



University of Colorado **Anschutz Medical Campus**

33rd ANNUAL STUDENT RESEARCH FORUM

COLLEGE OF NURSING

GRADUATE SCHOOL

SCHOOL OF DENTAL MEDICINE

SCHOOL OF MEDICINE SCHOOL

OF PHARMACY SCHOOL OF

PUBLIC HEALTH

DECEMBER 11th, 2018
ANSCHUTZ MEDICAL CAMPUS
Education 2, North and South

33rd ANNUAL
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS
STUDENT RESEARCH FORUM

Tuesday, December 11th, 2018

Poster Sessions

1:00-2:15 pm

2:15-3:30 pm

ANSCHUTZ MEDICAL CAMPUS
Education 2, North and South

The Student Research Forum organizing committee wishes to
acknowledge, with gratitude, the financial support for medical student
research provided by:

**The University of Colorado Denver
School of Medicine Dean's Office *And*
Undergraduate Medical Education Office**

Poster Session Judges

The organizing committee wishes to acknowledge their appreciation to the following serving as judges for the AMC Student Research Forum. Without their generous contribution of time and talent the forum would not be possible. Thank you!

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2018 AMC Student Research Forum Award and Funding Donors

The organizing committee is especially grateful to the following schools, departments, divisions, and programs for their generous contribution of financial support for the forum and/or a \$320 research prize awarded to the top scoring posters at the event.

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Department of Radiology

Primary Student Presenter: Andrew Pham

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Joaquin Espinosa

Poster Title: Protection from heart disease in people with Down syndrome is unlikely the result of changes in the canonical atherosclerotic pathway

Final Category: Cardiovascular

Abstract:

Purpose of Study: People with Down syndrome (DS), a condition caused by trisomy 21 (T21), present with unique co-morbidities. While these individuals are more likely to develop risk factors for heart disease – including obesity and hypothyroidism – few adults with DS develop this condition. Thus, T21 may confer a protective mechanism that mitigates traditional heart disease risk. This study therefore aims to investigate the effects of T21 on the atherosclerotic pathway, which is the underlying cause of heart disease.

Methods Used: We used published datasets to compare individuals with and without DS (Sullivan et al., 2016; Sullivan et al., 2017), including RNAseq of fibroblasts and monocytes, SOMAscan proteomics, and Meso Scale Discovery assay. We also used flow cytometry data on monocytes. These datasets were then compared to previously reported factors that either confer protection from or predisposition to atherosclerosis.

Summary of Results: Among monocyte subpopulations, there is a decreased percentage of CD14⁺⁺CD16⁻ monocytes ($p = 0.0005$) and an increased percentage of CD14⁺⁺CD16⁺ as well as CD14⁺CD16⁺⁺ monocytes ($p = 0.005$; $p = 0.002$). Moreover, there is an increase in absolute numbers of CD14⁺⁺CD16⁺ and CD14⁺CD16⁺⁺ monocytes ($p = 0.016$; $p = 0.019$). Among bulk CD14⁺ monocytes, RNAseq reveals decreased expression of ALOX5AP (FC = 0.540; $\text{padj} = 0.00002$) and increased expression of COLEC10A (FC = 1.541; $\text{padj} = 0.0007$), which are specific to classical and intermediate monocytes respectively. Proinflammatory cytokines, including TNF alpha (FC 1.434; $\text{padj} = 0.031$) and MCP1 (FC 1.305; $\text{padj} = 0.015$), have increased expression. Scavenger proteins, MSR1 (FC 1.302; $\text{padj} = 0.028$) and OLR1 (FC 1.310; $\text{padj} = 0.048$), are upregulated.

Conclusions: People with DS are predisposed to altered monocyte subpopulations, chronic inflammation, and increased scavenger receptor expression. All these factors should increase heart disease risk. Thus, changes in the canonical atherosclerotic pathway do not explain how T21 leads to protection from heart disease. Future studies are needed to examine lipids and their metabolism.

Primary Student Presenter: Keith Strand

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Mary Weiser-Evans

Poster Title: High-throughput screening (HTS)-based identification of novel, small molecule inducers of PTEN upregulation in smooth muscle cells

Final Category: Cardiovascular

Abstract:

PTEN is known for antagonizing PI3K/Akt signaling and our recent work shows that it functions as a transcriptional co-factor with SRF to regulate SMC contractile gene expression. SMC-specific PTEN deletion promotes spontaneous vascular remodeling and loss of PTEN correlates with increased atherosclerotic lesion severity in human coronary arteries. PTEN overexpression protects mice from AngII-induced pathological vascular remodeling, suggesting that pharmacologic PTEN upregulation could be a novel therapeutic approach to treat vascular disease. However, few small molecules are known to upregulate PTEN. To identify novel PTEN activators, we undertook an HTS using a fluorescence based PTEN promoter-reporter system. Using a pCHD-CMV-MCS-EF1-copGFP lentiviral vector backbone, we generated a pCDH-PTEN-mCherry-EF1-copGFP construct by inserting a cloned 4032-bp fragment of the proximal PTEN promoter+5'-UTR upstream of the mCherry ORF. Primary rat aortic SMCs were stably transduced with the vector, then flow sorted for GFP expression, yielding a pure population of construct positive SMCs. We screened ~2500 compounds dosed at 10 uM using mCherry induction as a readout for PTEN expression. A threshold of mCherry expression >2.0-fold above DMSO-stimulated PTEN promoter-reporter SMCs identified positive hits. 151 initial hit compounds were then screened in a dose-response format at 5.0, 1.0, and 0.2 uM, validating the activity of 57 compounds, which were narrowed to 13 final compounds based on their level of activity and mechanism of action. These 13 compounds were tested in vitro to validate PTEN upregulation and are being tested in vivo using pre-clinical mouse models of vascular remodeling to assess their anti-remodeling effects.

Primary Student Presenter: Brandon Sonn

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Andrew Monte

Poster Title: Advancing Personalized Medicine - Identifying Responders to Lisinopril

Final Category: Cardiovascular

Abstract:

Background: ACE inhibitors (ACEI) are the most commonly prescribed antihypertensive drugs and the third most commonly prescribed drug in the United States. Only about 50% of hypertensive (HTN) patients respond to ACE therapy. The objective of this study is to evaluate metabolic markers that predict individualized responses to ACEI (lisinopril) treatment.

Methods: Hypertensive patients were started on an ACEI at the initial visit and had blood pressures reevaluated at their next visit. Plasma samples and observed clinical parameters were collected at each visit. Pre-lisinopril treatment plasma samples were evaluated in conjunction with clinical data to predict post-lisinopril treatment clinical outcomes. Responders to lisinopril treatment were defined as individuals who had either a 10% decline in systolic blood pressure (SBP) between visits or SBP of <140 at the follow-up visit. Metabolomic analyses were performed. Regression analyses of metabolite and clinical values were completed in SPSS to identify predictive models using significant parameters from independent t tests.

Results: A significant difference in mean BMI was noted ($p=0.012$). The mean difference in GFR showed that it should be included in the linear regression model as well ($p=0.066$). In our multinomial regression model, the Wald statistic shows that we have identified GFR ($p=0.044$) and BMI ($p=0.017$) as significant factors to be used in conjunction with metabolite data to develop a predictive model for clinical outcomes. Several metabolites were found to have significantly different levels when comparing between the groups.

Conclusions: The data suggest that patients with higher BMI and levels of lipid oxidation may be less likely to respond to ACEI therapy.

Primary Student Presenter: Adam Carroll

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Chris Knoepke

Poster Title: The Impact of Procedural Approach and Comorbidities on Quality of Life Improvements at One and Twelve Months Post-TAVR: A Meta Analysis & Systematic Review

Final Category: Cardiovascular

Abstract:

BACKGROUND: TAVR is becoming the preferred treatment option for severe aortic stenosis. However, individual treatment decisions still hinge on the likelihood of quality of life (QOL) improvement, especially in the presence of comorbidities or need for alternative (non-transfemoral) access that may negatively impact these gains.

Many patients with severe aortic stenosis (AS) have the option of transcatheter aortic valve replacement (TAVR). Individual treatment considerations hinge on the likelihood of improvements to quality of life (QOL), especially when uncertainty is amplified by the presence of comorbidities or the necessity of non-transfemoral approaches.

METHODS: Using PRISMA guidelines, we conducted an ongoing multi-database search for all English language studies of TAVR including QOL assessment at 1 and 12 months post-procedure. Studies were included if they were published from 2013 and used either the KCCQ or SF-12 as outcome measures. We performed a mixed-effects meta-regression of extant study data to determine whether short and long-term QOL improvements after TAVR differed according to patient surgical risk (inoperable, high, or intermediate) or access approach (transfemoral or alternate).

RESULTS: We identified 29 total studies meeting inclusion criteria. After removing analyses in overlapping cohorts, we were left with 15 unique cohorts composed of 4383 patients who received TAVR. Due to heterogeneity of variance, random effects models were fit, illustrating a consistent positive effect on QOL across studies, both at 1month (log relative mean difference=-0.6, 95% CI: -0.91 to -0.37), and 12 months (lrm= -0.99, 95% CI: -1.25 to -0.73). At 1 month, QOL impact was moderated by alternate access use ($p < .02$), but not surgical risk. At 12 mos, neither factor moderated improvements to QOL.

CONCLUSION: TAVR is consistently associated with improved QOL at 1 and 12 months post-procedure. Pooled analyses suggest that short-term QOL improvement is moderated by procedural approach, but

not surgical risk, and longitudinal QOL is independent of both. These data support the adoption of TAVR among patients with varied surgical risk, even in need for alternative access approaches.

Primary Student Presenter: Allyson Adams

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Maryam Guiahi

Poster Title: Access to family planning in rural communities primarily served by Catholic hospitals: a mystery caller study

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Catholic hospitals account for one in six acute care hospital beds. A total of 46 hospitals are considered sole community hospitals, a designation that refers to care in remote locations. Catholic hospitals are expected to follow the Ethical and Religious Directives for Catholic Health Care Services, which applies the Catholic doctrine to the practice of medicine, prohibiting common reproductive services. Little is known about reproductive health care access in rural communities served primarily by Catholic hospitals. The purpose of this study is to understand access to family planning service appointments in the three rural communities in Colorado (Grand Junction, Durango, and Canon City) that are served by Catholic sole community provider hospitals.

We performed an online search of all general obstetrics and gynecology (ob/gyn), family practice, and midwifery practices in Grand Junction, CO. For each practice in Grand Junction, we called five different times, each one week apart, and queried about availability of short-acting reversible contraception (pill, injection), long-acting reversible contraception (intrauterine device [IUD], implant), emergency contraception (EC), tubal ligation (interval, postpartum), and abortion using structured telephone scripts.

We reached all 25 eligible practices for each of the calls. Nine practices were ob/gyn, 15 were family medicine, and one was a midwifery practice. Amongst these, 96% offered a contraceptive pill appointment, 88% injectable contraception, 76% IUD, 64% implant, 8% EC, 20% tubal ligation, and 4% abortion. No practices offered all services. Most denials to appointments were based on the practice not having a trained provider; Catholic affiliation was rarely cited (4-16% of denials).

There was little restriction to family planning services secondary to Catholic health care affiliation in Grand Junction, CO. We will survey two other rural communities with these methods to determine if this pattern is consistent.

Primary Student Presenter: Eniola Ogundipe

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Benjamin Mullin

Poster Title: An Examination of Neural Networks in Adolescents With and Without Severe Worry

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Severe worry, which frequently emerges during adolescence, involves persistent thoughts about potential negative events. The neural underpinnings of worry are poorly understood among adolescents. The current study sought to identify patterns of brain activity underlying the experience of worry in adolescents.

