

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### Keywords

Twins ADHD epigenetic MRI neural networks

### Abstract

Globally, attention-deficit/hyperactivity disorder (ADHD), affects children, adolescents and adults, and can cause reduced academic achievement, occupational struggles, and social disability. Past research has attempted to explain the contributions of genetic and environmental factors in the functional connectivity of the human brain using twin's studies. The variation in genetic risk factors for ADHD explain a minimal proportion of observed cases, which suggests how genes are expressed and appear to affect the likelihood of diagnosis. While differences in neural functional connectivity have been observed on ADHD and typically developing children, the extent which these epigenetic factors contribute to differential neural behavior has not been investigated. To investigate epigenetic factors, one needs a cohort of twins that has discordant ADHD diagnoses, high quality resting-state functional magnetic resonance imaging (MRI) data, and epigenetic markers. We found that methylation at specific DNA sites was significantly correlated with surface area of the visual, dorsal attention, and salience networks in the cortex. This suggest that these three networks are expressing certain genes deferentially due to environmental factors, which affects the topology of the brain and may account for diagnosis outcome.



# Research Week 2020

## Neurophysiological Correlates of Callous-Unemotional Traits in ADHD

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### Keywords

Callous-Unemotional, ADHD, ERP, EEG, Emotion, Regulation, Arousal, Heterogeneity, N170, LPP, Neurophysiology.

### Abstract

#### Introduction

Although ADHD is a highly heterogeneous disorder, some children experience difficulties not just with inattention and hyperactivity-impulsivity, but also with co-occurring emotional problems. This includes a group with elevated callous-unemotional (CU) traits and a lack of empathy. While the presence of CU traits in ADHD is well-documented, the neurophysiological mechanisms remain unclear. Here, we hypothesize that CU traits in ADHD are associated with blunted neurophysiological response to negative emotional stimuli.

#### Methods

Adolescents (ages 11-18; N=199; 96 with ADHD) underwent comprehensive diagnostic assessment for ADHD. Parents also completed the Inventory of Callous-Unemotional Traits. Teens completed an emotional go/no-go task while 32-channel EEG data were recorded. N170 and LPP event-related potential amplitudes to happy, fearful, and neutral emotional faces assessed early emotional arousal and later, regulatory processing of emotional stimuli, respectively.

#### Results

Individuals with low CU had larger N170 amplitude to fearful faces than those with moderate to high CU,  $F(2, 193)=5.46, p=.01$ , consistent with blunted early response to negative emotions. In addition, a significant ADHD\*CU interaction,  $F(2, 191)=3.85, p=.02$ , indicated that children with ADHD and high CU had larger LPP to happy stimuli than controls and children with ADHD and lower CU traits, suggesting enhanced elaborative processing of the happy stimuli.

#### Discussion

Children with high CU traits show blunted early response to fearful stimuli, consistent with literature suggesting less arousal to negative emotions in this group. The lack of interaction suggests a similar mechanism regardless of diagnosis. Children with ADHD and high CU traits also showed increased regulatory response to positive stimuli, which was not present for other groups. CU traits in the general population are not associated with dysregulated positive affect. However, the combination of under-arousal to negative stimuli and weaker regulation of positive affect may be a unique mechanism contributing to high CU in ADHD.



# Research Week 2020

## Improving Radiograph Analysis Throughput using Object Detection

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### Keywords

Radiographs, Machine Learning, Data Science, Orthopedic Surgery

### Abstract

SIGN Fracture Care International partners with surgeons in low-resource hospitals worldwide to provide access to effective orthopedic care. SIGN reaches across 52 countries and interacts with over 5,000 surgeons, but expanding their care has led to an overwhelming amount of medical data; SIGN's Online Surgical Database (SOSD) contains over 500,000 images spanning two decades and is continuing to grow. We apply machine learning tools to the SOSD to improve the throughput of radiograph analysis to assist SIGN in further expanding their reach and effectively helping surgeons and patients. We also outline a plan for future work on improving surgical outcomes using additional analyses and metadata about patients before and after surgery.

In our initial work, we used object detection methods to detect surgical implants in radiographs. From the SOSD, we generated a training set containing 2,510 radiographs with screws, nails, and plates labeled by bounding boxes. We then applied transfer learning using the Faster R-CNN architecture pretrained on the COCO dataset. Training a single model to recognize all three classes of implants gave a low average precision (AP) for the plate class, likely due to the low number of plates in our training set and the large variety of surgical plates used by SIGN-partnered surgeons. Applying standard image augmentation techniques to increase the plate count did not appreciably increase the AP of plate detection. We, therefore, trained a separate model to detect plates by redrawing the bounding boxes to account for correlations between screws and plates. This strategy increased the AP of plate detection by 75.3 percentage points. The AP of each class was 78% for screws, 93% for nails, and 89% for plates, while the sensitivity was 90% for screws, 85% for nails, and 78% for plates.



# Research Week 2020

## DNA METHYLATION ANALYSIS OF BICUSPID AORTIC VALVE IN TURNER SYNDROME

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### Keywords

Turner Syndrome, Bicuspid Aortic Valve, DNA methylation, Epigenetics, Methyl-Capture Sequencing

### Abstract

Turner Syndrome (TS) is a rare cytogenetic disorder caused by the partial or complete loss of a second sex chromosome, which occurs in 1 in 2,000 female live births. The most common cause of early mortality in TS is due to congenital heart defects. Bicuspid Aortic Valve (BAV) is the most common congenital heart defect in the general population with a prevalence of 0.5-2%. TS patients have the highest burden of BAV with a prevalence around 30% with near complete penetrance of aortic disease. It is unknown why there is such a large increase of BAV in TS. TS is associated with genome wide hypomethylation when compared to karyotypically normal female and male controls. Epigenetic alterations in BAV have been found with changes identified in circulating miRNAs and the DNA methylation profiles of patient derived aortic tissue. We hypothesize that BAV is associated with DNA methylation alterations in TS.

The purpose of this study is to investigate DNA methylation alterations when comparing 1) BAV to non-BAV in TS and 2) TS BAV to 46,XX Non-Syndromic BAV. Illumina TruSeq-Methyl Capture EPIC methylation sequencing (Methyl Capture Seq) will be performed on whole blood genomic DNA samples from 45,X TS BAV (n = 15), 45,X TS non-BAV (n = 22), and 46,XX Non-Syndromic BAV (n = 11). Capture region enrichment of these Methyl Capture Seq libraries will be performed as a quality control step. Differential methylation will be assessed using logistic regression on the whole genome tiled into 1kb regions adjusting for cell type composition using Surrogate Variable Analysis. These regions will be annotated and assessed for biological inference using transcription factor motif enrichment and resources such as DAVID, GREAT, and STRING. We anticipate that DNA methylation alterations will correlate to previously found changes in BAV and in TS.



# Research Week 2020

## Changes in the social network after a Safe Patient Handling Champions Program

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### Keywords

safe patient handling; social network analysis; champions

### Abstract

Safety champions who are best positioned to diffuse safety behaviors are commonly used in healthcare programs as a tactic to advance safety and quality improvement goals through their ability to influence peers and safety stakeholders. However, no study has documented how the safety-related interactions among co-workers change after the implementation of a Safe Patient Handling and Mobility Program (SPHM) that included champions. The program was pilot-tested at a rural critical access hospital (25 beds) in Oregon with a pre (n=38) and post (n=54) design. Social Network Analysis was applied to identify the most central workers in the flow of safe patient handling advice. Identified workers were subsequently invited to complete quality improvement and ergonomic practical training modules to become champions. We assessed changes in the network about safe patient handling interactions among peers and examined whether safety champions influence safer behaviors on their peers. Results showed that after adjusting for age, gender, and tenure, network density that represents the number of connections related to safe patient handling increased after the implementation of the program. Betweenness, which measures the level of network connectivity, also increased. An overall increase was found among all participants after the SPHM on equipment use, safety participation, and safety compliance regardless of the connection they had with champions. However, multiple regression results indicated that workers who sought advice for safe patient handling from a champion reported higher equipment use than co-workers who did not report any connection with the champions. In sum, SNA-selected champions have shown to influence safety behaviors and promote more safety-related interactions after the implementation of the program. More research is needed to assess the generalizability of these network changes.





# Research Week 2020

## Do changes in daily activity during an exercise intervention relate to improvement in motor symptoms in Parkinson's disease?

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### Keywords

Parkinson's Disease, Exercise, Rehabilitation, Mobility, Daily Activity

### Abstract

#### Introduction

Exercise interventions can improve mobility in people with Parkinson's disease (PD). Recently, it has been shown that an Agility Boot Camp intervention with Cognitive Challenge (ABC-C) successfully improved certain aspects of mobility in people with PD. However, it is unclear whether the ABC-C alters the daily activity levels of people with PD and if an individual's daily physical activity levels during the ABC-C are associated to their response to the intervention itself. This study aims to determine whether the ABC-C alters daily physical activity habits in people with PD and understand if daily activity correlates with their response to the ABC-C.

#### Design

A cross-over, single-blind, randomized control trial was employed to assess the efficacy of the ABC-C in 42 people with PD.

#### Methods

Clinical measures of disease severity (MDS-UPDRS III and PIGD) and balance were collected while subjects were off levodopa medication at baseline and after each intervention. Daily physical activity data was collected using an Actigraph sensor (GT3X) worn on the waist throughout the study (12 weeks). Outcomes measures of activity were averaged across 6-weeks of exercise and education for the following measures: step counts, Kcal, sedentary time, moderate to vigorous physical activity (MVPA). Paired t-tests were used to investigate differences after each intervention. Also, we performed a Pearson's correlation to investigate if the average activity measures during the 6-weeks of ABC-C were related to  $\Delta$ UPDRS III and  $\Delta$ PIGD.

#### Results

Subjects demonstrated significantly higher mean daily MPVA and Kcal expenditure during the ABC-C compared to education ( $p < 0.01$ ). A significant reduction in PIGD following the ABC-C was detected ( $p < 0.01$ ), but not in the total MDS-UPDRS III. The  $\Delta$ PIGD was significantly correlated with mean daily Kcal expenditure ( $r = 0.331$ ).

#### Conclusions

The ABC-C increased daily physical activity in people with PD, yielding greater mobility improvements among individuals with more severe mobility dysfunction.



# Research Week 2020

## Isl1 is Required for the Specification and the Morphological Maturation of Starburst Amacrine Cells

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### Keywords

cell fate, neurodevelopment, retina, starburst amacrine cell, transcription factor

### Abstract

During neuronal development, neuronal subtype differentiation is regulated by transcription factors (TF's) which control effector genes that define cell fate. TFs can regulate initial neuronal specification, the development of cell features (morphology, neurotransmitter expression, physiology) or both. The mammalian retina consists of 5 classes of retinal neurons with each type containing many subtypes. Specific transcriptional pathways that direct development for each subtype are unknown. The most diverse class of retinal neurons are amacrine cells (ACs), with over 45 distinct subtypes. Within the AC population, the TF Isl1 is expressed in a single subtype: starburst amacrine cells (SACs). Isl1 is also expressed in other retinal neuron classes, and pan-retinal deletion of Isl1 results in a loss of these retinal neurons, thus confounding conclusions about Isl1's role in SAC development. To examine Isl1's role in SACs, we developed two approaches to selectively delete Isl1 at distinct stages of development. The first deletes Isl1 from AC precursors using a Ptf1aCre;Isl1cKO mouse line, allowing us to examine its role in the initial specification of SACs. The second approach uses a ChATCre;Isl1cKO mouse line to delete Isl1 after SACs are specified and migrate to their correct target area, but before the completion of dendritic growth. This approach allows us to examine how Isl1 can regulate SAC-specific features. Preliminary data indicates that deleting Isl1 in Ptf1aCre;Isl1cKO results in an absence of SACs. If deleted in ChATCre;Isl1cKO, SACs adopt aberrant dendritic morphology and lamination. Together, these data suggests Isl1 is required for the initial specification of SACs and the subsequent development of proper morphological maintenance. Detailing the specific roles TFs have in neuronal subtype specification and differentiation is important for understanding how neural circuitry develops and how morphological properties contribute to overall circuit function.



# Research Week 2020

## Investigating mechanisms that connect Alzheimer's disease with circadian disruptions

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### Keywords

Alzheimer's disease; APP intracellular domain; Circadian rhythm

### Abstract

Recent research suggests that disruptions in circadian rhythms, including sleep-wake cycles, are early signs of Alzheimer's disease (AD) and may contribute to the pathological processes. The Amyloid Precursor Protein (APP) plays a key role in AD because when cleaved by  $\beta$ - and  $\gamma$ -secretase, it generates the toxic  $\beta$ -amyloid fragments. However, when  $\alpha$ -secretase activity is followed by  $\gamma$ -secretase cleavage of APP, no  $\beta$ -amyloid is produced. Interestingly both APP processing pathways produce the same C-terminal APP intracellular domain (AICD), which has been linked to transcription regulation. Previous studies in *Drosophila* have shown that overexpression of  $\alpha$ -secretase,  $\beta$ -secretase, or AICD in circadian pacemaker neurons disrupted locomotor activity rhythms. These studies suggest that the misregulation of APP processing and the consequent changes in AICD localization may contribute to the pathological processes in AD. To investigate how changes in the AICD function may contribute to AD, we used transgenic flies with induced AICD expression in circadian pacemaker neurons or mushroom body neurons. We determined that AICD overexpression caused a shortened lifespan, a decline in locomotor performance, and disrupted rhythmic activity in addition to increased sleep fragmentation (shorter but more sleep bouts). To study the subcellular localization of the AICD, transgenic flies expressing the fly or human APP tagged with GFP at the N-terminus and RFP at the C-terminus were used to follow cleavage products in pacemaker neurons *in vivo*. We found that the levels of nuclear AICD change during the day, with little AICD detectable in nuclei during the daytime while it accumulated in the nucleus in the night. Furthermore, the pattern of AICD nuclear localization is disrupted in aged flies and flies overexpressing secretases. Together, these data suggest the AICD as a functional link between AD and circadian rhythms, providing the basis to investigate whether similar mechanisms contribute to AD pathology in humans.



# Research Week 2020

## Species level bacterial classification of the human bladder microbiota.

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### Keywords

Human microbiome, bacteria, classification, bladder

### Abstract

It has been recently established that the human bladder contains a bacterial community not associated with acute infection. This discovery of the bladder microbiota naturally leads to the question of its influence on the health of the host. Recent results have shown that changes in the composition of the bladder microbiota are associated with bladder disorders. For example, studies have identified characteristics in the urinary microbiota that are associated with symptom severity of urgency urinary incontinence (UUI) and response to the common UUI drug treatment solifenacin. These studies collectively provide evidence that the bladder microbiota is clinically relevant and warrants further investigation.

Understanding the changes of the bladder microbiota and their relationship to human health requires the identification of the bacterial species. Common identification methods avoid culturing bacteria, and instead rely on the comparison of variable regions of the bacterial 16S ribosomal gene sequence obtained directly from biological samples. However, these methods are limited to resolving bacterial identity to the genus level, and obscures the true relation of the bladder microbiota to the host.

Recently, several new approaches to bacterial identification have become available which may improve resolution to the species level. Thus, our primary aim was to determine if species-level identification of bladder microbiota is currently possible using subsequences of the 16S ribosomal gene sequence. We evaluated the ability of taxonomic classifiers to correctly classify 16S ribosomal sequences from bladder microbiota when used with different publicly available databases and taxonomic classifiers. We further evaluated several 16S rRNA gene variable regions for their ability to accurately distinguish between urinary bacterial species. We show that species-level bacterial identification is possible with currently available resources. Our findings allow future studies of the bladder microbiome to understand the effect of changes in species diversity on the health of the human host.



# Research Week 2020

## The Impact of Lee Silverman Voice Treatment (LSVT® LOUD) on self-perception in individuals with Parkinson disease

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### Keywords

Parkinson's, dysarthria, communication, self-perception, voice therapy

### Abstract

#### Background

Individuals with Parkinson Disease (PD) often present with hypokinetic dysarthria which can impact intelligibility, ability to communicate with friends and family, and participation in socialization. Research has shown that PD may also impact how patients perceive themselves as communicators with specific negative impact on their sense of control, confidence, getting their message across, sense of adequacy, and independence. These changes in communication can lead to withdrawal and social isolation. Voice and speech deficits are frequently treated with Lee Silverman Voice Treatment (LSVT), an intensive 4-week program of voice therapy, which is regarded as the most well-researched, efficacious treatment for these symptoms. Although numerous studies have been published reporting acoustic and perceptual findings, none have assessed the impact of treatment on how patients perceive themselves. This is the first study to address changes in self-perception after LSVT in patients with PD.

#### Methods

Twenty-two individuals with idiopathic PD completed a self-perception questionnaire before and immediately after completing LSVT.

#### Results

Results indicated that there were significant positive improvements for seven of the twenty-two items including feeling confident, patient, withdrawn, equal, clear, getting their message across easily, and being talkative. Interestingly, three of these items were specific to communication but four of them were not. There were no items that showed a worsening of any personality traits evaluated.

#### Conclusions

The results of our study indicate that participation in an intensive voice therapy program positively impacts features of how patients with PD perceive themselves not only as communicators but also more generally and promote more positive self-appraisals. These findings complement our previous findings of improved communicative effectiveness and communicative participation and suggest that LSVT may promote positive self-perception in pts with PD.



# Research Week 2020

## Visualization of Intercellular Communication Channels in a Dual-Lipid Bilayer at Near-Atomic Resolution by cryoEM

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### Keywords

CryoEM, Gap Junction, Lipid, Nanodisc

### Abstract

Intercellular communication by the gap junctions is facilitated by a unique macromolecular architecture, in which transmembrane channels directly couple the plasma membranes of neighboring cells. In each membrane, six connexin (Cx) subunits oligomerize to form a "hemichannel". Docking between extracellular (EC) domains of two hemichannels forms the complete gap junction intercellular channel. Our current understanding of gap junction structure lacks crucial information about how these channels interact with their native phospholipid environment. To address this gap in knowledge, we used lipid nanodisc technology to incorporate native connexin-46/50 (Cx46/50) intercellular channels into a dual-lipid bilayer—closely mimicking a native cell-to-cell junction. Structural characterization of lipid-embedded Cx46/50 revealed a dramatic lipid-induced stabilization to the overall channel architecture. The cryoEM images were refined to 1.9 Å resolution, providing an unprecedented level of detail for this class of protein. The connexin subunit interactions within each hemichannel are supported by clusters of hexagonally-packed lipid acyl chains. Remarkably, the lipid stabilization is exclusive to the EC leaflet and extends well beyond the annular lipid shell, indicating that Cx46/50 binds to and stabilizes lipids specifically at the EC leaflet. In addition, nearly 400 water molecules are resolved throughout the channel, which appear to cement the rigid extracellular docking interactions and stabilize the architectural integrity of these channels. 3D heterogeneity analysis of the cryoEM images identified three distinct, yet overlapping, classes of annular phospholipid headgroup configuration. We found by all-atom equilibrium MD-simulation that many states, including those captured by cryoEM, are in rapid-exchange, indicating that Cx46/50 is stabilized by a non-specific and dynamic lipid environment. These findings demonstrate the dramatic influence of the phospholipid membrane on the structure of Cx46/50, and establish a model system with which to investigate the influence of lipid composition on gap junction structure.





# Research Week 2020

## Social Factors and Their Role in Pediatric Solid Tumor Outcomes

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### Keywords

Pediatric Solid Tumors, Environmental Factors, Financial Insecurity, Housing Insecurity

### Abstract

#### Introduction

Cancer is a leading cause of disease-related mortality in children, and malignant solid tumors account for approximately 40% of childhood cancers<sup>1</sup>. Hepatoblastoma, Neuroblastoma, and Wilm's tumor are some of the most common surgically treated solid abdominal tumors in the pediatric population. There is existing literature that states that environmental factors contribute to the development of Wilm's in pediatric populations<sup>2, 3</sup>. In preliminary chart review of these three diagnoses, treatment of Wilm's tumors, in particular, had a larger incidence of verbalized social, financial, and housing stress, demonstrating a need to investigate this discrepancy. This study will investigate the role of financial, housing, and social support needs and utilized resources in the perceived and measurable outcomes of patients of these three solid tumor populations.

#### Methods

Retrospective chart review and a prospective phone call/email survey will assess how variation from treatment protocol or delays in treatment of Hepatoblastoma, Neuroblastoma, and Wilm's Tumor were impacted by social stressors. IRB approval has been obtained. Variables will include location of residence, family structure, and financial and housing insecurity status both at the time of diagnosis and during treatment. It will be analyzed with completed retrospective review of tumor staging, pathology, tumor rupture, and relapse.

#### Preliminary Results

Unfavorable clinical outcomes have occurred across all three solid tumor types, including relapse and mortality, and are sometimes associated with tumor rupture and/or unfavorable biology. There is a large incidence of reported social stressors in Wilm's tumor patients, including financial, housing, and travel burden. Further investigation will be conducted to determine the statistical significance of these social stressors in relation to patient outcomes.

## Conclusion

The goal is to better understand the often-overlooked factors that impact patient outcomes. The focus is on enhancing multidisciplinary interactions between clinicians and care teams, perhaps tailored to the specific type of solid tumor.



# Research Week 2020

## A Scientific Investigation into the Therapeutic and Adverse Effects of Cannabis

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### Keywords

Cannabis Clinical Research Public Health

### Abstract

Amid spreading legalization of cannabis nationwide, the use of the drug for medicinal or recreation purpose alike is becoming increasingly commonplace. From customized cultivation practices to pharmaceutical developments, cannabis has changed from an illicit substance to a drug used for purposes of both therapy and indulgence. More data are becoming available pertaining to drug pharmacodynamics and pharmacokinetics, which may help guide clinical practices, and better define intoxication, toxicity, and safety profiles. Scientific research of varying quality highlights treatment with cannabis for symptoms related to chronic pain conditions, multiple sclerosis, seizure disorders, and HIV- and cancer-related sequelae, among others. Research also of various quality points to potential acute and chronic health effects associated with cannabis use that infer many clinical and public health implications, often disproportionately affecting vulnerable populations. Possible adverse effects may impact, but are not limited to, psychiatric, cardiovascular, pulmonary, and neurological domains, as well as the ability to operate a motor vehicle. Many therapeutic and side effects appear dose-dependent, though adverse effects are more likely to occur with cannabis dependence or abuse. The purpose of this conceptual framework is to briefly explore the pharmacology, demographics, and systematically-weighted evidenced-based therapeutic and adverse effects of cannabis (using the Scottish Intercollegiate Guidelines); highlight clinical, individual, and public implications related to cannabis use, dependence, and abuse; and identify gaps in the literature that could influence research in the future.



# Research Week 2020

## Effects of Immunopotential and Demyelination on Microglial Activation and Neuronal Injury in Two Genetic Mouse Models

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### Keywords

Multiple Sclerosis, Oligodendrocyte, Microglia, Inflammation, Neurodegeneration

### Abstract

Multiple Sclerosis is an inflammatory demyelinating disease of the central nervous system (CNS) in which the degeneration of axons causes cumulative disability. The relative contribution of myelin loss and inflammation to axonal degeneration was studied in a novel transgenic mouse model of demyelination. *Myrf*, a gene necessary for myelin production, was knocked out from mature oligodendrocytes. The density of activated microglia in the optic nerve was measured during acute demyelination, following remyelination, and in aged mice. A sustained inflammatory reaction was seen at all time points following demyelination relative to wild-type mice. Inducible nitric oxide synthase (iNOS) was not noted to be strongly expressed in the knockout mice, contrary to existing autoimmune models and pathologic analyses of human multiple sclerosis tissue. Immune boosting with intraperitoneal lipopolysaccharide (LPS) injections was used to induce microglial activation within the CNS as demonstrated by the upregulation of genes encoding known pro-inflammatory cytokines and iNOS. To assess if the additive insults of a heightened microglial cytokine response and demyelination could cause neurodegeneration, immune boosting was then used in a second mouse model in which remyelination is prevented following demyelination by knocking *Myrf* out of both mature oligodendrocytes and oligodendrocyte precursors. No statistically significant differences in neuronal injury, indicated by the activation of the stress pathway culminating in the phosphorylation of C-Jun, or outright neuronal loss indicated by the density of RBPMS-positive retinal ganglion cells (RGCs) were seen following LPS injection. However, demyelination coupled with impaired remyelination was sufficient to phosphorylate C-Jun suggestive of damage to these neurons with demyelination. Although microglial activation is intensified by both demyelination and LPS injection independently, together they were not enough to cause neurodegeneration within the visual system in this model.



# Research Week 2020

## Associations between urinary bacterial load and UUI symptoms

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### Keywords

urinary microbiome, urgency urinary incontinence, bacterial load, quantitative microbiome profiling

### Abstract

Women are impacted twice as likely as men by urgency urinary incontinence (UUI) with nearly one-third of women suffering from UUI in their lifetime. The etiology of UUI is complex, but evidence suggests that shifts in the normal urinary microbiome may play a role in UUI. We aim to understand whether women with UUI have different urinary bacterial loads compared to women without UUI and whether this is correlated with severity of UUI symptoms.

Our prospective cohort study compares urinary microbiome in women with and without UUI. We recruited 25 women with and 36 without UUI between the ages of 45-85. UUI was defined as daily urinary leakage with urgency. Women with known neurological conditions, active urinary tract infections, recent antibiotic use and symptomatic pelvic organ prolapse were excluded. UUI severity was measured using the ICIQ-OAB symptom questionnaire. Bacterial load was estimated from a random sample of 50 catheter-collected urine specimens using SytoBC and flow cytometry.

There was no significant difference between cases and controls in menopausal status, sexual activity, or comorbidities. Cases were slightly older (59.4 vs 53.1,  $p=0.05$ ), more likely to have had a hysterectomy ( $p=0.03$ ), use estrogen products ( $p=0.001$ ), and had higher BMI (29.6 vs 24.9,  $p=0.003$ ). Average bacterial load was doubled in women with UUI compared to women without UUI (8,749±6,883 bacteria/mL in UUI, 4,121±4,993 in controls,  $p=0.01$ ). Furthermore, we identified a significant negative correlation between bacterial load and symptom severity as measured by the ICIQ ( $r=-0.63, p=0.02$ ).

This study provides evidence that women with UUI have significantly higher urinary bacterial load, but the higher bacterial load was associated with less severe symptoms. Larger bacterial load in women with UUI symptoms may represent a mix of both pathogenic and commensal bacteria and that symptom severity is dependent on proportion between these two types of bacteria rather than the overall abundance



# Research Week 2020

## How Undergraduate Medical Students Identify and Respond to Educational Deficits

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### Keywords

Academic resilience,

### Abstract

#### BACKGROUND

Like many medical schools Oregon Health and Science University (OHSU) has shifted towards competency-based education (CBE). CBE relies on frequent testing and formative assessment to ensure knowledge, skill, and professional benchmarks are reached. When a benchmark is not reached, OHSU uses assessment data to focus the remediation process on specific learning gaps. However, there is no mandatory longitudinal program in place for learners who face repeated academic adversity. The goal of this study was to determine: 1) How students identify their learning gaps 2) What resources students use to address learning gaps 3) The association between past adversity and resilience in undergraduate medical students.

#### METHODS

An anonymous cross-sectional survey was emailed to all OHSU medical students. Survey sections: 1) Demographics 2) Past academic & career adversity 3) Perspective on OHSU academic support 4) Modified Academic Resilience Scale. Students were grouped into Low Adversity (LAG) and High Adversity (HAG) groups for quantitative analysis with independent samples t-test, Chi Square & Fisher's Exact Test.

#### RESULTS

Being white was associated with the LAG. Having dependents or a prior career was associated with the HAG. The HAG was more likely to have experienced persistent knowledge gaps, have remediated one or more blocks, or have had environmental/social circumstances that contributed to their adversity in medical school. There was no statistical difference in overall resilience score between the HAG and LAG.

#### CONCLUSIONS

Diverse student populations (racial/ethnic minorities, students with dependents & students with prior careers) make up a greater percentage of the HAG than the LAG, yet

both groups are equally resilient. Academic adversity status is not associated with a lack of resilience. The HAG identified different resource needs than the LAG, notably additional support for diverse student populations. Remediation programs should take an individualized longitudinal approach with students who face repeated academic adversity.



# Research Week 2020

## The Use of Acute Normovolemic Hemodilution in Pediatric Cardiac Surgery

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### Keywords

Acute normovolemic hemodilution, cardiopulmonary bypass, congenital heart surgery

### Abstract

#### Background

Acute normovolemic hemodilution (ANH) is considered safe and effective in decreasing perioperative transfusion in pediatric populations undergoing high blood-loss surgeries. We sought to determine the association between ANH and the intraoperative use of allogeneic blood products in pediatric cardiac surgery patients.

#### Methods

Single-center cohort study including pediatric patients between 0 and 36 months of age undergoing surgical repair or palliation of their cardiac defect with the use of cardiopulmonary bypass between November 2013 and November 2014. Our primary endpoint was the volume per kilogram of body weight of any blood product administered. Secondary endpoints were postoperative bleeding, coagulation profile, creatinine, vasoactive support, duration of mechanical ventilation, and hospital stay.

