University of Colorado **Anschutz Medical Campus**

34th ANNUAL STUDENT RESEARCH FORUM

COLLEGE OF NURSING

GRADUATE SCHOOL

SCHOOL OF DENTAL MEDICINE

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OF PHARMACY SCHOOL OF

PUBLIC HEALTH

DECEMBER 10th, 2019
ANSCHUTZ MEDICAL CAMPUS
Education 2, North and South

34th ANNUAL
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS
STUDENT RESEARCH FORUM

Tuesday, December 10th, 2019

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
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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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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.

Undergraduate Medical Education

Department of Family Medicine

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Department of Medicine

Department of Medicine-Division of Hematology

Department of Surgery

Department of Clinical Pharmacy

Primary Student Presenter: Alison Abele

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Steven Abman

Poster Title: Antenatal Exosome Treatment Preserves Lung Structure and Vascular Growth in an Experimental Model of Bronchopulmonary Dysplasia due to Chorioamnionitis

Final Category: Pulmonary and Critical Care

Abstract:

ANTENATAL EXOSOME TREATMENT PRESERVES LUNG STRUCTURE AND VASCULAR GROWTH IN AN EXPERIMENTAL MODEL OF BRONCHOPULMONARY DYSPLASIA DUE TO CHORIOAMNIONITIS

A Abele1 (MD SOM), N Wilson2, A Abikoye2, G Seedorf1, A Brooks1, S Kourembanas3, SH Abman1

1Dept of Pediatrics, University of Colorado, Aurora, CO. 2University of Notre Dame, Notre Dame, IN. 3Dept of Neonatology, Harvard University, Cambridge, MA

Purpose

Bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is characterized by severe respiratory disease due to early disruption of lung development. BPD is multifactorial, including increased risk due to prenatal stressor chorioamnionitis (CA). Mesenchymal stem cell-derived exosomes (MEx) have demonstrated promising results in animals with BPD due to postnatal hyperoxia, however, the antenatal efficacy of MEx for prevention of BPD is unknown. Thus, we hypothesized that antenatal treatment with MEx in a model of CA will prevent BPD.

Methods

Antenatal MEx treatment was studied using an established rat model of CA induced by ETX. At E20, litters were treated with intra-amniotic injections of saline, ETX (100uL/sac), or ETX+MEx. Pups were delivered at E22 (term) via C-section. Morphometric studies to assess airspace growth (by mean linear intercept; MLI), vascular growth (vessel density; VD), and lung function (FlexiVent) were performed at 2 weeks of age.

Results

Compared to controls, intra-amniotic ETX reduced alveolar growth (increased MLI) by 23.2% and reduced vascular growth (decreased VD) by 44.4% at 2 weeks of age ($p<0.05$). In rats treated with

antenatal MEx+ETX, MLI and VD were not different from saline controls. Lung resistance and compliance also improved with antenatal MEx treatment compared to ETX alone.

Conclusions

Antenatal treatment with MEx preserves lung structure and function in rats with experimental BPD induced by ETX. We speculate that early MEx treatment may prevent the development of BPD in premature infants, especially in the setting of CA.

Primary Student Presenter: Elizabeth Ambros

Additional Presenter(s):

Presenting School: Nursing

Degree Seeking: BS

Year: 2nd

Mentor: Kate Coleman-Minahan

Poster Title: Latinx Sexual Minority Women's Reproductive Health Perspectives and Experiences

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Latinx Sexual Minority Women's Reproductive Health Perspectives and Experiences. EL Ambros (BA) and K Coleman-Minahan, College of Nursing, Anschutz Medical Campus.

This secondary analysis of qualitative data from Dr. Coleman Minahan's parent study Structural Vulnerability and Reproductive Health among Mexican-origin Immigrants explored the compounding effects of multiple marginalized identities on reproductive health. Eighteen participants from the Denver metropolitan area were recruited during the summer of 2018 and were eligible for participation if they were: 1) born in Mexico and came to the U.S. before the age of 16 OR had at least one parent born in Mexico and 2) were between the ages of 18-34. The purpose of the present study was to 1) investigate how young women's gender, sexuality, and ethnic identities intersect to shape their perspectives and experiences with reproductive healthcare and 2) examine how Latinx sexual minority women's intersecting identities result in both protective factors and risk factors for reproductive health disparities. In-person, semi-structured interviews were conducted, transcribed, and then analyzed in Atlas.ti using a deductive approach with an initial coding scheme based on our theoretical frameworks of reproductive justice and intersectionality. We also allowed for an inductive approach to add emerging codes in vivo. Using various displays in Microsoft Excel, we identified thematic patterns. Four main themes emerged: 1) Latinx sexual minority women have varied experiences of discrimination vary based on visible versus invisible identities, 2) they face significant cultural stigma around sexuality, 3) they have inconsistent quality of healthcare, and 4) they have diverse experiences with contraception and largely pro-choice attitudes about abortion. Further research is needed to better understand reproductive health among sexual minority Latinx women.

Primary Student Presenter: Colin Anderson

Additional Presenter(s):

Presenting School: Pharmacy

Degree Seeking: PhD

Year: 4th

Mentor: James Roede

Poster Title: Methylation of the Dithiocarbamate Fungicide Maneb Reveals Potential Toxic Mechanisms in Neuroblastoma

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

The dithiocarbamate fungicide maneb (MB) has received research interest due to the increasing concern of the negative health effects of pesticides, as well as its association with Parkinson's disease (PD). However, few studies focus on the molecular mechanisms of MB in human cells, with identified toxicities including mitochondrial dysfunction, proteostasis disruption, and apoptosis of dopaminergic neurons. Our laboratory has previously reported distinct phenotypic changes of neuroblastoma cells exposed to acute, sub-toxic levels of MB including decreased mitochondrial respiration, altered lactate dynamics, and metabolic stress. In this study, we aimed to define specific molecular mechanisms of MB through the comparison of several thiol-containing compounds and their effects on energy metabolism and antioxidant defense. The Seahorse XFe96 extracellular flux analyzer was employed to evaluate alterations in energy metabolism of SK-N-AS human neuroblastoma cells after acute exposure of an array of chemicals including dithiocarbamates (maneb, nabam, zineb) and other thiol containing small molecules (glutathione, N-acetylcysteine). These studies revealed MB and its methylated form (MeDTC) as unique toxicants, with significant alterations to mitochondrial respiration, proliferation, and glycolysis. Next, we investigated glutathione and thioredoxin/peroxiredoxin redox homeostasis, finding decreased glutathione and altered thiol oxidation status of peroxiredoxin 3 (Prx3, mitochondrial) after acute MB exposure. We then used redox Western blotting to pinpoint a potential MB-specific modification of cellular and recombinant Prx3, which we subsequently confirmed by Mass Spectrometry (MS) techniques. Finally, an ELISA for S-adenosylmethionine (SAM) revealed a MB-mediated decrease cellular SAM after a 2 hour exposure, confirmed by MS. The data presented strengthens the argument that MB can preferentially target mitochondrial enzymes containing thiol or iron-sulfur moieties, giving further credence to the MB model of PD in which many disease associated proteins contain these functional groups (Ubiquinol-cytochrome c reductase, aconitase, ALDH2, etc.). Additionally, our data supports a novel cellular "detoxification" mechanism via enzymatic methylation, potentially contributing to the complex toxicity profile of MB.

Primary Student Presenter: Abigail Barnes

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Edward Jones

Poster Title: Endoluminal Vacuum Closure of a Duodenal Perforation

Final Category: Surgery

Abstract:

ENDOLUMINAL VACUUM CLOSURE OF A DUODENAL PERFORATION

Abigail L Barnes BS; Hazem T Hammad MD*; Matthew Reveille MD*; Edward L Jones MD, MS*

*Department of Surgery and Medicine, The University of Colorado and Rocky Mountain Regional VA Medical Center, Aurora, CO

Background and Aims

Perforation is a known complication of endoscopic resection and has been recently managed with endoscopic defect closure, antibiotics and close observation. Closure of duodenal perforations are more challenging due to the presence of gastric and pancreaticobiliary secretions. The use of endoluminal vacuum therapy to divert flow and aid closure of an esophageal, gastric or colonic luminal perforation is increasingly prevalent and may avoid high-risk surgery. We describe the use of endoluminal vacuum closure to salvage an iatrogenic duodenal perforation.

Methods

A 57-year-old male underwent an endoscopic mucosal resection of a 35mm polypoid lesion on the posterior wall of the second portion of the duodenum. The mucosal defect was closed with endoclips and developed evidence of perforation on post-procedure day 1. Multiple surgical and radiologic interventions were unable to control the leak and sepsis. An endoluminal wound vac was placed on post-procedure day 6 to control leakage.

Results

The endoluminal wound vac successfully controlled leakage allowing defect closure and eventually discharge on post-procedure day 50. Final pathology confirmed a tubular adenoma with focal high-grade dysplasia and clear margins.

Conclusions

The endoluminal wound vac is an emerging technique that can effectively manage complicated injuries throughout the GI tract. This may allow enhanced recovery by avoiding surgical salvage and its associated morbidity and mortality.

Primary Student Presenter: Abigail Barnes

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Edward Jones

Poster Title: Manufacturer and User Facility Device Experience Review of Endometrial Ablation Devices

Final Category: Surgery

Abstract:

Background: The Manufacturer and User Facility Device Experience (MAUDE) database was created in 1991 as a response to the growing number of device reports and the need for an organized presentation of the data to the public. Maude is used by the FDA to detect potential safety issues and to monitor device performance. It is also used by many researchers as a tool in analyzing patient injury or death related to various medical devices used in many fields of medicine including gynecology. Endometrial Ablation (EA) is indicated in the treatment of heavy menstrual bleeding in premenopausal patients who no longer desire fertility. A variety of devices are used for this procedure and reports of injury or death are available in the MAUDE Database.