Forty-five adolescents (ages 13-18) were recruited from Children's Hospital Colorado and the community. Worry severity was assessed via the Penn State Worry Questionnaire for Children (PSWQ-C). Participants underwent functional magnetic resonance imaging (fMRI) during which they completed a task to isolate regions of the brain activated during the viewing of emotional images. Negative and neutral images were presented following a negative, neutral, or ambiguous cue. We examined blood oxygenation level-dependent (BOLD) responses in the anterior cingulate cortex (ACC), insula, and amygdala during viewing of negative images preceded by a negative cue and contrasted these against BOLD responses to neutral images preceded by a neutral cue (threshold at $p < .001$, $k > 5$). Beta weights were extracted and correlations performed contrasting activation and PSWQ-C scores.

Analysis revealed significant activation of the ACC and insula in response to negative versus neutral images. A marginally significant negative association was found between PSWQ scores and activation in the insula ($r = -.266$, $p = .077$).

Our findings are consistent with previous studies, suggesting that the insula and ACC are implicated in the processing of negative emotion. Surprisingly, activation in the insula was negatively associated with worry severity, although this finding was only marginally significant. It may be that other brain regions are more central in determining the intensity and severity of worry.

Primary Student Presenter: Kelly Stanek

Additional Presenter(s): Kelly Stanek

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Shideh Majidi

Poster Title: An Examination of the Presence of Mental Health Diagnoses in a Clinical Sample of Individuals with Type 1 Diabetes

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Objective: To examine demographic and mental health diagnostic characteristics for individuals with type 1 diabetes (T1D) and current mental health diagnoses. Methods: The medical records of 397 individuals ages 10-25 with T1D (mean age = 15.3±3.1 years, mean T1D duration = 6.0±4.5 years) who were screened during routine T1D clinic visits for depressive symptoms using the Patient Health Questionnaire-9 (PHQ-9) were reviewed for current DSM-5 diagnoses, demographic information, and T1D management data. Results: Of those screened, 29% had a mental health diagnosis; 56% had 1 diagnosis, 26% had 2, and 18% had 3+. The most common diagnoses were depression (16% of total screened), anxiety (15%), and attention-deficit/hyperactivity disorder (10%). Other diagnoses included mood, learning, and eating disorders. Those with a mental health diagnosis were slightly older and they had higher PHQ-9 scores and higher HbA1c (Table). Sex, race, insulin regimen, continuous glucose monitor use, T1D duration, and insurance were not significantly different. Conclusions: Mental health diagnoses are common in adolescents and young adults with T1D. Those with mental health conditions may experience greater difficulties in T1D management, contributing to higher HbA1c. There is a need to develop tailored interventions to improve T1D management when specific mental health conditions are present.

Differences in Characteristics between T1D youth with and without a Mental Health Diagnosis.

	Mental Health Diagnosis (n=116)	No Mental Health Diagnosis (n=281)	p-value
Age (years)	15.8±2.9	15.0±3.2	0.023
PHQ-9 Score	7.5±6.4	3.8±4.3	<0.001
A1c	9.88±2.5	9.17±2.1	0.004

Primary Student Presenter: Katherine Drexelius

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Jenny Hsieh

Poster Title: Using Stem Cell Derived Cerebral Organoids to Model Prenatal Hypoxic Ischemic Encephalopathy

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Hypoxic-ischemic encephalopathy (HIE) due to neonatal asphyxia is a leading cause of mortality and severe impairment among infants, including motor impairment and a wide range of neurological deficits. Despite how common and how devastating HIE is, therapies are limited, as it has been difficult to create functional models with which to understand the disease process and potential treatments.

Our project examines the use of cerebral and cortical organoids derived from human embryonic stem cells as a potential disease model for HIE. These organoids are three-dimensional "mini-brains" that recapitulate the developmental processes and organization of the human brain. Cell death and subsequent upregulation of astrocytes in organoids exposed to hypoxic conditions would support their use as an HIE model, which would be an invaluable tool in understanding HIE and in developing new therapies for HIE patients.

Organoids were divided into chambers for chronic hypoxic (CH), acute hypoxic (AH), and normoxic conditions. After exposure to hypoxic conditions, we performed immunohistochemistry to stain for apoptotic cells and astrocytes, which are typically upregulated with cell stress. Results showed a qualitative increase in number of apoptotic cells and astrocytes in CH organoids. However, there was no qualitative difference in expression when comparing AH organoids to the controls.

Cell damage and upregulation of surrounding astrocytes under chronic hypoxic conditions reflects cell damage seen in HIE, supporting the use of organoids in modeling this disease, while exposure to acute hypoxic conditions did not show qualitative differences from control groups, suggesting that organoids may be an ineffective model for acute hypoxic-ischemia.

Primary Student Presenter: William Dewispelaere

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Marian Betz

Poster Title: Improving Firearms Conversations in the Emergency Department

Final Category: Education

Abstract:

Objectives: Emergency Department (ED) physicians are on the front lines of firearms violence. They also have opportunities to prevent firearm injury or death through intervention programs and counseling about reducing firearm access to prevent suicide. This opportunity is often missed because of a lack of comfort or knowledge about firearms. Specific firearm education may help in this regard, but there are few accessible resources. Here we investigate the impact of a short, in-person educational session on ED physicians' comfort and knowledge regarding firearms.

Methods: We hosted a 3-hour session for ED providers to learn about firearms, firearm violence, and counseling patients about firearms. The content was based on prior research and experiences within the ED. Participants completed a pre- and post-session assessment. Multiple-choice questions addressed knowledge about firearms and confidence talking about guns with patients. McNemar's Exact test for paired proportions was used to assess whether the lecture series had an impact on question responses.

Results: 26 ED physicians attended the event. 21 completed the pre-and post-event surveys. Pre-post comparisons showed an average increase of 2.24 (95%CI 1.63-2.85) correct answers on our test of gun knowledge ($p < 0.001$). Most (88%) of participants who were uncomfortable talking to patients about firearms before the event rated themselves as comfortable after the event ($p = 0.007$). Most (87%) of participants changed their mind about comfort identifying patients who need firearms counseling ($p = 0.016$).

Conclusions: Our firearms event demonstrated an effective model for improving firearm knowledge and comfort among ED physicians. Increasing knowledge could lead to more conversations about guns in the ED. Further research is needed to develop validated measures of firearm knowledge and to assess the effects of training on provider behavior.

Primary Student Presenter: Oliver Bawmann

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Katie Morrison

Poster Title: Is there an association between experiencing burnout and gratitude in medical students?

Final Category: Healthcare and Public Health

Abstract:

Burnout is a problematic issue for medical students with studies reporting a prevalence of burnout symptoms ranging from 45 – 71%. Gratitude is a positive emotion, and there is literature that has demonstrated that promoting gratitude has increased well-being, meaningfulness, and overall mental health in some populations. As such, we hypothesized that medical students who experience more feelings of gratitude would experience less symptoms of burnout – that experiencing gratitude would be inversely proportional to burnout.

In order to examine our hypothesis, we administered a validated gratitude questionnaire (GQ-6) that assesses participants' disposition toward experiencing gratitude, as well as a screening tool that has been validated to measure burnout in medical students [1]. These surveys were administered to all second and third year medical students at a university associated medical school. The survey items were administered as part of a larger end of year survey that is sent to all university medical students. 165 and 166 second year students completed the gratitude and burnout surveys respectively. Of the third year students, 161 and 164 completed the gratitude and burnout surveys respectively.

Our data demonstrated that in medical students there is a statistically significant association between experiencing gratitude and experiencing burnout. This was consistent in both classes ($r = 0.221$, $p = .004$, and $r = 0.218$, $p = .006$ for the second and third year classes respectively).

There are multiple possible explanations for our findings. One possibility is that those who experience gratitude have associated personality traits such as increased empathy or engagement that might predispose them to emotional exhaustion (one of the symptoms of burnout). In addition, much of the research that links gratitude with resilience is done on those with an active (often daily) practice of focusing on gratitude. While students may express having a lot of gratitude, that may not have the same positive effect as an active daily practice of focusing on gratitude.

While our hypothesis proved incorrect and in fact supported the association between gratitude and burnout it certainly raises interesting questions. Future research might focus on the effect of active

gratitude practices such as gratitude letters or journals on medical student burnout.

Primary Student Presenter: Zoe Panchal

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Charles Whitmore

Poster Title: What is LGBT-Friendly Healthcare? A Literature Review.

Final Category: Healthcare and Public Health

Abstract:

In 2010, One Colorado conducted a needs assessment of LGBT individuals in Colorado (n=4,600). Ten percent of respondents identified LGBT-friendly healthcare as one of their top-five social service needs. However, there is no current evidence-based consensus as to what constitutes LGBT-friendly healthcare, making it difficult to act on this finding. The purpose of this literature review was to better define LGBT-friendly healthcare. A keyword search of PubMed, Web of Science and PsycInfo was conducted to identify randomized control trials (RCTs), meta-analyses, systematic reviews, and data-driven reports regarding healthcare experiences and preferences of LGBT individuals. Only original research from the United States, in English, published between January 1, 1990 and January 6, 2018 were included. Among the 105 unique articles identified, seven articles were identified as most relevant to our research and analyzed to determine the factors most important to making healthcare LGBT-friendly. Preliminary analysis indicates that non-assumption of heterosexuality, respect for partners, discussion of sexuality only when relevant to specific healthcare needs, and knowledge of LGBT healthcare issues are consistently the most important aspects of LGBT-friendly healthcare. Of less importance seem to be visual displays of LGBT symbols such as the rainbow flag, or LGBT-specific pamphlets, etc. in the office as well as the gender or sexual orientation of their healthcare provider.

Primary Student Presenter: Walter Taylor

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Caleb Ing

Poster Title: Long-term Healthcare Utilization in Children with Neonatal Abstinence Syndrome

Final Category: Healthcare and Public Health

Abstract:

Background: Children exposed to opioids during pregnancy can develop neonatal abstinence syndrome (NAS) shortly after birth. The incidence of this complex withdrawal syndrome has increased dramatically in recent years and has resulted in significantly increased healthcare expenditures. The purpose of this study was to evaluate healthcare utilization in children with NAS over their first two years of life.

Methods: Data from a birth cohort of over 2.5 million children from Texas and New York were used for this study. Neonates with NAS during their birth admission were identified. Each NAS child was propensity score matched to 5 children without NAS using demographic and clinical covariates. Outcomes included birth length of stay (LOS), inpatient hospital days, outpatient hospital visits, physician office visits, and number of prescriptions.

Results: 3,799 neonates with NAS were matched to 18,995 children without NAS. Mean birth LOS for children with NAS was significantly longer than in children without NAS. Children with NAS had more inpatient days during the first 3 quarters of life. NAS children had more outpatient hospital visits but fewer office visits than non-NAS children. Children with NAS had more outpatient hospital visits Q2-Q8, whereas they had fewer outpatient office visits in each quarter except Q2.

Conclusions: NAS children were found to have significantly longer inpatient hospitalizations at birth compared to non-NAS children. However, no differences were seen in the number of subsequent inpatient hospital days or in prescription drug fills. Regarding outpatient care, NAS children had more outpatient hospital visits but fewer physician office visits.

Primary Student Presenter: Derek Wilson

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Kowalski

Poster Title: Significant Reduction in Prehospital Evaluation and Door-to-Treatment Times with a Mobile Stroke Unit.

Final Category: Healthcare and Public Health

Abstract:

Background: The University of CO Mobile Stroke Unit (UC MSU) provides ambulance-mounted CT scanning and tele-stroke neurologic assessment in the Denver, CO, metro area. As one of the first U.S. medical centers to utilize a mobile stroke protocol we sought to compare operational characteristics of the MSU during its first year with standard management (SM) of prehospital stroke alerts at a Comprehensive Stroke Center.

Methods: The study compared patient characteristics, ambulance response, neurologic evaluation, and treatment between the MSU, and SM patients. Variables included time from stroke alert to tPA administration, as well as time from arrival at the door of MSU or ED to first brain CT and to IV tPA administration. Patients were split into those with door to needle times greater and less than the American Stroke Association target study goal of 45 minutes.