#### Results

Fifty patients met eligibility criteria and were included. Of those 7 were exposed to ANH, while 43 patients were treated according to usual care. Baseline characteristics were similar in both groups. After adjustment for baseline characteristics including age, American Society of Anesthesiologists (ASA) classification, and Risk Adjusted Congenital Heart Surgery score, ANH was associated with reduced administration of allogeneic blood products, with the mean difference between groups of 57.5 mL/kg (95%CI:34.8,80.2). The ANH group had lower blood losses at 6 and 24 hours postoperatively. There were no differences in the duration of ICU or hospital stay.

#### Conclusions

We found a reduction in the administration of blood products and lower postoperative blood losses associated with the use of ANH in pediatric cardiac surgery patients. The data



suggest that ANH might be beneficial in reducing perioperative morbidity in this patient population.



# Research Week 2020

## Investigating cell migration inducing and hyaluronan binding protein in central nervous system development and disease

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### Keywords

Extracellular Matrix, Hyaluronic Acid, CEMIP, Myelination, Oligodendocytes

### Abstract

Myelin ensheathes axons and increases their conduction velocities. In the central nervous system (CNS) myelin is produced by oligodendrocytes (OLs) that differentiate from oligodendrocyte progenitor cells (OPCs) throughout life. Demyelination and neurodegeneration are observed in many forms of white matter injury and disease, one of which is multiple sclerosis (MS). OPCs accumulate and fail to differentiate into OLs within MS lesions, inside which there is an increase in the levels of extracellular hyaluronic acid (HA), a linear glycosaminoglycan polymer that can be mega-Daltons in size. HA fragments produced by the enzymatic digestion of high molecular weight HA have been shown to inhibit OPC differentiation and myelin formation. There is debate as to which specific hyaluronidase generates these smaller, inhibitory HA fragments. One promising candidate, CEMIP (cell migration inducing and hyaluronan binding protein), is expressed by OPCs and has increased expression levels in MS and an MS animal model called experimental autoimmune encephalomyelitis (EAE). Increased CEMIP expression leads to the breakdown of extracellular HA; this activity is blocked by a selective hyaluronidase inhibitor that was also shown to promote OPC maturation and remyelination in an animal model of white matter injury. Furthermore, increased CEMIP expression inhibits the differentiation of OPCs to OLs in vitro. Future studies will investigate if the HA fragments produced by CEMIP inhibit OPC differentiation and myelin formation, as well as if inhibition of CEMIP activity induces remyelination in white matter lesions and EAE. These studies could lead to the identification of CEMIP as a new therapeutic target to promote functional remyelination in a variety of demyelinated lesions, such as preterm white matter injury and MS.



# Research Week 2020

## The Prevalence of Swallowing Problems in Patients with Parkinson's Disease Prior to Deep Brain Stimulation

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### Keywords

Parkinson's Disease, Deep Brain Stimulation, Surgery, Swallowing

### Abstract

#### Background

Parkinson's Disease (PD) is a progressive neurodegenerative disorder affecting over 10 million people worldwide. Swallowing problems are common and aspiration pneumonia is the leading cause of death in this population. Deep brain stimulation (DBS) is a surgical method for managing the motor symptoms of PD when pharmacological management begins to fail. As DBS may have a deleterious effect on swallowing, it is important to identify baseline dysfunction, but no consensus regarding screening for abnormalities exists. This study was undertaken to identify the prevalence and characteristics of abnormal swallowing function prior to DBS.

#### Method

57 patients with idiopathic PD and no confounding medical conditions were examined consecutively prior to DBS. The patients were predominantly male (70%) with an average age of 65 years and an average PD duration of 10 years. Three screening measures, including the Swallowing Disturbance Questionnaire (SDQ), Peak Cough Flow (PCF), and the Timed Water Swallow Test (TWST), were completed prior to undergoing swallowing evaluation on videofluoroscopy.

#### Results

The prevalence of abnormal findings was as follows: 35% had abnormal symptoms on the SDQ; 45% had abnormal swallowing efficiency and 23% had aspiration symptoms on the WST; 57% had abnormal cough strength on the PCF; 35% had reduced airway protection and 18% had aspiration on videofluoroscopy. None of the screening measures was associated with reduced airway protection or aspiration on videofluoroscopy. Of the demographic and disease-related characteristics, only age was associated with reduced airway protection ( $r = .278$ ,  $p = .036$ ) and aspiration ( $r = .301$ ,  $p = .023$ ).

## Conclusions

Abnormal swallowing function is common in patients about to undergo DBS. Unfortunately, no screening measure we utilized significantly predicted abnormal airway protection on videofluoroscopy. As such, radiographic testing may be the most appropriate standard of care for preoperative work-up, particularly in older patients.



# Research Week 2020

## Association between Plasma PCSK9 levels and Computed Topographic Coronary Artery Calcium

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### Keywords

PCSK9, coronary artery calcium, atherosclerotic cardiovascular disease

### Abstract

#### Background

Given its central role in low-density lipoprotein (LDL) metabolism, there is interest in exploring proprotein convertase subtilisin/kexin type 9 (PCSK9) as a potential circulating biomarker of atherosclerotic cardiovascular disease (ASCVD) risk. Computed tomography for coronary artery calcium (CAC) scoring provides an accurate assessment of subclinical coronary atherosclerotic plaque burden and can be used to refine cardiovascular risk estimates in individuals without symptoms of ASCVD. In this study, we assessed the correlation of cross-sectional measurements of plasma PCSK9 concentration and CAC score in individuals free of clinical ASCVD.

#### Methods

Patients were recruited at routine clinic visits with providers at the OHSU Center for Preventive Cardiology. Only patients who had previously undergone CAC scoring as part of standard of care were included. Total plasma PCSK9 levels were measured using a commercially available ELISA assay (R&D Systems). Descriptive statistics were used to describe continuous and categorical variables. Wilcoxon rank sum and fisher exact tests were used to test significant differences between variables ( $p$ -value $<0.05$ ), when appropriate. Unadjusted and adjusted multiple logistic regression models were utilized to determine odds ratios (OR) of plasma PCSK9 concentrations to predict CAC $>0$  versus CAC=0 scoring.

#### Results

Of the 189 patients included in this analysis, 106 (56.1%) were female and the mean age was 58.8 (standard deviation: 12.3) years. There were 138 (73%) patients with CAC $>0$  scoring and median overall CAC score was 75 (interquartile range [IQR]: 0-251). Median plasma PCSK9 level was 374.8 (IQR: 289.9-467) for those with CAC $>0$  versus 333.2 (IQR: 266.9-441.3) for those with CAC=0. No significant association was observed between plasma PCSK9 concentration and CAC score in either an unadjusted (OR=1.0015;  $p=0.1740$ )

or adjusted (for age, sex, body mass index, LDL-C, and statin therapy) model (OR=1.0004; p=0.8126).

#### Conclusion

Plasma PCSK9 concentration was not associated with subclinical CAC in an asymptomatic preventive cardiology clinic population.



# Research Week 2020

## Humeral shaft fracture: a cost-effectiveness analysis of fixation techniques

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### Keywords

humeral shaft fracture, open reduction and internal fixation, intramedullary nail, functional brace, cost-benefit analysis

### Abstract

#### Background

Humeral shaft fractures account for 3% of managed fractures. Historically, in the absence of neurovascular injury, open fracture, or polytrauma they have been managed non-operatively with functional bracing. An upward trend in operative fixation rates has recently emerged. Operative fixation techniques for the humeral shaft include open reduction and internal fixation (ORIF) and intramedullary nailing (IM).

Although numerous studies have compared outcomes of these treatment modalities, there is no consensus on the ideal approach for isolated fractures. Moreover, no investigation has applied a value-based lens to differentiate the cost-effectiveness of these treatments, an increasingly pertinent consideration with U.S. healthcare spending surpassing \$3.2 trillion annually. Thus, the present study applies a decision tree model to investigate the value of operative treatment for humeral shaft fracture with ORIF or IM approaches, in comparison to functional bracing.

#### Methods

A decision tree model describing treatment of these injuries is utilized. For each treatment strategy, outcomes are estimated using weighted average via systematic review of the literature; outcomes include uneventful healing, non-union and revision, symptomatic hardware removal, and deep infection requiring debridement. Weighted averages define probabilities for each decision tree node. Cost-effectiveness is evaluated using incremental cost-effectiveness ratios (ICERs), defined as the ratio of the difference in cost and difference in effectiveness of each approach, measured in dollars per quality-adjusted life-year (QALY). The model is assessed at threshold ICERs of \$50,000/QALY and \$100,000/QALY. Sensitivity analysis of all outcomes will assess cost-effectiveness of each approach across a range of outcome values.

#### Results

Ninety-three papers met inclusion criteria. Data abstraction is underway. Preliminary results will be available for Research Week.

## Conclusions

Delivering value-based care has become an elevated priority as implementation of bundled payment models continues. Synthesizing understanding of intervention cost and outcome quality, this study serves to inform optimal value-based management of humeral shaft fractures.





# Research Week 2020

## Long-term *Centella asiatica* treatment improves cognition, increases synaptic and antioxidant markers and reduces plaque burden in $\beta$ -amyloid overexpressing mice

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### Keywords

beta-amyloid, NRF2, antioxidant, synaptic plasticity

### Abstract

#### Objectives

We have previously reported that short-term treatment with the water extract of *Centella asiatica* (CAW) activates the endogenous antioxidant response pathway and ameliorates cognitive deficits without altering plaque burden in mouse models of  $\beta$ -amyloid ( $A\beta$ ). Here we investigate whether prolonged CAW exposure in 5xFAD mice has similar effects on cognitive function and  $A\beta$  pathology, in addition to markers of antioxidant response and synaptic plasticity. We also used primary neurons isolated from 5xFAD mice to explore how the antioxidant response pathway contributes to these effects.

#### Methods

4-month-old male and female 5xFAD mice and wild-type (WT) littermates were treated with CAW (2g/L) in their drinking water for three months prior to one month of behavioral tests of learning, memory and executive function after which mice were sacrificed and expression of antioxidant and synaptic genes was assessed and  $A\beta$  plaque burden was quantified. Additionally, markers of synaptic plasticity and oxidative stress were evaluated in primary neurons treated with CAW and the NRF2 inhibitor ML385.

#### Results

Long-term treatment with CAW improved cognitive performance in 5xFAD animals. CAW also increased synaptic and antioxidant gene expression and reduced  $A\beta$  plaque burden. Interestingly, while this decrease in pathology was evident in the cortex of both male and female mice, only female animals also showed a reduction in plaque burden in the hippocampus. Additionally, CAW induced expression of NRF2-reduced oxidative

stress in primary neurons from 5xFAD animals and enhanced synaptic plasticity, but this effect was abrogated when cells were co-treated with CAW and ML385.

## Conclusion

These data indicate that long-term CAW treatment in 5xFAD mice can attenuate cognitive impairment, increase antioxidant and synaptic gene expression, and alter A $\beta$  plaque burden. This combined with the in vitro data suggest that the activation of the antioxidant transcription factor NRF2 may play an important role in these effects.



# Research Week 2020

## Pilot Feasibility and Acceptability of MBCT for Perinatal Women With Trauma History

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### Keywords

perinatal depression, mindfulness, cognitive therapy

### Abstract

#### Purpose

Postpartum depression (PPD) can have significant consequences for mothers and infants. Mindfulness-based cognitive therapy (MBCT) during pregnancy is an effective preventative intervention for PPD. However, little is known regarding the efficacy and potential mechanisms of action of MBCT for women with a trauma history. In this pilot trial, we attempted to establish the feasibility and acceptability of conducting an intergenerational translational study of the neurobiological mechanisms of action of MBCT during pregnancy for women with trauma histories.

#### Method

Pregnant women were recruited to participate in an MBCT group during pregnancy or treatment as usual (TAU). Maternal neuroimaging was completed six weeks postpartum, and infant neuroimaging was completed in the first four weeks following birth. The Maltreatment and Abuse Chronology of Exposure (MACE) and the Client Satisfaction Questionnaire — 8 (CSQ-8) were used to collect data on trauma history and participant satisfaction with their assigned group. Feasibility was calculated using percentage of attendance for greater than four MBCT sessions; acceptability was measured using the CSQ-8. Mean differences between groups on the CSQ-8 were tested using the Mann-Whitney U test.

#### Results

A total of  $N = 12$  women completed the study. Eighty-three percent met clinical cutoff for trauma history on the MACE. Four (80%) participants assigned to MBCT completed at least four groups. Mean CSQ-8 scores for the MBCT group were significantly higher than TAU,  $U = 1.500$ ,  $p = .008$ . All women and their infants eligible for an imaging session attended.

#### Conclusions

MBCT and maternal and infant neuroimaging is feasible and acceptable for pregnant women with trauma histories, who are at increased risk of PPD. These are promising results supporting further exploration of MBCT mechanisms at a neurobiological level from larger, randomized samples from this population to provide robust evidence to support this intervention.



# Research Week 2020

## A novel method for the quantification of platelet adhesion on biochemically-modified poly(vinyl alcohol) vascular grafts

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### Keywords

Vascular grafts, surface modification, platelet adhesion, thrombosis

### Abstract

The clinical standard for small diameter vessel treatment, currently, is the use of autologous vessels. However, due to limited availability and pre-surgical complications, many patients are ineligible for this treatment. In addition, synthetic vascular grafts have been shown to exhibit limited long-term patency at diameters less than 6 mm, creating a large unmet clinical need. By biochemically modifying the surface of small diameter poly(vinyl alcohol) (PVA) grafts, anti-thrombotic properties can be achieved. Previously, thrombogenicity has been investigated through an *ex vivo*, non-human primate, shunt model. However, this model only characterizes platelet attachment over the length of the entire graft, losing the ability for dynamic physical properties of the thrombus along the graft to be understood. This work introduces a novel method to quantify thrombus formation along the cross-sectional area of biochemically-modified PVA grafts.

MicroCT imaging was utilized to analyze thrombus formation within biochemically modified PVA vascular grafts. Using Amira, the physical properties of the grafts were segmented and labeled for all cross sectional voxels. The surface area and volume were then computed, and 3D renderings of the segmented features were generated for the biochemically-modified PVA grafts. Thrombus formation was then quantified for each cross-sectional area per slice over the entire length of the graft.

Through the methods established, the analysis of physical quantification of platelet adhesion was enhanced compared to previous methods and validated with direct measurement of the graft dimensions. The ability to quantify thrombus formation through microCT images along the cross-sectional area of each graft shows a novel method compared to the prior work using the *ex vivo* shunt model. Physical characteristics of the thrombus for each surface modification was compared for thrombus content and uniformity along the length.

The method developed using microCT images reflects and enhances shunt data through the physical evaluation of thrombus formation.



# Research Week 2020

## The aged rhesus macaque hippocampus exhibits previously undetected pathological tau

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### Keywords

Alzheimer's disease, aging, nonhuman primate, tau, neurodegeneration

### Abstract

Due to their genetic, behavioral, and physiological similarities to humans, rhesus macaques (*Macaca mulatta*) have long been used as a translational model in biomedical research. However, studies using very old monkeys have been impeded by lack of access to animals of advanced age. As the average lifespan of a rhesus macaque is reported to be 25 years, acquiring animals of this age can be both time- and cost-prohibitive. Our laboratory, via a collaborative pooling of resources, has access to postmortem tissue from a cohort containing some of the oldest known macaques in the world, with three animals having lived more than 40 years. Due to this unique resource, we are able to examine whether specific normative or pathological brain aging processes occur in the macaque brain. Specifically, we are interested in whether the rhesus monkey naturally develops Alzheimer's disease (AD) phenotypes. For decades, it has been known that macaque species naturally accumulate amyloid beta plaques as they age, similarly to both healthy humans and those with AD. These plaques, however, are controversial in terms of their contribution to cognitive deficits involved in aging and AD. Tau is another major hallmark of AD, with intracellular hyperphosphorylated tau tangles correlating much more strongly with declining cognition, and is historically undetected in even the oldest monkeys. Here, using immunohistochemistry with clinically-validated antibodies against phosphorylated tau, we present novel evidence of multiple forms of clinically relevant tauopathy in the aged rhesus macaque entorhinal cortex and hippocampus. Taken together, the rhesus monkey exhibits far more of the human brain aging condition than previously presumed. Therefore, it represents a highly appropriate translational animal model in which to investigate mechanisms that underlie the normal and pathological human brain aging, as well as to test pharmacologic, metabolic, and lifestyle interventions aimed at targeting physiological AD etiology and symptomology.



# Research Week 2020

## Plantarflexor Muscle Fatigue in People with Multiple Sclerosis Impairs Standing Balance

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### Keywords

Multiple Sclerosis, Fatigue, Biosensors

### Abstract

#### Background

People with Multiple Sclerosis (PwMS) experience fatigue differently than those without MS due to weakness, ataxia, and spasticity. This fatigue can play a role in balance during activities of daily living. Poor balance control poses a health concern for PwMS, resulting in falls, limiting independence, and reducing quality of life.

#### Objectives

To test the effects of motor fatigue on static postural balance control in PwMS compared to healthy controls (HC).

#### Methods

Eighteen PwMS and fifteen age-matched HCs underwent a fatiguing protocol consisting of a sustained maximum voluntary contraction of plantarflexor muscles for one minute. Plantarflexors were chosen for the fatigue assessment as these muscles significantly contribute to ankle strategy utilization in standing balance control. Standing balance data were collected immediately before and after implementing the fatiguing protocol using a single APDM wearable sensor placed on the lumbar spine to objectively capture postural sway (PS). Balance was measured as the area of PS while standing eyes-open on a flat firm surface for 30 seconds per trial.

#### Results

Increases in trunk sway during static PS tests were found statistically significant in PwMS after the fatiguing task. PwMS showed the greatest changes post-fatigue in trunk range of motion, velocity, jerk and the root mean square of the sway angle in the coronal plane after the fatiguing protocol ( $p < 0.05$ ), while HCs showed no significant changes.

#### Conclusion

Observed mediolateral sway instead of anteroposterior sway may be due to the unilateral fatiguing protocol. The increase in trunk sway in PwMS after PF fatiguing is consistent with impaired control of PS. This increased truncal sway also indicates decreased dependence on ankle strategy and increased hip strategy use to control stance posture. This type of "truncal ataxia" in PwMS exhibits a shift to using hip torque rather than fatigued ankle torque to control standing balance.





# Research Week 2020

## A Streamlined Approach to Using NIH's Updated Diversity Guidelines in a STEM Enrichment Program

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### Keywords

diversity, STEM, education, evaluation, demographics

### Abstract

The National Institutes of Health (NIH) guidelines defining populations that are underrepresented in biomedical research fields have changed four times since early 2018. The most recent guidelines include nine criteria for underrepresentation. To qualify, a person must be from a racial or ethnic minority or have a disability, or meet two of the other seven criteria: experience with homelessness, experience with foster care, eligibility for free/reduced-price lunch, status as a first-generation college student, eligibility for Federal Pell grants, eligibility for WIC, or come from an underserved area. The NIH provides a tool to assess an individual's qualification for only one criterion (i.e., underserved area) of the nine. Without asking applicants directly for extensive and sensitive demographic data, it is challenging to determine whether a person qualifies as underrepresented under NIH guidelines.

Diversifying STEM and providing opportunities to historically underrepresented populations remain national priorities, yet the aforementioned barriers make it difficult to comprehensively define "underrepresented" and then translate those definitions to an actual use case in a way that is not overly demanding of the applicant. For STEM enrichment programs aimed at supporting marginalized researchers, it is especially important to use consistent, inclusive, and minimally intrusive methods when determining if applicants qualify as marginalized.

We used the updated NIH guidelines on underrepresented populations to classify the statuses of 428 undergraduate students participating in a STEM enrichment program (BUILD-EXITO) based at Portland State University. Through simplified data-collection processes, we were able to assess participants on seven of the nine NIH criteria. (The two excluded criteria—eligibility for WIC and free/reduced-price lunch—require more extensive data-collection methods). The resulting streamlined approach can be used in a variety of applications to determine adherence to NIH diversity guidelines. Nuanced instances where neither our algorithm nor NIH guidelines fully identified underrepresented students will also be addressed.



# Research Week 2020

## Development of an anatomic landmark-based measurement of the Achilles tendon

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### Keywords

Achilles, rupture, repair, measurement

### Abstract

#### Introduction

A greater degree of Achilles tendon lengthening during surgical correction has been correlated with worse clinical outcomes. MRI and ultrasound techniques have been validated in measurement of Achilles tendon. We sought to develop a reproducible and accurate measurement technique utilizing the manual palpation of anatomic landmarks that will be cost effective and convenient to perform, particularly intraoperatively.

#### Methods

The length from the medial head of the gastrocnemius to the bottom of the non-compressed heel pad was measured on both lower legs of 10 healthy subjects by three raters using the ultrasound and anatomic landmark-based techniques. The measurements were performed by three raters for inter-rater reliability and repeated one week later for intra-rater reliability. Ultrasound measurements had excellent inter-rater (0.93) and intra-rater (0.82) correlation coefficients, while good inter-rater (0.76) and intra-rater (0.86) correlation coefficients were observed among anatomic landmark-based measurements. Achilles tendon length measured with ultrasound and anatomic landmark-based techniques were compared using a paired t-test.

#### Results

The anatomic landmark-based technique produces longer measurements of the Achilles tendon (23.2 cm (sd 2.6 cm)) compared to measurements made using ultrasound (22.4 cm (sd 2.6)) ( $p < 0.001$ ). On average, the anatomic landmark-based technique measures 0.8 cm (95% Confidence Interval: 0.4, 1.2) longer than the ultrasound technique. The intraclass correlation coefficient between the anatomic landmark-based and ultrasound measurements is 0.90.

#### Conclusions

While the anatomic landmark-based technique produces a longer measurement of the Achilles tendon, it may still be a reproducible measurement tool. If the change in tendon length is the variable of interest in Achilles tendon repair (ATR), this technique may be a valid and simple way to monitor that variable. Comparison with MRI may be warranted to confirm the accuracy of the anatomic landmark-based measurement and set the stage for evaluation of this technique in the operating room in subjects undergoing ATR repair.



# Research Week 2020

## A neural projection from the parastrial nucleus to the dorsomedial hypothalamus contributes to the activation of BAT thermogenesis

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### Keywords

Thermoregulation, BAT, PS, RPa, DMH

### Abstract

The parastrial nucleus (PS) is a lenticular formation located beneath the anterior commissure in the preoptic area. Anatomic and physiologic studies have demonstrated: 1) a direct projection from PS neurons to the dorsomedial hypothalamus (DMH), 2) increased cold-evoked Fos expression in PS, and 3) infected neurons in PS after injection of Pseudorabies virus into the interscapular brown adipose tissue (iBAT). However, it has not been assessed whether a specific population of PS neurons projecting to DMH is involved in the modulation of iBAT thermogenesis. We aim to determine if PS projecting neurons to DMH are selectively responsive to cold or warm stimuli, and if pharmacologic manipulation of these neurons activates iBAT thermogenesis. Two groups of male rats, previously injected with Cholera Toxin subunit-b (CTb) in DMH and FluoroGold (FG) in raphe pallidus (RPa), were respectively exposed to warm and cold ambient temperature to elicit Fos expression. A third group of rats, instrumented for recording iBAT sympathetic nerve activity (SNA) and skin and core temperature, were maintained at 38°C. Pharmacologic manipulations of PS were performed to determine whether PS projecting neurons to DMH modulate iBAT thermogenesis. Immunohistochemical analysis confirmed the existence of direct projections from PS to DMH and RPa, as well as increased Fos expression in the PS of cold-exposed rats compared to the warm-exposed group. We found that the majority of CTb-immunoreactive (ir) neurons and a small population of FG-ir neurons in PS express Fos in cold-exposed rats, suggesting the existence of an excitatory input from PS to DMH and RPa, most likely involved in the control of iBAT thermogenesis. This is consistent with the increased iBAT SNA and temperature observed after bilateral injection of the GABA-A antagonist bicuculline or NMDA in PS.



# Research Week 2020

## Low-dose methotrexate safety in dermatologic disease: incidence and timing of laboratory abnormalities during the first year of therapy

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### Keywords

methotrexate, lab monitoring, dermatology

### Abstract

#### Introduction

Methotrexate is a commonly used medication for inflammatory and autoimmune disorders. Dermatologic literature recommends frequent laboratory monitoring due to the potential of serious side effects although data supporting this recommendation is lacking. In this study, we aimed to identify the incidence and timing of laboratory abnormalities in a cohort of patients prescribed low-dose methotrexate during their first year of therapy.

#### Methods

Utilizing a web-based discovery tool available through Oregon Clinical and Translational Research Initiative (OCTRI), we identified patients who were seen at OHSU between May 2004 and October 2018 who were prescribed low-dose methotrexate (defined as 5-25 mg per week). Electronic health records were reviewed, and baseline and follow-up laboratory data over the first year of therapy were recorded. Changes in baseline laboratory values were identified and categorized using The Common Terminology Criteria for Adverse Events version 5.0 grading system.

#### Results

1376 patients who initiated low-dose methotrexate between 2004-2018 met criteria for inclusion in our study. Low-dose methotrexate-related grade 2-4 lab abnormalities developed in 2.3% of patients with normal baseline lab values and 10.4% of patients with abnormal baseline lab values (odds ratio = 5.0, 95% CI: 2.9 to 8.4;  $P < 0.001$ , Fisher's exact test); 0.8% of patients discontinued therapy secondary to these laboratory abnormalities. There were no cases of methotrexate-induced serious laboratory abnormalities in the first month of therapy. Serious lab value changes were equally probable throughout the first year of therapy.

## Conclusion

Methotrexate-related lab abnormalities are uncommon in patients without baseline lab abnormalities and do not occur more frequently in the first month of therapy. These findings suggest that monitoring frequency can be adjusted taking into account baseline risk factors. We recommend that monitoring can be performed at regular intervals over the first year of therapy in patients without a history of baseline lab abnormalities.



# Research Week 2020

## Question prompts to enhance patient engagement in care: An systematic review of the literature of AskShareKnow

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### Keywords

Patient activation, review, shared decision-making

### Abstract

#### Background/objective

The AskShareKnow (ASK) question set includes three basic questions that patients may ask to promote their understanding of their health and increase their care involvement. Despite the simplicity of these questions, ASK has been used in many health contexts with a wide array of results. Our objective was to conduct a systematic literature review (SLR) of the use of ASK.

#### Methods

An SLR of articles published from January 2011 to January 2020 was conducted using PubMed, Google Scholar, and MEDLINE. Inclusion criteria for review included original research, use of ASK, and reported outcomes related to ASK. Data extracted from each article included study outcomes, ASK deployment, effects and perceptions of ASK, potential harms, and study settings. Two reviewers independently extracted data from included articles. Disagreements were resolved by a third team member.

#### Results

Fourteen (14) records fulfilled inclusion criteria. Of these, four were qualitative, another four quantitative, and six mixed methods. Two studies reported study protocols. Across designs, studies focused on facilitation of shared decision-making (SDM) due to ASK (n = 6), personal perspectives of the questions (n = 5), and experiences of SDM related to ASK (n = 4). ASK appeared to increase the content of information presented by clinicians (n = 4), prompt patient questions (n = 4), and was recalled by many participants (n = 4). Challenges included difficulties understanding the questions' terminology among persons with limited literacy. ASK was most frequently used/tested in primary care and adult education settings.

#### Conclusion

This first SLR of the ASK question prompts, developed to facilitate patient engagement in care, indicates that ASK may help patients understand more about their health conditions. Despite this, there is a need for further research to quantify the efficacy of the question prompts and best clinical context in which to use them.





# Research Week 2020

## Fluorescence imaging technologies for in situ measurement of drug target engagement and cell signaling pathway reprogramming

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### Keywords

fluorescence, cancer, cyclic immunofluorescence,

### Abstract

Successful cancer treatment continues to elude modern medicine and its arsenal of therapeutic strategies. Therapy resistance is driven by tumor heterogeneity, complex interactions between malignant, microenvironmental and immune cells and cross talk between signaling pathways. Advances in molecular characterization technologies such as next generation sequencing have helped unravel this interaction network and identify therapeutic targets. Tyrosine kinase inhibitors (TKI) are a class of molecularly targeted therapeutics seeking to inhibit signaling pathways critical to sustaining proliferative signaling, resisting cell death, and the other hallmarks of cancer. While tumors may initially respond to TKI therapy, disease progression is inevitable due to mechanisms of acquired resistance largely involving cellular signaling pathway reprogramming. With the ultimate goal of improved molecularly targeted therapeutic efficacy, our group has developed intracellular paired agent imaging (iPAI) to quantify drug target interactions and oligonucleotide conjugated antibody (Ab-oligo) cyclic immunofluorescence (cycIF) imaging to characterize perturbed signaling pathways in response to therapy. iPAI uses spectrally distinct, fluorescently labeled targeted and untargeted drug derivatives, which correct for untargeted uptake and facilitate quantitative in situ assessment of drug target engagement. Ab-oligo cycIF exploits in situ hybridization of complementary oligonucleotides for biomarker labeling while oligo modifications facilitate signal removal for sequential rounds of fluorescent tagging. Ab-oligo cycIF is capable of generating multiparametric images for quantifying dephosphorylated and phosphorylated protein expression to quantify protein activation, expression, and spatial distribution. Together, iPAI and Ab-oligo cycIF can be applied to interrogate drug uptake and target binding along with changes to heterogeneous cell populations within tumors that drive variable therapeutic responses in patients. To date, we have successfully performed ratiometric iPAI on tissue sections after systemic iPAI probe administration to xenograft bearing mice and calculated epidermal growth factor receptor (EGFR) concentration with subsequent Ab-oligo cycIF imaging to measure EGFR signaling, cell viability and state on the same tissue.