Study Design: The FDA Manufacturer and User Facility Device Experience (MAUDE) database was searched for adverse events categorized as injury or death related to the use of endometrial ablation devises. Reports generated between May 1, 2009 and May 31, 2019 were included. Results were classified based on year, type of device, mechanism of injury, severity of injury and cause of death.

Results: A total of 1,220 reports were screened with 1,219 being injuries and 10 deaths. 251 Reports were excluded for insufficient information, duplicate, pain, or device malfunction without injury leaving 978 reports included. Our study suggests that specific devices have injury patterns such as uterine perforation, hysterectomy and bowel resection/ repair with Novasure and Minerva Surgical and thermal injuries with Genesys HTA/Thermablator and Thermachoice.

Conclusion: The advances in technology for endometrial ablation devices bring both opportunities for patients to gain relief from abnormal uterine bleeding but also expose patients to various risks of injury. These injury types are challenging to track which is why databases like MAUDE are beneficial. This information is important for providers to accurately counsel patients on the risks of undergoing an endometrial ablation procedure.

Primary Student Presenter: Sanjana Bukkapatnam

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Sana Karam

Poster Title: The Dichotomy of EphrinB2 Signaling in Modulating Proliferation and Invasion in Glioblastoma Multiforme

Final Category: Other

Abstract:

The aggressive nature of Glioblastoma Multiforme may be attributed largely to the complex invasive and proliferative pathways that these tumors commandeer to promote tumorigenesis. EphrinB2, a member of the Eph family of receptor tyrosine kinases, has recently emerged as a critical therapeutical target responsible for modulating those pathways, but is heavily embedded in controversy. The published literature is contradictory with either tumor-promoting or tumor-suppressive roles of ephrinB2, depending on the model system used. This study was initiated with a goal to decipher the true role of ephrinB2 in GBM. Based on data from public databases for transcript levels and methylation status of ephrinB2 in gliomas of differing grades and found that ephrinB2 was overexpressed and demethylated in GBM, correlating with poor survival outcomes. Hypothesizing an oncogenic role for ephrinB2, we initiated complex in vivo studies with concurrent analysis using advanced imaging systems, like computed tomography (CT) scans. In contrast to our initial hypothesis, our in vivo data illustrated that ephrinB2 was in fact decreasing tumor volumes and enhancing survival. To reconcile this contrast, we embarked on functional studies involving ephrinB2's cognate receptor, EphB4. We dissected the bidirectional axis of signaling between EphB4 and ephrinB2 and identified downstream effects on invasion and proliferation. Consistent with the established "go or grow" model in GBM, we found a dichotomous relationship between invasion and proliferation. Interestingly, our data show that activating or inhibiting forward EphB4 receptor versus reverse ephrinB2 ligand signaling have opposing effects on GBM tumor invasion and proliferation. These data highlight the importance of considering the signaling of both the receptor and ligand, rather than either one in isolation, to truly understand the downstream effects on GBM cell behavior, thus explaining the controversial results. This is of particular gravity when designing therapeutic interventions targeting the EphB4-ephrinB2 signaling complex in GBM, as one must consider the downstream effects of inhibiting or activating ephrinB2, as it also affects the signaling function of EphB4 in the adjacent cell.

Primary Student Presenter: Christian Curran

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Wagner

Poster Title: CD20 Expression is Elevated on T Helper Cells that Coexpress CD40 and CD4 in Newly Diagnosed Multiple Sclerosis Patients

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose of Study

Anti-CD20 monoclonal antibody therapy (rituximab, ocrelizumab) has demonstrated significant efficacy in treating relapsing remitting multiple sclerosis. Although it is postulated that these therapies' mechanism of action is to deplete peripheral B cells--the primary antigen presenting cells to effector T cells in the MS disease process--we sought to understand if CD4+/CD40+ T helper (Th40) cells, which are elevated in autoimmune states including T1D and MS may also be targeted by the drug.

Methods Used

Frozen peripheral blood mononuclear cell (PBMC) samples from 10 newly diagnosed MS patients were cultured in vitro with one of either IL-2, IL-3, or Interferon-γ, and then stimulated by either biotinylated CD3 or biotinylated CD3 and CD28. We stained these samples with anti-CD3, -CD4, -CD40, and -CD20 antibodies, then conducted flow cytometry at baseline and 24 hours post-stimulation.

Summary of Results

CD20 expression on Th40 cells was significantly elevated compared to the broader population of coexpressive CD40+/CD3+ T Cells both at baseline and 24 hours (Mean diff. = 22.9%, 95% CI: 20.4% to 25.3%, $p < 0.0001$; Mean diff. = 17.5%, 95% CI: 15.8 to 19.2%, $p < 0.01$, respectively). ANOVA demonstrated CD20 expression was also significantly elevated on all CD4+ cells compared to CD3+ cells $F(1, 408) = 126.3$, $p < 0.01$ at baseline and 24 hours (Mean diff. = 6.2%, 95% CI: 5.1% to 7.2%; Mean diff. = 6.9%, 95% CI: 6.0% to 7.7%, repectively). CD20 expression decreased on CD4+ cells between baseline and 24 hours (Mean diff. = -2.2%, 95% CI: -3.3% to -1.1%, $p < 0.01$) and on CD3+ cells between baseline and 24 hours (Mean diff. = -2.9%, 95% CI: -3.7% to -2.1%).

Conclusions

This research demonstrates that CD20 is preferentially expressed on cells that coexpress CD4 and CD40 (Th40 cells). Because Th40 cells are present at elevated proportions in patients newly diagnosed with multiple sclerosis and are implicated in autoimmune disease progression, these findings may indicate an alternative mechanism of action for anti-CD20 monoclonal antibody therapy. Next steps will include analyzing CD20+ Th40 cell counts in patients before and after commencing anti-CD20 antibody therapy for multiple sclerosis.

Primary Student Presenter: Lorraine Davis

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Daniel Sherbenou

Poster Title: Characterizing the Ikaros Pathway in Multiple Myeloma IMiD Drug Resistance

Final Category: Hematology and Oncology

Abstract:

Characterizing the Ikaros Pathway in Multiple Myeloma IMiD Drug Resistance. LN Davis (PhD, GS), …, DW Sherbenou. Department of Medicine.

Multiple myeloma (MM) is a malignant plasma cell neoplasm that afflicts more than 30,000 Americans each year. Although treatment options have significantly improved in the past 20 years, this remains an incurable disease, as nearly all patients will eventually relapse and develop drug resistance. Immunomodulatory drugs (IMiDs) exert direct anti-tumor effects by promoting the proteasomal degradation of critical MM transcription factors Ikaros (IKZF1) and Aiolos (IKZF3). However, the mechanisms of acquired IMiD resistance remain largely unknown. Based on the IMiD mechanism of action, we hypothesized that the Ikaros pathway would show a differential response to IMiD treatment in patients with IMiD resistance. We used flow cytometry to characterize IKZF1/3 degradation in response to ex vivo IMiD exposure in cell lines and eight patient samples. IMiD sensitivity was determined by ex vivo drug screens. After 24 hours, IKZF1/3 were significantly depleted in both IMiD-sensitive and -resistant cell lines (66/56% and 79/86% depletion, respectively). In patient samples, we found that IKZF1 degradation is retained in IMiD-resistant patients and that IKZF3 degradation did not differ based on IMiD sensitivity. Interestingly, patients with previous IMiD exposure had 25% greater IKZF1 depletion compared to IMiD-naïve patients ($p= 0.04$). These findings support that IMiD resistance is not mediated by preventing IKZF1/3 degradation, but that the Ikaros pathway is modulated in response to IMiDs. This suggests that the major mechanisms of IMiD resistance occur downstream of IKZF1/3 or through utilizing alternate pathways. To further elucidate the role of the Ikaros pathway in IMiD resistance, we are characterizing the response of IKZF1/3 downstream targets to IMiD treatment, as well as validating our findings with immunoblot and mass cytometry.

Primary Student Presenter: Katherine Drexelius

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kenneth Hunt

Poster Title: Patient Outcomes Differences Following Ankle Fracture Fixation With or Without Ankle Arthroscopy

Final Category: Surgery

Abstract:

Title: Comparison of patient outcomes following ankle fracture fixation with or without arthroscopy trend toward improved outcomes with the use of arthroscopy

Authors: K.D. Drexelius (MD, School of Medicine), K.S. Smith MD., S.S. Challa, D.K. Moon, MD., J.A. Metzl, MD., K.J. Hunt, MD.

Affiliation: University of Colorado Anschutz Medical Campus, Dept of Orthopedics

Rotational ankle fractures are among the most commonly treated orthopedic injuries, yet there is no consensus on the role of arthroscopy in the management of acute ankle fractures. The purpose of this study is to investigate the rate of chondral pathology and other intra-articular injuries in ankle fracture patients and compare the clinical and radiographic outcomes of the patients who underwent arthroscopy at the time of ankle fracture open reduction internal fixation (ORIF) with those patients who did not.

We recorded demographic data, injury characteristics, surgical details, and follow-up radiographs to determine the degree of osteoarthritis and to assess the final fracture outcome. We utilized the PROMIS Global Health Short Form and the PASS scale as our selected patient reported outcome scores.