Results: Between 1/15/2016 and 1/9/2017, 47 patients received management with the UC MSU, and 73 received standard management. Median age was 66 years (IQR 57-77), and 45% were female, with no difference between MSU and SM patients. Thirteen (28%) of patients were treated with IV tPA on the MSU, compared with 16 (22%) through SM. Median time was significantly shorter from door to first CT on the MSU than SM [4 minutes MSU vs. 9 minutes SM, $p < 0.001$]. Median time from dispatch to IV tPA administration was shorter on the MSU [39 minutes MSU vs. 65 minutes SM, $p < 0.001$], and for door to IV tPA [26 minutes MSU vs. 37 minutes SM, $p = 0.022$]. MSU patients were more likely to have door-to-needle times meeting the ASA goal of <45 minutes [13 (100%) MSU vs. 11 (69%) SM, $p = 0.048$].

Conclusions: Patients treated via the MSU benefited from quicker time to CT, neuro evaluation, and, shorter time from dispatch to tPA administration, compared with pre-hospital stroke alerts. These results suggest prehospital management with an MSU has potential to aid the goal of earlier thrombolysis after ischemic stroke symptom onset.

Primary Student Presenter: Katherine Turner

Additional Presenter(s): Daniel Grine Amrut Ambardekar

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Matthew Taylor

Poster Title: Characterization of the University of Colorado Human Cardiac Tissue Bank

Final Category: Healthcare and Public Health

Abstract:

Human cardiac tissue banks (HCTBs) are valuable yet high-cost endeavors restricted to a handful of academic medical centers. Many publications describe approaches for establishing HCTBs; however, little has been published describing their demographic and clinical characteristics. Here we describe the demographics and diagnoses of the University of Colorado HCTB (UC-HCTB).

Demographic and clinical phenotype data were extracted from the UC-HCTB and analyzed using R 3.5.1 and RStudio 1.1.456. Colorado transplant data was downloaded from the Organ Procurement and Transplantation Network website for comparative analysis.

The UC-HCTB contains tissue from 1,343 unique patients. Of these patients, 860 have complete clinical and demographic data on age, sex, race, year of transplant or device placement, and diagnosis. The 860 samples include 591 (69.7%) failing and 269 (31.3%) non-failing hearts. Common diagnoses include ischemic cardiomyopathy (26.7%), idiopathic dilated cardiomyopathy (22.7%), familial cardiomyopathy (4.3%), and retransplant (3.8%). The failing and non-failing samples are 21.7% and 52.8% female respectively. The racial distribution among the failing hearts is 77.5% White, 9.6% Black, 9.1% Hispanic, and 2.4% Asian. When compared to cumulative OPTN Colorado transplant data, females are under-represented in the UC-HCTB (21.7% vs. 31.3%). Black and Hispanic samples were more and less frequent in the UC-HCTB, respectively (Black 9.6% vs. 6.1%, Hispanic 9.1% vs. 13.3%).

These data provide insight into the demographic and diagnostic makeup of the UC-HCTB. Transparent reporting by other HCTBs will reveal whether similar demographic disparities between patients and banked tissues are present elsewhere, suggesting that under recruitment of women and minorities is a problem endemic in the field.

Primary Student Presenter: Colton Ladbury

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Sameer Nath

Poster Title: Estimated Dose of Radiation to Immune Cells Predicts for Overall Survival and Myelosuppression Following Chemoradiation for Locally-Advanced Non-Small Cell Lung Cancer. CL Ladbury, (MD, SOM), CG Rusthoven, DR Camidge, BD Kavanaugh, SK Nath, Department of R

Final Category: Hematology and Oncology

Abstract:

Purpose: Emerging data suggests that unintended radiation dose to the host immune system may contribute to tumor progression and death in patients undergoing treatment for locally-advanced non-small cell lung cancer (LA-NSCLC). Previously, a model for calculating the estimated dose of radiation to immune cells (EDRIC) was found to be associated with clinical outcomes in patients with LA-NSCLC treated with definitive chemoradiation on RTOG 0617. The aim of this study was to externally validate this association in an independent cohort.

Methods: From 2004 to 2017, 117 patients with stage III NSCLC were treated with curative-intent chemoradiation. EDRIC was calculated as a function of the number of radiation fractions and mean doses to the lung, heart, and the remaining body. The primary endpoint was overall survival (OS), and secondary endpoints were local progression-free survival (LPFS) and disease-free survival (DFS).

Results: The median follow-up for all patients was 16 months with 77% of patients followed until death. Median EDRIC was 6.1 Gy (range, 2.5-10.0 Gy). Use of intensity-modulated radiation therapy trended towards a lower EDIC ($p=0.07$). A higher EDRIC correlated with a lower absolute neutrophil count ($p=0.0007$) and absolute lymphocyte count nadir ($p=0.0007$). On multivariate analysis, EDRIC was significantly associated with OS (HR 1.17, $p=0.03$), LPFS (HR 1.17, $p=0.02$), and DFS (HR 1.15, $p=0.04$), whereas total radiation dose and planning target volume were not.

Conclusion: This study supports the association of estimated dose of radiation to immune cells in the host with increased myelosuppression and worsened tumor control and survival following the definitive treatment of LA-NSCLC. Tailoring radiotherapy to spare the immune system may be an important future direction to improve outcomes in this population.

Primary Student Presenter: Eliza Baird-Daniel

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jean Mulcahy-Levy

Poster Title: The assessment of therapeutic autophagy inhibition in NF1 mutated tumors

Final Category: Hematology and Oncology

Abstract:

Purpose: Upregulation of Ras-Raf-MEK-ERK pathway (also known as MAPK/ERK pathway) through various mutations is critical across many different tumor types including CNS tumors. Neurofibromin 1 (NF1) protein functions as a tumor suppressor by negatively regulating Ras proteins through GTPase activity. A loss of function mutation in the NF1 gene results in the activation of MAPK upregulation /ERK pathway. Neurofibromatosis type 1 (NF1) is one of the most prevalent brain tumor predisposition disorders. NF1 is associated with peripheral nerve sheath tumors (MPNST) as well as optic gliomas and is often resistant to surgical resection. MEK inhibition (MEKi) remains a standard therapy for tumors associated with NF1 although studies have shown development of resistance towards these therapies.

We have previously shown that CNS tumors harboring BRAFV600E mutation exhibit an increase in autophagy and a dependence to this cell survival pathway. Additionally, we have shown autophagy inhibition improves the response of both sensitive and resistant tumor cells to BRAF inhibition. There has been little investigation on the role of autophagy in NF1 cells. We hypothesize that these cells are autophagy dependent and therefore sensitive to autophagy inhibition. Targeting autophagy could provide a new therapeutic option for a difficult to treat patient population. Thus, our objective here was to evaluate the role of autophagy in NF1 cells.

Methods: NF1 wild-type and knockout HSC1 λ (immortalized human Schwann) cells were evaluated for response to autophagy inhibition. Pediatric SF188 cells were used as controls. MAPK/ERK pathway upregulation due to NF1 knockout was evaluated via Western Blot analysis. Autophagic activity was assessed via Western Blot analysis of autophagic flux. The efficacy of autophagy inhibition on decreasing cell growth and survival was analyzed via Incucyte growth and CellTiter Glo assays, respectively.

Results: NF1 mutated cells demonstrated upregulation of the MAPK/ERK pathway as expected.

Preliminary studies show increased autophagic flux in NF1 mutated cells compared to wild-type.

Conclusion: Evidence supports increased autophagic dependency in NF1 mutated tumors. Future studies will further characterize how autophagy regulate NF1 driven tumor cells and the specific role of

autophagy inhibition.

Primary Student Presenter: Michael Oliphant

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 6th

Mentor: Heide Ford

Poster Title: Six2 mediates late-stage metastasis via direct regulation of Sox2 and induction of a cancer stem cell program

Final Category: Hematology and Oncology

Abstract:

The ability of tumor cells to metastasize efficiently is directly linked to their ability to colonize secondary sites. Herein, we identify Six2 as a critical regulator of a breast cancer stem cell program that enables metastatic colonization. In several triple negative breast cancer (TNBC) models, we show that Six2 enhances the expression of genes associated with embryonic stem cell programs. We find that Six2 directly binds to the sox2 srr2 enhancer, promoting sox2 expression and downstream expression of nanog, both key pluripotency factors. Regulation of Sox2 by Six2 enhances cancer stem cell properties and increases metastatic colonization. Further, Six2 and Sox2 expression are highly correlated in breast cancers, including TNBC, where a Six2 expression signature is predictive of metastatic burden and poor clinical outcomes. Our findings demonstrate that a SIX2/SOX2 axis is required for efficient metastatic colonization, underscoring a key role for stemness factors in outgrowth at secondary sites.

Primary Student Presenter: Kathleen O'Neill

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Jennifer Richer

Poster Title: Elucidating a critical metabolic dependency in TNBC: regulation of cholesterol uptake and biosynthesis in epithelial-to-mesenchymal transition

Final Category: Hematology and Oncology

Abstract:

Triple Negative Breast Cancer (TNBC) is an aggressive subtype of cancer with poor prognosis, due to high metastatic potential and limited targeted therapies. TNBC have often undergone epithelial-to-mesenchymal transition (EMT), acquiring a phenotype associated with drug resistance and metastasis. Recent studies demonstrate that in addition to driving aggressive traits, EMT is accompanied by altered cell metabolism, which can offer novel vulnerabilities to be targeted therapeutically. Normal breast epithelial cells and hormone-responsive breast cancers express miR-200c, a potent suppressor of EMT. TNBC tend to have lost miR-200c through silencing or deletion, allowing aberrant expression of genes that confer an invasive and chemoresistant mesenchymal-like state. Reintroduction of miR-200c to TNBC is a powerful tool to reveal altered dependencies between epithelial and mesenchymal-like cancer cells.

We hypothesized that in addition to reversing EMT markers, restoration of miR-200c to TNBC would alter and thereby reveal metabolic dependencies of this subtype. Indeed, gene array and metabolomic approaches identified key components of cholesterol metabolism as being high in TNBC and decreased by miR-200c.

Herein, we demonstrate that TNBC lines are highly sensitive to inhibition of cholesterol biosynthesis and uptake relative to hormone receptor-positive cell lines. We identified direct targets of miR-200c within the cholesterol metabolism pathway including the lysosomal cholesterol-efflux protein NPC1. Further, restoration of miR-200c affects SREBP-1 and SREBP-2 signaling, suggesting that altered lipid and cholesterol signaling is a component of EMT. Delineating cholesterol dependency and homeostasis in TNBC may lead to novel therapeutics in TNBC.

Primary Student Presenter: Heather Caulkins

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Natalie Serkova

Poster Title: Ultrasmall Super-Paramagnetic Iron Oxide Nanoparticles to Image Radiation-Induced Inflammation in Tumor-Bearing Mice with Diverse Immune Phenotypes

Final Category: Hematology and Oncology

Abstract:

Background: Many patients experience inflammation after radiation therapy (RT). This study aims to develop quantitative T2-MRI to measure RT-induced inflammation in tumor-bearing mice with varying degrees of immunodeficiency. We hypothesize that using macrophage iron metabolism will allow us to assess inflammation using ultra-small superparamagnetic iron oxide nanoparticle (USPION) T2 contrast.

Methods: We used NOD.SCID (non-obese diabetic/severe combined immunodeficiency), nu/nu athymic, and wild-type mice (C57BL/65). Mice were implanted with tumor cells in the flank. Quantitative T2-weighted MRI was performed before USPION and 24 hours after USPION. Mice underwent RT of the tumor, followed by MRI. Tumors were harvested for *ex vivo* correlates.