# Research Week 2020

## Metformin Impacts Syncytiotrophoblast Mitochondrial Function in a Sexually Dimorphic Manner

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### Keywords

placenta, mitochondria, metformin, diabetes, pregnancy

### Abstract

#### Introduction

Placental mitochondrial respiration is impacted by obesity, type 2 gestational diabetes (A2GDM), and fetal sex. The mechanism of metformin, a GDM treatment, is unclear, but it may inhibit mitochondrial complex I, reducing mitochondrial respiration and ATP production. As previous studies examined the effect of metformin on cytotrophoblast but not syncytiotrophoblast (STB) we studied the effect on mitochondrial respiration in both male and female STB.

#### Methods

Placentas from lean (BMI<25), obese (>30), and A2GDM pregnancies (male or female fetus, n=4/group) were collected at term C-section. Isolated cytotrophoblasts were syncytialized (72 hrs) before 24 hr treatment with 0.01 $\mu$ M-30mM metformin. Mitochondrial respiration was assessed by Seahorse XF Mito Stress Test. Statistical analysis employed two-way ANOVA and Tukey post-hoc correction.

#### Results

STB of all groups showed a concentration-dependent decrease in basal respiration at 0.1-3mM metformin ( $p<0.0001$  at 300 $\mu$ M). Maximal respiration decreased from 0.1-30mM metformin ( $p<0.001$  at 1mM), but as the concentration response slope was significantly less than basal respiration ( $p=0.006$ ), spare capacity (maximal - basal) was not significantly decreased until 3mM metformin. Female STBs of A2GDM pregnancies had significantly greater spare capacity vs. both lean ( $p=0.006$ ) and obese women ( $p<0.001$ ) at 100 $\mu$ M metformin. Oxygen consumption due to proton leak increased from 1-30 $\mu$ M metformin in male STB of A2GDM vs lean ( $p=0.003$ ) and obese males ( $p=0.05$ ), and vs females from A2GDM pregnancies ( $p=0.01$ ). Male STB from lean pregnancies also exhibited proton leak compared to BMI-matched females ( $p=0.03$  at 30 $\mu$ M).

#### Conclusion

Metformin concentrations near therapeutic circulating levels decreased STB basal and maximal mitochondria respiration. Spare capacity improved in female STB of A2GDM pregnancies at 100-300 $\mu$ M. However, metformin increases proton leak, uncoupling respiration, in STBs from male fetuses especially from A2GDM pregnancies. Overall, metformin may differentially impact STB mitochondrial respiration, depending on concentration used: effects on male STB appear deleterious with some benefit for female STB.



# Research Week 2020

## Enhancing epidemiological safety in prehospital care by detecting adverse events in patient care records

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### Keywords

Adverse Safety Events, Patient Care Records, Chart Review, classification, neural network

### Abstract

#### Introduction

The term Adverse Safety Events (ASEs) refers to harm from medical errors and, if considered a disease, would rank third among the leading causes of death in the U.S. Patient safety research has traditionally performed manual review of patient care records (PCR) to characterize ASEs and develop prevention strategies. Manual review is labor-intensive, which prohibits continuous monitoring and improvement. Automating detection of ASEs would overcome these barriers and allow the healthcare community to address safety issues at a population scale.

#### Objective

To demonstrate the feasibility of automatically detecting safety events in PCRs.

#### Materials

88 PCRs of pediatric out-of-hospital cardiac arrests (OHCA).

#### Methods

Clinical experts manually reviewed the PCRs to establish ground truth determination of airway and medication ASEs. We extracted features from the structured and unstructured parts of the PCRs, built predictive models, and evaluated the predictions against ground truth using stratified K-fold (K=5) cross-validation and balanced accuracy. The unstructured narratives were transformed into vector-based feature embeddings using Bidirectional Encoder Representations from Transformers (BERT). We used logistic regression, decision trees, random forests, k-nearest neighbors, and neural networks to build predictive models.

#### Results

For structured data, decision trees had the best accuracy (77±4%) detecting airway events and random forests had the best accuracy (57±14%) detecting medication events. For unstructured data, logistic regression performed best detecting airway (50±7%) and medication (61±1%) events. Logistic regression using combined features detected airway (64±3%) and medication (62±1%) events with slightly better accuracy.

## Conclusion

The results are modest but compelling because they demonstrate the feasibility of automatically detecting ASEs after training on a very small dataset. The models performed best using structured data for airway events and unstructured data for medication events. Accuracy increased using both types of data. This suggests information about ASEs exist in different parts of the chart, which necessitates a holistic approach.



# Research Week 2020

## The Inter-relationship Between Shinrin-yoku/ Nature Therapy and Spirituality: A Scoping Review

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### Keywords

shinrin-yoku, nature, nature therapy, spirituality, awe, well-being, spiritual well-being, wonder

### Abstract

#### Background

Recent research has identified Shinrin-Yoku (SY), a Japanese term meaning "relaxing in nature to improve health," as an efficacious integrative practice to improve humans' physiological and psychological health and well-being. Nature Therapy (NT), also coined as Ecotherapy, includes a breadth of treatments to improve individuals' health in outdoor settings and it, too, has been noted to have beneficial health outcomes. However, research regarding the inter-relationship between SY/NT and human spirituality is limited.

#### Objective

The present study undertakes a scoping review on the inter-relationship between SY/NT and human spirituality to determine the extent spirituality research has been conducted. Conceptual frameworks, provision of key definitions and the integrative health outcomes associated with SY/NT and spirituality were highlighted.

#### Design

This review followed the 2018 protocol 21-item check-list for Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist [1]. Published papers from 1999 - 2019 were identified using online databases from which 30 publications were initially selected using keywords and following a secondary and tertiary search, 13 publications using spirituality as a primary or secondary outcome were identified.

#### Results

The majority of the publications (82%) were qualitative in design. Of the 13 publications, one was a Doctoral Thesis, one was a Masters' Thesis, and three were literature reviews. Of the three literature reviews, one was a book chapter. Overall, 100% (N=13) of the publications examined the role of spirituality in relationship with nature.

## Conclusions

Albeit the quality of the reviewed studies being high there is a dearth of quantitative and mixed-methods studies and literature/systematic reviews including spirituality in relation to nature and SY/NT.



# Research Week 2020

## Multimodal preoperative screening for recent nicotine and marijuana use in hip and knee arthroplasty patients at the Portland VA Medical Center

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### Keywords

Surgical Outcomes, Cigarette, Nicotine Replacement Therapy (NRT), Prevalence, Smokerlyzer

### Abstract

#### Background

Tobacco use is associated with increased post-operative complications and is often underreported by patients. Recent literature also suggests that cannabis use may be correlated with post-operative complications. The prevalence of tobacco has been reported as disproportionately high in the veteran population and little is known about the population's cannabis use. Traditional biochemical testing methods, including serum and urine cotinine assays, do not differentiate active smoking from nicotine replacement therapy (NRT), and total joint arthroplasty patients are not regularly screened for the use of cannabis. This study intends to determine the prevalence of cigarette smoking, nicotine replacement therapy (NRT), and cannabis use in the population and evaluate the effectiveness of a novel point-of-care carbon monoxide (CO) breath test to verify smoking status.

#### Methods

This is a single-institution, prospective cohort study of adult orthopaedic patients at the Portland VA Medical Center to implement and evaluate a point-of-care CO breath test, the Smokerlyzer® Micro EC50, for pre-operative smoking status verification. Patients who were indicated for surgery were offered inclusion. Self-reported cigarette, cannabis, and nicotine replacement therapy (NRT) use was obtained pre-operatively and cigarette smoking status was verified by serum cotinine levels and exhaled CO levels. Prevalence was calculated as the number of patients who reported use compared to the overall population (69 patients).

#### Discussion



Preliminary data from 69 veterans undergoing elective orthopaedic surgery showed a prevalence of current cigarette smoking of 9/69 (13%). The prevalence for cannabis, e-cigarette, and nicotine replacement therapy use was calculated as 14/69 (20%), 2/69 (3%), and 2/69 (3%) respectively. Further studies will evaluate the validity of the smoking questionnaire and the use of point-of-care testing to differentiate cannabis use, active cigarette smoking, and NRT use. Results will provide preliminary data to directly test NRT use, separate from tobacco use, and surgical outcomes.



# Research Week 2020

## Inpatient teledermatology: Diagnostic and therapeutic concordance among hospitalist, dermatologist, and teledermatologist

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### Keywords

Inpatient; dermatology; teledermatology; telemedicine; telehealth; concordance; agreement

### Abstract

Inpatient dermatology has been shown to improve patient outcomes at a reduced cost. Few hospitals have dermatologists available. Teledermatology may allow dermatologists to assess hospitalized patients remotely. Objective: To examine diagnostic concordance between hospitalist, dermatologist, and teledermatologist evaluating chart data and images remotely. Methods: For 100 consecutive cases requiring inpatient dermatology consultation, a survey was conducted by all 3 raters to convey diagnostic impressions and therapeutic recommendations. Complete and partial agreements were assessed using Cohen's kappa statistic. Results: Inpatient dermatology consultation often resulted in a change in diagnosis (50.9%), and a change in systemic therapy (41.5%). Likewise, virtual teledermatology consultation would have resulted in a change in diagnosis (54.7%) and a change in systemic therapy (47.2%) at similar rates. Comparing dermatologist and teledermatologist, diagnostic complete and partial agreement was 52.8% and 84.9% respectively. Systemic therapy agreement was 77.4%. Teledermatologists recommended biopsy more often (68.5% vs 43.5%). Limitations: Small sample size, tertiary academic medical center, single rater for inpatient teledermatology with specific inpatient niche. Conclusion: Teledermatologists performed comparably to an in-person dermatologist for diagnosis and management of hospitalized patients with skin conditions. Teledermatology may be a suitable alternative for delivery of inpatient care if no dermatologist is available.



# Research Week 2020

## Adolescent pleasure and novelty seeking is associated with greater neural response in reward and control circuitry during evaluation of risk and reward

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### Keywords

Adolescence, decision making, reward, risk

### Abstract

Adolescence is a period of neurodevelopment during which risky behaviors often increase. This may be explained by the mismatch in brain maturation between bottom-up reward processing networks (which develop early in adolescence), and top-down regulatory control networks (which develop later). However, there are significant individual differences in adolescent risk taking which could be attributable to a variety of factors, such as differences in temperament. This study investigated the neurobiological underpinnings of risk and reward evaluation as they relate to self-reported pleasure derived from novel or intense experiences on the Early Adolescent Temperament Questionnaire. Participants included 265 healthy 12-17 year-old adolescents (~50% female). Participants underwent functional magnetic resonance imaging during a modified Wheel of Fortune task, where they evaluated a series of choices between lower probability/higher reward options (10% probability of winning \$7 vs. 90% probability of winning \$1) and higher probability/lower reward options (30% probability of winning \$2 vs. 70% probability of winning \$1). Whole brain and a priori ventral striatal region-of-interest regression analyses revealed that greater novelty seeking was associated with greater activation in the ventral striatum, posterior cingulate cortex, and left middle frontal gyrus when evaluating higher potential for risk and reward, regardless of the decision made. Novelty seeking was not associated with the proportion of high risk/reward selections. Together, these findings suggest that while adolescents who enjoy novel and intense experiences have greater reward-related brain response in situations with greater potential for risk and reward, they also show greater activation in regulatory control regions, potentially counterbalancing the bottom-up driven reward response. Although there was no association between novelty seeking and risk taking behavior on this task, more research is needed to determine whether individual differences in brain activation related to novelty seeking are related to decision making in more ecologically valid settings (e.g. under peer influence).



# Research Week 2020

## PIN1 Provides Dynamic Control of MYC in Response to Extrinsic Signals

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### Keywords

MYC, PIN1, Isomerization, Cancer

### Abstract

PIN1 is a phosphorylation-directed member of the peptidyl-prolyl cis/trans isomerase family that facilitates conformational changes in phosphorylated targets such as c-MYC (MYC). Following signaling events that mediate phosphorylation of MYC at Serine 62, PIN1 establishes structurally distinct pools of MYC through its trans-cis and cis-trans isomerization activity at Proline 63. Through these isomerization steps, PIN1 functionally regulates MYC's stability, the molecular timing of its DNA binding and transcriptional activity, and its subnuclear localization. Recently, our group showed that Serine 62 phosphorylated MYC can associate with the inner basket of the nuclear pore (NP) in a PIN1-dependent manner. The poised euchromatin at the NP basket enables rapid cellular response to environmental signals and cell stress, and PIN1-mediated trafficking of MYC calibrates this response. In my presentation, I will describe the molecular aspects of PIN1 target recognition and PIN1's function in the context of its temporal and spatial regulation of MYC.



# Research Week 2020

## Sporadic Fatal Insomnia: A Case Report

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### Keywords

Fatal Insomina, Creutzfeldt-Jacob disease

### Abstract

The most common prion disease is Creutzfeldt-Jacob disease (CJD), usually sporadic sCJD), but in up to 15% familial due to mutations in the prion gene. CJD presents with myoclonus, ataxia, and rapidly progressive dementia with an average age of onset of 67 years.

Fatal Familial Insomnia (FFI) is a related uniformly fatal prion disease, with mean onset of dysautonomia and insomnia at 56 years and mean duration of 13 months. The same mutations that produce familial CJD cause FFI, with the different phenotypes attributable to different polymorphisms of codon 129 of the prion gene: V/V or M/V in the case of CJD versus M/M in FFI. Occasionally, Fatal Insomnia (FI) can present as a sporadic prion disease (sFI) in patients lacking mutations in the prion protein, appearing as a phenocopy of FFI. To date, 32 cases of sFI have been reported in the literature. A 33rd case was recently encountered at autopsy in a patient who was treated at OHSU.

### Clinical History

A 56-year-old female initially complained of gait abnormality and difficulty in speaking. Despite extensive evaluation at Mayo clinic with empiric trials of immunotherapy and steroids, her symptoms worsened significantly. The patient manifested a sleep disorder characterized by insomnia with moaning and thrashing of many hours duration. MRI of the brain did not show typical basal ganglia abnormalities diagnostic of CJD and her clinical diagnosis was multisystem atrophy versus prion disease.

Tissue was sent to the National Prion Disease Pathology Surveillance Center in Cleveland, Ohio, where the results of western immunoblotting for abnormal protease-resistant prion protein showed low-molecular weight forms of insoluble prion protein that have been reported to predominate in FI. Sequencing of the prion gene did not reveal mutations but demonstrated the M/M polymorphism, supporting the diagnosis of sFI.



# Research Week 2020

## Evidence for discontinuous cyclical Wnt/beta-catenin signaling

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### Keywords

Wnt signaling mechanism disease development

### Abstract

Wnt/beta-catenin signaling is critically important during development and for stem cell maintenance. Dysregulation of the Wnt pathway is implicated in numerous diseases, most notably cancer. Appropriate manipulations for intervention and therapy require an accurate understanding of the Wnt signaling mechanism. The consensus model for the Wnt pathway is surprisingly straightforward: In the OFF state of the pathway, the central regulator in the pathway, termed the destruction complex (DC) targets beta-catenin for degradation, thereby preventing it from nuclear signaling. In the ON state, ligand activation of the Wnt receptor inhibits DC activity, leading to beta-catenin accumulation and transcription of Wnt target genes. The prevailing model of Wnt signaling is predicated on continuous pathway activation at a proportional level to ligand concentration ("Standard" model). We deployed bimolecular fluorescence complementation (BiFC), a novel technology that enables investigations of dynamic changes in components of the signaling mechanism, within intact developing organs and at a single cell resolution. Thus, we identified DCs for the first time *in vivo*. Further, we detected catalytically active DCs in cells without pathway activity, which we distinguished from inactivated DCs in actively signaling cells. Our preliminary results reveal substantially different dynamics of the signaling pathway, leading us to propose a radically new model for Wnt signaling. We will present support for the hypothesis that Wnt/beta-catenin signaling is discontinuous and uses a cyclical mechanism.



# Research Week 2020

## Portland Pivot Kick Study: Can a novel physical exam maneuver for medial meniscus tears predict improvement after partial medial meniscectomy?

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### Keywords

Medical meniscus, Osteoarthritis, knee, meniscectomy, & mechanical symptoms

### Abstract

#### Objective

The efficacy of partial meniscectomies in patients with osteoarthritis is currently debated. The purpose of this study is to determine the effectiveness of a novel physical exam maneuver, the Portland Pivot Kick (PPK), in predicting the potential benefit of arthroscopic partial medial meniscectomy in treating mechanical symptoms, even in the presence of osteoarthritis.

We theorize that differentiating mechanical symptoms from degenerative joint disease in medial meniscus tears can be a prognosticator of improvement following surgical intervention. We hypothesize that patients with a positive preoperative PPK will have improvement of mechanical symptoms and subjective outcomes scores following arthroscopic partial medial meniscectomy.

#### Methods

This IRB approved retrospective study at the VA Portland Health Care System (VAPORHCS), included patients who received a partial meniscectomy for medial meniscal tears. Exclusion criteria included any patients with prior surgery on the index knee, an intraarticular loose body on MRI, an anterior and/or posterior cruciate ligament tear, a bucket handle tear, or meniscal tear deemed amenable to repair rather than partial meniscectomy.

Objective outcomes included the PPK maneuver before and after surgery. Subjective patient outcomes were evaluated pre and postoperatively using the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Western Ontario McMaster Osteoarthritis Index (WOMAC).

#### Results

Fifty-two patients with positive PPKs underwent partial medial meniscectomy for mechanical medial knee pain. At an average follow up of 9.1 months (range 8 days – 18.7 months), 51 of the 52 patients had a negative PPK. Patient outcomes scores were significantly improved postoperatively compared to preoperative values (Table 1).





# Research Week 2020

## Energy and Protein Composition of Water Buffalo Milk and Liquid and Dried Whey Products: A Pilot Study to Evaluate Suitability as a Nutritional Supplement for use in Low-Resource Countries

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### Keywords

Global Nutrition, Malnutrition, Protein Supplement, Milk Composition

### Abstract

#### Background

In Lao PDR, 33.5% of children under five years of age are stunted, 26% are underweight and 8% are severely wasted. Nutritional rehabilitation of malnourished children often requires dietary energy and protein supplementation. Water buffalo (WB), native to Southeast Asia, produce milk with higher energy and protein concentrations than dairy cattle (DC). Whey, a byproduct of cheese production and a source of protein and energy, is currently discarded in Lao PDR after making cheese. Energy and macronutrient concentrations of WB milk and liquid/dried whey were analyzed and compared to DC milk and whey data to determine suitability as a locally-sourced nutritional supplement.

#### Methods

WB milk and whey samples were obtained before and after making feta and mozzarella cheese. Nutrient analysis was performed by Mahidol University, Bangkok, Thailand. Crude protein concentrations were analyzed using the Kjeldahl method and energy concentrations were estimated by back calculation.

#### Results

Mean energy (107 kcal/100g) and protein (4.5g/100g) concentrations of WB milk were 51.2% and 28.7% higher than DC milk, respectively. The energy content of whey derived from liquid feta and mozzarella cheese was 30.5% and 26.8% higher than DC milk whey, respectively. Concentrations of protein in dried WB whey from feta and mozzarella cheese production were similar to and 4.3% lower than DC whey, respectively. Both WB dried whey products provide more than 11 g protein/100g whey and are suitable dietary protein sources.

#### Conclusions

WB milk contains higher concentrations of energy and protein than DC milk. Dried whey derived from WB mozzarella and feta cheeses meet the protein standards of an acceptable dried whey product. Development of a locally sourced, shelf-stable, powdered nutritional supplement derived from WB whey that is safe for human consumption is underway.

#### Funding Sources

OHSU and the Vejdusit Foundation. Milk/whey samples were donated by the Laos Water Buffalo Dairy



# Research Week 2020

## Transport of alpha-synuclein fibril aggregates in an in vivo mouse model of Parkinson's disease.

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### Keywords

Alpha-synuclein, age-related synucleinopathies, Parkinson's disease, neurodegeneration

### Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder for which there are currently no treatments to slow, halt, or reverse the disease process. The disease is defined by the accumulation of the protein alpha-synuclein into aggregates known as Lewy inclusions, but how these aggregates initiate and propagate to various locations throughout the brain is unknown. To develop targeted disease modifying therapies, it is important to understand how aggregated forms of alpha-synuclein are transported throughout the nervous system and to determine the effect aggregation of alpha-synuclein has on specific cell types and specific behaviors. The hypotheses of this research are that alpha-synuclein aggregates propagate through neuroanatomically connected pathways and that induction of Lewy pathology results in behavioral deficits. Current results support these hypotheses. In a new transgenic mouse model of PD we see direct evidence for axonal transport of aggregated alpha-synuclein using in vivo multiphoton and correlative light and electron microscopy (CLEM) imaging approaches. We also extend the findings of previous work and show that intramuscular injection of aggregated alpha-synuclein into the hind limb musculature not only leads to the formation of Lewy pathology in the cortico-spinal tract and brainstem motor system, but also to higher parts of the motor system, including primary motor cortex, strongly suggesting retrograde trans-synaptic spread through neuroanatomically connected pathways. Additional analyses also show differences in several behavioral assays including ultrasonic vocalizations, gross motor tasks, and cognitive behaviors following injection of aggregated vs monomeric forms of alpha-synuclein. Future work will target perturbation of possible mechanisms of transport to halt or reverse the accumulation of abnormal alpha-synuclein and reduce the resulting behavioral deficits in this mouse model of PD.



# Research Week 2020

## Using MLU to Evaluate the Reliability of ADOS Transcription

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### Keywords

autism, intra-annotator reliability, computational language analysis

### Abstract

Transcription of language samples is labor intensive and data on intra- and inter-annotator reliability is lacking. Mean Length of Utterance in Morphemes (MLUM) can be calculated from transcripts and used to evaluate intra-annotator reliability. We developed a computational method to determine transcriber consistency across a large speech corpus.

### Methods

Module 3 of the Autism Diagnostic Observation Schedule (ADOS) was administered to 137 children (IQ > 70; fluent/phrase speech), then transcribed according to modified SALT guidelines. Transcripts of Emotions, Social Difficulties and Annoyance, and Friends and Marriage conversations were split by even and odd lines and MLUM calculated separately for each half. Intra-annotator agreement was evaluated using Intraclass Correlation (ICC).

### Results

The sample comprised 66 children with ASD (mean age: 11.3 years; 80% male; mean IQ: 102) and 71 controls without ASD (mean age: 11.4 years; 58% male; mean IQ: 113). Across tasks and groups, mean MLUM ranged from 6.17 to 6.37. ICC between the even and odd MLUM was 0.732 for Emotions (95% CI: 0.644-0.801), 0.593 for Social (95% CI: 0.474-0.692), and 0.744 for Friends (95% CI: 0.658-0.81), indicative of moderate to good levels of reliability. Paired-t-tests between the two MLUM halves were all nonsignificant, indicating very good within task intra-rater agreement. ICC was comparable between the two clinical groups although reliability was higher in ASD than for controls on the three tasks. Using age and IQ median splits (11.4 years and 110, respectively), we further established that age had no discernible effect on ICC across tasks; a trend was found for lower reliability on one task among subjects with higher IQ. However, all ICCs across age and IQ groups remained in the moderate (>.50) range.

### Conclusions

Calculating MLUM for two random halves within each activity provides an efficient and valid measure of intra-annotator reliability.



# Research Week 2020

## Sex differences in effects of BMI on ADHD symptoms.

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### Keywords

Neuroscience, Psychiatry, ADHD, BMI

### Abstract

#### Introduction

Recent research suggests that higher Body Mass Index (BMI) may be associated with ADHD diagnosis and greater ADHD symptom severity, but results have been inconsistent. Emerging research indicates that failure to account for age, sex, and medication status may contribute to discrepant results. In addition, the relationships to specific symptom domains (inattention, hyperactivity-impulsivity) require further examination. The current study uses a large, well-characterized cohort of individuals with and without ADHD to characterize the relationship between ADHD symptoms and BMI in both males and females.

#### Methods

395 children ages 7-11 years old underwent a comprehensive diagnostic evaluation, including parent and teacher standardized rating scales of ADHD and other comorbid diagnoses, parent clinical interview, and child cognitive testing. BMI was measured using the Tanita scale, a body fat analyzer.

#### Results

Children with and without ADHD were not significantly different on BMI,  $t=1.03$ ,  $p=.30$  overall; however, those on stimulant medication had lower BMI than those not taking medication. Within the ADHD group, there was a significant interaction between sex and BMI on inattention symptoms,  $F(2, 388)=3.32$ ,  $p=.037$ . Females with high BMI had more inattention symptoms than their high BMI male counterparts, however, females with low-BMI have fewer inattention symptoms than low-BMI males. When stimulant medication was added to the model, the results were similar. There were no significant effects for hyperactivity-impulsivity symptoms, all  $ps > .10$ .

#### Conclusion

Females with ADHD and high BMI showed worse inattention symptoms than their male counterparts. Future research is needed to understand whether this is a biologically-

driven effect or whether this relationship may be due to other social factors, such as an increased BMI eliciting negative body image, low self-esteem, or other mood and anxiety problems that exacerbate inattention symptoms.



# Research Week 2020

## The tooth on-a-chip as model of dental pulp cell response to biomaterials and oral biofilm

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### Keywords

organs on a chip, stem cells, dental pulp, biomaterials

### Abstract

#### Objective

There is a shortage of in-vitro model systems that mimic the dentin-pulp interface while enabling a real-time evaluation of dental pulp cells, dentin and biomaterials. Here, we optimized an organ-on-a-chip model system, the 'Tooth-on-a-chip' and tested different biomaterials in real-time. Moreover, we developed a model of secondary caries on-chip co-culturing oral microcosm with dental pulp cells.

#### Methods

The tooth-on-a-chip is a micromolded polydimethylsiloxane (PDMS) device assembled onto a glass slide containing a dentin slice functioning as a semi-permeable membrane that separates two perfusable chambers. Human dental pulp stem cells (hDPSCs) cultured in osteoinductive medium were seeded on one surface of dentin, forming a monolayer after 24h. Next, collagen type I was added to emulate the extracellular matrix environment of the pulp. Dentin on the opposite chamber was treated with MTA (ProRoot), Biodentine, or Theracal and cell morphology was tracked for 7 days. Cells were fixed, stained with Actin Red/DAPI and imaged using a confocal microscope. The dentin release of transforming growth factor-beta (TGF- $\beta$ ) when in contact with biomaterials was determined using an ELISA test. To test the interaction of oral bacteria with pulp cells, we added an aliquot of oral microcosm biofilm on the opposite side of the hDPSCs monolayer. Cells were stained for live cell imaging and tracked in real time. As for the secondary caries groups, dentin was acid etched, restored with dental adhesive and flow resin and placed on-chip with bacteria co-culture.

#### Results

ProRoot and Biodentin showed biocompatibility on-chip and elicited more TGF- $\beta$  release. It was possible to co-culture oral microcosm on-chip and track hDPSC responses for 5 days. Live and dead stain showed hDPSCs viability for up to 3 days.



## Conclusion

The tooth-on-chip is a physiologically accurate platform and useful tool to study pulp response to biomaterials in near-physiologic conditions.



# Research Week 2020

## A Collaborative Multimodal Pathway Reduces Opiates after Total Hip and Knee Arthroplasty

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### Keywords

Opioid Reduction Hip Knee Arthroplasty

### Abstract

#### Intro

Degenerative joint disease affects much of the aging population making total hip arthroplasty (THA) and knee arthroplasty (TKA) two of the most prevalent procedures performed. The invasive nature of these procedures and the painful manifestation of degenerative joint disease is associated with opiate prescription. In an attempt to reduce the opiate consumption during TKA and THA we undertook a collaborative effort to improve our pathways for post-operative pain control. The aim of this investigation is to evaluate the effectiveness of our new multimodal pain control pathway.

#### Methods

This will be a retrospective review of all patients who underwent primary TKA and THA at a single academic institution from November 2018 to March 2020. The multimodal pain control pathway was implemented in November 2019. The primary outcome is total morphine equivalent dosing during inpatient stay, at discharge, and within the first six weeks from discharge. Secondary outcomes assessed were length of stay, visual analogue scale (VAS) pain score. Data collection will include basic demographics (age, sex, BMI, documented opioid usage), co-morbidity score (measured by ASA), cognitive score, psychiatric conditions, surgeon, discharge medications, day/time of discharge, and numerical pain scores.