Among patients who received ORIF with arthroscopy, there was a 48% rate of arthroscopic intervention beyond standard debridement of synovitis and hematoma. The mean PROMIS physical function score was higher in the ORIF plus arthroscopy group compared to the traditional ORIF group. 78% of the traditional ORIF group is satisfied with their ankle function compared to 89% satisfaction in the ORIF plus arthroscopy group.

We found that patients treated with arthroscopy in addition to ORIF for a rotational ankle fracture had superior patient reported outcomes for all tested metrics and across all specific fracture mechanisms and characteristics. Ankle arthroscopy is a useful adjunct to traditional ORIF and can

improve outcomes without a significant increase in operative time or complication rate.

Primary Student Presenter: Linda Driscoll Powers

Additional Presenter(s):

Presenting School: Nursing

Degree Seeking: BS

Year: 4th

Mentor: Paul Cook

Poster Title: Considering the Impact of Trauma and Abuse in the Etiology of Opioid Use Disorder: L Driscoll Powers, (BSN, CON) and P Cook, College of Nursing, University of Colorado, Denver, CO.

Final Category: Other

Abstract:

Opioid Use Disorder (OUD) is a public health crisis that affects a wide range of demographics and is challenging to treat. OUD is highly stigmatized, both socially and among healthcare providers. Negative stereotypes prove counter-therapeutic in healthcare settings, resulting in missed opportunities for non-pharmacological interventions. Twenty years of previous research shows correlations between OUD, lifetime history of abuse/trauma, and chronic pain.

Purpose: To determine whether changes should be made to healthcare intake and assessment procedures, it is necessary to determine what percentage of participants in a Medication Assisted Treatment (MAT) program for opioid use disorder (OUD) have a history of physical, sexual, and/or emotional abuse.

Methods: This is a secondary analysis of intake data from SB-74, the Pilot MAT Program, which was a 2-year, non-experimental cohort study coordinated by the CU College of Nursing and funded by the Colorado State Legislature. De-identified data was provided by 476 adult MAT patients between September 2018 and August 2019 using the Addiction Severity Index (ASI-6) screening tool, administered by trained clinicians. Secondary data analysis included descriptive statistics, chi squares, and t-tests.

Results: Among participants, 23% reported lifetime sexual abuse, 43% lifetime physical abuse, and 58% lifetime emotional abuse. A history of physical abuse was significantly associated with having a chronic pain diagnosis, $c2 = 4.49$, $p = .03$, and also with higher reported pain levels, $t(460) = 2.71$, $p = .007$.

Conclusions: History of physical abuse is associated with OUD and chronic pain, yet standard pain assessments do not assess for these factors. In healthcare settings, the implementation of standardized trauma-informed screening tools, prompt recognition of abuse- or trauma-associated OUD, and adjunct psychotherapeutic interventions may reduce stigma among patients and providers and ultimately help patients overcome OUD.

Primary Student Presenter: Mahmoud Elsayed

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 6th

Mentor: Nesren Omar

Poster Title: Knowledge, attitude and practice regarding Antibiotics use and resistance among Mansoura University in Egypt.

Final Category: Healthcare and Public Health

Abstract:

Background:

Antibiotics have been encroaching into Egypt's cities in the recent years. Thus, appropriate preventive measures should be taken into consideration.

Aim(s)/Objective(s):

Inappropriate use of antibiotics may contribute to the emergence of antibiotic resistance. The aim of this study was to evaluate the current knowledge, attitude and practice regarding antibiotics use among students and uncover the related factors.

Method:

A multistage, stratifie, cluster sampling technique was adopted, using a semi-structured questionnaire to collect the data from a total of 810 students. The questionnaire also included demographic data (such as sex, age, type of college and residence), sources of antibiotics used, and the frequency of use over the past year. Moreover, five-point Likert scales were used to determine the attitudes and practices, regarding students' self-medication with antibiotics.

Results:

Among the surveyed students 56.4% were urban while 43.6% were rural. The medical sector represented 20% while 80% were non-medical, about 37.5 % were in their last grade. The frequency of antibiotic use in the last year was three times or more among 54.9% of the students. Poor knowledge, attitude and practice were found among 74.6%, 31.6% and 48.4% of the students; respectively. 44.1% of the students reported the main source of last used antibiotic was purchased by them from pharmacies without prescription, 6% were left-over antibiotics, and 4.6% from other sources like friends.

Discussion, and/or Conclusion :

To conclude, gaps in the knowledge and practice of self-medication and the abuse of antibiotics were observed. Therefore, national education programs should target these gaps and enforcing antibiotics regulations at a national level is a must to help tackle one of the world's most pressing public health problems.

Primary Student Presenter: Joseph Fuchs

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Marilyn Coors

Poster Title: Religiously Affiliated Care: The Patient's Perspective

Final Category: Healthcare and Public Health

Abstract:

Religiously Affiliated Care: The Patient's Perspective. JR Fuchs, JW Fuchs, ME Coors, School of Medicine, Aurora, CO

The number of religiously affiliated acute care hospitals has grown over the past two decades. It is currently estimated that nearly 20% of hospital beds in community settings in the United States are provided by a religiously affiliated hospital. This study seeks to identify patients' attitudes towards religiously affiliated hospitals and clinics.

We conducted a survey using Likert scale-type and free responses of patients >18 years old who receive medical care in non-religiously affiliated primary care offices in Lincoln County, Colorado between July-September 2019. Demographic information, measures of religiosity and spirituality (R/S), and opinions regarding religious affiliation of providers and health care systems were obtained.

60 patients completed the survey (response rate 70.59%), representing more than 1% of the population of Lincoln County. Forty one patients (68.3%) surveyed were female, the average year born was 1971 (± 18.8 years), and 56 patients (93.3%) identified as white/Caucasian (non-hispanic). Forty two patients (70%) identified as belonging to a specific religion with the majority of patients identifying with a Christian denomination. When asked if patients preferred to receive care at a clinic/hospital affiliated with their own religion, 9 patients would prefer a clinic affiliated with their own religion, 2 patients would preferred a clinic affiliated with a religion other than their own, and 44 patients (73.3%) had no preference as to the religious affiliation. Only 5 patients (8.3%) would prefer to get health care at a clinic/hospital that is not affiliated with any religion.

Results of this study indicate that the majority of patients (73.3%) have no preference as to religious affiliation of their health care. This study provides a first step in understanding patients' attitudes towards religiously affiliated care.

Primary Student Presenter: Mason Gedlaman

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Christine Baugh

Poster Title: Association between Sports Related Injury and Risk Perceptions and Risk-Taking Behaviors

Final Category: Humanities and Bioethics

Abstract:

Purpose: Recent literature suggests that the likelihood an athlete discloses an injury or concussion decreases as they experience more such events. The mechanism behind this is unknown. However, one possibility is that after experiencing an injury, athletes' perceptions of the risk of injury changes. In this study, evaluate whether there is an association between athletes' history of sports related injury and their risk perceptions and/or risk taking behaviors.

Methods: Athletes on four NCAA Division I football teams completed surveys at their home campuses. The survey included the health-related sub-scale of the Domain Specific Risk-Taking (DOSPERT) scale, as well as questions about athletic information, demographics, and injury history. Poisson regression was used to evaluate the relationship between the number of career injuries and DOSPERT risk perceptions and risk-taking scores, controlling for total years of football, role on team, primary playing position, and maternal and paternal educational attainment. Logistic regression was used to evaluate the relationship between whether an athlete had experienced an injury in the previous football season and the same set of predictors.

Results: 292 athletes participated in the survey; 255 completed all items for this analysis.

For every one-point increase in an athlete's risk perception score, they are at 5% greater odds of having had a recent injury (OR=1.055, p=0.008). Compared to the average athlete, athletes one SD above average would have 35% increased odds of having had a recent injury (SD=7.13).

The incidence rate of career injury increases 1.2% for every point increase in an athlete's risk-taking score (IRR=1.01, p=0.005) and by 1.7% for every point increase in an athlete's risk perception score (IRR=1.02, p<0.001).

Conclusions: Athletes' risk-taking and risk perceptions are associated with their recent and career history of injury; however, the magnitude of this finding suggests that there are other influential factors.

Primary Student Presenter: Anne Gillespie

Additional Presenter(s):

Presenting School: Nursing

Degree Seeking: PhD

Year: 1st

Mentor: Madalynn Neu

Poster Title: The Youth and Pet Survivors Program: Exploring the experiences of pediatric oncology and bone marrow transplant patients in a virtual animal-assisted therapy pen pal program.

Final Category: Other

Abstract:

The Youth and Pet Survivors Program: Exploring the experiences of pediatric oncology and bone marrow transplant patients in a virtual animal-assisted therapy pen pal program. Background: The Youth and Pet Survivors Program (YAPS) is the only known virtual animal-assisted therapy (VAAT) program of its kind. Pediatric oncology and bone marrow transplant (BMT) patients are often excluded from receiving visits from therapy dogs due to infection risk. VAAT with animal pen pals allows these patients a "visit" without the associated risks. Purpose: To discover the impact of VAAT as experienced by the participants. Methods: A qualitative descriptive design using open-ended, in-depth, face to face interviews with participants in the YAPS program over time. N= 15 (8 girls, 7 boys) aged 7 to 16, receiving treatment for cancer or undergoing BMT. Participants exchanged letters with a dog or cat who had also been treated for cancer/serious illness (written by owners in the voice of their pet). Interviews were conducted at three points. Content analysis was completed by two investigators. Results: Three main themes: 1) Affinity for Animals – Characteristics of Animal and Shared Experience; 2) Why Be a Pen Pal – Emotional Reward and Entertainment; 3) Sustainability – Death of a Pen Pal. These findings include benefits similar to traditional animal-assisted therapy, such as distraction, happiness, and pleasure, and also demonstrate unique outcomes such as: ongoing friendship between the animal and the participant, bonding with the animal through a shared experience of similar medical challenges, and the emotional rewards of letter writing. Conclusion: The YAPS Program, in operation at a single hospital since 2001, now has evidence beyond the anecdotal to support dissemination. Leading the way in the emerging field of VAAT, YAPS is a nurse-led, innovative, non-invasive intervention that can be used to support pediatric oncology patients.