Results:

	Macrophages	$\Delta T2$, no RT (ms)	$\Delta T2$, RT (ms)	P-value
NOD.SCID MDA-231	none	-1.7	-2.6	Nonsignificant
Nu/nu MDA-231	moderate	-1.77	-18.35	0.00007
NOD.SCID UMSCC10	none	-1.7	-0.8	Nonsignificant
Nu/nu UMSCC10	Moderate	-2.0	-14.5	0.0002
Nu/nu U251	Moderate	-13.4	-12.3	nonsignificant
WT GL261	–	-17.6	-14.6	Too few animals received RT

Discussion: Previously, we have shown that highly inflamed immunocompetent models showed significant drops in T2 after USPION from macrophage uptake. Here we demonstrate that RT-induced inflammation is absent in SCID models and athymic nu/nu mice can produce macrophages after RT. SCID mice are inappropriate for studying the inflammatory microenvironment of cancer.

Primary Student Presenter: Emily Rao

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MS

Year: 2nd

Mentor: Brian Branchford

Poster Title: Improving Compliance with Institutional Risk Assessment Tool in Pediatric Patients at Risk for Hospital-Acquired Venous Thromboembolism

Final Category: Hematology and Oncology

Abstract:

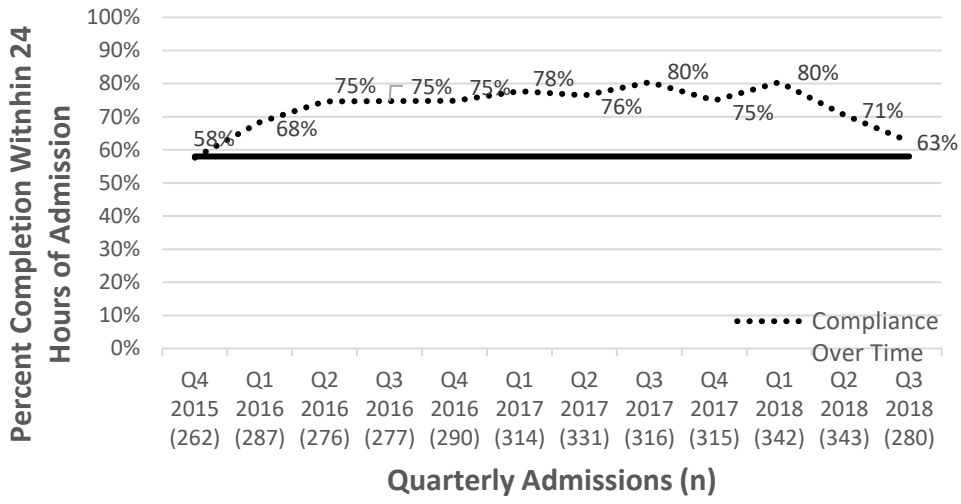
Background: The incidence of pediatric hospital-acquired venous thromboembolism (HA-VTE) is increasing, along with associated morbidity and mortality. An institutional risk assessment tool is in place with the goal of decreasing HA-VTE, but compliance has been poor.

Aim: To improve compliance with the HA-VTE risk assessment in patients admitted to the inpatient hematology, oncology, and bone marrow transplant unit.

Methods: Risk assessment completion was tracked for 3633 admissions to Children's Hospital Colorado hematology, oncology, and bone marrow transplant inpatient unit from 2015 – 2018. Providers were prompted by the electronic health record to complete risk assessments on admission to assess key risk factors and recommended prophylactic interventions. A HA-VTE was defined as a deep vein thrombosis or pulmonary embolism >48 hours after admission or at any time at the site of a central venous catheter. Compliance with the risk assessment was measured as percentage of risk assessments completed within 24 hours of admission, with goal compliance of 80% by the end of 2018. Interventions to improve compliance included reminder emails for incomplete assessments and monthly resident education. HA-VTE rate was also tracked and reported as number of events per patient days.

Results: Compliance with the risk assessment rose from a baseline of 58% in the first quarter of this project to 71% in the first three quarters of 2018. Rate of HA-VTE decreased from 0.30 to 0.21 events per patient days in the year prior to starting the project to 2018. Further work is needed to increase compliance to goal of 80%. Validation studies are underway to assess efficacy of risk assessment tool.

Risk Assessment Completion



Primary Student Presenter: Dylan Bergstedt

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kevin Deane

Poster Title: Antibody Isotype Changes Post Rheumatoid Arthritis Diagnosis

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose: Rheumatoid factor (RF) and anti-citrullinated protein Abs (ACPA) are known to be elevated in Rheumatoid Arthritis (RA). Less is known about the ways in which the specific isotypes of these antibodies change after RA diagnosis. Evaluating these changes may enhance our understanding of the ongoing inflammatory response in RA post diagnosis. We tested post RA diagnosis serum samples from the Department of Defense Serum Repository (DoDSR) and a Colorado-based RA cohort called "Studies of the Etiology of RA" (SERA) to better understand these changes.

Methods: From the DoDSR we obtained 214 post RA diagnosis serum samples. The samples were divided into two groups (less than two years post RA diagnosis and two years or greater post RA diagnosis). We evaluated for serum RF and ACPA immunoglobulin (Ig) IgA, IgG, and IgM isotypes. We then examined differences in the rates of positivity for all isotypes of both antibodies between the two groups. Following this, the same procedure was carried out on 1469 samples obtained post-RA diagnosis from patients from SERA with the exception that only RF isotypes were evaluated.

Summary of Results: Among the DoDSR sample set there was significantly higher rates of positivity for IgA RF and ACPA autoantibodies further from diagnosis. In the SERA data set all three RF isotypes were significantly increased in patients assessed ≥ 2 years from RA diagnosis compared to those who were tested < 2 years from diagnosis. Furthermore, when individuals were separated by age (< 40 and ≥ 40) there were no significant differences present in either the DoDSR or the SERA data sets.

Conclusion: Autoantibody positivity rates continue to rise after the initial diagnosis of RA. This indicates that there is likely an evolving autoimmune inflammatory response in RA despite therapy. In particular, the predominant change in IgA autoantibodies in the DoDSR data set lead us to believe there may be some degree of mucosal involvement in the early period following the diagnosis of RA. Further evaluation is necessary to help clarify the exact nature of this ongoing inflammation.

Primary Student Presenter: Amrita Chager

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jay Hesselberth

Poster Title: mRNA Targets of IRE1 during Unfolded Protein Response

Final Category: Immunology and Autoimmune Diseases

Abstract:

The unfolded protein response is triggered by stress from improperly folded proteins, mostly taking place in the ER. There are three associated pathways, with Inositol-requiring-1 (IRE1) being the most evolutionarily conserved. IRE1 has two isoforms – IRE1 α and IRE1 β . IRE1 α is ubiquitously expressed in mammalian cells, while IRE1 β is exclusively found in gastrointestinal epithelial cells. Its canonical target's (XBP1) downstream effects include protein expression contributing to proper execution of cellular stress responses. IRE1 also cleaves targets known as regulated IRE1-dependent decay of mRNA (RIDD). Unlike XBP1, RIDD is associated with unpredictable effects ranging from maintenance of ER homeostasis to cell death. Improper UPR activation has been appreciated in inflammatory processes and many autoimmune disorders (i.e. atherosclerosis, SLE). The main goal of this study is to find the mRNA targets of IRE1 during the UPR.

Primary Student Presenter: Rosalyn Savoie

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kristen Demoruelle

Poster Title: Does Pregnancy Lead to the Development of Anti-Cyclic Citrullinated Peptide (CCP) Antibodies?

Final Category: Immunology and Autoimmune Diseases

Abstract:

Objective. Rheumatoid arthritis (RA) is a systemic autoimmune disease that leads to joint inflammation. It affects women more often than men, and there is a 6-fold increased risk of developing RA during the postpartum period. The etiology of this increased risk is unknown. The goal of this study was to determine whether pregnancy is associated with increased prevalence of RA-related autoantibodies, specifically anti-cyclic citrullinated peptide (CCP) antibodies, which have been identified in the blood prior to the onset of joint disease in RA and are highly predictive of developing RA in the future.

Methods. Stored serum samples were obtained from 340 RA-free women in their 3rd trimester of pregnancy and 142 pre-menopausal, non-pregnant, RA-free women. All samples were tested for commercial anti-CCP ELISA assays, specifically CCP3 (IgG Inova) and CCP3.1 (IgG/IgA Inova). Questionnaires were used to assess women's health and smoking histories. Chi-square/Fisher's exact testing were used to compare groups.

Results. The prevalence of anti-CCP positivity did not differ between pregnant and non-pregnant women. [For CCP3, 2.1% vs. 1.2%, $p = 0.43$ and for CCP3.1, 1.4% vs. 1.5%, $p = 1.0$, respectively]. Within the pregnant women, there was no difference in anti-CCP positivity based on age, smoking history, or sexually transmitted infection during pregnancy.

Conclusion. We did not find an association between pregnancy and systemic anti-CCP antibodies. These data suggest that the increased risk of developing RA in the postpartum period is not due to increased systemic anti-CCP development during pregnancy. However, additional studies are needed to evaluate the influence of genetics on the development of anti-CCP antibodies during pregnancy and the postpartum period.

Primary Student Presenter: Andrew Tannous

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Nanette Santoro

Poster Title: Analysis of Inflammatory Signaling in Repro-Metabolic Syndrome

Final Category: Metabolism and Endocrinology

Abstract:

Purpose of Study: Obesity is characterized by elevated lipids, insulin resistance and relative hypogonadotropic hypogonadism; decreased LH, FSH, ovarian steroids and reduced pituitary response to GnRH, which we define as Repro-Metabolic syndrome. We have previously shown that this phenotype can be induced in healthy normal weight women by acute infusion of free fatty acids and insulin. Obesity is also a state of chronic inflammation. In order to identify potential mediators of insulin and lipid-related reproductive endocrine dysfunction, we examined serum levels of inflammatory markers.

Methods Used: 11 reproductive aged women of normal BMI (<25 kg/m²), with regular menses, were recruited with IRB approval. All were studied in the early follicular phase of the menstrual cycle. Each participant underwent infusion of either saline or insulin (40mg/kg/min) plus free fatty acid (Intralipid), for 6 hours, in sequential cycles in random order. Euglycemia was maintained by glucose infusion. Frequent blood sampling (q10 min) was performed to measure gonadotropin pulsatility.

To assess the inflammatory milieu, blood samples from 180-230 min (at which time steady state lipid and insulin levels were achieved) were pooled and analyzed using ELISA for a series of 33 inflammatory signaling molecules; cytokines, interleukins, chemokines, adipokines and growth factors (Table 1) and markers of endoplasmic reticulum stress (CHOP and GRP78). Mean levels in saline controls were compared to insulin/lipid infusions by paired t-test.

Summary of Results: Induction of Repro-Metabolic syndrome was confirmed by a decrease in LH and FSH pulse amplitude and the development of insulin resistance. No significant differences were observed in any of the inflammatory signaling or ER stress markers tested.

Conclusions: Infusion of lipid and insulin to mimic the metabolic syndrome of obesity was not associated with an increase in inflammatory markers. Our results imply that the endocrine disruption and adverse reproductive outcomes of obesity are not a consequence of the inflammatory environment, but may be mediated by direct lipotoxic effects on the hypothalamic-pituitary-gonadal axis.

Primary Student Presenter: Dustin Brown

Additional Presenter(s):

Presenting School: Pharmacy

Degree Seeking: PhD

Year: 3rd

Mentor: Vanessa Phelan

Poster Title: Examining the Effect of *Pseudomonas aeruginosa* Biofilms on Oxylipin Metabolism in Cystic Fibrosis

Final Category: Microbiology and Infectious Diseases

Abstract:

Background: In Cystic Fibrosis (CF), the lung microbiome becomes dysbiotic because of a mutation in the gene for the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), a chloride channel, leading to bronchiectasis, inflammation and oxidative stress. A hallmark of CF disease pathology is chronic *Pseudomonas aeruginosa* lung infections characterized by bacterial growth in biofilms. Biofilms provide protection from innate immune defense, antibiotics, and facilitate production of high titers of virulence factors. Virulence factors can be directly toxic to the host or can act indirectly to influence innate immunity. For example, virulence factors such as Cif protein can exacerbate CFTR trafficking issues and modulate host-derived inflammatory mediators (oxylipins), leading to chronic inflammation. The objective of the present study was to determine the effect of *P. aeruginosa* biofilms on activation of innate immunity in CF host bronchial epithelium (CFBE).