#### Results

Retrospective chart review is currently underway. We will compare TKA and THA patients prior to the initiation of the new pathway and compare these to the cohort of patients after the initiation of the multimodal pain pathway. Power analysis will be conducted after an initial pilot data collection to determine how many patients will need to be collected with appropriate power to detect a 10% reduction between cohorts.

#### Discussion

The results of this study could prove beneficial for patients undergoing TKA and THA by shifting away from opiates with a multimodal pathway and reducing their opiate consumption. Future investigations should evaluate this protocol on different populations and in different settings.



# Research Week 2020

## Epilepsy surgical outcomes

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### Keywords

Epilepsy, Surgery, Outcomes

### Abstract

Medically refractory epilepsy is defined as failure to control recurrent seizures with two or more anti-seizure medication trials. Among patients with refractory focal epilepsy localized to the mesial temporal lobe, amygdalohippocampectomy is a well-established treatment that can result in seizure freedom in up to 75% of appropriately selected patients. Laser Interstitial Thermal Therapy (LITT) is a newer, minimally invasive alternative to resection, although the safety and efficacy of LITT is less well defined. This study aimed to compare outcomes among patients who underwent LITT vs. resections.

A retrospective chart review was done for patients who underwent LITT or resection of the hippocampus at OHSU from 2015-2019, and included 46 resections and 10 laser ablations. Data obtained included pre-surgical evaluation details, adverse effects, and seizure outcomes. Seizure frequencies were examined pre-operatively as well as 3 and 6 months post-operatively.

At 3 months post-surgery, 66.7% of resection patients and 75% of LITT patients were free of disabling seizures (Engel Class I). At 6 months, 65.9% of resection patients and 85.7% of LITT patients were Engel Class I. 26% of resection patients experienced adverse events. 2 out of 46 resection patients had a complication necessitating surgical intervention and one additional patient underwent redo epilepsy surgery to obtain a better outcome. 30% of LITT patients experienced an adverse event with one complication requiring surgical intervention.

LITT began being offered at our institution in 2018 and limited postoperative data may affect rates of seizure freedom. Selection bias may be present as patients were not randomized to either procedure. Our data supports the finding that laser ablation is non-inferior to resection for treatment of medically refractory mesial temporal lobe epilepsy at six months post-surgery. More research is warranted to draw conclusions about the safety and efficacy of LITT compared to open resection.



# Research Week 2020

## Transgender Health in Orthopaedic Care: A Literature Review

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### Keywords

Orthopaedics, Surgery, Transgender

### Abstract

#### Background

Approximately 1.4 million adults in the United States identify as transgender. This population has been identified as a group that experiences disparities in healthcare. Although transgender individuals present with unique considerations for surgical and perioperative care, there is a paucity of research evaluating transgender health in orthopaedics.

#### Methods

We carried out a scoping review of existing literature to identify physiological and social factors of transgender care pertinent to orthopaedics.

#### Results

As transgender individuals can be in different stages of transition, the decision to evaluate risk factors based on either a patient's biologic sex or their gender identity must be given special attention. Many transgender individuals undergo gender-affirming hormone therapy (GAHT) and may experience effects of exogenous estrogen and testosterone on bone mineral density and bone geometry. These are important indicators of fracture risk and possibly fracture healing. Hormone therapy may also affect rates of tendon and ligament injury. Several unique perioperative characteristics bear consideration, most notably an increased risk of venous thromboembolism among transgender women on GAHT. Numerous studies have emphasized that increased social stresses and discrimination experienced by transgender individuals contribute to an elevated prevalence of drug use, HIV, and homelessness. These factors may lead to more frequent interactions with the orthopaedic trauma community and could place them at risk for poorer surgical outcomes. Providers may benefit from increased awareness of the barriers to care faced by transgender individuals, including financial stress due to limited coverage of transgender-related services and previous negative healthcare experiences that discourage individuals from seeking future care.

## Conclusions

Effective care of transgender individuals in the orthopaedic setting must take into account physiological, psychological, and socioeconomic considerations. Further research is needed to evaluate fracture risk, elucidate surgical complication profiles, and optimize operative and perioperative care of transgender individuals in orthopaedic settings.



# Research Week 2020

## Shared Decision Making in Dermatology: A Scoping Review

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### Keywords

shared decision making, dermatology, patient decision aids, physician-patient relationship

### Abstract

#### BACKGROUND

Shared decision making (SDM) is a standardized method to integrate patient values with the best clinical evidence. SDM is appropriate for any medical decision with multiple options and is now a formalized, Medicare-reimbursed, part of medical practice. Dermatologists often guide clinical decisions by patient preference and personal characteristics due to the nature of dermatologic diseases and the lack of evidence for single therapeutic answers. However, dermatology has lagged behind other medical specialties in developing SDM in clinical practice.

#### METHODS

We performed a systematic scoping review of the published literature on SDM in dermatology. The purpose of our research was to look at the characteristics and range of methodologies used in SDM for dermatology. Our search string was developed with several SDM MeSH terms to search Ovid Medline, Sciverse, Scopus, Cochrane, and PsychInfo. We screened 1701 published papers and identified 74 studies relevant for full text screening. Forty-four of these studies were chosen for full text review. Qualitative coding of the 44 papers was done by two researchers using Dedoose and themes were described using coded excerpts.

#### RESULTS

The majority of SDM papers mentioning dermatology were focused on complex medical problems like cancer and rheumatologic disorders and concentrated on satisfaction with care as an outcome. Qualitative analysis identified the advantages and disadvantages of SDM, types of patients that are most likely to benefit from SDM, factors that affect decision making, tools and patient decision aids used in SDM, and the strategies as well as barriers to implementing SDM.

#### CONCLUSION

There is a lack of research on SDM in dermatology despite unique opportunities inherent to dermatology for collaborating with patients in deciding which treatment is best for them. Employing SDM in clinical practice increases patient adherence to treatment, physician and patient satisfaction, and reduces time in follow up consultations.





# Research Week 2020

## “Bending the Curve” in Medically and Socially Complex Youth: Pilot of Novel Interventions in Children’s Health Care (NICH)

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### Keywords

Social vulnerability, medical complexity, pediatrics, behavioral health

### Abstract

#### Introduction

Children with medical complexity account for a relatively small percentage (0.4-0.7%) of children but approximately 15-33% of pediatric US healthcare spending. This is often attributed to recurrent hospitalizations that may be tied to social vulnerability. Few, if any, programs have effectively decreased utilization in this population.

Novel Interventions in Children's Healthcare (NICH), an intensive community-based, family-focused intervention, was developed for youth experiencing suboptimal disease management due to social determinants of health. NICH provides 24/7 support from a single 'interventionist' who provides strategic family and systems based interventions, health systems integration, patient needs alignment, and resource access for family and patient. This pilot study examines the effectiveness of NICH on reducing avoidable healthcare utilization and overall cost of care.

#### Methods

Youth (n=15) enrolled in the NICH pilot met the following criteria: 1) presence of a complex or chronic health condition, 2) avoidable hospitalizations, and 3) lack of response to existing services. Predominately represented medical conditions included type 1 diabetes, cystic fibrosis, and chronic pain. Mean youth age was 14.2 years (SD=4.66), 60% were female, and 80% were non-Hispanic white. Retrospective EHR reviews captured relevant healthcare utilization one year prior to and one year post NICH initiation. Medicaid paid claims data were examined for per-member, per-month (PMPM).

#### Results

In the year prior to enrollment, youth averaged 3.4 admissions, 25.3 days admitted, and 4.2 ED visits per youth as well as \$4,647 per-member, per-month (PMPM) in paid claims. In

the year following NICH enrollment, youth experienced on average 1.8 admissions, 9.7 days admitted, 3.4 ED visits and an associated \$2,243 PMPM per youth.

#### Discussion

The NICH pilot offers a promising intervention that addresses the challenges of social vulnerability compounded with medical complexity for pediatric patients in preventing unnecessary health system use. Further study is required to understand its effects and external validity.



# Research Week 2020

## A Real-time miRNA-based Machine Learning Approach for Precision Cancer Therapeutics

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### Keywords

Cancer, drug prediction, machine learning, miRNA

### Abstract

Recent research shows that microRNAs (miRNAs) may be potential biomarkers of cancer. MiRNAs are noncoding RNA molecules that regulate gene expression in the post-transcriptional phase. When miRNA count is depleted, gene expression can become dysregulated, consequently leading to progression or drug resistance in cancer. Therefore, many researchers have begun to investigate the role of miRNA as a potential biomarker of cancer, and its role in targeted drug therapy.

Artificial Intelligence has emerged as a recent breakthrough to identify cancer types with high accuracy. Even though cancer is a complex and extremely heterogeneous condition, the current practice of treating cancer – which entails surgery, radiation therapy, chemotherapy, and immunotherapy – is a one-size-fits-all approach that results in the prescription of the same drug for every patient with the same type and stage of cancer. This approach is expensive, time-consuming, causes the patients to suffer, and worse, prescribed cancer drugs are ineffective for 75% of the time. Machine learning can be used to deliver precision cancer therapeutics based on genomic profiles of patient's tumors. The solution is a machine learning platform that analyzes pharmacogenomic data of various cancer types and predicts targeted drug efficacy with a high accuracy. In this research, models were built and implemented in Python and its libraries using miRNA and drug response data from the Cancer Genome Atlas, a publicly available data repository. The classification algorithms tested in this research were OneVsRest, K-Nearest-Neighbors, AdaBoost, and DecisionTree. As an ensemble learning method combining multiple weak learners, OneVsRest was able to predict drug efficacy with the highest accuracy. The results show that the approach is superior to current research that uses miRNA and machine learning to predict drug efficacy using cancer cell line data and not real patient data.



# Research Week 2020

## To flow or not to flow: Considerations for quantitative microbiome profiling

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### Keywords

microbiome, 16S rRNA gene sequencing, quantitative microbiome profiling

### Abstract

Culture-independent methods are changing the way scientists interrogate microbes in complex environments such as the human body. Specifically, targeted sequencing of the conserved 16S rRNA gene is relatively simple, inexpensive, and high-throughput. However, the analysis of such data quantifies each microbe as a fraction of the total read count, which can lead to misinterpretations of microbes that differ between communities associated with disease. To address this limitation, quantitative microbiome profiling (QMP) methods have been developed. QMP methods complement 16S rRNA gene sequencing with estimates of microbial load by quantifying bacterial cells or 16S rRNA copy number. Several QMP methods have been proposed, but their performance on biological samples have not been thoroughly evaluated. Here, we present our results benchmarking QMP methods to investigate the strengths and limitations of each on samples originating from high and low microbial biomass environments.

### Methods

We compared three modalities for estimating microbial load: quantitative PCR (qPCR), droplet-digital PCR (ddPCR), and cell counting using SYTO BC staining with flow cytometry (flow). For each method of estimating microbial load on a mock microbial community dilution series, we evaluated variation as percent error and accuracy as log<sub>2</sub> fold change from expected.

### Conclusions

The method of estimating microbial load must be carefully considered and evaluated for QMP. We found that ddPCR was more precise but less accurate than flow, and flow was highly accurate but not precise. ddPCR had the least variation in repeated measures of the same sample, indicating that the reproducibility and error introduced with this method is minimal compared to qPCR and flow. The high variability of flow cytometry is likely due to complications in sample preparation which is simpler for ddPCR and qPCR. Both ddPCR and flow appear to have a larger dynamic range where the accuracy is within reason.



# Research Week 2020

## A Community-based Assessment of Skin Care, Allergies and Eczema (CASCADE)

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### Keywords

Atopic Dermatitis, Allergy, Emollient, Infant

### Abstract

#### Background

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that affects approximately 13% of children in the United States. Typically, it develops in those less than 2 years old, resulting in a lifelong condition that is often connected to other disorders such as allergies and asthma, degrading the individual's quality of life. Skin barrier dysfunction allows for these disorders to develop, therefore targeting the skin's barrier potentially prevents disease.

#### Methods

CASCADE is a randomized, multi-site, single-blind pragmatic clinical trial to discover the adequacy of emollient on the skin. From 25 clinics that are connected to practice-based research networks (PBRNs) in Oregon, Colorado, Wisconsin, and North Carolina, a total of 1,250 participants are to be enrolled. These participants are parent-infant dyads with infants 0-63 days old and the parents as 18 years or older. Those who are English or Spanish speaking are to be enrolled. The participants will use surveys to determine their eligibility, enrolling in either the control arm or the emollient arm. Those in the control arm are to apply moisturizer onto their child if dry skin develops. Those in the emollient arm are to apply moisturizer daily. The parent-child dyad will then record their findings in surveys every 3 months for 2 years.

#### Results

CASCADE is in year 3 of 5 years. As of March 4th, 2020, 865 participants have been enrolled. Data has yet to be analyzed.

#### Conclusion

Ultimately, the rate of each arm developing AD will be recorded, other associated disorders connected to AD will be taken into account, and the overall effect that AD has on individuals suffering from it will be noted.



# Research Week 2020

## Healthy Eating Index and Bone Mineral Density in Middle to Older-Aged Women: Evidence from NHANES, 2005-2010

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### Keywords

bone mineral density; Healthy Eating Index; nutrition surveys; women; United States; menopause

### Abstract

#### Purpose

Low bone mineral density (BMD) is a risk factor for osteoporosis, which can increase the risk of fractures and associated morbidity. Diet quality, as measured by the Healthy Eating Index (HEI), may be associated with bone mineral density. The relationship between the HEI and BMD was assessed in a U.S. population-based cohort of pre- and postmenopausal women, 40 years of age or older. Methods

Cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) from 2005-2010 were analyzed to assess the relationship between HEI and total femur and femoral neck BMD among pre- and postmenopausal women (n= 3,597). The Healthy Eating Index score was calculated based on data from two separate 24-hour dietary recalls.

#### Results

Linear regression analysis showed the lowest quartile of the HEI was associated with lower BMD, compared to those in the highest quartile of HEI score (fully-adjusted beta= -0.029, -0.021 for pre- and postmenopausal women, respectively). After adjusting for confounding factors, there was support for a linear trend in both pre- and postmenopausal women; increasing HEI score was associated with successively greater total femoral BMD (p= 0.02, test of trend in premenopausal women, p= 0.002, test of trend for postmenopausal women). After adjustments, the regression coefficients indicated femoral neck BMD were similar to those in minimally adjusted total femur BMD models (fully-adjusted beta= -0.036, -0.011 for pre- and postmenopausal women, respectively). A linear test of trend demonstrated increasing HEI score was associated with higher femoral neck BMD in premenopausal women (p= 0.01). Although not statistically significant, the associations between HEI score categories and femoral neck BMD in postmenopausal women followed similar patterns in premenopausal women (p= 0.12).

## Conclusion

Higher HEI scores, reflecting improved diet quality, were associated with higher BMD, suggesting a subtle yet important role of overall diet quality in bone health outcomes.



# Research Week 2020

## Longitudinal surveillance of health outcomes in response to a stable housing intervention for low income residents

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### Keywords

Housing insecurity, housing quality, disparities, quality of life

### Abstract

Poor housing quality is associated with negative health outcomes, even after controlling for socioeconomic factors. Using Coordinated Care Organization funding, a low income housing complex was built to support residents in central Oregon. This study explored whether stable housing could improve the health outcomes of low income individuals. Residents completed baseline survey measures within two weeks of move-in, with follow up assessment of health outcomes after one year. A total of 18 individuals received housing (61% female, 89% white, and 22% Hispanic or Latino). The age of residents ranged between 26-72 years, with an average age of 47. In baseline screening, 88% of residents reported fair to poor health-related quality of life, 72% reported moderate stress, 29% reported low life satisfaction, and 65% reported poor sleep. No residents met recommendations for fruit and vegetable intake and 69% exceeded sugar intake recommendations. No residents reported alcohol use, although 50% were current smokers. Residents reported an average of 8.8 pack years, categorizing 66% as high risk. Residents reported an average of 3 medical conditions, with 94% reporting at least one. Back and neck problems and mental health were most prevalent and impacted daily activities. Strong correlations were observed between mental health, life satisfaction, fatigue, and pain (all  $p < 0.001$ ). Followup measures were completed in February 2020 and are undergoing statistical analysis for individual-level change.





# Research Week 2020

## Clinical Dosimetry Tool Implementation of I-131 MIBG Therapy for Pheochromocytoma and Paraganglioma

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### Keywords

MIBG, Iodine-131, theragnostic, dosimetry

### Abstract

#### Purpose

To calculate a therapeutic activity that assures the limit doses are not exceeded for critical organs in patients undergoing the I-131 MIBG / AZEDRA (Progenics Pharmaceuticals, Tarrytown, NY) therapy for pheochromocytoma and paraganglioma.

#### Methods

A dosimetry calculation tool was developed based on the guidelines provided by the AZEDRA dosimetry protocol. The tool is designed to process the count data obtained from regions of interests drawn in scintigraphs of patients injected with 5 mCi of MIBG labeled with Iodine-131 and imaged three times over a period of 72 hours. The count data for the organs of interest was fitted with a mono-exponential curve. The estimates of radiation dose to each of the relevant organs at risk (kidneys, liver, lungs) are evaluated using a MIRD-equivalent formalism. More specifically, the dose factors (S values equivalent) were obtained from OLINDA/EXM software (Hermes Medical, Sweden) and imported into the tool. To account for each patient's unique anatomy, the organ masses were obtained from CT. The nominal therapeutic activity of 1000 mCi (injected in two sessions) was scaled down as necessary to ensure that the dose to the organs at risk is not exceeding the limits.

#### Results

The doses to the OARs obtained from the tool were compared and ultimately validated with the OLINDA software calculations. The calculated therapeutic activity varied between patients due to the difference in the clearance rate and tumor burden.

#### Conclusion

The implementation of the dosimetry protocol within a single tool allows for streamlined performance of patient-specific data analysis, organ dose estimation, and therapeutic

activity calculation. The tool has proven to be clinically useful in determining dose estimates to the OARs of two patients who have already been successfully treated.



# Research Week 2020

## Dendritic spine morphology and excitatory neurotransmission in prefrontal cortex is altered after early life sleep disruption

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### Keywords

Dendritic spines, Sleep, excitatory neurotransmission

### Abstract

Sleep deprivation studies indicate an essential role for sleep in the pathophysiology of many conditions, with sleep at a lifetime maximum during early life. Previous research in our lab using an early life sleep disruption (ELSD) paradigm has shown long lasting deficits in complex social and cognitive behaviors in adult prairie voles. We hypothesized that increased time spent awake during ELSD may cause a transient increase in excitatory neurotransmission, leading to morphological changes in dendritic spines and long lasting changes in excitatory neurotransmission. Here, we measured spine density and morphology on pyramidal neurons in layers 2/3 of the prelimbic cortex, a region of the brain involved in the behavioral changes observed in this model. Our approach combined light microscopy of Golgi-Cox stained brain tissue and ultrastructural examination of spines using electron microscopy. We found that ELSD resulted in an increase in thin spines, consistent with spines that are more immature. We also found a decrease in the area of nerve terminals expressing the vesicular glutamate transporter 1 (VGLUT1), a protein that is essential for quantal release of glutamate in presynaptic terminals, and a decrease in the size of the postsynaptic spine contacted by these VGLUT1 labeled presynaptic terminals, all within layer II of the prefrontal cortex. Our results suggest that early life sleep is important in development of excitatory connections and may play a causative role in the pathophysiology of neurodevelopmental disorders featuring impaired social and cognitive behaviors.



# Research Week 2020

## Effects of chronic and fractionated space radiation on behavioral and cognitive performance

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### Keywords

space, radiation, cognition, behavior

### Abstract

Project 4 of the NASA Specialized Center of Research on Carcinogenesis is focused on neurobehavioral characterization following space radiation exposure and testing potential countermeasures against the detrimental effects of space radiation exposure on the brain. The space radiation environment consists of multiple species of charged particles that may impact brain function during and following missions. In mouse studies, C57BL/6J and C57BL/6Jx DBA/2J F1 (B6D2F1) wild-type mice are often used for assessing effects of <sup>28</sup>Si irradiation on cognition. The marked differential effects of <sup>28</sup>Si ion irradiation on contextual fear memory in the hybrid strain and the pure C57BL/6J strain underline the importance of considering strains with distinct genetic backgrounds when evaluating the effects of space irradiation on the brain. As part of Project 4, we are also behaviorally and cognitively testing mice following exposure to fission spectrum neutron irradiation (<sup>252</sup>Cf neutrons at 1 mGy per day) to simulate the chronic, low dose rate exposures to high LET radiation that will be experienced by spaceflight crew beyond low Earth orbit. In the Fall of 2019, we assessed the effects of acute neutron exposure and the effects of long term, low dose aspirin on behavioral and cognitive performance on mice exposed to chronic neutron irradiation. Finally, we will behaviorally and cognitively tested C3H male mice irradiated with 0.4 Gy GCRsim in a single fraction or delivered in 19 fractions over 1 month, along with sham-irradiated C3H male mice. This presentation will provide a progress report of the ongoing work as part of Project 4.

This study is supported by a NASA Specialized Center of Research on Carcinogenesis grant, NNX15AK13G.



# Research Week 2020

## Patient Satisfaction Not Impacted by Antibiotic Prescribing for Viral Upper Respiratory Infections

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### Keywords

antimicrobial stewardship, patient satisfaction

### Abstract

Treating viral upper respiratory infections (URI) with antibiotics contributes to the rise of antimicrobial resistance. Major drivers of unnecessary prescribing are a patient's expectation to receive antibiotics for acute illness and the physician's desire to provide satisfactory care. Our objective was to determine if receiving an antibiotic prescription for URI is associated with increased patient satisfaction.

We identified emergency department (ED) and ambulatory care (AC) visits with an acute URI diagnosis code (9/2015-5/2016) that had an associated patient-satisfaction survey. The survey queried patients' overall satisfaction using a Likert-type scale ranging from 1-Very Poor to 5-Very Good. We assessed survey responses for visit satisfaction among patients receiving and not receiving antibiotics using the Wilcoxon rank-sum test, comparing ED and AC visits separately.

We collected survey responses from 282 ED patients and 1306 AC patients with acute URI. Compared to non-recipients, ED respondents receiving an antibiotic were more likely to be female (67% vs 55%) and on Medicare (28% vs 21%); AC respondents receiving a prescription were more likely to be female (68% vs 61%) and have private insurance (63% vs 53%). Median responses did not differ by antibiotic prescription status in either group (rank-sum p-value=0.4 and 0.8 for ED and AC respectively). When dichotomizing the satisfaction score, more patients receiving antibiotics reported satisfaction of good to very good than those not receiving antibiotics (84% vs. 76%; p=0.1) among ED patients, but not AC patients (95% vs. 94%; p=0.5).

Patient satisfaction was not strongly associated with antibiotic receipt among ED and AC patients with URI in our study. This finding suggests that providers may limit the spread of antibiotic resistance by ceasing to unnecessarily prescribe antibiotics without jeopardizing patient satisfaction. Given low response rates to visit satisfaction surveys, further work is needed to validate this study and evaluate its generalizability.



# Research Week 2020

## Towards an automated method for quantifying pedantic language in children with Autism Spectrum Disorder.

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### Keywords

autism spectrum disorder, natural language processing, speech and language disorders, pedantic speech, corpus linguistics

### Abstract

The language of children with Autism Spectrum Disorder (ASD) is sometimes described by clinicians as having a pedantic quality: overly formal, adult-like, and inappropriate for the conversational setting. The term, "pedantic speech", does not have a standard definition in ASD literature, but typically includes speech that is lengthy, containing too much detail, and more similar to written language than spoken language. Current measures of pedantic speech in ASD are subjective in nature and may not be consistent across examiners. Few automated measures have been proposed that do not involve additional manual coding by a transcriber. We have developed a fully automated method that attempts to measure pedantry at the unigram-level.

Our dataset consists of 109 transcribed Autism Diagnostic Observation Schedule (ADOS) sessions of 4-8 year-old children, across three diagnostic groups: ASD (n = 46), Typically Developing (TD; n = 43), Specific Language Impairment (SLI; n = 20). All participants have a full-scale IQ > 90 and a mean length of utterance (MLU) > 3.0.

For each unique word a child produced, we compute a "pedantic-index" score using the ratio of the frequencies of occurrence in two external corpora: the CHILDES corpus, to represent child-like speech; the Wall Street Journal Corpus (WSJ), to represent adult-like speech. Our hypothesis is that pedantic words will occur more frequently in WSJ than in CHILDES. The higher the pedantic-index of a word, the more pedantic it will be. Our overall pedantry score for a child is the 95th percentile of the pedantic-index scores for every unique word they said.

We are currently evaluating the performance of our measure as a diagnostic classifier and are exploring validation methods using various language assessment scores available to us. Future work includes substituting the WSJ corpora with other corpora that might function as a proxy for formal speech.



# Research Week 2020

## Quantifying Nest Building Behavior in Mice (*Mus musculus*) and Prairie Voles (*Microtus ochrogaster*) to Measure Functional Outcomes

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### Keywords

Nest building, behavior, rodents, disease models, health

### Abstract

Nest building is observed in a wide variety of rodents to provide shelter and as a means to thermoregulate in changing environmental conditions. Motivation and ability to build a functioning nest are therefore critical to health and survival and monitoring nesting can illuminate problems in normal functioning. Tests to quantify nesting are quick, easy, and capture behaviors inherent to an animal's day-to-day routine. Although many rodents build nests, the mouse strain-C57BL/6 is most commonly used in nest building research for its distinct nest building behaviors. However, there is limited research describing the nest building behavior of other rodent species. The socially monogamous prairie vole (*Microtus ochrogaster*) displays social behaviors that are more similar to humans than mice, such as opposite sex pair bonding and co-parenting, and thus can be used to study models of disease focused on social functioning such as autism, schizophrenia, or PTSD. Despite the prairie vole's natural motivation to build nests, there is currently no standardized test to measure nesting in this rodent species. We examined differences in nesting behaviors of mice and prairie voles in our lab, including time to begin nesting, shape of the nest created, and the amount of nesting material integrated into a nest. Given species differences in nest building, we propose a new system of scoring nests specific to prairie voles. This new method combines approaches designed for mice but also includes variables such as texture, volume, and spread that showcase the individual variation amongst prairie voles, and may improve assessing the functional outcomes in this species. Better understanding the specific nest building behaviors of prairie voles may provide an early or more subtle indication of impaired functional outcomes, for example in routine post-operative procedures, and that interventions may be needed to prevent the progression of disease.



# Research Week 2020

## Barriers to Maintaining Standard Precautions Compliance among Healthcare Workers

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### Keywords

Infection control, occupational health, environmental health, public health

### Abstract

Despite guidelines set by OSHA and CDC as well as literature showing the benefits of high standard precautions (SP) compliance, adherence with SP remains low (Gammon & Gould, 2005; Harris et al, 2017; Reddy et al., 2009). This paper evaluates current literature relating to the barriers associated with poor SP compliance with among health care workers (HCW), as well as a couple current strategies implemented to improve compliance rates. Two databases were searched, including PubMed and Google Scholar. The following search terms were used in each database: (Standard Precautions OR Universal Precautions) AND compliance AND United States AND (interventions OR barriers). The searches ranged from 27 to 17,000. Of these, 5 fit the inclusion criteria and were included in the literature review. Much of the literature focuses on individual behavior, knowledge and lack of training. While these are important factors to consider and find solutions to, it is suggested that more studies and intervention strategies focus on factors outside of the individual HCWs control, such as management support, workplace environment and safety climate of the unit. By creating multifaceted SP interventions that target multiple levels of the hierarchy of controls, proposed by the Total Worker Health (TWH) framework, overall compliance with SP will increase and ensure that compliance can be sustained over time.





# Research Week 2020

## Improving Machine Learning Models of Paraphasia Classification Using Crowdsourced Semantic Features

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### Keywords

Natural Language Processing, Machine Learning, Aphasiology, Language Assessment

### Abstract

Confrontation naming tasks such as the Philadelphia Naming Test (PNT) are essential tools for the assessment and treatment of people with aphasia. One challenge to clinical use of the PNT is the complexity of its scoring guidelines. We build on work towards automatic classification of paraphasias by (1) demonstrating that machine learning models substantially improve performance on the paraphasia classification task, (2) providing insight into the behavior of the highest-performing model, and (3) reporting results on experiments with contextual semantic and item-level information. Our best model improves 8.1 F1 points over a manually-constructed decision tree classifier. For development of the semantic features, we used crowdsourcing methods to construct a dataset of linguistic contexts from the visually presented items on the PNT assessment.



# Research Week 2020

## Safety of Intra-arterial (IA) Chemotherapy and Blood Brain Barrier Disruption (BBBD) for treatment of patients with malignant brain tumors

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### Keywords

Intra-Arterial Chemotherapy, Blood Brain Barrier Disruption, Brain Tumor

### Abstract

#### Background

Administration of chemotherapy via intra-arterial (IA) route results in a higher concentration of targeted chemotherapy against resilient brain malignancies with a decreased systemic chemotherapy side effect. Osmotic blood-brain barrier disruption (BBBD) further intensify drug delivery and effects on brain malignancies. The aim of this study is to determine the safety of the use of intra-arterial chemotherapy and blood brain barrier disruption to treat malignant brain tumors.