Primary Student Presenter: Sara Gracie

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MS

Year: 2nd

Mentor: Kathleen Brown

Poster Title: Novel de novo loss of function mutation in PTDSS1 in a child with autism and without skeletal dysplasia

Final Category: Other

Abstract:

The phosphatidylserine synthase 1 (PTDSS1) gene encodes the enzyme phosphatidyl serine synthase 1 (PSS1). PSS1 functions in the production of phosphatidylserine, a membrane phospholipid involved in many cell processes, including apoptosis, blood coagulation, cell signaling and is significant in the development of brain and bone mineralization. Heterozygous de novo missense variants that result in gain of function in the PTDSS1 gene are associated with Lenz-Majewski hyperostotic dwarfism (LMHD-MIM 151050). LMHD is characterized by the combination of sclerosing bone dysplasia, intellectual disability and distinct craniofacial, dental, cutaneous and distal limb anomalies. The progressive generalized hyperostosis associated with this syndrome affects the cranium, the vertebrae and the diaphyses of tubular bones, leading to severe growth restriction. Of note, loss-of-function mutations have yet to be reported. We describe a female with typical growth, developmental delay and autism spectrum disorder. Multi-gene panel for neurodevelopmental disorders revealed a novel de novo variant in exon 4 of the PTDSS1 gene (p.L137F). This variant has not been published as a pathogenic variant nor has it been reported as a benign variant. The variant is not observed in large population cohorts. The p.L137F variant is a conservative amino acid substitution, which is not likely to impact secondary protein structure as these residues share similar properties. However, in-silico analyses, including protein predictors and evolutionary conservation, support a deleterious effect. Skeletal survey revealed no evidence of LMHD for our patient. Since it is known that characteristically different clinical syndromes can result from different types of mutations in genes we pursued additional functional studies of the p.L137F variant. These studies confirmed that the function of the gene would be impacted. This evidence supports that our patient's variant in PTDSS1 is likely pathogenic due to loss of function and is associated with her specific clinical features typical growth, developmental delay and autism spectrum disorder. We propose a new phenotype for individuals with loss of function variants in PTDSS1.

Primary Student Presenter: Hayley Hawkins

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Todd Pitts

Poster Title: Examination of Wnt signaling as a therapeutic target for pancreatic ductal adenocarcinoma using a pancreatic tumor organoid library.

Final Category: Hematology and Oncology

Abstract:

Examination of Wnt signaling as a therapeutic target for pancreatic ductal adenocarcinoma using a pancreatic tumor organoid library. HJ Hawkins (MD, GS), BW Yacob, CD Brindley, SJ Hartman, SM Bagby, WA Messersmith, PJ Dempsey, TM Pitts. University of Colorado Anschutz Medical Campus, Aurora, CO

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers, commonly presenting at advanced stages and refractory to most treatment modalities. Wnt pathway mutations are rarely detected in PDAC, but Wnt signaling is activated by pancreatic duct ligation injury and plays a critical role in the proliferation and chemotherapeutic resistance. Patient derived pancreatic tumor organoid libraries (PTOL) allow for more accurate investigation of the biological phenotypes that might lead to additional therapies. This study aims to subclassify PDAC organoids based on Wnt dependency to determine if combinatory treatment with Wnt inhibitors and chemotherapy would be a feasible treatment.

Nine PDAC organoids were grown in Human Pancreatic Stem Cell medium. Minimal media conditions were assessed with depletions of various niche factors and organoids were treated with three Wnt inhibitors to confirm Wnt dependency. Growth was assessed with CellTiter Glo 3D.

Minimal media conditions, growth factor dependency, and Wnt dependency were determined as described above. Five organoids demonstrated Wnt dependency and two demonstrated a Wnt independent phenotype. Minimal growth media was determined for two additional organoids, but Wnt dependency has yet to be assessed.

Each pancreatic organoid demonstrated different niche factor dependencies providing an avenue for targeted Wnt inhibition therapy. WES and gene expression analysis will allow for correlation between genotype and Wnt (in)dependency observed in vitro. Combinatory treatment with Wnt inhibition and chemotherapy will be assessed in vitro and confirmed in patient-derived xenograft models.

Primary Student Presenter: Joseph Hsieh

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MD/PhD

Year: 2nd

Mentor: Paul Jedlicka

Poster Title: The Function and Regulation of PODXL in Fusion-Positive Rhabdomyosarcoma

Final Category: Hematology and Oncology

Abstract:

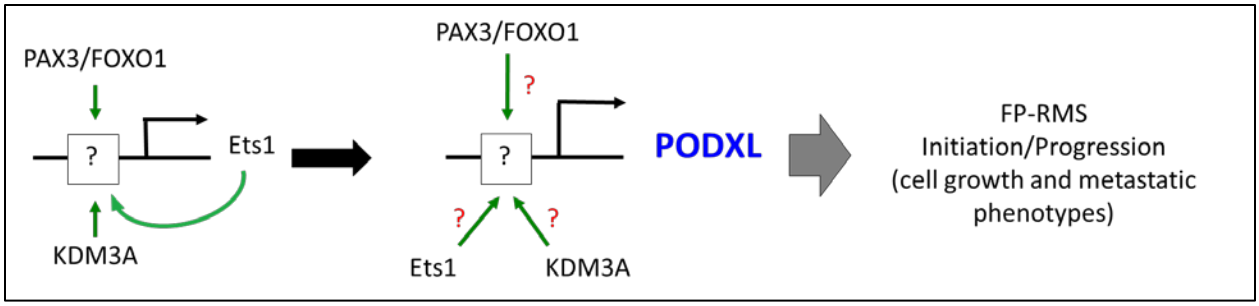
Rhabdomyosarcoma (RMS) is the most common cancer of soft tissue in children. RMS can be divided into two molecular subtypes: fusion-positive (FP) and fusion-negative (FN). FP-RMS carries a worse prognosis with less chemoresponse, more metastasis, and higher recurrence than FN-RMS. FP-RMS is a mutationally quiescent disease driven by fusion oncogene from chromosomal translocations. PAX3/FOXO1 (P3F) is the driver oncofusion in 70% of FP-RMS. P3F is an aberrant regulator of gene expression with metastatic effects.

Jumonji histone demethylase KDM3A and transcription factor Ets1 constitute an important disease-promoting regulatory axis in FP-RMS. Stable shRNA-mediated knockdown of KDM3A and Ets1 in FP-RMS cell lines inhibits clonogenic growth and transendothelial invasion *in vitro* and metastasis in a tail vein model *in vivo*. RNA-seq shows that KDM3A and Ets1 knockdown each result in significant downregulation of genes subject to positive regulatory control by P3F.

PODXL (Podocalyxin Like) is an EMT-induced cell-surface protein. PODXL has been shown to be a metastasis promoter, specifically in enhancing extravasation via interaction with cytoskeleton and downstream signaling axis.

In vitro analysis of PODXL knockdown in FP-RMS cell lines RH30 and RH41 reveals inhibition of clonogenic growth and transendothelial invasion. Integrated genomic analysis with public ChIP data reveals association between P3F, promoter, and enhancers in the PODXL genomic locus with potential interaction sites for KDM3A and Ets1.

Thus, **I hypothesize PODXL to be a key disease-promoting gene downstream of the P3F/KDM3A/Ets1 regulatory axis in FP-RMS**. Further investigation into the function and regulation of PODXL may yield valuable molecular insight into FP-RMS disease progression and additional therapeutic approaches.


PAX3/FOXO1
?
Ets1
KDM3A
PAX3/FOXO1
?
?
?
Ets1
KDM3A
PODXL
FP-RMS
Initiation/Progression
(cell growth and metastatic
phenotypes)

Primary Student Presenter: Austin Jolly

Additional Presenter(s):

Presenting School: Other

Degree Seeking: MD/PhD

Year: 4th

Mentor: Mary Weiser-Evans

Poster Title: Epigenetic control of pathological vascular remodeling: Role of smooth muscle-derived AdvSca1-SM cell induction of HDAC9-Brg1

Final Category: Cardiovascular

Abstract:

Throughout life, blood vessels are challenged with a complex combination of genetic and environmental factors that lead to pathological vascular remodeling. The remodeling process can affect all layers of the blood vessel, including the intima, media, and adventitia. For example, intimal hyperplasia obstructs the arterial lumen, decreasing perfusion to tissues that depend on oxygen rich blood to carry out cellular functions. Additionally, adventitial expansion leads to vascular fibrosis that reduces vascular compliance and leads to dysregulated vascular tone. Most studies that address the dynamics of cell movement between these vessel layers focus on migration of vascular smooth muscle cells (SMCs) from the arterial media into the intima contributing to intimal hyperplasia. Much less attention has been paid to the outer adventitia and, in particular, to the possibility that SMCs migrate in the opposite direction, into the adventitia. The discovery of resident adventitial Sca1+ vascular progenitor cells (AdvSca1 cells) raised new and important questions about roles these cells play in growth, remodeling, repair, and disease of the artery wall. Using a highly specific SMC lineage-mapping approach, our group conclusively demonstrated that mature SMCs move into the adventitia, are reprogrammed into a subset of AdvSca1 progenitor cells (termed AdvSca1-SM cells), and reside in an adventitial progenitor niche. The finding that AdvSca1-SM cells derive from mature SMCs through physiological reprogramming opens up the possibility that AdvSca1-SM cells could be manipulated in vivo to promote differentiation into reparative SMCs while blocking their differentiation into alternative pro-remodeling cell types (e.g. pro-fibrotic myofibroblasts, pro-inflammatory macrophages). For this study, we generated a high-precision fate-mapping system to selectively track AdvSca1-SM cells over time and monitor their behavior. Using this system in the setting of carotid artery injury, we found that AdvSca1-SM cells greatly expand in the adventitia in response to injury and are major contributors to adventitial fibrosis. Some AdvSca1-SM cells migrate to the arterial media and differentiate into reparative SMCs, but very few contribute to intimal hyperplasia. Using unbiased RNAseq analysis, our data show that, in response to injury, AdvSca1-SM cells downregulate stemness-associated genes, but upregulate genes associated with myofibroblast and macrophage phenotypes, inflammatory cytokine/chemokine genes, and several epigenetic regulators, including HDAC9 and Smarca4/Brg1. These data suggest AdvSca1-SM cells are central

regulators of pathological vascular remodeling and are a potential target for novel therapeutics. Currently, we are interested in how epigenetic modulation regulates AdvSca1-SM cell phenotype and function. Recent work in the field has shown that HDAC9 and Brg1 form a complex to repress SMC contractile gene expression in dysregulated SMCs. Inhibition of HDAC9 restores SMC contractile genes and attenuates ligation induced vascular remodeling. Our qPCR and immunofluorescence data reveal that HDAC9 and Brg1 are induced in AdvSca1-SM cells in injured vessels as compared to uninjured vessels leading us to investigate the role of these epigenetic regulators in AdvSca1-SM cells. Our ongoing studies are addressing the hypothesis that injury-induced activation of AdvSca1-SM cells promotes vessel fibrosis, inflammation, and remodeling through upregulation of HDAC9 and Brg1, which functions via epigenetic modulation to block AdvSca1-SM cell differentiation into reparative SMCs while promoting differentiation into pro-remodeling cell types. Inhibition of HDAC9 and Brg1 will promote differentiation toward the SMC contractile phenotype and improve vessel homeostasis.

Primary Student Presenter: Brandi Krieg

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Nolan Wessell

Poster Title: Comparison of adverse outcomes following placement of Superion interspinous spacer device versus laminectomy and laminotomy

Final Category: Surgery

Abstract:

Background Current evidence suggests placement of Superion interspinous spacer (SIS) devices compared with laminectomy/laminotomy surgery offers an effective, less invasive treatment option for patients with symptomatic lumbar spinal stenosis. Both SIS placement and laminectomy/laminotomy have risks of adverse events (AE) that have not been previously compared. The purpose of this study is to compare the short-term complications of the SIS with LL and highlight device-specific outcomes with LL

Methods Via retrospective review, 189 patients who received lumbar level SISs were compared with 378 matched controls who underwent primary lumbar spine laminectomy/laminotomy collected from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. AE analyzed included rates of wound infection, pulmonary embolism (PE), deep venous thrombosis (DVT), urinary tract infection (UTI), sepsis, septic shock, cardiac arrest, and death. Differences in groups were analyzed using the Chi-square test. Device-specific complications (DSC) were assessed including device malfunction/misplacement (DM), device explantation (DE), spinous process fracture (SPF), and reoperation.

Results No differences in demographics or comorbidities existed between groups. There was no significant difference in rates of wound infection, PE, DVT, sepsis, septic shock, cardiac arrest, or death Only UTI was significantly different, occurring in 2.1% of the SIS group and 0% in the control ($p < 0.05$). DSC in the SIS group showed 11.1% of patients experienced DM, 21.1% experienced a SPF, 20.1% required DE and 23.8% required re-operation.

Conclusion Aside from a higher risk of UTI with SIS, rates of AE in the SIS group were not significantly different from patients undergoing laminectomy/laminotomy. Rates of DSC with the SIS and cumulative risk associated with these complications should be studied further as they likely represent a substantial added cost to healthcare.

Primary Student Presenter: Vishal Krishnan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Victoria Pelak

Poster Title: Patient Characteristics From the Colorado Posterior Cortical Atrophy Bioregistry

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Posterior cortical atrophy (PCA) is a neurodegenerative syndrome characterized by prominent impairment of visuospatial/perceptual, literacy, and praxis skills. The natural history of PCA is largely unknown. To assess the feasibility of a multicenter, longitudinal investigation of PCA, we have established and gathered data from the Colorado PCA BioRegistry.

Patients diagnosed with PCA at our institution meeting 2017 PCA Consensus Criteria were consented or included if deceased. Longitudinal, standard clinical data were collected from the medical record utilizing a secure online database platform (REDCap). Variables collected include patient demographics, clinical history and course, Montreal Cognitive Assessment (MoCA) scores, Dementia Severity Rating Scale (DSRS) results, and results of threshold visual field perimetry.

38 patients are enrolled. Age of symptom onset is higher for men (65y) compared to women (60y). The median duration of illness is 8y and 6.5y for men and women, respectively. The median age of death was 73y, with survival after symptom onset ranging from 3-12y. Variable rates of decline in MoCA scores, with sizable fluctuation, are evident. DSRS results show improvement and fluctuation following an initial visit. Visual field loss was greater in the left than right hemifield.

A 5-year difference in age at symptom onset between men (older) and women is noted and has not been previously characterized. Median survival is 7.5y with a large range. Fluctuation in global cognitive and functional scores is present and important to explore further before deciding upon outcome measures in longitudinal PCA studies. It is likely that global cognitive outcome measures do not adequately capture the neuropsychological changes that occur in PCA. The Colorado PCA BioRegistry offers important data that inform the feasibility of an international, multi-center PCA longitudinal investigation.

Primary Student Presenter: Steven Lada

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Cara Wilson

Poster Title: Interferon Beta Increased Siglec-1 Expression on Human Gut Macrophages

Final Category: Microbiology and Infectious Diseases

Abstract:

Interferon Beta Increased Siglec-1 Expression on Human Gut Macrophages. SM Lada, (MD, SoM), CM Purba, SM Dillon, ML Santiago, CC Wilson, Division of Infectious Diseases, University of Colorado Anschutz Medical Campus, Aurora, CO.

Siglec-1 (CD169) expression, induced by Type 1 Interferons (IFN-1s) on myeloid dendritic cells (mDC) and macrophages (MΦ), binds HIV and has been implicated in HIV trans-infection of CD4 T cells. We previously showed elevated levels of IFN-1 interferon beta (IFNβ) in gut tissue of people living HIV. CD169 is expressed on murine gut MΦ, but few have investigated expression in human gut. We hypothesized that exposure to IFNβ or bacterial products would increase CD169 expression on human gut MΦ.

Human jejunum lamina propria mononuclear cells (LPMC), obtained from healthy discarded surgical tissue (N=4), were cultured for 18hrs with IFNβ (1000-1pg/mL; 10-fold dilutions), Escherichia coli lysate (10μg/mL), or were unstimulated. Flow cytometry was used to evaluate expression of CD169 on MΦ or mDC pre (baseline) and post in vitro culture.

MΦ were identified as HLA-DR+CD64+CD11c± cells within viable CD45+CD3-CD19- LPMC. At baseline MΦ constituted 0.16±0.03% (Mean±SEM); of these MΦ 7.95±4.1% expressed CD169. HLA-DR+CD64-CD11c+ mDC within viable CD45+CD3-CD19- LPMC, constituted 0.11±0.02% of baseline; there were few mDC expressing CD169 (0.95±0.59%). In the presence of 1000pg/mL IFNβ, 27±4% of MΦ expressed CD169, a 6.2-fold increase over unstimulated. With 100pg/mL IFNβ, 20±5% of MΦ were CD169+, a 4.2-fold increase over unstimulated. At lower doses of IFNβ, CD169 expression by MΦ only increased by 1.5-fold versus unstimulated. Exposure to E. coli lysates increased CD169 expression on MΦ by 2.3-fold.

IFNβ induced CD169 expression on human gut MΦ in vitro in a dose dependent manner; additionally, E. coli lysates increased expression although to a lesser degree. Future studies will investigate the role of CD169+ gut MΦ in T cell HIV infection.