Methods: CFBE41o- cells, homozygous for the $\Delta F508$ mutation, and CFBE41o- pCEP-WT cells, complemented with WT-CFTR, were provided by Dr. Dieter Gruenert at the University of California San Francisco. *P. aeruginosa* PA14 and a Cif deletion mutant (Δ Cif) were provided by Dr. George O'Toole at Dartmouth University. In all studies, CFBE were grown as monolayers using standard cell culture techniques. Separately, *P. aeruginosa* biofilms were grown in artificial sputum media (SCFM2) and cell-free supernatant was collected. Then, CFBE monolayers were treated with biofilm supernatants. Following co-culture, culture medium and cell lysates were collected and analyzed. Non-targeted and targeted metabolomics were performed on biofilm supernatants and culture medium, respectively, to reveal the suite of virulence factors produced and their subsequent effect on pro-inflammatory oxylipin profiles. qRT-PCR and Western blotting were used to determine effect of co-culture on oxylipin metabolic gene and enzyme expression. Finally, Redox Western blots were performed to look at the effect of biofilm supernatant treatment on compartmental redox balance.

Results: CFBE41o- CFBE challenged with *P. aeruginosa* PA14 biofilm supernatants display lower oxylipin metabolic gene expression, protein expression, and a lower titer of pro-inflammatory oxylipins

compared to CFBE41o- pCEP/WT CFBE. Additionally, increases in mitochondrial, cytosolic, and membrane oxidation were observed following treatment. When CFBE41o- CFBE was challenged with Δ Cif-PA14 biofilm supernatants, levels of innate immune activation were increased and oxidative stress was decreased compared to WT-PA14 biofilm supernatant treatment.

Conclusions: Cif protein and other enzymatic virulence factors represent a key link between chronic infections and the damaging inflammatory and oxidative environment observed in cystic fibrosis.

Primary Student Presenter: Norhan Alhajjar

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Kelly Doran

Poster Title: Development of a murine model of *Enterococcus faecalis* vaginal colonization

Final Category: Microbiology and Infectious Diseases

Abstract:

Enterococcus faecalis is a Gram-positive bacterium of the human gastrointestinal tract that can cause opportunistic infections. *E. faecalis* is associated with aerobic vaginitis (AV), a state of abnormal vaginal microbiota that is caused by a displacement of *Lactobacillus* species with aerobic pathogens that trigger a localized vaginal inflammatory immune response. We hypothesize that *E. faecalis* expresses factors that mediate interaction with the vaginal epithelium and other AV bacteria to promote vaginal niche establishment. To model this in vivo, we have adapted our previous mouse model of Group B *Streptococcus* (GBS) vaginal colonization. Because bacterial colonization peaks at estrus, mice were treated with β -estradiol 1 day prior to vaginal inoculation with *E. faecalis* V583. On successive days the vaginal lumen was swabbed and recovered bacteria was quantified to determine changes in bacterial load over time. We observed 100% colonization within the first 24 hours post-inoculation which persisted over one week. When inoculating germ-free mice with V583, persistence was observed in the vaginal tract in the absence of the natural microbiota. However, V583 was completely displaced following inoculation with GBS. We have further observed that V583 can attach to human vaginal epithelial cells in vitro. Lastly we demonstrated that treatment with a lytic bacteriophage resulted in vaginal clearance of V583, suggesting that bacteriophage treatment may be utilized as an alternative therapeutic for vaginal bacterial infections. Future studies include understanding the mechanisms of polymicrobial interactions involving *E. faecalis* and other AV bacteria, as well as investigating the use of bacteriophage as an effective form of treatment for Enterococcal and other bacterial vaginal infections.

Primary Student Presenter: Zoe O'Donoghue

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Jeffrey Kieft

Poster Title: Exploration and Characterization of Pathogenically Relevant RNA Structures in Flaviviruses

Final Category: Microbiology and Infectious Diseases

Abstract:

Flaviviruses like Dengue, Zika, and West Nile infect millions of people every year, making them prominent global health threats. The family flaviviridae contains viruses that are vector borne, enveloped, and have positive sense single stranded RNA genomes. During infection, viral replication produces high levels of genomic RNA, but the buildup of smaller regions of the viral 3'UTR is also observed. These subgenomic-flaviviral RNAs (sRNAs) are made via incomplete degradation of the viral genome by the host 5' to 3' exonuclease Xrn1, which halts at highly structured regions of the 3'UTR called Xrn1 resistant RNAs (xrRNAs). sRNAs have been shown to be necessary for both cytopathicity and pathogenicity during WNV infection. Using a reconstituted in vitro study system, we demonstrate that several diverse members of the flaviviridae family, including Modoc, Montana Myotis Leukoencephalitis, Cell Fusing Agent, and Tick-Borne Encephalitis viruses also produce sRNAs following Xrn1 degradation. Further, using SHAPE chemical probing we have characterized these divergent xrRNAs into two distinct structural "classes", indicating that while the ability to produce sRNAs may be conserved across the flavivirus genus, the sequences required for Xrn1 halting are more variable than previously suspected. This observation may imply a generalized role for sRNAs during flavivirus infections and currently we are working to more fully characterize the structural mechanism(s) of enzyme halting in these different classes of xrRNAs. We have also found that West Nile Virus xrRNAs are capable of stopping other exonucleases as well, including bacterial enzyme RNase J1. Ongoing studies include infection models and large-scale manipulations of xrRNAs in the Dengue Virus 3'UTR to explore the structure-function mechanisms of sRNAs during infection in both mosquito vector and vertebrate host models.

Primary Student Presenter: Ashley Knox

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Linda van Dyk

Poster Title: Host and Viral Non-Coding RNA: Regulation and Roles in Pathogenesis

Final Category: Microbiology and Infectious Diseases

Abstract:

While viral RNA is known to play vital roles in viral infection and replication, the regulation of viral RNA polymerase III (pol III)-transcribed non-coding RNAs (ncRNAs) remains unclear. The gammaherpesviruses (γ HVs) contain multiple ncRNAs that are highly expressed during infection. The γ HV68 TMER ncRNAs are required for pathogenesis and Epstein-Barr virus ncRNAs (EBERs) contribute to B cell transformation. Additionally, several host ncRNAs have been shown to be upregulated during gammaherpesvirus infection and play integral roles in pathogenesis. These include the B2 SINEs, which stimulate NF- κ B signaling that ultimately increases viral gene expression, and vault RNAs that protect B cells from apoptosis and allow enhanced viral establishment. Therefore, detailing how these ncRNAs are regulated is integral to understanding their role in pathogenesis. To compare the transcriptional regulation of pol III ncRNAs, we cloned several types of pol III promoters into a newly generated luciferase reporter we have optimized to measure pol III promoter activity during infection. Promoters include those of host ncRNAs (5S rRNA, tRNA, U6 snRNA), and of the γ HV68 TMERs, the EBV EBERs, and the adenovirus VA RNA. Infection with γ HV68 drives simultaneous repression of the human U6 promoter activity and stimulation of the γ HV68 TMER promoters. This TMER promoter induction was prevented by an inhibitor of viral protein synthesis, indicating that this aspect of infection is vital for driving transcriptional regulation. This analysis of pol III promoter activity indicates shared and unique regulation patterns and identifies the critical promoter and polymerase features for preferential expression during infection.

Primary Student Presenter: Hadrian Sparks

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: J. David Beckham

Poster Title: Investigating the Impact of Zika Virus 3' Untranslated Region Structural Interactions on Viral Infection

Final Category: Microbiology and Infectious Diseases

Abstract:

Similar to other mosquito-borne flaviviruses, Zika virus encodes two RNA structures (xrRNA1 and xrRNA2) in the 3' untranslated region (UTR) of the viral genome that resist degradation by host 5'-3' exonuclease 1 (Xrn1). Viral RNA-mediated Xrn1 resistance results in accumulation of fragments of the flavivirus 3' UTR called sub-genomic flaviviral RNAs (sfRNAs) which accumulate during infection of the host cell. Previous studies have shown that the presence of xrRNAs and subsequent sfRNA production is necessary for replication and pathogenicity of several flaviviruses. However, little is understood about the impact of specific structural elements in one or both xrRNAs on sfRNA production, viral replication, and virus-host interactions. A recent study solved the tertiary structure of Zika virus xrRNA1 and identified a stabilizing interaction within this structure that is essential for resistance of host Xrn1 degradation. Based on this information, we hypothesize that disrupting this interaction in either Zika xrRNA structures will decrease the production of sfRNA during infection leading to reduced viral replication and pathogenicity. To investigate this, we have generated infectious Zika virus clones in which xrRNA1 or xrRNA2 stability has been disrupted by a single nucleotide mutation. Currently, we have shown that these xrRNA mutants do not exhibit decreased viral replication during infection when compared to wild type (WT) Zika virus in both mosquito and mammalian cell lines. Continuing research will seek to determine if destabilization of both Zika xrRNAs results in reduced viral pathogenesis.

Primary Student Presenter: Francis Santoriello

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Stefan Pukatzki

Poster Title: A Competitive Mechanism of *Vibrio cholerae* Originated from a Phage-like Element

Final Category: Microbiology and Infectious Diseases

Abstract:

Vibrio cholerae (Vc) is a pathogen that thrives in coastal waters. It encodes a type VI secretion system (T6SS), a harpoon-like complex that exports effector proteins to kill neighboring competitor cells. The T6SS is encoded in three loci (a main cluster and two auxiliary clusters), each terminating in a modular effector-immunity (E/I) protein pair. E/I modules are highly diverse among Vc strains, conferring intra- and interspecies killing capacity and allowing a strain to clonally colonize its niche. We recently provided phylogenetic support for horizontal module transfer, as Vc effector sets do not align with the evolutionary lineage of Vc strains. Vc in the estuarine environment is regularly exposed to exogenous DNA, suggesting that the aquatic environment is a reservoir for new E/I module acquisition.

A fourth T6SS locus (Aux3) encoding the E/I module tseH/tsiH was recently characterized. Analysis by our lab identified a nearby phage integrase. Here we show that this locus is highly conserved in pandemic Vc (Aux3Pan) and six nontoxicogenic environmental isolates (Aux3Env). Interestingly, Aux3Env encodes approximately 42 extra genes with bacteriophage homology, and is dispersed sporadically across environmental strains. Taken together with sequence alignment of Aux3Pan and Aux3Env, this indicates that Aux3Pan is the degraded remnant of a putative Aux3Env prophage circulating horizontally in the aquatic reservoir. We further demonstrate by inverse and quantitative polymerase chain reaction that both Aux3Env and Aux3Pan excise from the chromosome by phage-like site-specific recombination to form a circular DNA element. These findings support the potential for contact-independent transfer of this pandemic-associated E/I module to naïve Vc strains in the environment.