#### Methods

This is a single-institution, retrospective cohort study of malignant brain tumor patients at the Oregon Health and Science University (OHSU) to determine the safety of the use of IA and BBBD. Four hundred and thirty-six patients who were treated with IA and BBBD at OHSU from 1997-2018 were included in the study (4,940 procedures). Treatment complications were documented along with procedural outcomes and life expectancy after diagnoses. The data will be analyzed to determine if the safety of IA and BBBD.

#### Preliminary Results

Review of the 4,940 procedures shows a complication rate of 2.8% when utilizing IA and BBBD. This complication rate includes both major and minor complications. The major complication rate is approximately 0.8%. Further analyses will be performed to determine how the specific complications arose.

#### Discussion

Intra-arterial chemotherapy provides many benefits, including increased chemotherapy concentration at the tumor site and decreased systemic chemotherapy side effects. These benefits must be carefully compared to the potential risks associated with surgical

procedures in order to ensure physicians make correct treatment decisions when facing patients with malignant brain tumors. This study aims to determine if the benefits of intra-arterial chemotherapy outweigh the risks associated with the procedure. Results will also provide preliminary data to directly test the efficacy of intra-arterial (IA) chemotherapy infusion vs. traditional chemotherapy should the procedure be determined safe by this study.



# Research Week 2020

## Novel Interventions in Children's Healthcare for Youth with T1D: Does Mental Health Moderate Outcomes?

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### Keywords

behavioral health intervention, health outcomes, pediatrics, type 1 diabetes

### Abstract

#### Objective

Novel Interventions in Children's Healthcare (NICH), an intensive behavioral health program, has demonstrated promise in improving health outcomes in youth with type 1 diabetes (T1D) with social risks that impact disease management. Given that mental health (MH) concerns can impact T1D outcomes and are prevalent in youth with social risks, this study aims to examine 1) the presence of MH diagnoses in NICH youth and 2) potential impact on health outcomes.

#### Methods

Youth (n=70) served by NICH were included. EHR review included complications (DKA) and HbA1c one year prior and two years following NICH initiation. EHR review and family report (FR) were used to examine presence of MH conditions. Mean age was 14.4 years; 40% male; 77% non-Hispanic white.

#### Results

MH condition prevalence ranged from 17% (EHR review) to 40% (FR). When comparing the year prior to NICH initiation to the following 2 years, youth with MH via EHR (n=12) demonstrated reductions in yearly DKAs (2.0 to .95) and increased HbA1c (11.3 to 11.6) while those without (n=58) experienced fewer yearly DKAs (1.3 to .84) and decreased HbA1c (11.3 to 10.9). When comparing the same time frames using FR, youth with MH (n=28) had fewer yearly DKAs (2.0 to 1.4) and decreased HbA1c (11.2 to 10.9), and those without MH (n=42) experienced less yearly DKAs (1.0 to .5) and increased HbA1c (11.3 to 11.0).

#### Conclusion

Findings are variable depending on methods used to establish presence of MH diagnoses, with more than 50% of MH diagnoses reported by families not being present in EHR. When using FR for MH identification, youth with MH had significantly ( $p<.05$ ) more DKA

events prior to NICH initiation than those without. No other outcomes were significantly different when comparing those with and without MH, regardless methodology, suggesting that NICH outcomes are robust to MH concerns.



# Research Week 2020

## NRF2 activating dimethyl fumarate improves mitochondrial function, reduces oxidative stress and enhances synaptic plasticity a neuronal model of synucleinopathy

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### Keywords

alpha-synuclein, antioxidant, NRF2, mitochondrial function, synaptic density

### Abstract

Lewy bodies comprised of aggregated alpha synuclein ( $\alpha$ Syn) protein are a pathological hallmark of the Parkinson's disease (PD). Increased oxidative stress, mitochondrial dysfunction and synaptic loss are also features of the PD brain. NRF2 regulates the antioxidant response pathway and has been shown to be neuroprotective in many models of neurodegenerative diseases. Dimethyl fumarate (DMF) is a NRF2 activator that is FDA approved for treatment of multiple sclerosis making it an attractive candidate to be repurpose for use in PD. Here we investigate the antioxidant, mitochondrial and synaptic effects of DMF in neurons isolated from the A53T  $\alpha$ Syn mouse model of synucleinopathy.

Embryonic hippocampal neurons were isolated from A53T  $\alpha$ Syn mice as well as wild-type (WT) littermates. Cells were treated with either DMF or the NRF2 inhibitor ML385 and mitochondrial function was evaluated along with markers of synaptic plasticity and oxidative stress.

Relative to WT neurons,  $\alpha$ Syn neurons had impaired dendritic arborization and DMF treatment restored this deficit. Increased reactive oxygen species and impaired mitochondrial function were also seen in the  $\alpha$ Syn neurons and DMF treatment likewise improved these endpoints. Inhibition of NRF2 with ML385 resulted in a greater impairment of mitochondrial function, further increases in oxidative stress and a greater reduction in markers of synaptic density in  $\alpha$ Syn neurons.

These data show that NRF2 activation can reduce oxidative stress, improve mitochondrial function and restore synaptic plasticity in neurons isolated from A53T  $\alpha$ Syn mice whereas NRF2 inhibition exacerbates these endpoints. Taken together these data suggest that NRF2 may be a viable therapeutic target in PD.



# Research Week 2020

## The Association of Communication Quality Regarding Incidental Nodules on Psychosocial Outcomes

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### Keywords

health communication, pulmonary nodules, psychosocial harms, lung cancer worry, communication quality

### Abstract

#### Purpose

Millions of patients are diagnosed annually with a pulmonary nodule and related follow up can cause psychosocial harms such as lung cancer worry, depression, and anxiety. High quality patient-centered communication of nodule results could help reduce those psychosocial harms over time.

#### Methods

We conducted a prospective, repeated-measures, cohort study of participants with newly reported, incidentally detected pulmonary nodules. The primary exposure was quality of communication regarding nodules that was measured using the Consultation Care Measure (CCM), which is based on the patient-centered communication model. We assessed the primary outcomes of lung cancer worry, depression, and anxiety with the Lerman Breast Cancer Worry Scale (CWS), the Center for Epidemiologic Studies Depression Scale (CES-D), and the Hospital Anxiety and Depression Scale (HADS), respectively. We performed multivariable-adjusted linear regression models between study visits of each participant to compare the association of high-quality communication with those outcomes.

#### Results

We included 121 participants with an average of 3 (SD 1.24) assessments. Participants with excellent communication had a 0.36 (n=206, 95% CI: 0.04, 0.67, p=0.03) unit increase in their worry score at the next visit, compared to participants with less than excellent communication. We observed no difference (n=210, b=0.90, p=0.40) in depression score change or in the anxiety score change (n=211, b=0.15, p=0.81) between participants who reported excellent communication compared to participants who reported less than excellent communication at the following visit.

## Conclusions

We found that high quality communication is not associated with reduced psychosocial harms and there was even a small increase in lung cancer worry. We suspect that clinicians may tailor their communication based on their patient's risk of lung cancer. Higher quality communication strategies may appropriately influence patients' worry but does not influence other, possibly more severe harms such as depression and anxiety.





# Research Week 2020

## Linking Traumatic Brain Injury, and Post-Traumatic Headache: a Potential Role for Glymphatic Pathway Dysfunction

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### Keywords

Traumatic Brain Injury, Headaches, Glymphatic System, MRI, Pediatrics

### Abstract

Headaches are frequently reported by patients with traumatic brain injury (TBI). The relationship between TBI and headaches is poorly understood. Disruption of the glymphatic pathway, a brain-wide network of perivascular spaces, could explain this link. The glymphatic pathway allows the exchange of fluid, solutes, and wastes between the cerebrospinal fluid and the brain interstitium. MRI-visible enlarged perivascular spaces (ePVS) may be putative surrogates of glymphatic function. The purpose of this study is to: a) characterize the ePVS burden in a cohort of healthy adolescents; b) determine if ePVS burden is increased in individuals with post-concussive symptoms.

### Methods

Characterize ePVS burden. One hundred and eighteen 12-21 year old subjects received T1- and T2-weighted 3T MRI. ePVS were identified in white matter on T2-weighted imaging and their characteristics were calculated using a local heterogeneity approach.

Evaluation of ePVS burden in subjects with post-concussive headaches. Twenty subjects with post-concussive headaches received a 7T MRI (T1, T2, FLAIR, GRE). ePVS burden was estimated as above, and compared to 20 healthy individuals (preliminary data).

### Results

Total ePVS number ranged from 16 to 287. ePVS were found more often in frontal and parietal WM lobes ( $p < .01$ ). Males had a significantly higher number of ePVS than females (mean [SD]; 98.4[50.5] males vs. 70.7[36.1] females,  $p < 0.01$ ). Age and pubertal status were not significantly associated with ePVS burden when controlling for gender.

Preliminary results in one subject scanned under this protocol show that there is an asymmetry in the ePVS burden, which correlated with the injury location, and surrounds an area of microhemorrhage.

## Conclusion

In our cohort, males have a higher ePVS burden than females, regardless of age and pubertal status. We provide the first evidence, although preliminary, of regional changes on ePVS burden in a subject with post-traumatic headaches, seen with high resolution MRI.



# Research Week 2020

## Automatic Characterization of Temporal Properties in Verbal Fluency Tests

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### Keywords

Neuropsychological tests, Animal Fluency, Biomarkers, Mild cognitive impairment, Computerized assessment

### Abstract

#### Introduction

In the VF test, participants are asked to retrieve as many words in a category (e.g., animals) as possible in a short duration of time, typically one minute. Conventionally, the count of uniquely generated correct words comprises the final score. However, this does not consider other clinically relevant information such as the sequential pattern of produced words in a semantic fluency test.

#### Method

Capitalizing on the temporal aspects of the animal fluency test, we hypothesize that time related measures of the response will be useful in distinguishing mild cognitive impairment (MCI) from cognitively intact (CI) controls. Measuring temporal properties of the VF is costly and time-consuming as it requires a precise annotation of timestamps (i.e., when in time a word begins and ends). To address this drawback, we propose a computational approach that utilizes an automatic speech recognition (ASR) system, in which temporal properties of the verbal response is automatically characterized. Our model semantically clusters animal names and automatically characterizes the semantic search strategy of subjects in retrieving words from animal name clusters. Extracted time-based measures along with standard count-based features are then used in a support vector machine (SVM) classifier to examine the utility of these measures in distinguishing those with MCI from CI controls.

#### Results

We experimentally showed that the conventional test score cannot capture other clinically useful information from the test and once it is solely used for training a support vector machine (SVM) classifier, the resulting model achieved a poor performance. The combination of both count-based and time-based features, automatically derived from the test response, achieved 77% on AUC-ROC of the SVM classifier, outperforming the model

trained only on the raw test score (AUC, 65%), and well above the chance model (AUC,50%).



# Research Week 2020

## Sex differences in Big Five personality trajectories among adolescents and young adults

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### Keywords

Development, Personality, Sex Differences

### Abstract

Personality plays a role in phenotypic risk and resilience across the lifetime. Research on personality development during adolescence is mixed and suggests both increases and decreases in individual traits (e.g. extroversion, agreeableness, etc.) with age. To address these disparate findings, this study capitalized on a relatively large study, with multiple waves of longitudinal data, to investigate linear and non-linear changes in personality across adolescence and young adulthood and as a function of sex. Select data from the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA) study, a 5-site, cohort-sequential longitudinal study of adolescent neurodevelopment (age 12 to 21 at study entry) were analyzed. 829 participants completed the Ten-Item Personality Inventory (TIPI) at baseline and 4 annual follow-up visits, with most completing 3 out of 4 follow-ups. To assess for both linear and non-linear changes on the 5 TIPI subscales (agreeableness, conscientiousness, emotional stability, extroversion, and openness), generalized additive mixed models (GAMM) were fit for each subscale, separately. There were significant developmental effects across all five factors of the TIPI. Males had lower overall levels of conscientiousness and agreeableness, compared to females, but both males and females demonstrated linear increases in these factors with increasing age. Males and females decreased in extroversion in early adolescence then deviated in development in late adolescence, with males demonstrating steeper decreases than females. Females decreased in emotional stability in early adolescence then increased in late adolescence, while males showed the opposite pattern. This study replicated previous reports of increasing conscientiousness and agreeableness with age, and provides novel evidence of non-linear changes in extroversion and emotional stability as a function of sex. These sex differences and non-linear patterns in personality development help reconcile conflicting reports of personality change. Future research should attempt to replicate these sex differences in development on more comprehensive measures of personality.



# Research Week 2020

## Social Determinants as Indicators for Medication Adherence and Graft Function in Pediatric Kidney Transplant Recipients

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### Keywords

Social Determinants, Transplant, Adherence, Nephrology, Pediatrics

### Abstract

#### Introduction

Social determinants of health (SDoH) affect the outcomes of medical interventions. We examined the association of SDoH documented pre-kidney transplant (Tx) with medication adherence and graft function within the first year after kidney Tx in children.

#### Methods

We conducted chart review of patients with a first kidney Tx at Doernbecher between 2012-2017, receiving tacrolimus therapy. SDoH data were collected from social workers' notes documented during pre-Tx evaluation. Medication adherence was assessed by calculating the coefficient of variation of tacrolimus trough levels (TCV) as well as the presence of donor specific antibodies (DSA) over 12 months post-Tx. TCV > 30% was considered high risk for medication non-adherence. Graft function was estimated using the bedside Schwartz equation (eGFR) at 12 months post-Tx. Data were analyzed in R. Summary statistics were calculated. Appropriate model assumptions were checked for linear and logistic regression. Multiple variable regression was used to examine the impact of SDoH variables on TCV, eGFR, and DSA.

#### Results

39 patients were included in the analysis, mean  $10.9 \pm 6.7$  years at Tx, and 54% male. Based on the regression, patients who lived in a single caregiver household were estimated to have a TCV 6.04% higher (95% CI: -3.66 to 15.73%), an eGFR 10.78 mL/min/1.73m<sup>2</sup> lower (95% CI: -36.6 to -3.09 mL/min/1.73m<sup>2</sup>), and 2.98 times the odds of DSA (95% CI: 0.24 to 45.51) compared to their counterparts.

#### Conclusions

Our results are limited by sample size and retrospective design, but indicate that SDoH of children who are evaluated for kidney Tx may be important indicators of medication adherence and graft function post-Tx. SDoH variables that act as risk factors can often be addressed pre-Tx. For example, the results suggest that strengthening support for primary caregivers may improve post-Tx outcomes, particularly among single caregivers or those with a chronic illness.



# Research Week 2020

## A Novel Treatment for Melanoma: Targeting the MIF/CD74 Inflammatory Pathway

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### Keywords

Melanoma, immunotherapy, MIF, CD74, DRQ

### Abstract

Melanoma is one of the more aggressive skin cancers with a high mortality rate once it metastasizes. New breakthroughs in the treatment of melanoma have come from the introduction of immune checkpoint blockade (ICB). Targets of ICB include programmed cell death protein 1 (PD-1), program death-ligand 1 (PD-L1), and cytotoxic T-lymphocyte associated protein 4 (CTLA-4). However, these therapies that target ICB proteins are only effective in 30-40% of melanoma cases. Combinations of these drugs can lead to better outcomes but also increase the risk of severe side effects. A new inflammatory pathway is being investigated, the receptor CD74 and its known ligands macrophage migration inhibitory factor (MIF) and its homolog D-dopachrome tautomerase (D-DT). This pathway is highly inflammatory in autoimmune diseases like multiple sclerosis (MS). However, studies in melanoma have shown the MIF/CD74 pathway creates regulatory/pro-tumorigenic macrophages and can potentially induce tumor cell survival through phosphorylated extracellular-related kinase (pERK1/2) signaling. We have developed a partial MHC class II construct, DRQ, that inhibits ligands from binding to CD74 and blocks downstream signaling through CD44 to increase pERK1/2. We hypothesize that DRQ can be used at low doses to treat melanoma. Mice survive significantly longer with metastatic melanoma when treated with a lower dose of DRQ than the higher, immunosuppressive dose, or vehicle. Additionally, B16F10 mouse melanoma cells produce MIF in culture and have a baseline expression of CD44. When the cells are cultured with interferon gamma (IFN $\gamma$ ) for 48h, the cells express significantly more CD74 and PD-L1 compared to baseline. These results suggest targeting the MIF/CD74 pathway by inhibiting CD74 with DRQ could provide a novel treatment for melanoma as a monotherapy for patients that fail ICB or as an adjuvant therapy with ICB therapy.





# Research Week 2020

## Study protocol for the review of adverse safety events in the EMS care of children with out-of-hospital cardiac arrest in the United States

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### Keywords

Patient Safety; Medical Errors; Cooperative Behavior; Patient Care Team; Emergency Medical Services; Teamwork; Child; Humans

### Abstract

#### Introduction

Efforts to improve the quality of Emergency Medical Services (EMS) care for adults with out-of-hospital cardiac arrest (OHCA) have led to improved survival over time. Similar improvements have not been observed for children with OHCA, who may be at increased risk for preventable adverse safety events during prehospital care. The proposed study aims to identify patient and organizational factors that are associated with adverse safety events during the EMS care of pediatric OHCA.

#### Methods and analysis

We propose a large multi-site EMS study in the United States (US) consisting of chart reviews and agency surveys to measure, characterize, and evaluate predictors of adverse safety events in pediatric OHCA. Using the previously validated Pediatric prehospital adverse Event Detection System (PEDS) tool, we will review EMS charts for 1,500 children with OHCA from 2013-2019 to collect details of each case and identify severe adverse safety events (ASEs). Cases will be drawn from multiple EMS agencies in at least five states in geographically diverse areas of the US. EMS agencies providing charts will also be invited to complete an agency survey to capture organizational characteristics. We will describe the frequency and proportion of severe ASEs in pediatric OHCA across geographic regions and clinical domains, and identify patient and EMS organizational characteristics associated with severe ASEs using logistic regression.



# Research Week 2020

## An Ambulatory Intensive Care Unit (“A-ICU”) for Medically and Socially Complex Patients Improved Mental Health Functioning, Patient Well-Being, and Outpatient Engagement at 6-months: Interim Results of SUMMIT Randomized Controlled Trial.

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### Keywords

social determinants of health, addiction, primary care, improving quality of care

### Abstract

#### Background

People experiencing homelessness, co-morbid chronic medical conditions, and substance use disorder (SUD) make up a disproportionate number of high-cost, high-need patients. Intensive ambulatory care unit (“A-ICU”) interventions aim to improve patient engagement, quality of care, and reduce hospitalizations.

#### Methods

This is a preliminary analysis of a randomized trial of SUMMIT, an A-ICU for high-utilizers at a federally qualified health center that serves patients with high rates of poverty. SUMMIT is a stand-alone team consisting of care coordinators, an addictions-boarded physician, social workers, complex care nurse, pharmacist, and team manager, with a low staff-to-patient ratio and increased appointment flexibility. Patients were randomized to enroll in SUMMIT immediately or to remain in usual care. We assessed functional status using the 12-item short form survey (SF-12) and wellbeing from the Edmonton Symptom Assessment System (ESAS) at 6-months. We also examined primary care (PCP), mental health (MH), and hospital utilization.

#### Results

Of 139 patients enrolled, 52% (n=73) were randomized to SUMMIT. Average age was 54.7 years (+/-10.1), with the majority male (62.6%); a majority (60.4%) had high school education or less, 84.2% had very low income (<\$1000/month), 27.3% reported having an opioid use disorder, and 51.1% reported being homeless within the past year. In the six months prior to enrollment, participants averaged 7.3 (+/-1.2) PCP visits and 2.6 (+/-1.7)

hospitalizations. At follow up, SUMMIT patients had higher SF-12 Mental Health scores (46.5 vs 42.0,  $P<0.01$ ), and higher self-reported wellness rating (ESAS 6.3 vs 4.9,  $P<0.01$ ). SUMMIT patients had higher number of PCP visits (12.3 vs 4.9,  $P<0.01$ ) and MH visits (7.8 vs 6.4,  $P<0.01$ ) but hospital admissions did not differ between groups (1.94 vs 1.91,  $P=0.72$ ).

### Conclusions

SUMMIT improved mental health functional status and well-being, perhaps mediated through increased engagement in outpatient care. Six-months may be too soon for SUMMIT to impact utilization.



# Research Week 2020

## Blood Loss in Acetabular Surgery; Consequence of Fracture Pattern and Surgical Approach

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### Keywords

acetabulum fracture bloodloss

### Abstract

#### Purpose

Intraoperative blood loss (IBL) in acetabular fracture care is rarely minor; accurate IBL prediction and measurement may improve intra and postoperative care in high blood loss operations. The purpose of this study is to determine the impact of fracture pattern and surgical approach on IBL during acetabular surgery, investigated using a novel, quantitative, formulaic approach.

#### Methods

All patients presenting to our Level 1 academic trauma center receiving unilateral acetabular ORIF were reviewed (2008-18, n=371) for patient, injury, pre & post operative hematocrit, surgical details, and intraoperative transfusions. Fractures were classified and approach categorized as: Kocher-Langenbech, Iliioinguinal (full or 1st & 3rd windows), Stoppa only, or percutaneous. IBL was calculated using adaptations of the Gross and Nadler formulas which utilize changes in hematocrit and, through the "blood volume" factor, account for patient differences in height, weight, and gender:

$$\text{Blood loss} = \text{Blood Volume} \times ((\text{Hct0} - \text{HctF} + \text{Units Transfused} \times 1.9) / \text{HctAVG})$$

A multivariate model was created & variables were prioritized via backwards stepwise multivariate linear regression.

#### Results

349 patients (94%) were included in the model; 67% of patients (233/349) sustained associated patterns. IBL was similar across fracture patterns, and all potential groupings. A difference existed between approaches (Figure 1), with highest IBL via the Kocher-Langenbech approach (df=3, F=3.59, p=0.01). In multivariate modeling, percutaneous approach (-448 mL, p<0.01), height (+13.3 mL per cm, p<0.01), and delayed surgery (-48 mL, p<0.01) were all associated with IBL.

## Conclusion

IBL is influenced by surgical approach & technique, patient height, and time to surgery as calculated by formula, as opposed to intraoperative estimation.



# Research Week 2020

## Towards Developing Quantum Proof of principle Applications for the Biological Sciences

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### Keywords

Algorithms Computational Biology Quantum Information

### Abstract

There has been a growth of interest in the application of quantum computation and quantum simulation to the many intractable computational problems in the biological sciences. While theoretical results imply the value of quantum information processing (QIP) to many of the challenging problems resident in this research domain, such as molecular dynamics simulation, oncogenic mutational signature inference, and phylogenetic tree inference, a framework to guide the realization of quantum proof of principle applications has yet to be clarified. Here, we present such a framework, comprised of five components; Assessment, Complexity, Problem Instance, Hardware Implementation, and Validation, that has been assembled to fill this crucial gap and aims to orient domain practitioners as they begin exploring applications of QIP. While motivated by applications of quantum computing to the biology domain, the framework is sufficiently general that it may find use in other domains – guiding the development of quantum proof of principle applications across the many scientific domains that stand to benefit from this rapidly advancing technology.



# Research Week 2020

## Head Computed Tomography (CT) Volumetrics to Quantify Cerebral Edema using 3D SLICER

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### Keywords

Traumatic Brain Injury (TBI), Cerebral Edema (CE), Brain Volume (BV), Head Computed Tomography(CT), 3D Slicer

### Abstract

#### Introduction

Following traumatic brain injury (TBI), fluid can accumulate in damaged brain tissue (e.g. "cerebral edema" or CE), and cause irreversible injury. Currently, there is no single accepted method to quantify CE. The purpose of this study was to measure the accuracy of a protocol using an open source software platform for medical image informatics(3D SLICER) to evaluate changes in brain volume (BV) on Head CT in order to quantify CE.

#### Methods

A subset of patients with TBI were identified from a prospectively enrolled cohort of critically ill

trauma patients. Using 3D SLICER, three independent novice readers were trained on a

standardized protocol measured BV on head CTs using a semiautomated tool to segment brain regions based on a threshold (20-50) of Hounsfield units. Total BV was calculated with

adjustment for the presence of lesions where applicable. We assessed intra-rater reliability with a two-way random-effects model, reporting an intraclass correlation coefficient. Descriptive statistics were calculated to quantify change in BV between scans; significance was set at  $p < 0.05$ .

#### Results

A total of 70 patients with 124 scans were measured for BV, while 16 scans (11%) were

excluded(missing (n=5), poor quality(n=11)). The ICC=0.97 (95% CI: 0.96 to 0.98,  $p < 0.001$ )

indicating excellent agreement between the 3 raters. The mean standard deviation between scan reads was 30mL, which represents 2.7% of the mean BV (1140mL). Fifty-four patients had paired scans that were assessed for BV change between initial and follow up scans. Follow up scans were obtained a median of 7 [6-41] hours after the initial, and on average, BV increased by 2.0% (SD  $\pm$ 5.6%), but ranged from -14% to 19% in the cohort.

### Conclusions

Novice readers can produce highly reliable brain volume measurements on CT after TBI. Future work will examine the correlation between measured % BV change and clinical measures of CE.





# Research Week 2020

## Diagnostic instruments used to diagnose Posttraumatic Stress Disorder and measure symptom severity in randomized controlled trials

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### Keywords

Posttraumatic stress disorder, assessment, diagnosis, randomized controlled trial

### Abstract

Randomized controlled trials (RCTs) of PTSD interventions use many different instruments to diagnose PTSD and assess symptom severity, which may limit the ability to compare findings across trials or pool data for meta-analysis. Understanding and comparing these differences can provide guidance on instrument selection for future research and evidence synthesis efforts. We analyzed data from the PTSD-Repository, a database of 318 PTSD RCTs on adults, to describe the instruments used, the assessment types (structured clinical interview, clinical diagnosis, or self-report questionnaire), and the relationship between assessment type and study characteristics (e.g., pharmacologic vs. nonpharmacologic). Across these RCTs, 26 different instruments were used to diagnose PTSD or measure patients' symptom severity. To diagnose PTSD, 63% of studies used a structured clinical interview, 15% used a clinical diagnosis, 10% used a self-reported survey, and 12% used multiple methods. The Clinician Administered PTSD Scale (CAPS) was the most common instrument used to diagnose PTSD (36.79%). To measure PTSD symptom severity, 67% of studies used structured clinical interviews and 33% used self-reported surveys. Pharmacologic studies primarily used the CAPS (71%) and the Impact of Event Scale (8%). Nonpharmacologic studies primarily used the CAPS (47%) and the PTSD Checklist (14%). There is significant variation in the instruments used to measure symptom severity. Prioritizing the use of PTSD symptom severity measures that are directly comparable would facilitate synthesis of PTSD outcome data across RCTs.



# Research Week 2020

## Novel Interventions in Children's Healthcare (NICH): Examining Access to Diabetes Technology Among Socially Vulnerable Youth with Type 1 Diabetes

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### Keywords

behavioral health intervention; health outcomes; pediatric; type 1 diabetes

### Abstract

#### Objective

Recent advancements in technology (insulin pumps, continuous glucose monitors (CGMs)) for youth with type 1 diabetes (T1D) hold promise for better outcomes, but multiple barriers to access exist. Novel Interventions in Children's Healthcare (NICH), an intensive behavioral health program, was designed to improve care for vulnerable youth and is associated with improved health for youth with T1D, but less is known regarding technology access for these youth. This study aims to 1) identify prevalence of technology use prior to and following NICH initiation and 2) examine whether technology access moderated NICH youth outcomes.

#### Methods

Youth with T1D served by NICH (n=69) were included. EHR review included T1D complications (DKA), HbA1c values, and presence of T1D technology one year prior and two years following initiation of NICH services. Youth mean age was 14.2 years (SD=3.5); 57% were female; 78% were non-Hispanic white.

#### Results

5.8% of youth had access to some form of technology prior to NICH (pump=5.8%; CGM=0%) and 14.5% had access to some form of technology 2 years post NICH initiation (pump=11.6%; CGM=10.1%). Youth were significantly more likely to gain access to CGMs ( $p<.01$ ) and general T1D technology ( $p<.05$ ) while in NICH. While there were no significant differences in health outcomes for those who gained technology while in NICH compared to those who did not, youth who already had technology prior to NICH had significantly fewer days admitted prior to NICH (M=1.0 days; SD=2.0) compared to those without access (M=5.8 days; SD=8.3).

## Conclusion

With clinic level rates of tech access hovering around 50% for CGMs and 40% for pumps, this study demonstrates that 1) youth referred to NICH experience substantial barriers to accessing T1D technology, 2) NICH participation is associated with increased access to T1D technology for socially vulnerable youth, and 3) despite program involvement, technology access inequities persist.