Primary Student Presenter: Jonathan Layne

Additional Presenter(s): Samuel Merrill Hunter LaCouture

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jason Stoneback

Poster Title: Classification and incidence of bacterial infections in infected nonunion and osteomyelitis patients

Final Category: Bone or Skeletal

Abstract:

Osteomyelitis (OM) and infected nonunions (INU) present unique and serious problems to patients as the multitude of factors and variable infective sources make treatment uncertain. Together these represent two of the most challenging complications to address for orthopaedics trauma and fracture surgeons. OM is commonly seen in patients who have sustained complex fractures, especially those with open fracture types graded Type II or worse and those that are debrided greater than five hours post-injury. Prior research in the military setting has concluded that 9% of trauma cases developed OM. While it is difficult to extrapolate this information to the civilian sector, OM has been reported in similar proportions in the noncombatant population and continues to rise with the increased use of posttraumatic surgical implants. OM is also associated with the development of fracture nonunion as this underlying infection history may be a reason for healing complications. However, the etiology of INU is unclear. The management of INU, on the other hand, has remained consistent for many years. Treatment typically involves surgical debridement, tissue reconstruction, extended periods of antibiotics, and opioids for pain management. As a result of the extensive intervention requirements, some of these patients are at an increased risk for severe complications including recurrent infections and loss of functionality. The purpose of this retrospective chart review is to analyze OM and INU cases and determine the most prevalent types of bacterial organisms along with their respective antibiotic treatment regiments to propose an evidence-based method for treating these infectious diseases. Using a query related to OM/INU diagnoses codes, pre-existing data from patient records was collected to include bacteria types, treatment methods, comorbidities, lab values, complications, and other treatment variables to deduce the commonalities among cases. Preliminary data from this cohort provides initial insight into the treatment of this population. The preliminary cohort included 38 individuals, 86.8% male (33/38) with a mean age of 56.4 ± 12.3 years. Thirty-eight patients experienced OM alone and one patient experienced both OM and INU. The majority of infection sites were located in the lower extremity, with 48% of sites occurring at the foot or toes. The lone INU saw heavy mixed anaerobic flora, mixed gram positive and gram negative flora culture, and staphylococcus species. Among all patients, Methicillin-sensitive Staphylococcus aureus (MSSA) was the most prevalent bacteria

(40.4%) while vancomycin was the most commonly used antibiotic (23.0%) within the sample. Twenty-four (36.9%) patients experienced wound healing complications and 16 (24.6%) patients experienced a recurrent infection. In conclusion, gram-positive bacteria were most prevalent and were most often treated with an appropriate antibiotic, though the rate of complications illustrates an opportunity for more targeted interventions. Additional data collection is needed to strengthen these findings and further extrapolate a clinical recommendation.

Primary Student Presenter: Jacob Leary

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Timothy Vollmer

Poster Title: Patient demographic factors predict likelihood of improvement on patient-reported outcome measures in multiple sclerosis

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Patient demographic factors predict likelihood of improvement on patient-reported outcome measures in multiple sclerosis. JB Leary (MD, SOM), S Sillau, B Vollmer, KV Nair, and TL Vollmer, Department of Neurology, University of Colorado, Aurora, CO.

Purpose of Study: Functional improvement is seen in some patients with multiple sclerosis (MS) being treated with high-efficacy disease-modifying therapies (DMTs), but the factors influencing improvement are unknown. We examined the impact of patient demographics, disease characteristics, and brain volumetrics on the likelihood of clinical improvement in patients treated with these agents, using patient-reported outcome (PRO) measures.

Methods Used: This retrospective chart review included adults with MS who completed ≥2 PRO measures across 2 time points separated by ≥10 months, taking a high-efficacy DMT at baseline. Qualifying DMTs included fingolimod, dimethyl fumarate, natalizumab, rituximab, and ocrelizumab. We examined the influence of demographics, disease characteristics, and brain volumetrics on the likelihood of clinical improvement. PRO measures included 10 domains of the NeuroQOL Short Form battery. NeuroQuant MRI reports were used for volumetric data. Patients were grouped as Improved vs. Failed to Improve by each NeuroQOL domain. Statistical analyses utilized Spearman correlations and logistic regression.

Summary of Results: 318 patients met inclusion criteria. Factors significantly predicting the likelihood of clinical improvement included race (Fatigue; Odds Ratio = 2.325, CI 5, 95 = 1.122, 4.817, p = .023), age (Depression; odds ratio = 0.976, CI 5, 95 = 0.952, 1.000, p = .049), and type of MS (Sleep Disturbance; PPMS v. SPMS odds ratio = 0.101, CI 5, 95 = 0.012, 0.842; RRMS v. SPMS odds ratio = 0.346, CI 5, 95 = 0.166, 0.721, p = .0069).

Conclusions: Patient demographic factors appear to be the most likely predictors of clinical improvement, as compared to disease characteristics and brain volumes.

Primary Student Presenter: Pierce Lewien

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Juan Lessing

Poster Title: A Common Drug Causing An Unusual Eruption: Furosemide Triggering Bullous Pemphigoid

Final Category: Other

Abstract:

Case: A 65 year-old man with no known autoimmune disease history was hospitalized for shortness of breath and peripheral edema, diagnosed with decompensated heart failure, and treated with IV furosemide. Within a day, he developed a 1 cm, tense, fluid-filled bullous lesion on his lower abdomen. The next day, three larger bullous lesions with surrounding erythema appeared nearby. Based on clinical appearance and timing, he was diagnosed with drug-induced bullous pemphigoid. Furosemide was stopped and treatment switched to bumetanide. Symptoms improved with no further bullae formation and he was sent home with PO bumetanide and follow-up. Furosemide was added to his list of allergies and he was counseled to avoid this medicine.

Discussion: Furosemide, a loop diuretic, is the 20th most prescribed medication in the United States. This case illustrates a rare adverse effect known by few of a medication prescribed exceedingly commonly in the clinic and hospital. Bullous pemphigoid (BP) is an IgG-mediated autoimmune subepidermal blistering disease that targets hemidesmosomes that hold the dermis and epidermis together, causing the two layers to separate and blisters to form. Along with idiopathic causes, drugs are BP inducers, with furosemide included among them. The mechanism for drug-induced BP is poorly understood; one postulated mechanism involves drug induction of antibodies against the basement membrane through binding to a lamina lucida protein thus changing its antigenic properties. Unlike Stevens-Johnson syndrome or toxic epidermal necrolysis, in BP bullae tend to be tense, rarely involve mucosal surfaces, and often affect the lower abdomen, thighs, and forearms. Questions remain why this reaction happens with furosemide but far less commonly with bumetanide, another sulfa loop diuretic. The drug reaction in this case occurred over one day while most reported cases presented days to weeks after exposure. Still, the fact the eruption occurred with drug initiation and ceased after discontinuation strongly implicates furosemide in our patient. As immediate medication discontinuation is critical, it is important to recognize that furosemide, a common drug used in patients, can cause this reaction. Bullous pemphigoid should be considered in all older adults who develop tense bullae, and an exhaustive drug exposure history is critical to recognizing and discontinuing possible inciting medications.

Primary Student Presenter: Nguyen Lu

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Yihan Lin

Poster Title: Cardiac Surgery Publications in Africa Over the Last 20 years: A Literature Review

Final Category: Cardiovascular

Abstract:

There is a significant burden of surgically correctable cardiovascular disease in Africa. The goal of this research is to review the last 20 years of literature on this topic.

A systematic search was performed, including PubMed, Embase, and African Index Medicus for the period 1996 - 2016. Title screening was performed in duplicate. Data abstraction included researcher affiliations, study design, country, hospital type, procedures, and outcome measures.

209 articles and abstracts met criteria. Publications originated from 29 countries, 13 of which were low-income (44.8%), 11 lower-middle income (37.9%), and 5 upper-middle income (17.2%). Research output increased more than 15-fold over the study period. Publications were mostly authored by local teams (71.4%) compared to visiting (4.9%) and mixed teams (23.7%). Public hospitals were the most common sites for research (79.5%). 43.8% of articles described adult cases, 35.6% pediatric, and 20.6% described mixed populations. Less than half of publications (45.9%) reported inpatient care data, and 40.7% reported outpatient follow-up. Mortality was reported in 62.7% of studies; health-related quality of life measures in 4.8%. Collaborations between high-income countries and African researchers were more likely to produce lower evidence quality (commentaries, case reports, etc.) than literature produced by local teams.

Clinical reporting on cardiac surgery is limited in Africa. More published data should be encouraged to better benchmark and improve research capacity. Reporting of surgical outcomes should also be emphasized in future publications, as should collaborations that produce high-quality evidence.

Primary Student Presenter: Amrita Mahajan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Julia Sanders

Poster Title: Seasonal Trends in Operative Pediatric Supracondylar and Femur Fractures at a Pediatric Level 1 Trauma Center

Final Category: Surgery

Abstract:

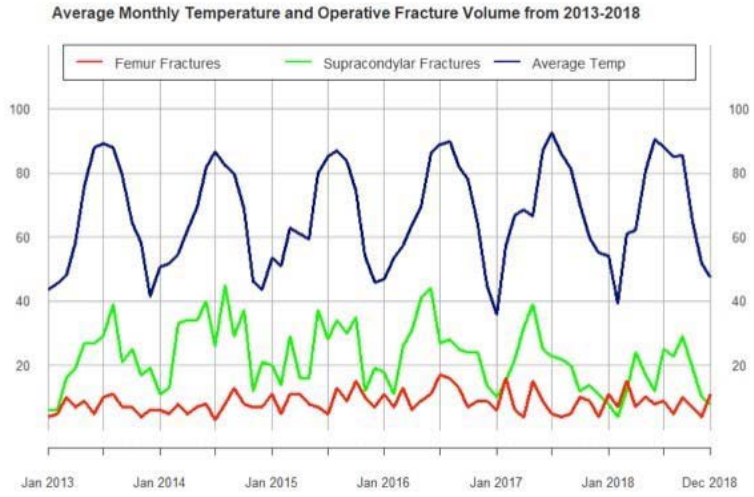
Purpose: Supracondylar humerus and femoral shaft fractures are two common injuries managed by pediatric trauma centers. While anecdotally we see an increase in many injuries with warmer weather, no studies in the United States have evaluated this subjective trend. The purpose of this study was to describe the seasonal variation in the incidence of operative pediatric supracondylar humerus and femur fractures, and the relative burden of these injuries on hospital census.