Primary Student Presenter: Jaclyn Essig

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Gidon Felsen

Poster Title: Functional circuits for goal-directed behavior in the superior colliculus

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Decision making is a fundamental process of the nervous system for generating goal-directed behaviors. The midbrain superior colliculus (SC) contributes to sensorimotor decision making by integrating cortical and subcortical inputs to guide orienting movements of the eyes, head, and body towards spatial goals. The SC is topographically organized and encodes for specific regions in retinotopic space, however the underlying circuitry for how the SC selects where to orient is unknown. Multiple models of excitatory/inhibitory interactions have been proposed to describe SC function, but these are based on cellular anatomy, ex-vivo slice physiology, and in-vivo recordings in the absence of behavior, or on recordings during behavior from unknown cell types. Here, we record and manipulate the activity of GABAergic neurons in mice performing a spatial-choice task to determine the functional role of inhibition during spatial choice. We train mice to select a left or right reward port based on a binary odor mixture. Importantly, after odor delivery, mice wait for a 'go tone' before orienting to the reward port, giving us access to neural activity during the decision. We hypothesized that GABAergic neurons would shape spatial choice locally by inhibiting SC motor output neurons promoting contralateral choice, and therefore predicted that these cells would be most active before an ipsilateral choice. However, optogenetic identification (i.e., "optotagging") and activation of channelrhodopsin-expressing GABAergic neurons revealed that GABAergic neurons are active before contralateral choices and driving their activity during the 'decision epoch' biases mice to select the contralateral port. These findings support a role for long-range inhibitory interactions in the SC. We are incorporating these data into a bump attractor model as a framework for understanding how the dynamics of excitation and inhibition give rise to nodes of activity in the SC underlying spatial choice.

Primary Student Presenter: Phuong Nguyen

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Brian Berman

Poster Title: Neural Responses Are Abnormal During Reflexive Blinking in Blepharospasm: An Event-Related fMRI Study

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Aim: Use fMRI to investigate neural mechanisms underlying reflexive blinking in blepharospasm (BSP).

Background: Blepharospasm is an isolated focal dystonia characterized by increased blinking and involuntary muscle spasms of the eyelid. While the etiology of BSP remains unknown, many studies suggest it is associated with dysregulated inhibition and abnormal sensorimotor integration.

Methods: 15 BSP patients and 15 healthy controls (HC) were recruited. Randomly timed air-puffs to the left eye were used to induce reflexive eye blinks during an 8-min fMRI scan. Continuous surface EMG and video recordings were used to monitor blink responses. Data were analyzed using an event-related design with SPM12. Significance for voxel-wise analysis was defined as $p < 0.05$, corrected for multiple comparisons.

Results: Data from one BSP subject was excluded due motion artifact. Data from 15 HC (11F, age 60.9 +/- 5.5) were compared to that of 14 BSP (10F, 61.6 +/- 8.0). Reflexive eye blinks in HC were associated with activation of the anterior cingulate and insular cortices. Compared to HC, BSP patients showed increased activation in the post-central gyrus, precentral gyrus, and occipital cortex. BSP disease duration negatively correlated with reflexive-blink activity in the cerebellum and in the temporal gyrus. Disease severity (Jankovic Rating Scale) negatively correlated with activity in the dorsal pons and occipital cortex.

Conclusions: Reflexive blinking in BSP is associated with increased activation in sensorimotor cortices suggesting a loss of inhibition within the sensorimotor network. Decline in cerebellar activity with disease duration suggests an adaptive role, while reduced response during reflexive blinking in the pons with increasing disease severity suggests that changes in the corneal blink reflex circuitry are linked to the manifestation of symptoms.

Primary Student Presenter: Nicole Rumian

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Ulli Bayer

Poster Title: S-Nitrosylation regulates CaMKII targeting and plasticity

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Hippocampal long-term potentiation (LTP) is a form of synaptic plasticity underlying learning, memory, and cognition. Further, it is well established that LTP requires the Ca²⁺/calmodulin (CaM)-dependent protein kinase II (CaMKII), its Ca²⁺-independent autonomous activity, and its movement to excitatory synapses. Autonomous CaMKII can be generated by protein modifications such as autophosphorylation of residue T286 or simultaneous S-nitrosylation of residues C280 and C289. Autonomous CaMKII activity generated by T286 autophosphorylation is well known to play a key role in LTP, and, by extension, learning, memory and cognition. However, the role of CaMKII S-nitrosylation in LTP remains unknown. Recently, a study has suggested that CaMKII S-nitrosylation may play a role in age-related cognitive decline. My preliminary imaging data suggest that S-nitrosylation of wild-type (WT) CaMKII, induced by the nitric oxide donor, DEA-nonoate, is sufficient to induce CaMKII translocation to excitatory synapses under basal conditions and that this effect is abolished in non-nitrosylable CaMKII mutants (CaMKII Δ SNO, C280/289V; CaMKIIC280V; CaMKIIC289V). Other preliminary data from the lab suggests that theta-burst stimulation-induced, but not high-frequency stimulation-induced, LTP is impaired in Δ SNO mice, similar to what is seen in aged animals, as compared to WT. The results of this project elucidate the physiological role of CaMKII S-nitrosylation in regulating synaptic targeting and plasticity and may contribute to a better understanding age-related cognitive decline.

Primary Student Presenter: Alexis Sunshine

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Cristin Welle

Poster Title: Vagus Nerve Stimulation May Enhance Motor Learning Through Modulation of Cholinergic Basal Forebrain

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Vagus nerve stimulation (VNS) is currently used to treat drug-resistant epilepsy and depression. There are results indicating that VNS may also be useful in treating a wide range of autoimmune, metabolic, and neurological disorders. Preclinical studies show that VNS can induce cortical plasticity and improve rehabilitation after stroke or SCI. Albeit showing tremendous potential, the underlying mechanism of VNS remains ambiguous. We aim to tease apart the specific circuitry that underlies VNS-induced cortical plasticity in a healthy mouse model. Identifying these specific anatomic pathways will help guide future research on the use of VNS in patients with motor deficits and may illuminate the mechanisms of other therapeutic benefits.

We used immunohistochemistry staining of an immediate early gene, cFos, to identify neuronal activation in key neuromodulatory centers such as the cholinergic basal forebrain and noradrenergic locus coeruleus. We then performed electrophysiological recordings in the basal forebrain during VNS and confirmed neural activity driven by vagal stimulation. To ensure that these changes reflected the state of a brain with increased cortical plasticity, we paired these experiments with behavioral investigations of a motor learning task.

Our results indicate that the enhancement of motor learning may be mediated by the excitation of basal forebrain, a neuromodulatory nuclei that widely projects to cortex. The projections from vagus nerve to the basal forebrain are still not fully defined, and may be mediated through locus coeruleus. To further dissect this, we will employ tracing experiments using a retrograde tracer in basal forebrain and an anterograde tracer in the Nucleus of Solitary Tract, where vagal afferents terminate.

Primary Student Presenter: Jennifer Gile

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Tobias Eckle

Poster Title: Per2 as a novel therapeutic target in midazolam induced delirium

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Delirium occurs in 30% of critically ill patients, and the risk of dying during admission doubles in those patients. Molecular mechanisms causing delirium are unknown, however, critical care units consistently disrupt patients' circadian rhythms which is highly associated with the occurrence of delirium. Exposure to benzodiazepines (e.g. midazolam) is a major contributor to the development of delirium. Thus we tested the effects of midazolam on the regulation of the circadian rhythm protein Per2 in the mouse brain. We analyzed the effects of midazolam on Per2 mRNA expression in wild-type mouse brains and found a robust and significant downregulation of Per2 transcript levels. Using midazolam in a T-maze alternation model, in open field studies (line crossing/center square entries) or in novel recognition tests, we were able to establish a novel mouse model for delirium. Following studies using midazolam in a T-maze alternation model, we found up to 72h after midazolam treatment that mice exhibited significant deficits in a T-maze alternation model with significant downregulation of Per2 protein in the hippocampus and the SCN. Following studies in Per2^{-/-} mice confirmed a functional and specific role of Per2 in midazolam induced delirium. Using the recently identified small molecule nobiletin as a Per2 enhancer, we were able to abolish the midazolam induced delirium phenotype in wild type mice. Based on these preliminary studies we hypothesize that Per2 plays a major role in the pathogenesis of delirium and that Per2 stabilization in the brain attenuates delirium. These results suggest Per2 as a potential drug target using the Per2 enhancer nobiletin as therapy in delirium.

Primary Student Presenter: Ryan Phan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: John Repine

Poster Title: Increased Brain Inflammation and Decreased Heme Oxygenase-1 (HO-1) Response in Control and Tolerant Rats Following Repetitive Traumatic Brain Injury (TBI)

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Traumatic Brain Injury (TBI) induces secondary mechanisms of injury that center on inflammation, cell death, and neurologic dysfunction, leading to a substantial risk of hypotension, hypoxemia, and brain swelling. In our studies of continuous exposure to 100% O₂ (hyperoxia) in Acute Respiratory Distress Syndrome (ARDS), a single Sprague-Dawley control rat survived while all other control rats (n>1000) died. A unique hyperoxia tolerant rat strain was developed that shows less lung inflammation and injury following a lung insult. Here, we studied the differences in heme oxygenase-1 (HO-1) and nitrotyrosine (NT) concentration after both single TBI and repetitive TBI in hyperoxia tolerant and control Sprague Dawley rats. HO-1 is an anti-inflammatory antioxidant induced by oxidative stress involved in the breakdown of heme and has an immunomodulatory role in monocyte and macrophage recruitment via IL-4 and IL-10 production. NT is produced via tyrosine nitration and is a marker of reactive nitrogen species, inflammation, and cell damage. Rats received either a single TBI or TBI on 3 consecutive days. Brains were subsequently harvested and stained for presence of HO-1 and NT, with images being taken at the site of injury in the cortex. Our data shows that HO-1 expression was decreased and NT expression was increased in the cortex after repetitive TBI across control and tolerant rats. These changes suggest increased inflammation and cellular damage along with decreased response to oxidative stress after repetitive TBI.

Primary Student Presenter: Elsa Alaswad

Additional Presenter(s): Elsa Alaswad

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: D. Ryan Ormond

Poster Title: Current applications of diffusion tensor imaging tractography in intracranial tumor resection

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Surgical intervention for the treatment of primary brain tumor remains a common and highly ameliorative therapeutic option. Recent advances in neuroimaging have provided the neurosurgeon with new tools to overcome the challenge of differentiating healthy from tumorous tissue, with the aim to increase the likelihood of maximizing the extent of resection volume while minimizing destruction of healthy, and critically, eloquent regions. Novel applications of diffusion tensor imaging (DTI) tractography and derived diffusion coefficients have demonstrated that preoperative non-invasive mapping of eloquent cortical regions and functionally relevant white matter bundles is critical during surgical planning to reduce postoperative deficits which can decrease quality of life and survival rates. In this review, we summarize the latest developments in the use of DTI in the context of tumor resective surgery and highlight its utility within every stage of the clinical workflow: preoperative planning, intraoperative management, and postoperative outcomes.

Primary Student Presenter: Edward Husarcik

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Michael Kahn

Poster Title: Limitations of a Synthetic Patient Population Generator Using EMR Data

Final Category: Other

Abstract:

Purpose of Study: Strict confidentiality rules often prevent data scientists from having access to real-world patient data. Synthetic data designed to replicate real-world patients is one approach to solving this problem. Synthea is a synthetic patient generator which utilizes disease-specific state transition probability modules to synthesize patients on a population level. Although Synthea has been used to model patients at a country, state, and city level, it has not been used to model hospital-specific patient populations. This study focuses on creating Synthea disease modules reflecting observed hospital-specific transition probabilities.

Methods Used: De-identified electronic medical record (EMR) data from 997,235 patients containing 25,640,495 conditions was used as a localized hospital data set. Synthea was utilized to generate patients based upon transition state probabilities computed from the dataset. Due to their simplicity, transition probabilities for Synthea's sinusitis and appendicitis disease modules were implemented.

Summary of Results: The modules included in Synthea contain disease transition states and probabilities that could not be calculated using available EMR patient data. For example, the Synthea sinusitis module requires probabilities for bacterial versus viral infection. This distinction was not documented by clinicians in the EMR so no local probability could be calculated. Conversely, clinically relevant transition states occurred in the EMR that were not present in Synthea modules.

Conclusions: The two disease modules in Synthea could not be modified to represent a local hospital population using EMR data either due to data not recorded in the EMR or clinically important transition states missing in the Synthea models. New Synthea models containing transition probabilities actually recorded in EMR data need to be developed to create localized synthetic patient populations for data scientists.