# Research Week 2020

## Retrospective Analysis of Mild Traumatic Brain Injuries at Oregon Health Science University

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### Keywords

Concussion, mTBI, balance, retrospective

### Abstract

Mild traumatic brain injury (mTBI) is a major public health concern and patterns of referral and time from injury to clinic visit is not well understood. The purpose of this study is to describe the patient demographics and time to clinical care in patients with an mTBI seeking care at Oregon Health Science University (OHSU). This study, a retrospective chart review, examined records from 2016-2018. Inclusion was a diagnosis of mTBI and people with hospitalization, skull fracture and positive neuro-imaging were excluded. Data extraction included age, gender, county of residence, time from injury to OHSU visit, cause of mTBI, history of mTBI, total previous mTBI, loss of consciousness, whether imaging performed, and total symptom score at time of clinical care (Sport Concussion Assessment Tool [SCAT]). Across these 2 years, a total of 3,870 people were seen in the OHSU for an mTBI. People were between 3-89 years old (median age 31) and 51.4% female. 71% came from the Portland Metro area, specifically Multnomah county (36%), Clackamas county (12%), Washington county (19%), and Clark County (4%). Of these 3,870 people, 1,010 were seen by a sports medicine provider. This subset of patients had a mean time from injury of 143 days and 52% of these people received CT scan. The most common mechanism of injury was motor vehicle accident (37%) and sporting injury (32%). A history of prior mTBI was present in 49% of people with a median of 2 prior occurrences. Lastly, these patients reported an average symptom score of 46 out of a possible 132. Understanding the pattern of patients being treated at OHSU can help maximize clinical care for this complex patient population. We plan to further examine points of entry into OHSU including which departments first see these patients and what percent are referred to rehabilitation.



# Research Week 2020

## Low parental criticism prospectively predicts the development of self-efficacy in children

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### Keywords

Self-efficacy, self-efficacy in children, parental criticism, ADHD, resilience

### Abstract

#### Introduction

Self-efficacy is a central component to mental wellness and resilience across the lifespan (Bandura, 1997; Muris, 2002; Prince-Embury and Saklofske 2013; Joët., Usher, & Bressoux, 2011). Family environment, including positive parental support, is related to the development of self-efficacy (Prince-Embury and Saklofske 2013; Dyvorsky and Langberg, 2016). At the group level, children with attention-deficit/hyperactivity disorder (ADHD) have low self-efficacy, but little is known about mechanisms supporting development of self-efficacy in this group. Here, we focus on parental criticism—one important aspect of the parent-child relationship—and its prospective relationship to self-efficacy in children with and without ADHD. We hypothesize that low parental criticism in early childhood will prospectively predict higher self-efficacy in later childhood and adolescence.

#### Method

606 children (nADHD=509) ages 7-11 years old underwent a comprehensive diagnostic evaluation, including parent and teacher standardized rating scales, parent clinical interview, and child cognitive testing. Evaluation was repeated annually for three years. Parental criticisms were coded from five-minute speech samples (FMSS). Child self-efficacy was measured via California Q-sort items selected based on self-efficacy items from the Resiliency Scales for Children and Adolescents.

#### Results

Children with ADHD had lower self-efficacy ( $M=4.92$ ,  $SD=1.16$ ) compared to those without ADHD ( $M=6.16$ ,  $SD=.97$ ) at baseline,  $p<.001$  and at Year 3,  $p<.001$ ). Baseline self-efficacy predicted Y3 self-efficacy,  $b=.67$ ,  $p<.001$ . In addition, lower levels of parental criticism at baseline predicted greater self-efficacy at Y3,  $b=-.08$   $p=.023$  after controlling for baseline self-efficacy.

#### Conclusions

Findings confirm that low parental criticism prospectively predicts higher self-efficacy, an important component of resilience, even after controlling for baseline self-efficacy. Results help clarify processes contributing to development of self-efficacy and provided a treatment target for building resilience. Improving parent-child relationships, and specifically attenuating parental criticism in early childhood, may be one way to increase self-efficacy and build resilience in children with ADHD.



# Research Week 2020

## Creating future leaders in women's health research: A goals-based evaluation of OHSU's oldest K12 career development program

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### Keywords

Women's Health, Training, Career Development, BIRCWH

### Abstract

#### Background

The Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program is an NIH-funded K12 award with the goal of supporting junior faculty to research independence. The Oregon BIRCWH program is one of 20 nationwide and is the longest standing K12 training program at OHSU. The program aims to develop junior faculty members through mentorship, salary support, and protected time with the ultimate goal of producing high-level, independent researchers in women's health and/or sex/gender differences research. Over 18 years, the Oregon BIRCWH has funded nearly 30 interdisciplinary junior-faculty members.

#### Objectives

We aim to quantify the success of the program through the analysis of scholar productivity through metrics such as receipt of independent K-series and R-series grants, publication output preceding and following their appointment as an Oregon BIRCWH K12 scholar, and impact score. Non-quantifiable metrics, such as obtaining leadership positions both within and outside of academia, will also be considered as a measure of scholar success.

#### Results

Leveraging nearly two decades of scholar narratives and incorporating conventional metrics of research success such as publications, citations, federal grant funding, and academic appointments, the Oregon BIRCWH Program is effectively meeting its mission of supporting and elevating junior researcher careers at OHSU.

#### Conclusion

As a long-running training program with set metrics for success, it is valuable to periodically engage in self-reflective evaluation to ensure the program is meeting or exceeding its federally-mandated mission. This evaluation shows that the Oregon BIRCWH Program has continued to fulfill its mission over the last 18 years.





# Research Week 2020

## Transcriptome-wide Characterization of Alternative Splicing Variants in Drug Resistant AML

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### Keywords

Bioinformatics, Genomics, Cancer, Alternative Splicing, RNA-Seq

### Abstract

Abnormal splicing events can promote drug resistance in a variety of cancer types, however, the full extent of genome-wide splicing in therapy-resistant AML is not fully characterized. Further, expression changes of splice variants do not occur independently, but rather in a coordinated fashion in order to maintain proper cellular function. Therefore, in order to understand how aberrant splicing confers drug resistance in AML, alternative splicing needs to be studied on a systems-wide level. This research utilizes a network-based approach to characterize coordinated alternative splicing variation and identify potential splicing event signatures of drug response in AML.



# Research Week 2020

## Role of genetic background in behavioral and cognitive phenotypes of NF1 mice

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### Keywords

Neurofibromatosis, Genetics, Behavior, Cognition

### Abstract

Neurofibromatosis type 1 (NF1) is a genetically determined neurodevelopmental disorder and tumor syndrome with an incidence of approximately 1/3000 live births. It is caused by loss of function mutations in the neurofibromin gene (NF1) and is estimated to effect 100,000 people in the US. Approximately 50% of the patients inherit the condition in an autosomal dominant pattern; the remaining 50% are the result of de novo mutations. Cognitive deficits have been found in 70% of children with NF1. They include specific problems with attention, visual perception, language, learning, attention, and executive function. These symptoms are observed in the absence of tumors or macroscopic structural abnormalities in the central nervous system. No effective treatments for the behavioral and cognitive disabilities of NF1 exist. It is currently unclear how the parental gene carrier may affect the offspring's cognitive abilities, therefore we tested whether the parental carrier of the mutated NF1 gene and/or genetic background strain affected behavioral and cognitive performance in mice. The experimental mice are on a mixed C57BL6/J x 129/SvJ background where either the mother or the father was a heterozygous NF1 carrier. Preliminary results indicate that the parental carrier does significantly influence the behavioral and cognitive phenotype of the offspring. A progress report on this study will be presented during the Research Week.

This project is supported by DoD Award W81XWH-17-1-0193.



# Research Week 2020

## Factor Structure of Short Forms of the Barratt Impulsiveness Scale (BIS-15 and BIS-Brief) in an Adolescent, Non-clinical Population

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### Keywords

Impulsivity, factor analysis

### Abstract

The Barratt Impulsiveness Scale (BIS) is a widely used tool for measuring impulsivity and has been influential in shaping current theories of impulse control. Studies have found that BIS factor structures can vary between youth and adults. The present study examines the factor structure of two widely used short versions of the BIS (BIS-15 and BIS-Brief) within an adolescent population. The BIS-15 has fifteen questions thought to assess three factors of impulsivity: non-planning, motor, and attentional impulsivity. The BIS-Brief has eight questions thought to assess impulsivity as a unidimensional factor. This study applied exploratory and confirmatory factor analysis to a cross-sectional sample of 612 middle school students in grades six through eight. The factor structures for both BIS-15 and BIS-Brief will be reported as will model fit and internal reliabilities of total scores and subscales for these instruments. This work provides evidence for how these scales can be used with non-clinical adolescents to understand the impact of impulse control on health and educational outcomes.



# Research Week 2020

## Characteristics of Cardiac Memory in Patients with Implanted Cardioverter Defibrillator: the CAMI study

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### Keywords

Cardiac Memory, Vectorcardiogram, GEH

### Abstract

#### Introduction

The goal of this study was to determine factors associated with cardiac memory (CM) in patients with implantable cardioverter-defibrillators (ICD).

#### Methods

Patients with structural heart disease (n=20; mean age 72.6±11.6 y; 80% male; mean left ventricular ejection fraction (LVEF) 31.7±7.6%; history of myocardial infarction (MI) in 75%, ventricular tachycardia (VT) in 85%) and preserved atrioventricular (AV) conduction received primary (80%) or secondary (20%) prevention dual-chamber ICD. Standard 12-lead ECG was recorded in AAI and DDD mode, before and after 7 days of right ventricular (RV) pacing in DDD mode with short AV delay. Direction (azimuth and elevation) and magnitude of spatial QRS, T, and ventricular gradient (SVG) vectors were measured before and after 7 days of RV pacing. CM was quantified as the degree of alignment between QRSDDD-7 and TAAI-7 vectors (QRSDDD-7-TAAI-7 angle). Circular statistics and mixed models with a random slope and intercept were adjusted for days 1-7 change in cardiac activation, LVEF, known risk factors, and use of medications known to affect CM.

#### Results

QRSDDD-7-TAAI-7 angle strongly correlated (circular  $r = -0.972$ ;  $P < 0.0001$ ) with TAAI-7-TDDD-7 angle. In the mixed models, history of MI ( $-180^\circ$  (95%CI  $-320^\circ$  to  $-40^\circ$ );  $P = 0.011$ ) and female sex ( $-162^\circ$  (95%CI  $-268^\circ$  to  $-55^\circ$ );  $P = 0.003$ ) counteracted CM-T azimuth changes ( $+132^\circ$  (95%CI  $80^\circ$ - $184^\circ$ );  $P < 0.0001$ ). History of VT ( $+27$  (95%CI  $4$ - $46$ ) mV\*ms;  $P = 0.007$ ) amplified CM-T area increase ( $+15$  (95%CI  $6$ - $24$ ) mV\*ms;  $P < 0.0001$ ).

#### Conclusions

Existing cardiac remodeling affects CM in response to RV pacing. Women develop less CM than men. Activation memory is another manifestation of CM.



# Research Week 2020

## Instrumented Balance Assessment: Normative Values and Descriptive Data for Acute, Sub-Acute, and Chronic Mild Traumatic Brain Injury Populations

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### Keywords

mild Traumatic Brain Injury (mTBI), modified Balance Error Scoring System (mBESS)

### Abstract

Balance deficits are common following mild Traumatic Brain Injury (mTBI) and can persist well beyond the standard recovery period. Recent advances in wearable technologies, such as inertial measurement units (IMUs), have increased utilization of instrumented balance assessments, increasing the sensitivity of common clinical balance tests. However, there are limited studies providing normative ranges for instrumented balance assessment to help characterize abnormalities in people with mTBI. The aim of this study was to provide normative ranges for healthy controls and populations of acute, sub-acute, and chronic mTBI. Instrumented data were derived from four studies where participants completed the modified Balance Error Scoring System (mBESS). Testing took place at either an athletic facility or in a laboratory at OHSU/VA. Data from 142 healthy participants and 169 people with mTBI were collected. The mBESS test consists of three standing conditions (e.g. two-feet, one-foot, tandem stance) completed with eyes closed. The primary outcome measurement was the medial/lateral Root Mean Square of sway (ML\_RMS\_Sway). ML\_RMS\_Sway was averaged across conditions. For healthy controls, the 25th percentile for average ML\_RMS\_Sway was 0.12m/s<sup>2</sup>, 50th percentile 0.18m/s<sup>2</sup>, and 75th percentile 0.25m/s<sup>2</sup>. For people with mTBI, calculated percentiles were stratified by time since injury (acute <4 days), sub-acute (4 days-3 months), and chronic (>3months). For acute mTBI, the average ML\_RMS\_Sway was 0.13m/s<sup>2</sup> for the 25th percentile, 0.18m/s<sup>2</sup> for the 50th percentile, and 0.24m/s<sup>2</sup> for the 75th percentile. For the sub-acute group, the 25th percentile was 0.18m/s<sup>2</sup>, the 50th percentile 0.27m/s<sup>2</sup>, and the 75th percentile 0.41m/s<sup>2</sup>. Finally, for the chronic group, the 25th percentile was 0.24m/s<sup>2</sup>, the 50th percentile 0.35m/s<sup>2</sup>, and the 75th percentile 0.46m/s<sup>2</sup>. The control percentiles provide normative ranges for ML\_RMS\_Sway to assist clinicians in taking appropriate rehabilitation measures. Further analyses should be completed to determine any clinically or statistically meaningful differences between the mTBI and control ranges.



# Research Week 2020

## Post-Post Mobilization Radiographs for Stable Pelvic Ring Injuries: When is Enough, Enough?

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### Keywords

Pelvic Ring, Stable Pelvic Ring, Non-Operative, LC1, Radiograph

### Abstract

#### Purpose

Recent literature has demonstrated limited utility obtaining routine in-hospital post mobilization radiographs in LC1 pelvic ring injuries unless patients cannot mobilize (Winston, 2019). The literature does not address whether this specific cohort of conservatively treated, stability proven pelvic ring injuries require clinical films after discharge. The purpose of this study was to determine how many of these injuries displaced late and proceeded to operation. We predicted that most pelvic fractures determined to be stable from initial post-mobilization films will not end up displacing and requiring surgical fixation.

#### Methods

All patients presenting to our Level 1 academic trauma center from 2008 to 2018 were reviewed for the following criteria: pelvic fractures treated conservatively, with stable post mobilization films, and who returned to clinic with outpatient radiographs. This yielded 219 unique patients. Patient characteristics (age, comorbidities, tobacco use, BMI), Young-Burgess classification, mechanism of injury, weight-bearing status, length of follow up, number of clinic visits, and number of outpatient x-ray images were collected. The primary outcome was late operation after a trial of non-operative management.

#### Results

Zero patients received late operation for displacement after a trial of non-operative management over the past decade. The patients included 123 females and 96 males. Mean clinic follow up was 20.3 weeks (1.4 - 134.7 weeks, SD 27.6) post injury. 185 fractures (84.5%) were classified as LC1 injuries and 12 (5.4%) were classified as LC2. Patients received a mean of 6.4 radiographs (1 - 22 radiographs, SD 4.3) in outpatient follow up.

#### Conclusion

Pelvis fractures that demonstrated stability via post-mobilization radiographs likely do not require significant post-discharge radiographic follow up. The lack of late displacement suggests that we can reduce patients' radiation exposure by minimizing follow up radiography. A future pathway with fewer clinical radiographs is likely possible for stable, low acuity pelvic ring injuries.



# Research Week 2020

## Placental Glucose Uptake in a Nonhuman Primate Model of Western-Style Diet and Chronic Hyperandrogenemia

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### Keywords

Placenta Glucose Diet Hyperandrogenemia

### Abstract

#### Introduction

During pregnancy, glucose is predominantly transported to fetus by the placenta via facilitated diffusion through glucose transporter (GLUT) proteins. Our group has previously demonstrated altered placental perfusion and levels of GLUT proteins in a nonhuman primate model of Western-style diet (WSD) with and without hyperandrogenemia. Therefore, we hypothesized that there would be dysregulation of placental glucose uptake in this model.

#### Methods

Female rhesus macaques were randomly assigned at puberty to one of four treatment groups: controls receiving subcutaneous cholesterol implants + standard chow diet (C); testosterone implants + standard chow diet (T); cholesterol implants + WSD (WSD); and testosterone implants + WSD (T+WSD). After ~6 years of treatment, animals were bred and the pregnancies were delivered by Cesarean section at G135 (term is G168). Placental villous explants were harvested for radiolabeled glucose assay, and glucose uptake was measured over 120 seconds. Villous tissue was also harvested for western blot and immunohistochemistry analysis of GLUT proteins.

#### Results

Linear glucose uptake was observed between 0 and 30 seconds. At 20 seconds, glucose uptake did not differ across the four treatment groups. Glucose uptake values (mean  $\pm$  SD) at 20 seconds were as follows: C:  $25.5 \pm 6.33$  pmol/mg (n=6), T:  $22.9 \pm 0.404$  pmol/mg (n=3), WSD:  $27.0 \pm 3.24$  pmol/mg (n=5), T+WSD:  $33.0 \pm 3.12$  pmol/mg (n=3). Western blot analysis showed no difference in GLUT profiles. Immunohistochemistry showed that GLUT1 primarily localizes on the basal membranes and fetal capillaries. GLUT4 localizes to the syncytiotrophoblasts.



## Conclusion

We anticipated that decreased placental perfusion would impact glucose transport. However, no change in uptake nor transporter expression was observed between groups. This suggests that the primate placenta has sufficient capacity to compensate for these effects to maintain normal nutrient transport and optimize fetal growth.



# Research Week 2020

## Novel Interventions in Children's Healthcare: Outcomes of Minority Youth with Type 1 Diabetes

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### Keywords

Behavioral Health Intervention, Health Outcomes, Pediatric, Type 1 Diabetes

### Abstract

#### Introduction

Significant advancements in pediatric care have been made over the years, but racial and ethnic inequities in health outcomes persist. Novel Interventions in Children's Healthcare (NICH), a family-based intervention program for youth with chronic medical conditions and psychosocial stressors, is associated with better health outcomes for youth with type 1 diabetes (T1D). However, little is known about whether race/ethnicity may moderate such outcomes.

#### Objective

Compare NICH T1D outcomes of minority youth to non-Hispanic white youth.

#### Methods

Youth with T1D participated in NICH (n=53); those of non-white race and/or Hispanic background were grouped as "minority" (n=11). Retrospective chart reviews comprised ED visits, admissions, days admitted, and DKA events 1 year prior through 2 years after NICH initiation.

#### Results

There were no significant differences in mean admissions, days admitted, and ED visits among minority youth throughout the three time periods. Minority youth had a substantial but statistically non-significant decrease in DKA events from pre-NICH to 1 year (1.36 to 0.27;  $p=0.59$ ). Majority youth displayed significant ( $p<0.05$ ) reductions in admissions (1.9 to 1.1), days admitted (5.9 to 2.8), and DKAs (1.5 to 0.8) after 2 years. There were no significant differences between improvements experienced by minority and non-Hispanic white youth.

#### Conclusion

Although both non-Hispanic white youth and minority youth both demonstrated fewer acute complications following program initiation, the trends seemed to differ. Minority youth appeared more likely to experience large reductions in utilization in the first year with some regression in the second year, while non-Hispanic white youth showed smaller improvements in the first year but continued reductions in utilization during year 2. This second year often represents post-program outcomes and could reflect the continuation of inequities experienced by minority youth post program support; however, small sample size limits definitive conclusions. Further research is needed to assess racial/ethnic disparities in pediatric interventions.



# Research Week 2020

## Novel Poly(2-oxazoline) Micelle Formulation of PARP/PI3K Induces Immunogenic Cell Death, Enhancing Response to Triple Combination Therapy

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### Keywords

radiation, PARP/PI3K, polymeric nanoparticles

### Abstract

Radiation therapy is commonly employed in cancer treatment regimens in concert with other treatments but is rarely effective as a monotherapy. Radiation can be enhanced by the application of small molecule checkpoint inhibitors. These drugs are hydrophobic, necessitating a drug delivery agent, such as a polymer. This approach has been applied to breast and ovarian cancer, but has not yet been explored in colorectal. The efficacy of chemo-radiation combination therapy has the potential to further be improved by the addition of immunotherapy. With the recent clinical approval of immunotherapy for metastatic colorectal cancer, triple combination therapy (i.e. radiation, chemo, immuno) is an area that warrants exploration.

PARP and PI3K inhibitors were screened in colon cancer CT26 cells to find an optimal combination, then loaded into a poly(2-oxazoline) micelle. A poly(2-oxazoline) polymer was chosen over traditional PEG and Pluronic as a delivery excipient for the high loading capacity, low toxicity, and enhanced uptake. The drug-loaded micelles were characterized and tested out in vitro with radiation for cell uptake, cell toxicity, double strand break induction, and ability to induce reproductive cell death and immunogenic cell death. The micelles were tested in vivo with radiation and anti-CTLA-4 antibodies for efficacy, tumor volume, safety, and immunogenic cell death.

The PARP/PI3K inhibitor combination was able to induce immunogenic cell death (ICD) both in vitro and in vivo when injected intratumorally. The triple combination therapy was able to increase the cure rate of mice implanted with CT26 tumors and had a slightly improved tumor volume curve relative to the radiation and anti-CTLA-4 only controls. The ability of the drug combination to induce ICD is important in the immune suppressive tumor environment and paired with CTLA-4 may lead to better outcomes. Increased tumor infiltrating lymphocytes were observed with intratumoral injection. However, the dosing and timing of therapy is critical. A mere 0.4% of the injected dose was able to reach the tumor, yet histological differences were still visible with only three injections of the

micelles. With increased and more frequent dosing of micelles, we would expect to see increased separation between the tumor volume curves.



# Research Week 2020

## Role of Cellular Microenvironment in Intracellular mRNA Delivery for Applications in Tissue Engineering

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### Keywords

Tissue engineering, Mechanotransduction, mRNA

### Abstract

#### Introduction

The use of synthetic mRNA-based gene modification offers several advantages over traditional DNA based gene therapy including faster translational kinetics, transient expression and mitigation of risks associated with insertional mutagenesis and genomic integration. Accordingly, mRNA technology holds particular promise for applications in tissue engineering where spatiotemporal control of gene expression is crucial. Recent advances in non-viral delivery technologies have significantly increased the efficiency of intracellular delivery of synthetic mRNA by modulating mTOR signaling, which has been identified as a crucial player in mRNA translation. However, mTOR signaling is regulated by matrix stiffness through mechanotransductive pathways. Therefore, the mechanical properties of the engineered tissue must be tailored for optimal translation and expression of mRNA.

#### Methods

Human Mesenchymal Stem Cells (hMSCs) seeded on plastic culture dishes were transfected with 100 ng/ml Green Fluorescent Protein (GFP) encoding mRNA packaged into lipid nanoparticles (LNP). 4 hours post transfection, the cells were trypsinized and encapsulated in GelMA (7% (w/v)) hydrogels constructs at a density of  $2 \times 10^6$  cells/ml in order to study mRNA expression in physiologically relevant 3D models. The mechanical properties of the hydrogel constructs were modulated by photopolymerization for 25, 50, 75 and 100s (blue light, 20 mW/cm<sup>2</sup>). GFP expression was measured at 6, 24, 30 and 48 hours post transfection by fluorescence microscopy. mTORC1 activation was measured by intensity of fluorescence signal from immunostaining and imaging with Confocal Microscopy. Mechanical signaling inhibition studies used a ROCK inhibitor (Y27632, 30 mM).

#### Results

We observed a stiffness dependent response expression where intensity and efficiency of expression of GFP reduced with stiffness of the hydrogels. Lower expression of the mRNA in stiffer hydrogels correlated with reduced activation of mTORC1. When mechanical signaling was inhibited, both mRNA expression as well as mTORC1 activation were significantly reduced irrespective of stiffness of the hydrogel. The results show that the cellular microenvironment plays a significant role in the mechanisms of intracellular delivery and translation of synthetic mRNA with significant implications for both design of in vitro models as well as for translational applications.



# Research Week 2020

## Cross-Sectional Brain Volumetrics in the Rhesus Macaque: Effects of Age and Sex

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### Keywords

rhesus macaque, age, sex, MRI

### Abstract

The number of US individuals affected by dementia is expected to rise significantly during the next decade, as the age of the population continues to increase. Unfortunately, the underlying causes of dementia are poorly understood and currently there are no effective therapies. Furthermore, the prevalence of dementia is higher in women than in men, yet the cause of this sex difference is unclear. To help shed light on underlying causal mechanisms of dementia there is a great need for the development of appropriate animal models. To this end, we evaluated the rhesus macaque as a model of human aging by performing cross-sectional T1-weighted structural MRI brain scans of male and female animals across a wide age range. Our goal was to assess volumetric differences due to sex and age (N=74; 37 males, aged 5-29 years, 37 females aged 6-32 years). Using the INIA19 template, we assessed a number of brain regions functionally related to cognition and memory and which decline with age, including the prefrontal cortex and hippocampus, along with other regions of interest. Volumes were all normalized to total brain volume to allow for comparison between animals of varying size due to gender and individual differences. To date this is the most comprehensive dataset prepared of in vivo rhesus macaque brain volumes and will provide novel insight into the changes occurring in the macaque brain during aging, with a focus on differences due to biological sex. By observing these changes in macaques and comparing them to those observed in humans we will determine the value of the rhesus macaque as a comparative model of aging in humans.





# Research Week 2020

## Muscle Assessment through the Nutrition Focused Physical Exam Compared to Skeletal Muscle Index Measured by CT Imaging.

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### Keywords

Nutrition focused physical exam, computed tomography, mid upper-arm circumference

### Abstract

#### Research Outcome

The Nutrition Focused Physical Examine (NFPE) is a tool, primarily used by Registered Dietitian Nutritionists (RDNs), to assess subcutaneous fat and muscle stores to aid in the diagnosis of malnutrition. The overall goal of this study is to compare and contrast muscle assessment from the NFPE to skeletal muscle index (SMI) measured by CT imaging.

#### Methods

SMI was calculated from single cross-sectional CT scans of the 3rd lumbar in 14 oncology and 12 organ transplant patients. Mid upper-arm circumference (MUAC) was also measured in all participants. We described the relationship between SMI, MUAC and muscle status using unpaired t-test. Cohen kappa was used to evaluate inter-rater reliability of muscle assessment from the NFPE.

#### Results

Participants with moderate and severe muscle loss had significantly lower SMI compared to individuals with normal or mild muscle loss (unpaired t-test; p-value: 0.0126). MUAC was also significantly lower in those with moderate and severe muscle loss (unpaired t-test; p-value: 0.0180). There was substantial agreement between observers for the NFPE (Cohen kappa: 0.649; SE: 0.111).

#### Conclusion

Muscle status evaluated by NFPE strongly correlates with SMI and MUAC. Results from this study suggest that NFPE is an effective tool in capturing broad muscle status in transplant and oncology patients. Furthermore, our results demonstrate that those competent in NFPE assessment procedures demonstrate good inter-rater reliability.

Future studies are needed to determine if SMI and NFPE can delineate more specifically between normal, mild, moderate and severe muscle loss.



# Research Week 2020

## Sex differences in behavioral responses to standard laboratory stressors in arctic ground squirrels (*Urocitellus parryii*)

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### Keywords

hibernation, aggression, animal behavior

### Abstract

Arctic ground squirrels are obligate seasonal hibernators found in the arctic tundra of North America and Siberia. In the wild as well as in the laboratory, AGS hibernation lasts approximately 7 months, during which time their body temperature reaches values as low as  $-2.9^{\circ}\text{C}$  without appreciable physiological impairment of their organ function at return to normothermia.

In biomedical research, AGS is an ideal rodent model to understand thermoregulation and the natural entrance and arousal from torpor. However, unlike other laboratory rodents, we know very little about their behavioral responses to typical laboratory stressors, making standardization of research difficult across laboratories.

In this study, male and female wild caught, laboratory housed, AGS were video recorded in their home cages for two hours after either cage checks or gentle handling over 6 weeks. Behavioral ethograms were created by continuously recording behaviors from videos collected during both morning and afternoon time periods starting approximately one month after the completion of their natural breeding season.

We found that male AGS were more socially aggressive towards same sex conspecifics than females. Furthermore, males, but not females, showed increased social aggression as dates got closer to the annual timing for re-entrance into torpor.

In response to handling, males responded with more agonistic behaviors than females. However, both male and female AGS returned to their normal baseline behaviors within 30 minutes, consistent with habituation times expected in laboratory rats, a species that does not naturally hibernate. To our knowledge, these results are the first to report home cage agonistic and social behaviors in response to typical laboratory activities over time in the wild caught AGS and suggest that standard handling procedures produce minimal disruptions to their behavior.