Methods: We performed an IRB-approved, retrospective review of 1626 supracondylar humerus and 607 femur fractures treated operatively between 2012 and 2018 at a single level 1 pediatric trauma center. Dates of injury were identified as weekday versus weekend, and temperature and precipitation data was obtained through the National Weather Service.

Results: Together, supracondylar humerus and femur fractures account for between 6% and 25% of orthopedic admissions. For every 10 degree (F) increase in temperature, there was a 10% increased likelihood of femur fracture and a 25% increased likelihood of supracondylar humerus fracture (p=0.03 and p=<0.0001 respectively). Femur fractures were less likely to occur on weekdays compared to weekends (OR 0.65, p=0.0001) and less likely to occur on days with precipitation (OR 0.39, p= 0.03), while supracondylar humerus fractures demonstrated no significant weekly or precipitation-related trends.

Conclusion: As often anecdotally reported, supracondylar humerus fracture volumes mirror temperature variations annually. Femur fractures appear to have more complex trends, with higher volumes on weekends regardless of season. Geographic variation in temperature, precipitation and proximity to seasonal activities such as snow skiing may contribute to injury volumes.

Significance: Given the large relative burden of trauma on orthopedic admissions, further understanding of seasonal trends in pediatric orthopedic injuries can provide valuable information to develop strategies for more efficient resource allocation at pediatric trauma centers.


Average Monthly Temperature and Operative Fracture Volume from 2013-2018
Femur Fractures
Supracondylar Fractures
Average Temp
100
80
60
40
20
Jan 2013
Jan 2014
Jan 2015
Jan 2016
Jan 2017
Jan 2018
Dec 2018

Primary Student Presenter: Derek Mason

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Rosemary Rochford

Poster Title: Measles Vaccine Response Varies in 12-Month-Old Kenyan Children Which May Increase Measles Transmission

Final Category: Microbiology and Infectious Diseases

Abstract:

Measles is a preventable infectious disease, but still presents a large burden of disease throughout the world. In 2017, measles caused roughly 110,000 deaths worldwide. While the measles vaccine is used in Africa, reduced measles vaccine efficacy has been reported in Sub-Saharan Africa. The aim of this study was to determine the response to measles vaccine following routine 9-month vaccination in infants living in a malaria endemic region of sub-Saharan Africa. Plasma samples were collected from children from Kisumu, Kenya, at 12 months of age, three months after routine vaccination for measles. These plasma samples were tested by indirect ELISA to measure anti-measles antibodies. Samples that had one well with an optical density > 0.5 that different from the other two wells were trialed again to account for pipetting error. If on reanalysis the wells of a sample no longer had a well with a difference > 0.5, the sample was included in analysis with its original wells excluding the well that differed > 0.5. If the sample again had a well that differed in optical density from the other two wells by > 0.5, the sample was considered an outlier and excluded from analysis. Eleven samples were excluded, leaving 143 samples included in the final analysis. The mean optical density was 1.83 (SD ± 0.72; 95% CI 1.71-1.94). Twenty-two participants had an OD of 1.0 or less, raising concern of not being immunoprotective against measles. These twenty-two participants represent 15% of the total participant sample. For the measles vaccine to be protective, roughly 95% of the community must be vaccinated to prevent transmission. This then represents a possibility for transmission of measles to occur in these communities, particularly in young children who are more at risk of infection. The variability in levels of anti-measles antibodies following routine measles vaccination in this sample are not entirely understood and will be the subject of ongoing analysis.

Primary Student Presenter: Nick Mason

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Meguid

Poster Title: Comparative Assessment for Patient Surgical Risk By Surgeons vs A Universal Parsimonious Risk System

Final Category: Surgery

Abstract:

Introduction: The literature lacks evidence on preoperative prediction of surgical outcomes by surgeons. The Surgical Risk Preoperative Assessment System (SURPAS) provides accurate procedure-specific preoperative risk prediction of 30-day postoperative adverse outcomes including mortality, overall morbidity, & 9 other surgical complications. SURPAS predicts these values using 8 variables including procedure-specific risk and American Society of Anesthesiologists Physical Status Classification (ASA class). These risk algorithms were developed from American College of Surgeons National Surgery Quality Improvement Program (NSQIP) data.

Methods: We compared the surgeons' predictions of morbidity & mortality for a variety of surgical procedures to SURPAS predicted values, and the postoperative outcomes. 30 patients' NSQIP data was presented to surgeons in standardized vignettes, including the procedure performed & each patient's comorbidities. Vignettes in ASA classes I-V were randomly presented to the participants. Surgeons were asked to predict each patient's 30-day postoperative mortality & morbidity.

Results: Preliminary results from general surgery residents show that surgeons were able to accurately & precisely predict both the morbidity & mortality risk amongst low risk patients (ASA class 1 & 2). In high risk patients (ASA class 3-5) the agreement amongst surgeons on both mortality & morbidity was variable. Surgeons were also less accurate at predicting risk in the high-risk patient pool.

Conclusions: The data supports continuing the study in attending surgeons of different specialties. Each specialty will be administered a survey using procedures from their field of expertise.

Primary Student Presenter: William Mundo

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Colleen Julian

Poster Title: Environmental hypoxia during perinatal life enhances erythropoiesis and pulmonary vascular dysfunction in response to chronic hypoxia during adulthood: lessons from a murine model

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Chronic hypoxia contributes to the development of cardiopulmonary disease at high-altitude (HA) residence and the factors influencing susceptibility are not well understood. Previous studies demonstrate that young HA males with pulmonary dysfunction were 6-times more likely to have experienced hypoxia during perinatal life, however, the data did not allow fully account for the effect of unknown environmental exposures between gestation and adulthood. An experimental murine model in which the degree and timing of environmental hypoxia could be strictly controlled was used to assess the impact of perinatal hypoxia on pulmonary function and the development of polycythemia. Hypoxic exposure during adulthood increased RVSP by 79 % (25.2 vs. 45.2 mmHg, $p<0.0001$), raised hematocrit by 34 % (40.2% vs. 53.8%, $p<0.0001$), enhanced RV:LV+septum weight ratio 15 % (0.24 vs. 0.27, $p<0.05$), reduced PAAT 15% (18.32 vs. 15.93, $p<0.001$), and increased the magnitude of pulmonary vascular dysfunction and polycythemia in response to a secondary hypoxic exposure during adulthood in male offspring only. Perinatal hypoxia exaggerated the hypoxia-associated reduction of PAAT (15.9 vs. 12.8, $p<0.0001$) and PV peak flow velocity (765 vs. 886, $p<0.001$) and enhanced the hypoxia-associated increase of RVAW thickness (0.91 vs. 0.69, $p<0.0001$) and hematocrit (57.7% vs. 53.8%, $p<0.001$). This study highlights that perinatal hypoxia alone can induce lasting effects on pulmonary vascular function even in the absence of a secondary hypoxic exposure during adulthood. This study demonstrates that perinatal hypoxia increases the susceptibility to polycythemia and pulmonary dysfunction in early adult life in hypoxic and normoxic conditions.

Primary Student Presenter: Margaret Mary Nguyen

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Ken Maclean

Poster Title: Altered Expression of Thioredoxin, Peroxiredoxin, and Thioredoxin Reductase 1 Activity in CBS-Deficient Homocystinuria in the Presence and Absence of Homocysteine-Lowering Treatment: Possible Implications for Oxidative Stress

Final Category: Metabolism and Endocrinology

Abstract:

Purpose of Study: Cystathionine □-synthase-deficient homocystinuria (HCU) is a poorly understood, life-threatening, inborn error of sulfur metabolism. If left untreated, it can lead to cognitive impairment, connective tissue disturbances, and thromboembolic complications. Multiple lines of evidence from both the transgenic HO mouse model of HCU and human HCU patients indicate oxidative stress as a major pathogenic factor in this disease. Previous work has shown that impaired antioxidant defense may contribute to the generation of oxidative stress in HCU.

Methods Used: We investigated the hepatic expression of antioxidants thioredoxin (TRX), thioredoxin reductase 1 (TRD), and peroxiredoxin (PRDX) in the presence and absence of the homocysteine-lowering therapy in the HO mouse model of HCU.

Summary of Results: Western blotting analysis revealed significant induction of hepatic levels of PRDX1 in HO mice, while treatment to lower homocysteine normalized hepatic levels of this antioxidant in the HO mice. Our results indicate that hepatic PRDX1 levels in HCU are directly related to homocysteine levels.

Conclusions: This may suggest that decreased expression of PRDX1 is a contributory factor for oxidative stress in HCU.

Primary Student Presenter: Regan Pelloquin

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Kristine Erlandson

Poster Title: Frailty, Physical Function Impairment, Comorbidity Burden, and Falls are Predictive of Mortality Among Middle-Aged Adults with HIV

Final Category: Other

Abstract:

Higher than expected rates of frailty and functional impairment are described among people with HIV (PWH). Whether these impairments, particularly among middle-aged persons, are predictive of poor outcomes including death are not well established. The objective of this study was to determine if frailty and physical function impairments are associated with long-term mortality among middle-aged adults with suppressed HIV.