Primary Student Presenter: Anne Strong

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jeffrey Olson

Poster Title: Novel PAN Fiber for treatment of Macular Degeneration shows efficacy and biocompatibility in Eye

Final Category: Vision Sciences

Abstract:

Age related macular degeneration (AMD) is one of the leading causes of blindness in the United States. Currently, there is no effective treatment for dry AMD, and treatment for wet AMD involves monthly intraocular injections. The AmpVision Intravitreal Implant, is composed of a protein adsorbing polyacrylonitrile (PAN) polymer that has been shown to bind complement factor (CF). It is hypothesized that the permanent implant will decrease the amount of CF in the eye, thereby slowing disease progression of AMD. We tested the degree of CF affinity, biocompatibility, and efficacy of AmpVision.

Ex Vivo efficacy was tested by subjecting diabetic human vitreous fluid to PAN fibers for 30 minutes. Biocompatibility was tested in Brown Norway rats (n=5) with endpoint ERG and histology, and New Zealand White cross rabbits (n=5) with histology. In vivo efficacy was tested in an AMD mouse model homozygous CFH -/- (n=19) with serial ERG, OCT thickness, and cell counts to measure changes in the retina. Devices were implanted in the right eye, and the left eye was used as a control in all animals.

Ex vivo, the vitreous exposed to PAN fiber showed a significant decrease in CF in comparison to the control group (19.7 ± 3.2 ng/ml vs. 596.0 ± 21.1 ng/mL, $p=0.0003$, Student's t-test). The PAN fiber was well tolerated, showing no difference in the outer nuclear layer cell counts between eyes (Rabbit: RE= 172.8 ± 5.8 , LE= 176.5 ± 4.4 , $p=0.5721$ Student's t-test, Rat: RE= 145.5 ± 4.3 , LE= 140.5 ± 4.1 , $p=0.4190$ Student's t-test). Endpoint ERGs in the rats demonstrated no difference in step 3A between right and left eyes (RE= -79.3 ± 16.8 , LE= -103.4 ± 15.8 , $p= 0.0762$ Student's t-test).

In summary, our preliminary studies have shown biocompatibility of the PAN device in two animal models and efficacy in removing CF from vitreous ex vivo. We will continue testing in vivo efficacy in the CFH -/- model.

Primary Student Presenter: Erin Drake

Additional Presenter(s): Kira Grush

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Kristina Tocce

Poster Title: The effect of immediate postpartum etonegestrel implants on postpartum depression.

Final Category: Other

Abstract:

Objective: To compare rates of postpartum depression among adolescents who initiate immediate postpartum contraceptive implants (IPI) and those initiating other methods.

Methods: We assessed prenatal and postpartum depression in patients enrolled in an adolescent prenatal-postnatal program. Depression was assessed at prenatal intake using the Center for Epidemiologic Studies Depression (CES-D) scale and postpartum with the Edinburgh Postnatal Depression (EPDS) scale. We compared rates of prenatal (CES-D \geq 24) and postpartum (EPDS \geq 10) depression between the IPI and comparison group.

Results: 875 patients were enrolled between 1/1/13 and 12/31/16: median age 19 (range: 13-22 years), 75% primiparous, 51% Latina, 25% black, 16% white. 32.7% of the cohort initiated IPI (n=170). Those initiating IPI were similar to the rest of the cohort in age, race/ethnicity, and parity. Prenatally, 13.3% had an elevated CES-D (12.0% IPI vs 15.2% comparison, p=0.77). At 6-weeks postpartum, 7.8% had postpartum depression; this rate was significantly less for those receiving IPI compared to those choosing other methods (4.3% vs 9.6%, p=0.04). In subgroup analyses, immediate postpartum DMPA-users (n=67) had similar rates of postpartum depression as those initiating other methods (10.4% vs 9.6%, p=0.84).

Conclusion: In this study, IPI users had lower rates of postpartum depression than those initiating other methods. Providers should encourage adolescent mothers to choose whichever highly-effective contraceptive method they prefer for postpartum use and be reassured that progestin-containing methods do not increase postpartum depression.

Primary Student Presenter: Ian Coulter

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Slobodan Todorovic

Poster Title: Different roles of T-type calcium channel isoforms in sex-specific hypnosis induced by an endogenous neurosteroid epipregnanolone

Final Category: Pharmacology and Physiology

Abstract:

Common general anesthetics (GAs) induce hypnosis by blocking neuronal NMDA receptors and/or potentiating GABA-A currents. However, these effects may be the basis for their developmental neurotoxicity. It has been demonstrated that the endogenous neuroactive steroid epipregnanolone blocks T-type calcium channels (T-channels) but lacks any GABA-mimetic and NMDA receptor-blocking properties. This work investigates the sedative/hypnotic properties of epipregnanolone and characterizes its adjuvant use to GAs.

Epipregnanolone was injected intraperitoneally to adult wild-type (WT) mice and T-channel (Cav 3.1, 3.2, 3.3) knockout mice of both sexes. Onset and duration of Loss of Righting Reflex (LORR) and Loss of Withdrawal Reflex (LOWR) were assessed as measurements of hypnotic/anesthetic state.

We found that epipregnanolone is an efficacious hypnotic with an LORR ED50 of 55.5mg/kg in WT males, and 41.2mg/kg in WT females. We noted a prominent sex-dependent difference. Across all genotypes and doses, females were sedated for longer than males. We also report a difference in the hypnotic responses between WT mice and T-channel KOs. Specifically, 3.1KOs were less sensitive to hypnosis while 3.2 and 3.3KOs were more sensitive. Finally, we found that epipregnanolone administration lowered the concentration of isoflurane necessary to induce LOWR and LORR in WT mice.

Neuroactive steroids devoid of GABA-mimetic properties that target neuronal T-channels may have an important role as adjuvants. To our knowledge, this work is the first to report on the hypnotic properties of epipregnanolone in rodents. These results indicate that epipregnanolone may be useful in lowering amounts of GAs used to induce surgical anesthesia. This is important because there is mounting research that GAs administered in early life can induce neurotoxicity.

Primary Student Presenter: Simon Feseha

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Slobodan Todorovic

Poster Title: Use of T-type Calcium Channel Blockers as Adjuvants for General Anesthesia

Final Category: Pharmacology and Physiology

Abstract:

It is generally accepted that general anesthetics (GAs) induces hypnosis by targeting neuronal GABAA and NMDA receptors, which in turn may cause learning deficits in both rodents and children (Jevtovic-Todorovic et al., 2003; Ing et al, 2014). Previous in vitro study documented that CaV3.3 isoform of T-type calcium channels (T-channels) in the reticular thalamic nucleus (nRT) are inhibited by clinically-relevant concentrations of volatile GAs, including isoflurane (Joksovic et al, 2005). Little is understood of the role CaV3.3 channels in anesthetic induced unconsciousness. The goal of this study is to first determine the effects of TTA-P2, a T-type calcium channel blocker, on the quality of isoflurane-induced anesthesia in WT mice; and second, to better characterize the role of CaV3.3 channels in anesthetic induced unconsciousness. The hypnotic effects and surgical depth of an anesthesia was measured by the % of Isoflurane at Loss of Righting Reflex (LORR) and Loss of Withdrawal Reflex (LOWR) respectively. Additionally, the quality of anesthesia was measured by the % isoflurane at which characteristic neuronal oscillations of 70% burst suppression ratio (BSR) was elicited during EEG. We found that i.p injection of TTA-P2 showed a dose-dependent decrease in the requirement of isoflurane to reach LORR and LOWR in WT mice. There was an even greater decreased requirement of isoflurane to reach LORR and LOWR in Cav3.3 KO mice. EEG recordings following injections of 60 mg/kg of TTA-P2 showed that mutant mice required significantly less isoflurane to reach 70% BSR when compared to WT. We propose that T-Type calcium channel blockers should be further explored as a valuable adjunct to reduce the usage of potent volatile anesthetics, and potentially decrease GA-induced neurotoxic effects of the developing brain. Our findings point to the value of CaV3.3 channels in anesthetic induced unconsciousness.

Primary Student Presenter: Ivelisse Cruz-Torres

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Paco Herson

Poster Title: Characterization and optimization of the novel TRPM2 antagonist tat-M2NX

Final Category: Pharmacology and Physiology

Abstract:

We and others have identified TRPM2, a non-selective cation channels highly expressed in the brain, as a contributor to neuronal injury caused by stroke or cardiac arrest. However, the lack of specific inhibitors hinders the study of TRPM2 in pathophysiology. Our lab designed tat-M2NX to prevent ligand binding and TRPM2 activation. Tat-M2NX reduces ischemic injury in wild-type male mice. The lack of effect of tat-M2NX treatment in TRPM2 knockout mice provides evidence of specificity. . In the current study, we performed mutagenesis of tat-M2NX to determine potency, binding affinity, and antagonistic mechanism. We assessed tat-M2NX antagonism on heterologously expressed human TRPM2 channels in HEK-293 cells. To determine potency, we used whole-cell patch clamp recordings in the presence of ADPR (agonist) and tat-M2NX in the pipette. TRPM2 currents were quantified using maximal peak amplitude in the absence and presence of tat-M2NX, followed by bath application of the pore blocker clotrimazole. Binding interaction of tat-M2NX to TRPM2 was tested with co-immunoprecipitation. Tat-M2NX mutant and truncated peptides were tested: scramble, single point mutations, and truncations. Statistical significance was established as $p < 0.05$ for all groups using t-test or One-Way Analysis of Variance. Tat-M2NX inhibits >90% of TRPM2 channel currents suggesting, that tat-M2NX is an effective TRPM2 antagonist. Moreover, tat-M2NX is a potent antagonist with an IC_{50} of approximately 214nM. Our results from tat-M2NX mutagenesis experiments indicate that specific residues within the tat-M2NX C-terminus are required to confer antagonism on TRPM2. Therefore, the peptide tat-M2NX represents a new tool for the study of TRPM2 function in cell biology to enhance our understanding of neurological diseases and stroke.

Primary Student Presenter: Ian Stancil

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: David Schwartz

Poster Title: The Jamming Transition is Dynamically and Structurally Delayed in Idiopathic Pulmonary Fibrosis Bronchial Epithelia

Final Category: Pulmonary and Critical Care

Abstract:

Rationale: There is a temporally-controlled physical transition during differentiation of human bronchial epithelial cells (HBECs) from a fluid-like to solid-like state, known as the jamming transition. Recurrent microinjury to lung epithelia is thought to be a significant contributor to the pathogenesis of IPF resulting in an aberrant epithelial phenotype. We hypothesize, IPF HBECs demonstrate a delayed jamming transition, in which they maintain a prolonged unjammed phenotype.

Methods: HBECs from non-IPF and IPF donors were cultured at air-liquid-interface (ALI). Particle Image Velocimetry was utilized to compute cell velocity vector fields. Mean squared displacement (MSD) and four-point correlation function (Q) of the monolayer were computed. F-actin staining delineated cell boundaries, and projected area and perimeter were computed.

Results: Non-IPF HBECs undergo the jamming transition between days 5 and 8 of ALI; during the migratory phase of non-IPF HBECs, the average cellular speeds are $8.5 (\pm 2.9) \mu\text{m/hr}$. IPF HBECs maintain a prolonged unjammed phenotype through day 28 of ALI with an average speed of $14.1 (\pm 2.3) \mu\text{m/hr}$. MSD and Q are concordant with speed data, demonstrating a jamming transition before day 8 of ALI for non-IPF samples and prolonged unjamming for IPF samples. Structural analysis of non-IPF HBEC monolayers revealed an elongated cell shape during the fluid phase, but a hexagonal epithelium during the solid phase. This hexagonal phenotype is absent in IPF cultures, with persistent polarization of the monolayer.