# Research Week 2020

## Integrating domain knowledge, interpretable deep learning, and uncertainty quantification for computational prediction of cell response to drug combinations

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### Keywords

Precision Oncology, Drug Response, Deep Learning, Graphical Models, Graph Convolutional Networks, Visible Neural Networks, Uncertainty Quantification, Bayesian Modeling

### Abstract

A major challenge in precision oncology is accurately modeling the molecular machinery that governs cellular sensitivity or resistance to a given drug or drug combination. While predicting drug response is an active area, model performance and interpretability vary depending on the method and prediction task, and leaves room for improvement. Challenges for drug response prediction include high feature dimensionality, measurement variability, low volume of functionally annotated tumor genomes, and limited understanding of drug-target interactions. Moreover, while domain literature describes many of the molecular interactions critical to drug response, it can be difficult to systematically encode this information in a framework conducive to predictive modeling. One effective family of methods use graph-based representations of domain knowledge captured in databases such as Reactome [3], KEGG [4], STRING [2] and Pathway Commons [8]. Graph structures are well-suited to encode numerous feature types and narrow the model hypothesis space by limiting feature (nodes) and interactions (edges) according to supporting domain evidence. Recently, the deep learning field has proposed applications specific to graph structures, such as Graph Convolutional Networks (GCN) [7], that show promise. The flexibility and predictive value of deep learning is renowned across fields such as machine learning, signal processing, and image recognition; however, this often comes at a loss of interpretability since the latent (or underlying) representations rarely map to real world concepts. To address this issue, Visible Neural Networks (VNNs) were proposed [1,6] to constrain latent space representations to hierarchies based on real-world pathway domain knowledge. Further, the rise in popularity of Bayesian methods have made uncertainty quantification highly approachable, and are well suited for high-dimensional and data-poor problems such as drug response prediction. In this talk, I'll discuss how these methods may be combined in a biology-centric framework that provides robust drug-response prediction, an interpretable latent space, and uncertainty quantification.



# Research Week 2020

## Implementation of pharmacist-driven penicillin allergy evaluation and testing at an academic medical center

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### Keywords

Penicillin Allergy, Graded oral challenge

### Abstract

#### Background

Penicillin allergies are reported by approximately 10% of the US population, however, studies reveal that >90% of those patients are not allergic to penicillins. Penicillin allergies are associated with negative health outcomes due to reduced efficacy and increased adverse effects of alternative antibiotics.

Patient interview, penicillin skin testing (PST) and/or an oral graded challenge can be used to evaluate penicillin allergy.

#### Methods

Adult patients ( $\geq 18$  years) admitted with a history of penicillin allergy were evaluated for eligibility between September 2019 and March 2020. Pregnant and critically ill patients as well as those receiving medication that would invalidate testing were excluded. Patients were evaluated and tested using institutional protocols. Allergies were removed from the medical record with standardized documentation to discourage relabeling. Data collected included but were not limited to, the number of patients challenged and delabeled, number of delabeled patients who were relabeled, and number of patients whose change in allergy status resulted in change of therapy.

#### Results

Thirty patients were interviewed. One patient was evaluated by PST while 20 patients underwent a graded amoxicillin challenge. Nine patients were delabeled as a result of chart review and patient interview alone. One patient failed oral challenge with minor itching that did not require any rescue medications, while 20 patients passed. Twenty-nine penicillin allergies were removed or modified. At time of review, 1 patient who was delabeled had been relabeled with a penicillin allergy with no record of a new reaction. Of patients who had a penicillin allergy removed, 50% received a penicillin for treatment following removal, either during that admission or as future therapy.

## Conclusions

Penicillin allergies can be evaluated and removed using a standardized algorithm and protocol. Risks of a reaction are low, and removal leads to change in treatment in a significant portion of patients.



# Research Week 2020

## Comparing BMP-9 with TGF- $\beta$ 1 for Tissue Engineering Stable Articular Cartilage

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### Keywords

Cartilage, BMP-9, TGF- $\beta$ , Progenitor

### Abstract

#### Introduction

When damaged by acute injury or chronic degeneration, articular cartilage has limited ability to repair itself. Earlier studies indicated that articular cartilage progenitor (ACP) cells are good candidates for creating articular cartilage as they produce a matrix that more closely resembles the stable cartilage of the native tissue than that created by other stem/progenitor cell types, which produce hypertrophic cartilage. Previously, bone morphogenic protein 9 (BMP-9) was shown to increase matrix production in chondrocytes, but also increased hypertrophy. We aimed to determine the effects of BMP-9 on ACPs as part of ongoing efforts to develop optimal methods for tissue engineering stable articular cartilage.

#### Methods

We isolated and expanded multiple ACP clones from human cartilage of healthy donors and subjected them to the in vitro 3D chondrogenesis assay with either TGF- $\beta$ 1 (control) or BMP-9 (experimental) groups. We analyzed the effects of the growth factors at the gene and protein level after 14 days of differentiation.

#### Results

BMP-9 induced significantly greater sulfated glycosaminoglycan (sGAG) accumulation (a measure of proteoglycan production) and higher gene expression of SOX9 and PRG4 compared with TGF- $\beta$ 1 with no significant increase in COLXA1 gene expression or collagen X protein levels. However, total collagen production was lower with BMP-9 and matrix organization was less ordered.

#### Discussion

We found that BMP-9 increased proteoglycan accumulation in pellets without a significant shift towards hypertrophy. While there was a small increase in COLXA1, the collagen X

protein levels measured by ELISA were still far below the levels found in mesenchymal stromal cell (MSC) pellets, which are known to exhibit a hypertrophic phenotype. However, because BMP-9 induced less collagen production and a diminished matrix organization, it may not be a better alternative to TGF- $\beta$ 1 for generating biosimilar articular cartilage tissue.





# Research Week 2020

## The Calcium-Sensing Receptor: A Novel Endocannabinoid Receptor

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### Keywords

anandamide, calcium-sensing receptor, synaptic transmission, endocannabinoid

### Abstract

Endogenous cannabinoids, such as anandamide (AEA), have multiple important functions in the brain including modulation of the reward response and neuroplasticity. There are numerous identified and unidentified target receptors for AEA in the nervous system. We have previously determined the calcium-sensing receptor (CaSR), a G-protein coupled receptor, is present at the vast majority of nerve terminals and that it stimulates spontaneous release of glutamate. Preliminary experiments indicate that AEA is an allosteric agonist at the CaSR. Thus, we hypothesized that AEA stimulates spontaneous release via the CaSR. We examined the action of AEA (10  $\mu$ M) on miniature excitatory post synaptic currents (mEPSCs) recorded in neocortical neurons in tetrodotoxin (TTX, 1  $\mu$ M) and gabazine (10  $\mu$ M), voltage-clamped at -70 mV after 14-36 days in culture. AEA strongly increased mEPSC by 15-fold compared with vehicle control after 10 minutes ( $P=0.005$ ). However, in age-matched neurons isolated from CaSR-deficient (KO) mice, there was substantial attenuation of the response to AEA. Specifically, the rate of increase following AEA application was delayed by 4.3 min (time to 50% maximum value). This was confirmed by comparing the integration of average mEPSC frequency following AEA application, which was reduced by 55% in the CaSR KO neurons ( $n= 15$  and 7 for wild-type and KO respectively;  $P = 0.0003$ , Kolmogorov-Smirnov test). Our findings indicate the CaSR mediates the rapid increase of spontaneous glutamate release by AEA but that AEA can still slowly trigger spontaneous release in the absence of the CaSR. These data support the hypothesis that the CaSR is an endocannabinoid receptor.

This work was supported by a grant awarded by U.S. Department of Veterans Affairs (BX002547) to SMS. The CaSR null mutant mice were kindly provided by Dr. Wenhan Chang, UCSF and San Francisco VAMC



# Research Week 2020

## Survey of tauopathy in mitochondrial protein associated neurodegeneration

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### Keywords

tauopathy, a-synucleinopathy, neurodegenerative disease

### Abstract

Tauopathy and a-synucleinopathy often occur together in human brain diseases but most commonly in the context of  $\beta$ -amyloidosis. Tauopathy induced by a-synucleinopathy in the absence of  $\beta$ -amyloid has been demonstrated in vitro and in cultured cells but compelling examples of this in human disease are rare and limited largely to instances of familial Parkinson's disease due to mutations in the a-synuclein gene. Mitochondrial protein-associated neurodegeneration (MPAN) due to mutations in C19orf12 produces neurodegeneration with brain iron accumulation as well as widespread a-synucleinopathy. Four patients with genetically confirmed MPAN were referred for brain autopsy and a complete histologic and immunohistochemical evaluation was undertaken for lesions and proteinopathies of common neurodegenerative diseases as well as the specific reported lesions of MPAN. All patients had hallmark pathologic features of MPAN including atrophy, gliosis, and iron accumulation involving the globus pallidus as well as abundant a-synucleinopathy manifest as Lewy bodies and neurites throughout the brain. Tauopathy was present in each case with neurofibrillary tangles distributed in Braak stages I to V with pretangles and more widely distributed tau-positive dystrophic neurites. The distribution and regional burden of tauopathy was less than that of a-synucleinopathy in each case.  $\beta$ -amyloid or TDP-43 abnormalities were not identified in any case. The lesional burden and distribution in MPAN are consistent with a pathogenetic model in which dysmetabolism of a-synuclein is sufficient, in the absence of other common neurodegenerative pathologies, to induce tauopathy. Study of rare familial diseases such as MPAN may enhance our understanding of the pathogenesis of common idiopathic neurodegenerative diseases.



# Research Week 2020

## Use of spirometry to evaluate breathing-swallowing coordination with solid foods

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### Keywords

breathing-swallowing coordination; dysphagia; spirometry

### Abstract

#### INTRODUCTION

Breathing-swallowing coordination (BSC) is an important pulmonary defense that aids airway protection. However, commonly used measurement methods are prone to artifact and limited to measuring the presence and direction of airflow. Spirometry offers an alternate method to measure BSC with reduced artifact while also measuring air volume and flow. The purpose of this study is to determine the utility of using spirometry to measure BSC with solid food consistencies

#### METHODS

Ten healthy participants (6F, 4M; ages 20-43, mean 30) wore a head-mounted nasal mask (Philips Wisp) connected to a pneumotachograph (Hans Rudolph 3813) and spirometer (ADInstruments, Inc.) to collect airflow data during swallowing. Participants were observed with 3 bites of applesauce and 1 bite of cracker. Tidal breathing was measured for 3-5 cycles per swallow. Data were analyzed with LabChart 8.

#### RESULTS

Measurement of BSC was quick and easily tolerated. Consistent with prior literature, the average swallow apnea duration (SAD) with bites of applesauce was 0.94s (SD=0.69) with an expiratory/inspiratory respiratory phase pattern (RPP) in 93% of swallows. For bites of cracker, the average SAD was 0.75s (SD=0.22) and an expiratory/inspiratory RPP was observed in 80% of swallows. Additional measures of RPP volume and flow of air, expressed as a percentage of the participants' average tidal volume, were found to be much smaller than the average inspiratory tidal volume. For instance, with bites of applesauce, the average volume of the pre-SAD RPP was 0.14% (SD=0.11) and the post-SAD RPP was 0.40% (SD=0.23) of average tidal volume, respectively. With bites of cracker, the average volume of the pre-SAD RPP was 0.27% (SD=0.27) and the post-SAD RPP was 0.28% (SD=0.31) of average tidal volume, respectively.

#### CONCLUSIONS

Measurement of BSC via spirometry is valid, feasible and useful in describing additional characteristics of RPP.



# Research Week 2020

## PLC Mediates Spontaneous Glutamate Release Triggered by Extracellular Calcium

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### Keywords

Calcium-sensing receptor, PLC, spontaneous release, mEPSC, calcium

### Abstract

Chemical neurotransmission is the major form of communication between neurons and is essential for CNS function. Glutamate is an excitatory fast-acting neurotransmitter that mediates inter-neuronal communication. Evoked and spontaneous release of neurotransmitter are proposed to have distinct roles and rely on divergent vesicle pools and receptors. Moreover, changes in extracellular  $[Ca^{2+}]_o$  are shown to differentially affect the probability of release for each mechanism.  $Ca^{2+}$  entry via voltage-gated calcium channels (VGCCs) is responsible for evoked release however the same pathway does not contribute to spontaneous release. How does extracellular  $[Ca^{2+}]_o$  stimulate spontaneous release? Previous experiments demonstrate that the G-protein coupled receptor (GPCR), the calcium-sensing receptor (CaSR), is involved and accounts for ~30% of basal miniature excitatory postsynaptic currents (mEPSCs). Downstream of GPCRs, phospholipase C (PLC) is activated by G protein subunits and hydrolyzes the phospholipid phosphatidylinositol 4,5-bisphosphate (PIP<sub>2</sub>), resulting in inositol triphosphate (IP<sub>3</sub>) and diacylglycerol (DAG), both of which affect mEPSC frequency. Using whole cell patch clamp in primary neocortical neuronal cultures, we determined that median mEPSC frequency was increased (270% of baseline, n=13) by elevation of  $[Ca^{2+}]_o$  from physiological (1.1 mM) to high (6.0 mM). Inhibition of PLC with U73122 (5  $\mu$ M) substantially reduced the sensitivity of mEPSC frequency (95% of baseline, n=8) to the  $[Ca^{2+}]_o$  increment compared to controls (ANOVA  $P=0.0002$ , Dunnett's multiple comparisons,  $P<0.001$ ), though vehicle (n=14,  $P>0.99$ ) and the inactive analog, U73343 (n=13,  $P=0.3295$ ), did not. In PLC1B null mutant mice (n=10), the effect of high  $[Ca^{2+}]_o$  on mEPSC frequency was attenuated 31% (Dunnett's,  $P=0.045$ ), and the residual response to high calcium was still reduced by U73122 (n=9, Dunnett's,  $P<0.01$ ). Taken together these data indicate that PLC strongly links changes in  $[Ca^{2+}]_o$  to mEPSC frequency and that a substantial fraction of this is mediated by isoform PLC1B.

This work was supported by a grant awarded by U.S. Department of Veterans Affairs (BX002547) to SMS. The null mutant- mice were kindly provided by Dr. Hee-Sup Shin, S. Korea.



# Research Week 2020

## Testing whether alpha-synuclein binds specific DNA conformations

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### Keywords

Alpha-Synuclein, Synucleinopathies, Neurodegenerative Diseases, Parkinsons, Lewy Body Dementias

### Abstract

The abnormal accumulation of the intracellular protein  $\alpha$ -synuclein has been implicated in the pathogenesis of several neurodegenerative disorders, including Dementia with Lewy Bodies (DLB), Lewy Body variant Alzheimer's Disease (LBVAD) & Parkinson's Disease (PD). In these diseases, known as "synucleinopathies", the accumulation of aggregated  $\alpha$ -synuclein in the cytoplasm, known as Lewy inclusions, is correlated with cellular dysfunction and death. Although the presence of Lewy inclusions are used as a marker for a definitive diagnosis of synucleinopathies, their specific role in neurodegeneration still remains unclear. The Unni lab has discovered a previously unrecognized function for the protein  $\alpha$ -synuclein in repairing nuclear DNA damage. Based on this discovery, we have proposed a new hypothesis that during disease,  $\alpha$ -synuclein protein is sequestered in cytoplasmic Lewy bodies, decreasing its nuclear DNA damage repair function and potentially leading to cell death of Lewy body-containing neurons. We have examined which conformations of DNA  $\alpha$ -synuclein preferentially binds for further insight into  $\alpha$ -synuclein's normal function in the nucleus.

We utilize electrophoretic mobility shift assays with subsequent fluorescence imaging to visualize the biochemical interactions between  $\alpha$ -synuclein and DNA, both in the presence and absence of small molecule reagents known to alter DNA conformations. Through the use of DNA bending dyes (DAPI, Hoescht), which both bind to the minor groove of DNA, we have characterized a shift in synuclein's concentration-dependent binding to DNA. Increasing amounts of DAPI and Hoescht in a 10% polyacrylamide gel system, shifted the  $\alpha$ -synuclein bound DNA to higher apparent molecular weights. Our data suggests that  $\alpha$ -synuclein binds preferentially to non-linear DNA conformations and may have a role in DNA bending. Understanding the mechanism by which  $\alpha$ -synuclein binds DNA will help to elucidate the mechanistic role  $\alpha$ -synuclein plays in DNA repair, as well as potentially inform the creation of new therapies that could ameliorate cell death caused by loss of  $\alpha$ -synuclein function.



# Research Week 2020

## Overcoming technical hurdles in intramuscular pH monitoring for acute compartment syndrome: A pilot study

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### Keywords

Compartment Syndrome, Orthopaedic Surgery

### Abstract

#### Purpose

One promising technology to diagnose compartment syndrome is intramuscular pH monitoring. In 2019, we began a prospective pilot investigating anterior tibialis intramuscular pH, with a transcutaneous probe, in patients with tibial shaft and plateau fractures. One technical challenge remains probe stability and "pH drift" (Fig 1A) as described by Elliott, in which intramuscular pH values increase with time during monitoring. The purpose of this study is to explore whether a portion of this drift can be explained by systemic factors, including changes in venous pH after surgical management of a fracture of the tibial plateau or shaft.

#### Methods

All adults ages 18-89 presenting to a single Level 1 academic trauma center (2019-20) with fractures of the tibial plateau and/or shaft (AO/OTA 41 and 42) were considered. After obtaining informed consent, patients received standard fracture care. During surgery, the probe was placed into the anterior tibialis percutaneously, remaining for 48 hours with continuous monitoring. Data was collected and analyzed by a separate research team; no study data was available to the treating orthopaedic traumatologist. Association between intramuscular and venous pH measurements was assessed via Pearson coefficient, significance set at  $p < 0.05$ .

#### Results

The pH probe was implanted in eight subjects. Venous and intramuscular pH were correlated, with a Pearson coefficient of 0.734 ( $p < 0.01$ , Fig 1B), indicating a strong correlation.

#### Conclusion

A significant component of the variation in anterior tibialis intramuscular pH in the 48 hours after fracture of tibial plateau and/or shaft appears to be explained by systemic changes in venous pH, rather than an artifact intrinsic to the probe such as sensor oxidization. This may be a critical finding. The pilot study remains ongoing.





# Research Week 2020

## Comparisons reintervention rates using traditional thoracostomy tubes versus pigtail catheter for the management of traumatic thoracic injuries at a level 1 trauma center

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### Keywords

thoracostomy, Pigtail catheters

### Abstract

#### Introduction

Options for tube thoracostomy include smaller bore pigtail style catheters (12-14 French) as an alternative to traditional large bore thoracostomy tubes (>20 french). Pigtail catheters (PC) and their association with less pain has led to increased use for trauma patients. The need for repeat interventions after pigtail versus traditional thoracostomy tubes (TTT) in the setting of acute trauma is unknown. We hypothesized that pigtail catheters would be associated with more complications.

#### Methods

All trauma patients admitted to our level 1 trauma center who required tube thoracostomy placement from 2016-2019 were prospectively enrolled into our study. The type of thoracostomy tube (pigtail vs. traditional), demographics, injury data, blood transfusions, length of stay, ICU and ventilator days, and complications were collected. Repeat interventions were defined as patients requiring a second intervention on the same side of their chest as a previously placed thoracostomy tube.

#### Results

During the 3-year study period, 335 trauma patients requiring tube thoracostomy were enrolled with 83 (24.7%) initially having a pigtail catheter placed and 252 (75.3%) having a TTT placed. TTT Patients with initial pigtail chest tube placement were less likely to require a repeat intervention on the same side of the chest (8.4% vs 31.4%,  $p < 0.0001$ ). Of the patients with initial pigtail catheter placement who required reintervention, 0 of 7 (0%) required >1 intervention. Of the patients with an initial TTT who required a reintervention, 36 of 79 (45%) required >1 intervention.

## Conclusions

TTT tend to be placed in more severely injured patients than pigtail catheters. After placement, patients with pigtail catheters require fewer reinterventions than TTTs. If patients with traditional thoracostomy tubes require reintervention on their chest, many will require more than one reintervention.



# Research Week 2020

## I-CONNECT (Internet-Based Conversational Engagement Clinical Trial): Reconnecting with a Forgotten Population; Can Social Interaction Improve Cognitive Functions among Socially Isolated Older Adults?

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### Keywords

Isolation; Conversation; Social; Benefit; Dementia

### Abstract

There are currently 5.8 million Americans living with Alzheimer's disease. Alzheimer's disease and other dementias have cost the United States upwards of \$290 billion this year. By the year 2050, the number of Americans with Alzheimer's disease and other dementias is projected to climb to 14 million and costs are expected to rise to \$1.1 trillion. We hypothesize that increasing social interaction in older adults with normal cognition or mild cognitive impairment (MCI) could significantly improve or sustain cognitive function. Increasing daily social contact through communication technologies offers a cost-effective home-based prevention program that could slow cognitive decline and delay the onset of dementia.

Over the last 10 years, we have conducted several NIH-funded randomized controlled trials (RCTs), observing whether digital, face-to-face conversations can improve cognitive functions and enhance cognitive reserve. While our previous studies have shown positive results in our primary cognitive aims, and we expect our current project to follow this trend, there has also been a less visible, but important individual, personal, and human benefit to connecting to and socializing with isolated older adults. After working with hundreds of research volunteers in Portland, OR and Detroit, MI, we will share the study background and aims, the current status of recruitment, and some of the unexpected personal outcomes of our intervention from those volunteers who have completed our year of video chats.



# Research Week 2020

## Examining the Narratives of Military Sexual Trauma (MST) Survivors

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### Keywords

Military sexual trauma (MST), Sexual assault prevention and response efforts; U.S. Military

### Abstract

#### Background

Reports of sexual harassment and sexual assault in the military (also known as military sexual trauma or MST) have increased significantly, especially in the last ten years. However, there exists a wide gap between the military's official efforts and survivors' experiences. Consequently, more research is needed to understand how survivors perceive the military's efforts, how these efforts affect their experiences, and how future responses can be improved.

#### Objectives

The goals of this dissertation study were to: 1) identify how current messaging in the military affects the experience of MST survivors; 2) explore what a survivor-centered MST prevention and response program might look like as defined by survivors, and 3) obtain recommendations for how the military's prevention and response services can be improved.

#### Participants

This national sample included twenty-one servicemembers from various military branches who experienced sexual harassment and/or sexual assault during their military service between 2003 and 2019. The participants identified as women (95%), non-white (15%), Hispanic/Latina (19%), LGBT-Q (24%), and have college or masters-level degrees (62%).

#### Methods

The data for this qualitative study was collected during phone interviews, using an open-ended, semi-structured interview protocol and were transcribed for further analysis. Using the interview transcripts, a thematic analysis was conducted by the researcher and a secondary coder, identifying semantic and latent themes.

## Results

Four main themes emerged from the participant interviews: 1) The military's culture of sexism and misogyny contribute to MST, 2) The leadership and chain of command matters, 3) Prevention efforts are inadequate, and 4) The military's response is often (re)traumatizing.

## Conclusions

These four themes often intersect with each other, and their interdependence is reflected in the recommendations provided by the participants to improve the military's prevention and response efforts.



# Research Week 2020

## Sudden Cardiac Death in Young Adults with Long-Chain 3-Hydroxyacyl CoA Dehydrogenase Deficiency (LCHADD)

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### Keywords

fatty acid oxidation disorders, sudden cardiac death, stem cell research, genetic diseases, cardiology

### Abstract

Long-chain 3-Hydroxyacyl CoA Dehydrogenase Deficiency (LCHADD) is an autosomal recessive defect in fatty acid oxidation that presents with hypoketotic hypoglycemia and/or hypertrophic cardiomyopathy in infancy, and recurrent rhabdomyolysis in adolescence, however, sudden cardiac death has not been a previously reported complication of LCHADD. We have conducted a case review study comparing young adult LCHADD patients who have experienced sudden cardiac arrest events (n=5) to similar patients who have not (n=5) for the purpose of evaluating associated cardiac risk factors. We reviewed medical records from ECG tests, hospitalization reports, acylcarnitine and complete metabolic panels, clinic notes, and autopsy reports. Retrospective chart review has led to no certain etiology however, electrolyte derangements, low free carnitine and elevated total to free carnitine ratios have been noted upon hospitalization in sudden cardiac arrest cases. At the time of the sudden death event, only one subject was noted to be in metabolic crisis with elevated creatine phosphokinase levels. Life threatening ventricular arrhythmias appear to be a newly recognized life-threatening complication in the adolescent and young adult age groups of LCHADD patients. The exact mechanism underlying the sudden death events are not understood and there are no current therapies. Recent advances in human induced pluripotent stem cell (hiPSC) technology has provided extraordinary progress in understanding the mechanisms in generating induced pluripotent stem cell derived cardiomyocytes. Future directions of this study seek to generate LCHAD deficient patient derived iPSC-CMs in order to assess mitochondrial function, force of contraction, oxygen consumption rates and calcium retention capacities. Assessing the disruption of bioenergetics and mitochondrial function in hiPSC-CMs will provide a meaningful exploration to understand the potential pathways that contribute toward the severe cardiac clinical manifestations observed in affected LCHADD patients who have experienced sudden cardiac death events.



# Research Week 2020

## Correlative Super-resolution Fluorescence and Electron Microscopies Unravel the Nanocluster Formation of Ras proteins on the Cell Membrane

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### Keywords

Ras, Nanocluster, SRM, SEM

### Abstract

Physical and functional partitioning of the biological membrane have been implicated in regulating heterotypic and homotypic interactions of proteins on the membrane. Among others, human Ras small GTPases are prototypical examples of membrane proteins that have been shown to preferentially compartmentalize on the plasma membrane. All three Ras isoforms, namely H-, N-, and K-Ras exhibit nanoclusters at different locations within membrane, which is primarily dictated by their isoform-specific membrane-targeting motifs. This spatial preference among the isoforms could explain why Ras proteins have non-redundant biological functions and distinct mutational spectra in human cancers despite the high homology in their functional (globular) domains. Thus, understanding how Ras is partitioned into nanoclusters on the plasma membrane is critical for devising mutant Ras-targeted cancer therapy. Using quantitative super-resolution fluorescence microscopy (SRM), we observed that two mutant Ras forms, K-Ras and H-Ras, can form either dimers or higher clusters on the cell membrane when expressed at near-endogenous expression levels. Furthermore, the correlative SRM and scanning electron microscopy revealed that both H-Ras and K-Ras dimers/nanoclusters are independently associated with distinct subsets of plasma membrane ultrastructures, such as cortical cytoskeleton, clathrin-coat pits, and caveolae. Additionally, we found that the membrane clustering properties are dominated by the C-terminal membrane targeting motifs of both Ras isoforms. Together, these results expand our understanding of structural and functional properties of Ras nanoclusters on the cell membrane and offer guidance to future studies defining membrane structures associated with Ras.



# Research Week 2020

## Bone-on-a-chip - A biomimetic organ-on-a-chip model system to study cancer metastasis

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### Keywords

Microfluidics, bone, organ-on-a-chip

### Abstract

Bone tissue is a common site of metastasis, affecting a large number of patients with advanced cancer. The specificity of bone for extravasation of many types of cancers appears to be tightly related to the specific chemo-attractant molecules secreted by bone stromal cells, as well as possible interactions with other non-cancer cells, such as platelets, leukocytes, and monocytes/macrophages. Current bone models of metastasis do not replicate the real complexity of the native bone tissue. However, recent efforts in our lab have shown a rapid fabrication method for the engineering of vascularized bone models that mimic the key hallmarks of the bone cellular and extracellular microenvironment. In this study, we combined our rapid bone fabrication method with microfluidic systems to create an organ-on-a-chip system that can mimic the nanoscale mineralization of the native bone tissue and aspects that are relevant to cancer metastasis.





# Research Week 2020

## The feasibility of a prospective cohort to assess improvement after partial medial meniscectomy by the Portland Pivot Kick physical exam maneuver?

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### Keywords

Orthopaedic Surgery, Knee Surgery, Meniscus Tear

### Abstract

#### Objective

The efficacy of partial meniscectomies in patients with osteoarthritis is currently debated. The purpose of this study is to determine the effectiveness of a novel physical exam maneuver, the Portland Pivot Kick (PPK), in predicting the potential benefit of arthroscopic partial medial meniscectomy in treating mechanical symptoms, even in the presence of osteoarthritis.

We theorize that differentiating the presence of mechanical symptoms from those of degenerative joint disease in medial meniscus tears can be a prognosticator of improvement of symptoms following surgical intervention. We hypothesize that patients with a positive preoperative PPK will have improvement of mechanical symptoms and significantly improved subjective outcomes scores following arthroscopic partial medial meniscectomy.

#### Methods

This IRB approved prospective observational cohort study of orthopedic patients at the VA Portland Health Care System (VAPORHCS). All adult veteran patients who are seen at the Sports Orthopedic Clinic at VAPORHCS with a medial meniscal tear proven on MRI will be offered inclusion in the study. Exclusion criteria include any patients with prior surgery on the index knee, an intraarticular loose body on MRI, an anterior and/or posterior cruciate ligament tear, a bucket handle tear, or meniscal tear deemed amenable to repair rather than partial meniscectomy.

Patients are evaluated using a standard physical examination, including the PPK. Radiographs of the affected knee are evaluated to determine the extent of osteoarthritis via the Kellgren Lawrence grading system. Questionnaires include subjective patient outcomes scores, specifically the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Western Ontario McMaster Osteoarthritis Index (WOMAC).

An a priori power analysis was performed assuming a power of 0.8 and an alpha of 0.05 which predicted a sample size (n) between 50-64 patients. We anticipate around a 10% drop out rate due to loss of follow up after surgery. We plan to enroll 75 patients over the course of a 24-month period.

#### Data

Forty-one patients have consented to the study (since October 2019), 21 of the 41 have elected for surgical intervention, and 9 of the 21 are currently in the postoperative phase. It is predicted that enrollment will be completed within approximately nine months.



# Research Week 2020

## Time to cessation of acute heavy menstrual bleeding in adolescents after high versus standard dose combined oral hormonal pills

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### Keywords

Menstrual Bleeding, Medical Management

### Abstract

#### Objective

While multiple hormonal treatment strategies are effective in decreasing both acute and chronic heavy menstrual bleeding (HMB) in adolescents, there are few comparative studies that evaluate hormone dosages. Because estrogen-dependent endometrial repair mechanisms occur through gene signaling pathways, opposed to direct endometrial effect, we hypothesized that time until resolution of acute HMB in teens is independent of ethinyl-estradiol (EE) dose.

#### Design

We performed a retrospective chart review over a ten-year period (2008-2018) of adolescents aged 9-19 years receiving treatment for acute HMB at our urban tertiary care institution. We used billing codes to identify subjects at encounters with HMB and hemoglobin <12 mg/dl. Our primary outcome was the number of days from initial presentation until patient-reported resolution of acute HMB. We identified the initial medical management, including combined EE-progestin, EE-only, or progestin-only treatments. We then compared the number of days until resolution of acute HMB between subjects grouped by step-down taper dosing versus standard dosing (EE 20-35 mcg/day) of oral combined regimens.

#### Results

We identified 207 subjects based on coding criteria, of whom 90 met study criteria. We excluded subjects for lack of acute HMB (n= 103), pregnancy (n= 18), trauma or other etiologies of bleeding (n=11). Most teens received hormonal therapy (72/90; 80%); only nine were prescribed a progestin-only method. Of those who received oral combined EE-progestin, 32 (50%) received a step-down taper regimen and 32 (50%) received standard dosing. Time to resolution of acute bleeding was available for 57/90 (63.3%) subjects with overall median time to resolution of 2 days (range 0-15), with 75% experiencing cessation

in 4 days. Those prescribed standard dosing of a combined pill experienced resolution of HMB in  $2.3 \pm 2.3$  days (mean  $\pm$  standard deviation), compared to those using a step-down taper regimen ( $4.3 \pm 4.3$  days;  $p=0.07$ ).

### Conclusion

Our chart review suggests that time to resolution of acute HMB is no different between teens who start a variety of dose regimens for menstrual suppression at time of acute presentation with anemia. Current dosing guidelines should be re-evaluated in comparative clinical studies.



# Research Week 2020

## Allergy reporting in the hospital and outpatient settings following an antibiotic graded challenge

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### Keywords

Penicillin, Antibiotic graded challenge, antibiotic allergy

### Abstract

#### Purpose

This project aims to retrospectively evaluate patients who received an antibiotic graded challenge following the implementation the OHSU order set, to determine the success of the challenge and if the results were updated within the healthcare system, specifically outpatient pharmacies.

#### Methods

This is a retrospective cohort study. Data were collected from a repository of OHSU's electronic health records between January 1, 2017 and May 31, 2019. We identified antibiotic challenge orders using low dose antibiotic orders or the recently approved order set. Antibiotic allergies were obtained from patient reported allergy records. Outpatient pharmacies were obtained from patient records and each pharmacy was called to verify allergies in their system.

#### Results

The most commonly challenged antibiotic allergy was penicillin (54%) and the most frequently reported reaction was hives (34%). Twenty-six (52%) of the challenges tested amoxicillin, and the majority (92%) included either a penicillin or cephalosporin antibiotic. Forty-five (90%) patients passed the challenge and deemed to not have a true allergy. One (2%) patient failed, and 4 (8%) were classified as unknown. In patients that passed the challenge, 36 (84%) institution electronic health records were updated, with 20 (47%) of the patient allergies removed and 16 (37%) updated with a note to the allergy field documenting that the patient had passed the challenge. Sixteen (43%) outpatient pharmacy electronic health records were consistent with the results of the test and 21 (57%) still had the allergy listed as active.

#### Conclusion

Allergies were not updated in more than half of the outpatient pharmacy systems, which may delay patient care and result in inappropriate antibiotic prescribing. The majority of graded challenges were well tolerated without serious sequelae.



# Research Week 2020

## Degradation Resistance and Biocompatibility of Novel Multi-Functional Acrylamides

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### Keywords

Acrylamide, Degradation, Biocompatibility

### Abstract

#### Objective

(Meth)acrylamides have been proposed as ester-free alternatives to (meth)acrylates. The objective of this study is to evaluate novel multi-functional acrylamides in terms of resistance to degradation and biocompatibility.

#### Materials and Methods

Hydroxyethyl methacrylate (HEMA), N,N'-Diethyl-1,3-bis(acrylamido)propane (DEBAAP) and novel multi-functional acrylamides N,N'-bis[(3-methylaminoacryl)propyl]methylamine (BMAAPMA), tris[(2-methylaminoacryl)ethyl]amine (TMAAEA), and N,N'-bis(acrylamido) 1,4-diazepane (BAADA) were dissolved in methanol (50 mM) followed by dilution (1:100) with either acidic water (pH 1), phosphate buffered saline (PBS), or PBS + 2 units/mL each of cholesterol esterase (CE) and pseudocholinesterase (PCE). Samples were incubated for 5 days (water: RT; PBS 37°C). Remaining intact monomer concentration post-incubation was determined by NMR. OD-21 cell viability was tested in serial dilutions (10 to 0.05 mM) using MTT assay. Monomers were mixed with 60 wt% UDMA, 0.2/0.4 wt% 2,2-dimethoxy-2-phenylacetophenone/DPI-PF6 (initiators), and 0.1 wt% BHT Inhibitors), and photopolymerized into discs. Final conversion (DC) was assessed in NIR prior to incubation in ethanol for 2 days. The extracted compounds were quantified by <sup>1</sup>H NMR using 4-fluoro-2-nitrobenzamide as the internal standard. Results were analyzed with one-way ANOVA/Tukey's test ( $\alpha=0.05$ ).

#### Results

The multifunctional acrylamides showed minimal or no degradation in all conditions, especially BMAAPMA, DEBAAP, and BAADA. TMAAEA showed slight degradation but much less than the methacrylate control, HEMA. BAADA showed the lowest conversion, followed by TMAAEA. All others had similar conversion. Cytotoxicity was observed only at high concentrations. All monomers had at least 80% cell viability up to 0.5 mM, higher than the maximum concentration of unreacted monomers extracted after ethanol incubation.

## Conclusion

The novel diacrylamide monomers showed improved resistance to degradation compared to a methacrylate control in both acidic conditions and in the presence of enzymes. OD-21 cells showed similar survival for all monomers tested at concentrations determined relevant by leachate analysis of unreacted monomers.

## Support

NIH-NIDCR U01-DE023756; K02-DE025280; R01-DE026113





# Research Week 2020

## Does cognitive dual-task performance relate to disease severity in Parkinson's disease?

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### Keywords

Parkinson's Disease, Dual-Task, Cognitive, Disease Severity

### Abstract

Parkinson disease (PD) is a progressive neurodegenerative disease associated with motor and cognitive impairments. People with PD commonly have more difficulty performing two tasks simultaneously (dual-task performance) than healthy people. The purpose of this study was to investigate the relationship between a novel dual-task (DT) paradigm and cognitive performance, as well as clinical measures of disease severity.

Twenty-two subjects with PD (Off medication, age

$67 \pm 5.5$  MDS-UPDRSIII:  $41[\text{MM1}] \pm 14.5$ ) and six healthy control (HC, age:  $69[\text{MM2}]$ , SD:  $8.5$ ) performed two, two-minute, DT test; a sitting test and a turning in place test.

Participants were required to push a handheld button as quickly as possible after hearing an "AI" sequence, via an auditory modified AX-Continuous Performance Task. Reaction times (RT) and accuracy (AC) were computed for both sitting and turning. Cognitive function was assessed with the MoCA and disease severity with the MDS-UPDRSIII.

The PD group showed less AC ( $p=0.005$ ), but similar RT, in performing the cognitive DT compared to the HC group when sitting; while no differences were observed between groups when turning. Only for the cognitive DT while turning, a higher MoCA was associated to lower RT ( $r= -0.526$ ,  $p= 0.014$ ) and higher AC ( $r= 0.599$ ,  $p= 0.003$ ); and a higher MDS-UPDRSIII scores significantly related to lower AC ( $r= -0.539$ ,  $p= 0.008$ ).

Our findings indicate that AC while performing a cognitive task requiring attention may be impaired in people with PD when Off dopaminergic medication. No differences among PD and HC were found in the cognitive DT when performed while turning, as in general turning in place is a difficult motor task in the elderly. Lastly, we found significant associations between motor and cognitive severity of PD and the cognitive DT while turning, indicating that disease severity and cognitive dysfunction contribute to deterioration in cognitive performance only when two tasks occur simultaneously.



# Research Week 2020

## Sports Participation and Activity Practices in Pediatric Patients with Bicuspid Aortic Valves

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### Keywords

bicuspid aortic valve, activity, sports, restrictions, pediatric cardiology

### Abstract

#### Background

Children with a bicuspid aortic valve (BAV) are at risk of developing sedentary lifestyles and cardiovascular disease in adulthood. All children should participate in daily physical activity, and competitive sports are an important avenue for this. In 2015, the American Heart Association (AHA) released guidelines for competitive sports participation in patients with heart disease. Thus far, there have been no studies examining provider adherence to current guidelines in comparison to actual patient practices, or to evaluate how competitive sport restrictions affect activity levels.

#### Objective

To determine (1) are pediatric cardiology providers following AHA guidelines regarding competitive sports restriction, (2) are patient practices in keeping with AHA guidelines, and (3) are children restricted from competitive sports less active than those who are not restricted.

#### Methods

This is a retrospective cohort study of otherwise healthy youths aged 8 to 18 years with an isolated BAV who were seen in OHSU pediatric cardiology clinic between January 1st 2015 and October 1st 2019. Charts were reviewed for last cardiology visit and concurrent echocardiogram. Parents participated in a phone survey to determine current level of activity and participation in sports. Patient characteristics were summarized using counts, percentages, and means. Means were compared using a t-test statistic.

#### Results

Preliminary analysis of the 16 patients in our pilot study demonstrated that only 50% of provider recommendations agreed with AHA guidelines. In practice, 56% of patients complied with AHA. Additionally, children restricted from competitive sports were found to be less active compared to children who were not restricted ( $p < 0.05$ ).

## Conclusion

Only half of the pediatric cardiology providers in our study followed the AHA guidelines regarding competitive sports restriction. Our initial data suggests that children who are restricted from competitive sports participation are more likely to be less active.



# Research Week 2020

## Single-Cell Transcriptomics and Epigenomics Analysis of Tendon Development

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### Keywords

single-cell, transcriptomics, epigenomics, tendons, development

### Abstract

Despite tremendous advances in knowledge of most of the organs in our bodies, tendons largely remain a mystery. Yet tendons are implicated in a number of disorders, including over 400 that are characterized by congenital joint contractures—a condition known as arthrogyposis multiplex congenita. To investigate tendons and how they develop, I am performing single-cell transcriptomics analysis of tendon tissues taken from mouse limbs at eight different stages of development. I also plan to supplement this analysis with investigation of single-cell epigenomics data. The aim of this research is to gain insight into various aspects of tendon biology and development, including how tendons can molecularly be distinguished from other tissues, what the distinct stages of tendon development are, how tendon progenitors transition from one developmental stage to the next, and what distinct cell populations exist in the tendon. The tendons come from standard Black6 mice, as well as Scx-GFP mice, which are mice on a Black6 background that express GFP whenever the tendon biomarker Scleraxis (Scx) is expressed. This exogenous Scx-GFP is expressed at a very high level, dwarfing the expression of endogenous Scx. As a result, the level of endogenous Scx is unclear, so an additional aim is to quantify the natural level of Scx in the tendon at each stage. While bioinformatics cannot definitively answer all of these questions on its own, it can inform hypotheses that can then be tested in the wet lab. Ultimately, by improving our understanding of normal tendon development, we can also begin to understand what happens during abnormal development. Furthermore, this new insight could suggest ways to utilize developmental pathways to lengthen tendons, reducing and perhaps eliminating joint contractures.



# Research Week 2020

## Development and in vivo implantation of LEGO-like 3D printed bone scaffolds

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### Keywords

Bone Regeneration, Tissue Regeneration, Implant

### Abstract

The leading cause of failure for current bone replacements, is lack of vascularization. Ideal synthetic bone scaffolds provide structural rigidity, allow cellular migration, vascularization, have a modular design to fit defect geometry. Advancements in 3D printing technology offers materials such as Beta tricalcium phosphate ( $\beta$ TCP) ceramics and Gelatin methacrylate (GelMA). GelMA is a biocompatible, mechanically tunable, photocrosslinkable, and 3D printable material with the potential to seed both stem cells and growth factors into the medium. The present studies in-vitro development and preliminary in vivo implantation of a novel, modular, LEGO-like synthetic scaffold comprised of rigid  $\beta$ TCP scaffold and embedded GelMA matrix, and compares cellularization, vascularization and tissue invasion of two different GelMA designs within the construct.

TCP scaffolds were designed as modular, open, interlockable pieces with hollow core and wall openings analogous to LEGO blocks.  $\beta$ TCP scaffolds were SLA 3D printed (Lithoz) while GelMA microgels were printed using an Ember 3D printer. Microgels contained VEGF, PDGF-BB, and BMP-2 and were placed in the hollow core structures.

Hydrogel-impregnated' samples consisted of LEGO-like constructs filled with GelMA hydrogel containing growth-factors and photopolymerized. The second group, termed 'Microgels' consisted of growth-factor laden GelMA microgel using 3D printing to, fabricate microgels before placement in the construct

In vitro cellular migration and penetration into Hydrogel-impregnated and microgel constructs was examined by seeding constructs with 1:1 HUVECs and hMSCs and examined via confocal microscopy. In vivo cellularity, tissue invasion and vascularization were immunohistologically examined via subcutaneous implantation in rats.

Microgel incorporation increased hydrogel macro porosity and diffusion of nutrients to the core of the construct. In both the in vitro and the in vivo studies, microgels constructs showed increased cell spreading and invasion farther into the core than hydrogel-

impregnated samples. Both in vitro and in vivo, microgel samples showed increased cellularity over bulk hydrogel.

3D printed LEGO-like constructs demonstrated promising signs of cellularization and vascularization both in vitro and in vivo. These constructs, which are modular, synthetic, and do not require living tissue culture, may eventually provide an answer to critical-size bone defects.



# Research Week 2020

## Inference of Functional Redundancy in Cancer Genes via a Co-Mutation Frequency Network

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### Keywords

Cancer, genetics, networks, pathway analysis

### Abstract

I have developed a co-mutation frequency network to infer functional redundancy between pairs of cancer genes. In order for a population of cells to progress through tumorigenesis, a series of phenotypic changes must occur. Each of these changes is typically driven by mutations in various cancer-related genes. Often, there are several possible genetic or genomic changes a population of cells can undergo to achieve a given phenotypic modification. This approach rests on the biological assumption that the likelihood that a tumor with a relatively low mutation burden will independently develop two functionally redundant genomic alterations is low. Adjusting for mutation burden, two genes that are each frequently mutated in sequenced tumor samples but mutated in the same sample much less than expected (defined by the joint probability) may be functionally redundant, and will be assigned a high edge weight. By overlaying known biological pathway information, gene pairs inferred to be functionally redundant due to low co-mutation within a given tumor sample can be nominated with higher confidence. This analysis builds on previous work that leverages mutual exclusivity, or low co-mutation frequency, as a way to investigate the genetic mechanisms of tumorigenesis.



# Research Week 2020

## Automatic topic segmentation of ADOS transcripts

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### Keywords

autism, machine learning, natural language processing

### Abstract

#### Introduction

The Autism Diagnostic Observation Schedule (ADOS) is a widely used instrument for the diagnosis of Autism Spectrum Disorder (ASD). It includes tasks designed to elicit conversational language between the subject and an examiner.

Atypical language use and repetitive speech are features of the disorder as characterized by the DSM-5. Quantifying what is atypical about the language of subjects with ASD is challenging.

To answer questions like "Are subjects more or less verbose when discussing loneliness than their typically developing peers?" researchers have to manually label large sections of the ADOS. This is exceptionally time consuming.

We applied statistical sequence tagging together with state-of-the-art Natural Language Processing (NLP) tools to leverage the structure of the ADOS and automatically label each sentence with its framing question.

#### Methods

Our data consists of 115 ADOS module-3 transcripts (64 TD, 51 ASD) from children in an autism study. We manually annotated a randomly selected subset of 40.

ADOS conversations are guided by a set of scripted questions the examiner asks the subject. A subject might be asked "What makes you feel happy?" or "What are the things you're afraid of?" We marked each utterance with a tag representing which of these questions it was related to.

We created features from vector representation of the words in each utterance, and the similarity of the previous examiner utterance to each of the scripted questions (using the BERT vector semantic model). We trained a conditional random field (CRF) model on the tags and features, which can then predict tags on an unlabeled transcript.

#### Results



Tags generated using our model appear reasonable (f1 = .87, sd=.06). Preliminary tests suggest they generalize well to unlabeled transcripts. This work will allow us to perform new analyses via NLP and other computational methods.



# Research Week 2020

## Stress Relaxation Mechanisms in Low-stress Polymer Networks with Alternative Chemistries

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### Keywords

Polymers, dental materials, kinetics, polymerization stress

### Abstract

#### Objective

Polymerization stress may contribute to dental composite restoration failure. This study evaluated the stress relaxation mechanisms involved in low-stress resin composites based on chain-transfer reactions, modulated photopolymerization, and network reconfiguration.

#### Materials and Methods

BisGMA:UDMA:TEGDMA (50:30

20 wt%) were mixed with 0 (control) or 20 wt% thiourethane oligomer (trimethylol-tris-3-mercaptopropionate+dicyclohexylmethane-4,4'-diisocyanate; Bacchi et al., 2015). Composites were made with 50wt% methacrylate-silanized or thiourethane-silanized filler particles. 0.2/0.8 wt% CQ/EDMAB and 0.5 wt% BHT were the photoinitiator and inhibitor, respectively. Commercial composites included two "low-stress" materials (Surefil SDR Flow, Dentsply and Filtek Bulk Fill, 3M ESPE) and one conventional control (Filtek Supreme, 3M ESPE). Photopolymerization was done with LED light (Demi Plus; Kerr) at 600 mW/cm<sup>2</sup> for 20s. Real-time kinetics was assessed in near-IR. Polymerization stress was assessed with the Bioman system (10 min run time). Stress-relaxation was assessed by dynamic mechanical analysis (DMA) in tension mode (0.1% strain, 1 Hz, 30 min deformation time) between 25 to 145°C. Data were analyzed with one-way ANOVA/Tukey's test ( $\alpha=0.05$ ).

#### Results

Of the commercial composites, SDR Flow showed the highest maximum rate of polymerization (RPMAX), degree of conversion (DC) at RPMAX, and Final DC while also having the lowest stress (1.86 MPa vs 3.25 for Filtek Supreme). TU-modified composites displayed statistically similar Final DC compared to the experimental control, though RPMAX was reduced by more than 50% for the TU group. Polymerization stress was reduced by nearly 70% in the composite modified with TU oligomer (0.61 MPa vs. 1.98 MPa

for Control). TU and TU-Fil exhibited faster stress relaxation times than Experimental Control at all tested temperatures.

### Conclusion

The results of this study suggest that composites modified with TU oligomers may show improved performance compared with current commercial "low-stress" resin composites, via chain transfer reactions during polymerization and enhanced stress relaxation after polymerization.



# Research Week 2020

## Resilience-Building in a Residential Aftercare Facility for Young Women Rescued from Commercial Sex Trafficking in Indonesia

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### Keywords

Resilience, Adverse Childhood Events, PTSD

### Abstract

#### Background

Adverse Childhood Events (ACE) are associated with poor health outcomes. ACE scores are consistently elevated in those who have been sexually trafficked. Resilience, or the ability to overcome hardships, is associated with positive outcomes such as lower rates of depression, improved self-rated health, and lower mortality risk in the elderly. This study examines the effects of a resilience-building program (RBP) on resilience scores in a cohort of young women rescued from sexual trafficking.

#### Methods

This is a prospective cohort study analyzing surveys collected over 18 months. Study participants are female, Indonesian citizens under the age of 18, survivors of sexual trafficking, who reside in a residential treatment facility. Surveys were collected by facility staff to assess ACE scores, baseline and follow-up symptoms of PTSD, and resilience scores using the Connor-Davidson Resilience Scale. Data was analyzed by descriptive summary statistics and Mann-Whitney U test.

#### Results

18 participants were analyzed with a mean age of 14.4 years. The average self-reported ACE score was 5.4 (SD 1.7). For those enrolled in the RBP for at least 1 year, 8 of the 9 participants showed an increase in resilience score with an average increase of 5.5 (SD 5.9). Study participants that entered the RBP upon intake took on average 21 less days to complete the stabilization phase compared to participants without the RBP, although this was an insignificant difference ( $p=0.28$ ).

#### Conclusions

Study participants consistently had ACE scores high enough to put them at risk of long-term negative outcomes. The RBP demonstrated early success, with nearly all participants showing an increase in resilience score after one year in the program. The decrease in days spent in the stabilization phase did not reach statistical significance, but this trend could indicate increased stability secondary to the Resilience-Building Program. Data collection will continue in the coming years.



# Research Week 2020

## When is pre-operative imaging of head and neck dermoids cysts necessary to evaluate for possible intracranial extension?

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### Keywords

dermoid; dermoid cyst; intracranial extension

### Abstract

#### Introduction

Dermoid cysts are congenital masses which occur frequently in the head and neck region along lines of embryonic fusion. Anatomic locations can be categorized in four areas: nasoethmoidal, periorbital, frontotemporal and neck. Traditionally, imaging of midline dermoid cysts is recommended given the potential for intracranial communication. Although less so, non-midline locations are also at risk for intracranial communication. This study aims to quantify our institutional experience with lateral dermoid intracranial extension and discuss potential need for preoperative imaging.

#### Methods

Institutional Review Board approval was obtained. Patients with dermoid cysts presenting to the pediatric otolaryngology clinic from 2015-present were reviewed. Data collected included patient demographics, imaging modality if any (CT, MRI, US, x-ray), anatomic location, size of lesion and presence or absence of intracranial extension. Lesions were classified as midline and non-midline.

#### Results

Seventy-six patients with surgically removed dermoid cysts or sinuses were included for analysis. Of these, 41 were female and 35 were male. Mean age at surgery was 4.4 years (range 0.6 - 17 years). Thirty-nine dermoids were midline: nasoethmoidal (17) and neck (22). Of these, 31 underwent pre-operative imaging (79%): US (17), MRI (12), and CT (2). Thirty-seven dermoids were non-midline: frontotemporal (9), neck (1), and orbital (27). Of these, 12 underwent pre-operative imaging (32%): US (9), MRI (1), CT (1) and plain films (1). Interestingly, none of the midline dermoids in our series were found to have intracranial extension. One patient with a frontotemporal dermoid cyst had no pre-operative imaging and was found to have intracranial extension to the dura identified intraoperatively.

## Conclusion

The risk of intracranial extension of midline cranial dermoid cysts is well established. While the vast majority of laterally located head and neck dermoid cysts do not have intracranial communication, the incidence of intracranial extension is not zero. Given the low morbidity, low cost and the potential benefit, pre-operative US imaging of all head and neck dermoid cysts, particularly midline and frontotemporal, may be prudent to determine the need for MRI and/or CT imaging prior to surgical resection.



# Research Week 2020

## Dipeptidyl Peptidase IV inhibition protects against developmental programming of metabolic diseases in maternal obesity

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### Keywords

Obesity, Type 2 Diabetes, Maternal Obesity, Developmental Programming, Inflammation

### Abstract

The obesity pandemic produces immense health and economic burdens globally. More than 65% of women entering pregnancy in the US are overweight or obese and maternal obesity leads to the developmental programming of obesity and metabolic diseases in the offspring. Although maternal obesity is recognized as a major driving force behind the obesity pandemic, there are currently no effective therapies to address the detrimental effects of maternal obesity. Dipeptidyl peptidase IV (DPPIV) is a ubiquitous aminopeptidase that regulates development, metabolism, and inflammation. Emerging evidence indicates that increased plasma DPPIV activity is an early marker of obesity. Furthermore, DPPIV inhibitors such as Sitagliptin improve systemic metabolism and promote weight loss in diabetics. We found that at term, maternal obesity in human mothers and offspring is associated with a fetal-sex dependent dysregulation in plasma DPPIV activity. We also found that baboons and mice born to obese VS lean mothers had increased plasma DPPIV activity regardless of fetal sex and that this effect persists into adulthood. These findings prompted us to determine the effects of DPPIV inhibition using Sitagliptin on developmental programming in maternal obesity. In a pre-clinical study using female FVB/N mice fed either a regular (RD) or high fat diet (HFD), we administered oral Sitagliptin (3 mg/kg/day) to RD and HFD-fed mothers prior to pregnancy and until weaning (Mat-Sita), or to offspring (Off) after weaning (Off-Sita). We found that compared to controls, Mat-Sita and Off-Sita prevented obesity and metabolic dysfunction in Off of HFD (Off-HFD) and had no effect in Off of RD (Off-RD) -fed mothers. Furthermore, Off-HFD VS Off-RD had increased inflammation in vital organs such as the heart, kidney and liver, and Off-Sita decreased these effects. Therefore, these findings suggest that DPPIV inhibition is a viable therapeutic strategy to address the detrimental effects of developmental programming in maternal obesity.





# Research Week 2020

## Cortical Evoked Potentials in Reverberant Speech Perception

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### Keywords

Auditory Rehabilitation, Speech Perception, Evoked Potentials, Brain Behavior Relationships

### Abstract

Individuals with similar hearing abilities often vary greatly in their ability to successfully understand reverberant speech. Our poor understanding of reverberant speech perception hinders the development of effective treatments. Reverberation temporally smears speech, diminishing onsets which aid successful speech perception. Cortical auditory evoked potentials (CAEPs) can be elicited in response to these onsets in continuous speech. This study analyzed the effects of reverberation on CAEPs and related them to perceptual difficulties in reverberant speech perception. We hypothesized that greater reverberation would degrade the cortical responses and increase perceptual difficulties.

A naturally produced /ba/ syllable was modified by increasing the voice onset time (VOT) to produce 11 tokens that sounded increasingly /pa/-like. These 11 tokens were concatenated with a naturally produced /da/ to create two-syllable tokens. Two additional reverberant versions of each stimulus (a mild and high level) were also generated. CAEPs (the P1-N1-P2 complex) were elicited to a subset of these stimuli. Listeners also separately labeled the second syllable of the clean and reverberant /daba/ - /dapa/ stimuli and provided a rating of confidence in their label. Electrophysiological recordings and behavioral responses were obtained from 20 young normally hearing adults (9 female; mean age: 28.3; 23 – 37 yrs.).

A comparison of CAEPs obtained in response to clean and reverberant stimuli revealed the effect of reverberation on the neural coding of speech: while the responses to the first syllable were minimally affected by the reverberation, the responses to the second syllable were increasingly degraded with increasing reverberation. Preliminary analyses of the behavioral responses showed that increased reverberation not only caused listeners to label a greater number of tokens as a /ba/ but also increased the variability in labels assigned to a stimulus across listeners. Listeners were also less confident when labeling reverberant stimuli. These data serve as baseline data in the further study of reverberation-related changes in speech processing in populations with impairments. In the long term, these results will aid the design of diagnostic tests for use in hard-to-test

populations and lead to individualized rehabilitation strategies to improve speech perception in difficult listening situations.

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# Research Week 2020

## Novel Protein-Protein Interactions with c-Myc at the Nuclear Pore Basket

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### Keywords

c-Myc, PDAC, RIME, Nuclear Pore Complex

### Abstract

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In recent studies, c-Myc has been shown to localize to the nuclear pore complex (NPC) after specific post-translational modifications. The localization of c-Myc to the NPC can mediate aspects of stress response to environmental signals, and separate studies show a role for c-Myc in gene gating at the NPC. The c-MYC interacting protein partners at the NPC are still unknown and could potentially contribute to oncogenic responses governed by c-Myc. We utilized a Rapid Immunoprecipitation Mass spectrometry of Endogenous proteins (RIME) experiment to identify proteins, which interact with C-Myc (N-262 Abcam), TPR, and other nuclear pore proteins (Mab414). The identified protein targets from the RIME experiment were then tested in mouse embryonic fibroblasts, pancreatic cancer, and lymphoma cell lines. Currently, we are examining the role of c-Myc and RIME-identified protein interactions to uncover potential therapeutic targets in PDAC.