Conclusions: We have demonstrated an aberrant epithelial phenotype only present in IPF patient HBECs in which prolonged migration and cellular polarization persist throughout monolayer development. These results demonstrate a previously unknown physical characteristic of IPF epithelia.

Primary Student Presenter: Jacob Michalski

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Schwartz

Poster Title: Muc5b-Overexpression Promotes Increased ER Stress in Mouse Models of Pulmonary Fibrosis

Final Category: Pulmonary and Critical Care

Abstract:

Rationale: A gain-of-function promoter variant in the MUC5B gene is the strongest risk factor for the development of idiopathic pulmonary fibrosis (IPF). Endoplasmic reticulum (ER) stress occurs with disruption to cellular proteostasis and is increased in IPF lungs. The purpose of this study is to understand the relationship between ER stress and MUC5B-overexpression.

Methods: Two mouse lines for Muc5b-overexpression were used: Scgb1a1-Muc5b and SFTPC-Muc5b. Pulmonary fibrosis was induced using bleomycin. Relative mRNA expression was assessed using qRT-PCR. Protein expression was assessed using immunofluorescence staining for CHOP and Muc5b. Nuclear CHOP-positive and Muc5b-positive cells were counted and normalized to total cells per field of view.

Results: While no differences in whole-lung mRNA expression of ER stress markers were found in saline-treated mice, increased CHOP-positive cells were observed in distal airways of Scgb1a1-Muc5b mice (2.3-fold increase; $p = 0.0002$) and in alveoli of SFTPC-Muc5b mice (8.6-fold increase; $p < 0.0001$). Preliminary analysis also shows intracellular co-expression of both CHOP and Muc5b in Muc5b-overexpressing mice. Bleomycin treatment in Muc5b-overexpressing mice was associated with decreased CHOP-positive cells.

Conclusions: These results indicate that although there is no apparent difference at the transcriptional level, there is an increase in baseline number of CHOP-positive cells in the lungs of Muc5b-overexpressing mice. These data, along with evidence of Muc5b and CHOP co-expression, suggests a direct connection between ER stress and Muc5b-overexpression. The decrease in CHOP expression in Muc5b-overexpressing mice is potentially due to increased cell death of CHOP-positive cells, which would suggest that ER stress plays an important role in lung injury.

Primary Student Presenter: Brett Wiesen

Additional Presenter(s): Micheal R. Bronsert Davis Aasen

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Meguid

Poster Title: Use of the SURPAS tool to Assist Informed Consent Improves Patient Satisfaction and Surgeon Efficiency

Final Category: Surgery

Abstract:

The purpose of this study was to determine the efficacy of use of the Surgical Risk Preoperative Assessment System (SURPAS) in aiding in the surgical informed consent process when compared to different routine consents.

Patient (pt) perception of the consent process was surveyed in two cohorts; the first was pts who were consented using the "routine" process employed in 10 surgeon's clinics. The same 10 surgeons were then taught to use SURPAS and employed it for guiding informed consent on a subsequent cohort of pts. The SURPAS tool is an individualized risk prediction tool with visual displays of common adverse surgical outcomes. Pts were surveyed after completion of the "routine" or SURPAS-guided consent process to evaluate their perception of the consent process. The responses were compared using Fisher's exact test and the Cochran-Mantel-Haenszel test.

Pts ages, gender, race-ethnicity, and complexity of surgery were similar in the two cohorts ($p \geq 0.10$). Of 169 pts, 100 underwent the "routine" consent process (RTNE), and 69 underwent SURPAS-guided consent (SRPS). 100% of SRPS reported surgeons spent enough time discussing risks, vs. 72% of RTNE ($p < 0.0001$). Mean time of the consent process estimated by pts was 28 mins for RTNE vs. 11 mins for SRPS ($p < 0.0001$). 100% of SRPS were satisfied or very satisfied with the risk discussion vs. 88% of RTNE ($p < 0.0001$). 81.2% of SRPS reported the risk discussion made them more comfortable to have surgery and 98.5% reported somewhat or greatly decreased anxiety vs. 19% and 20% of RTNE, respectively (both comparisons: $p < 0.0001$).

The SURPAS tool improved the informed consent process for pts: SURPAS provides preoperative pts a level of comfort and understanding that current practice is unable to do. In addition, it does so in a more efficient manner, and increases pt satisfaction despite their perception that it requires less time.

Primary Student Presenter: Tessa Zangara

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Lisa Ferrigno

Poster Title: A stitch in time saves clots: A multicenter analysis of venous thromboembolism chemoprophylaxis in patients with traumatic brain injury

Final Category: Surgery

Abstract:

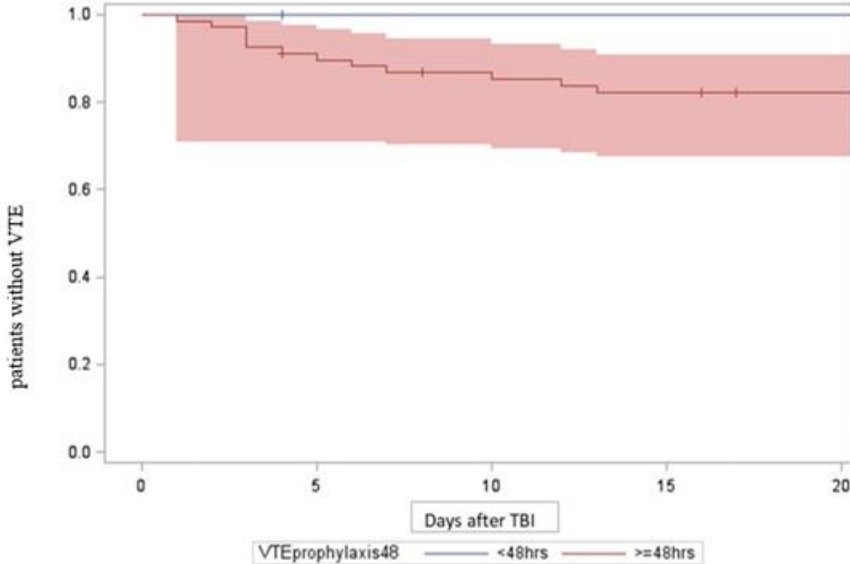
Purpose: Venous thromboembolism chemoprophylaxis(VTE-CHEMO) in traumatic brain injury(TBI) is often delayed due to bleeding concern, however, this poses risk of thrombosis. We sought to describe rates and timing of VTE-CHEMO and correlation with VTEs or intracranial hemorrhage(ICH) progression.

Methods: We include adult patients admitted to 5 trauma centers between 2014-2016 with head AIS \geq 2; \geq 2 head CTs(CTH); and length of stay(LOS) $>$ 72 hours. Outcomes of early($<$ 48hrs) versus late(\geq 48hrs) VTE-CHEMO were compared. Multivariate analysis(MV) was done with Cox proportional hazards regression.

Results: 1,803 patients were included, 8% developed VTE. VTE patients were older, with higher BMI ($>$ 30, 27% vs 15%, $p=0.0002$), more severely injured (TRISS 0.9 vs. 0.8, $p<0.001$), and more likely to have pelvic(16% vs. 7%, $p<0.001$) or femur(13% vs 4%, $p<0.0001$) fractures. After MV, BMI $>$ 30, ISS and pelvic/femur fractures were significantly associated with VTE. There was a significant interaction between VTE-CHEMO and early(24hrs) or late($>$ 24hrs) neurosurgical intervention(NS). Among late NS, early VTE-CHEMO had a lower VTE rate compared to late VTE-CHEMO(HR: 0.76, 95% 0.64-0.91, Figure1). 580(32%) had ICH progression: 22% without VTE-CHEMO, 50% before VTE-CHEMO, and 28% after VTE-CHEMO. Of those with ICH progression after VTE-CHEMO, VTE-CHEMO was started early in 36% and late in 64%($p=0.59$).

Conclusions: Late VTE-CHEMO was associated with higher VTE incidence in patients not requiring immediate NS. Early prophylaxis with severe injury, obesity, and/or high-risk fractures may reduce VTE in TBI. While these data do not suggest harm with early VTE-CHEMO, this merits investigation.

Figure 1. Time to venous thromboembolism (VTE) diagnosis by early versus late VTE chemoprophylaxis initiation among those who underwent late neurosurgical intervention



VTE=venous thromboembolism, TBI=traumatic brain injury

Primary Student Presenter: Bryn Launer

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: John Mitchell

Poster Title: Tracheobronchoplasty for Severe Tracheobronchomalacia: Patient Demographics

Final Category: Surgery

Abstract:

Background. Tracheobronchomalacia occurs when the cartilaginous walls of the trachea weaken, causing airway collapse during respiration. Severe tracheobronchomalacia may lead to complete airway collapse, causing distressing symptoms such as shortness of breath, fatigue, recurrent infections, and chronic cough. Placement of a silicone stent has been shown to improve these symptoms but is associated with a high rate of complications such as infection and formation of granulation tissue. Surgical intervention involving pleating and anchoring the excess membranous wall to a propylene mesh in order to stabilize the airway has been shown in smaller series to significantly improve quality of life. This study aims to examine the demographic factors in a retrospective review of the largest series to date of patients who have received tracheobronchoplasty for tracheobronchomalacia.

Methods. Retrospective chart review was performed for 64 patients who underwent tracheobronchoplasty at the University of Colorado Hospital from 2008 to 2018. Demographic factors such as age, gender, race, and ethnicity were obtained, as well as information regarding medical history such as presenting symptoms and concomitant diagnoses. Surgical variables such as length of operation, length of stay, and complication rates were collected. Frequency of these variables was calculated using excel.

Results. The average patient age at time of surgery was 57 years. 25 patients (39%) were male, and 62 (97%) were white. The most common presenting symptom was “dyspnea on exertion,” endorsed by 51 patients (80%). 30 patients (47%) had also been diagnosed with asthma in addition to tracheobronchomalacia. 28 patients (44%) had comorbid sleep apnea, while 37 (58%) had comorbid GERD. The average length of surgery was 229 minutes, and the average length of stay was 6.8 days. 12 (19%) patients had complications related to the procedure, 4 (6%) patients were readmitted to the hospital, and 0 patients passed away as a result of the surgery.

Primary Student Presenter: Anthony Scott

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Paula Pecen

Poster Title: Ophthalmic Medication Price Variation Across the United States: Anti-Inflammatory Medications

Final Category: Other

Abstract:

Purpose of Study: Cost-related nonadherence to medication can impact outcomes for patients with uveitis. We aimed to determine whether medication prices vary between U.S. cities and between different types of pharmacies within one city.

Methods: We conducted a phone survey of eight nationwide and five independent pharmacies in five cities across the United States: Boston, Massachusetts; Charlotte, North Carolina; Denver, Colorado; Detroit, Michigan; and Seattle, Washington. A researcher called each pharmacy asking for price without insurance for four common anti-inflammatory ophthalmic medications: prednisolone acetate, prednisolone sodium phosphate, difluprednate (Durezol[®]), and loteprednol (Lotemax[®]). Drug prices were also obtained from GoodRx.com.

Results: Medication price for prednisolone sodium phosphate could only be obtained by a small subset of pharmacies (29%) and was excluded from additional analysis, however preliminary data demonstrated a lower mean cost of prednisolone sodium phosphate over prednisolone acetate. Three-way ANOVA revealed no interaction between type of pharmacy (chain vs. independent), city, and drug ($p=0.92$). A significant interaction was identified between type of pharmacy and drug ($p=0.008$), but not between city and type of pharmacy ($p=0.62$) or city and drug ($p=0.97$). When combining data across cities, loteprednol demonstrated a significant simple main effect ($p<0.001$) of type of pharmacy on medication price, not seen for prednisolone acetate ($p=0.559$) or difluprednate ($p=0.297$).

Conclusions and Relevance: Medication prices do not differ significantly between U.S. cities. High variation in drug prices between type of pharmacies in the same city demonstrate how comparison shopping can provide cost savings for patients and may reduce cost-related nonadherence