PWH ages 45-65 with ART-suppressed HIV-1 RNA for a minimum of 6 months were evaluated in 2010-2011 (baseline) using the Fried Frailty Phenotype (composite score and grip strength alone), Short Physical Performance Battery ([SPPB] composite and chair rise alone), 400-m walk, Veterans Aging Cohort Study (VACS) Index, and any fall in the prior year. Medical records were reviewed in 2018 to determine vital status. For participants who were not able to complete the 400-m walk or the chair rise they were assigned a pace of zero. Hazard ratios were used to estimate survival by baseline frailty, function, comorbidity burden, or falls, stratified by age ≥/<50 years. Patients without a confirmed date of death were censored at last follow-up visit. Time-dependent area under the ROC (ROC-AUC) curves were estimated to compare the predictive accuracy of mortality between each physical function measure, where values of 0.5 and 1.0 represent random chance or no predictability and perfect predictability, respectively.

Of 351 participants, 299 (85%) identified as male, 52 (15%) as female, 16% were Black and 19% Hispanic. At baseline, the mean (SD) age was 51.9 (5.2) years and the majority (58%) had a CD4 count of >500 cells/μL; all had an HIV-1 RNA <200 copies/mL. Twenty-three (7%) were frail and 164 (47%) pre-frail, 103 (29%) had ≥1 fall in the prior year, 74 (21%) had an SPPB score of ≤10, 33 (9%) had weak grip strength. The mean (SD) 400-m walk pace (m/sec) was 1.4 (0.4) and the mean (SD) chair rise pace (rises/sec) was 0.5 (0.2). The mean (SD) follow-up time was 6.7(2.4) years. All physical function measures except grip strength were associated with mortality. 8-year overall survival differed significantly between participants who were pre-frail/frail compared to participants who were non-frail (HR=3.2[95%

CI=1.4,7.3], p-value=0.008) as well as between participants who had more than one fall compared to participants who had no falls (HR=2.8[95% CI=1.4,5.7], p-value=0.004). VACS score was associated with increased hazard of death (10-unit increment, HR=1.6[95% CI=1.3,1.9], p-value<0.0001). Individually, the 400-m walk was the best predictor of mortality with time-dependent ROC-AUC=0.82, followed by VACS index: 0.80, SPPB: 0.70, chair rise pace: 0.67, frailty 0.63, falls: 0.61 and average grip: 0.49.

In middle-aged adults with suppressed HIV, frailty, physical function, falls, and comorbidity burden (VACS Index) are associated with long-term mortality. These simple clinical measures can be useful tools to guide clinical decisions by aiding in the identification of participants with higher mortality risk.

Primary Student Presenter: Binhan Pham

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mark Petrash

Poster Title: Two Founder Lines of Aldose Reductase Knockouts Created Using CRISPR/Cas9

Final Category: Vision Sciences

Abstract:

Two Founder Lines of Aldose Reductase Knockouts Created Using CRISPR/Cas9. B Pham (MD, SOM), B Shieh, MG Pedler, P Lenhart, and JM Petrash, Department of Ophthalmology, University of Colorado School of Medicine.

In high glucose environments such as diabetes, the enzyme aldose reductase (AR) acts to metabolize glucose to sorbitol which is thought to contribute to diabetic complications, including cataract, posterior capsular opacification, retinopathy, and neuropathy. It is therefore imperative for the research community to use a standardized model to understand AR-linked pathologies. In this study, we took advantage of CRISPR/Cas9 to create mutations in the AR gene that knocked out AR activity (ARKO), which may reduce the risk of diabetic complications. DNA sequencing, protein western blot analysis, and tissue histology verified a 16 nucleotides deletion and 4 nucleotides insertion of ARKO mice. Transmission of mutant alleles followed expected Mendelian patterns in pedigrees from both founder lines. Functional deletion of AR gene expression was shown in ARKO eye, heart, and kidney tissues where AR is more abundant in wild type mice. Furthermore, structural differences were not seen in these tissues when compared to wild type mice. We believe that these lines can serve as important models in tackling diabetic pathologies and understanding their mechanisms.

Primary Student Presenter: Andy Phan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Sana Karam

Poster Title: Radioresistant anaplastic thyroid cancers display a unique gene signature and respond to hypofractionated radiotherapy

Final Category: Hematology and Oncology

Abstract:

Purpose: Patients diagnosed with anaplastic thyroid (ATC) cancer display heterogeneous tumor responses to radiation therapy. It remains unclear how the molecular profiles of ATC subtypes mediate a radiosensitive or radioresistent phenotype. Furthermore, the optimal fractionation for ATC remains controversial. In this study, we sought to identify genetic determinants of tumor radioresistance in ATC subtypes. We further compared the role of hypofractionated radiotherapy to conventional fractionation in a novel orthotopic model of ATC.

Methods: Eight human ATC and PDTC cell lines (C643, SW1736, BCPAP, T238, CAL62, KHM-5M, 8505C, and KTC-2) were profiled using microarray analysis. Clonogenic survival assays were performed for each cell line. Irradiation (IR) was performed at 0, 2, 4, 6, and 8 Gy and cells were incubated for 8-10 days post-IR. Data were fitted to the linear quadratic model. Cell lines were classified as radioresistant (RR) or radiosensitive (RS) based on SF2 and SF4 values. Hierarchical clustering was performed to determine the genomic profile of RR and RS cell lines. For in vivo studies, mice were surgically implanted with the luciferase-tagged 8505C ATC cell line. Mice were randomized on the day of treatment initiation (day 14-15) based on BLI photon radiance signal to receive hypofractionated (HF), conventional fractionation (CF) or no irradiation. A total dose of 20Gy was delivered in 2 weekly doses for the HF group and daily 10 doses for the CF group.

Results: We identified five radioresistant cell lines and three radiosensitive cell lines. Microarray gene-expression analysis revealed an inflammatory gene signature associated with radioresistance. In particular, CXCR4 was increased by more than 2-fold in RR cell lines. CXCR4 has been shown to play a role in mediating tumor growth, metastasis and resistance to therapy and its targeting has shown efficacy in various tumor animal models. Longitudinal analysis of weekly BLI revealed significant differences in tumor growth in the HF group compared to the control and CF groups. On the last day in which all mice were alive (day 36), average photon radiance in the HF group was significantly lower compared to mice in the control group (125-fold decrease) and mice in the CF group (16-fold decrease).

In addition to its effect on primary tumor growth, HF resulted in significantly improved survival compared to mice in the control and CF groups.

Conclusions: Our study provides evidence that hypofractionated radiotherapy is superior to conventional radiotherapy in a radioresistant model of ATC. Hypofractionated RT significantly retarded tumor growth and prolonged survival. Gene-expression analysis revealed targetable pathways that may be associated with radioresistance. These findings have direct clinical implications for enhancing treatment outcomes and survival in ATC patients.

Primary Student Presenter: Nisha Pradhan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Meguid

Poster Title: Understanding Techniques of and Attitudes Towards Preoperative Risk Assessment

Final Category: Surgery

Abstract:

Purpose of Study: In the era of electronic patient data, formal surgical risk assessment tools have developed to predict risk of adverse postoperative patient outcomes. These tools help patients understand their risks and increase shared decision making. Yet, formal surgical risk assessment tools are underutilized. We studied the attitudes towards & techniques of how surgeons preoperatively assess risk.

Methods Used: 203 surgical faculty (108) & surgical residents (95) at the University of Colorado were emailed a 16-question survey between 8/19-9/19. Surveys were excluded if the surgeon was no longer practicing or if the respondent did not complete the survey.

Summary of Results: 92/203 surgeons responded: 51 faculty; 41 residents. 55% of residents sometimes rely on online risk calculators, while 58.0% of faculty never or rarely use them ($p<.001$). 82.0% of faculty & 35.5% of residents rely on prior experience to estimate risk most of or all of the time ($p<.0001$). Barriers to use of a formal risk assessment tool include the amount of time needed to use the tool (40.0% report this a moderate barrier), lack of integration into the EHR (33.3% reported this a moderate barrier), & inaccessibility of the tool during the patient visit (38.9% reported this a moderate barrier).

Conclusion: Surgeons heavily rely on their prior experience & on current literature to guide their assessment of surgical risk. Surgical faculty communicate surgical risk directly instead of relying on residents. Time constraints & the lack of accessibility are moderate barriers to using an objective, evidence-based risk assessment tool.

Primary Student Presenter: Kendra Prutton

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: James Roede

Poster Title: Effect of trisomy 21 on the differentiation of induced pluripotent stem cells to neural progenitor cells

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Down syndrome (DS) is a complex genetic insult caused by triplication of chromosome 21. The ubiquity of cognitive deficits in DS has made structural and cellular changes in the brain the focus of much research effort. However, no prior studies have utilized DS induced pluripotent stem cells (iPSC) to assess the effect of trisomy 21 on embryoid body (EB) formation and neurogenesis. We aim to define, evaluate, and compare neural differentiation in DS and euploid iPSCs through the formation and maturation of EBs to neural progenitor cells (NPC). Here we show that DS iPSCs produce larger EBs compared to their euploid counterparts. We found that several neural differentiation markers, such as TuJ1 (neurons) and GFAP (glial cells), are upregulated in DS EBs. Furthermore, DS EBs showed increased expression of several genes involved in the TGF-β pathway – a critical regulator of pluripotency in embryonic stem cells and lineage determination in progenitor cells. In particular, DS EBs showed increased gene expression of several bone morphogenetic proteins (BMP) which have been shown to switch progenitors to an astrocytic fate. These observations and the lack of proper neural rosette formation in DS iPSCs suggest accelerated neural and glial differentiation and reduced progenitor cell development. Irregular cell fate specification in DS iPSCs is consistent with the fact that DS individuals show an increased number of astrocytes. Our results demonstrate dysregulation in cell lineage specification early in development of the DS brain, which may lead to altered synapse formation, function, and elimination, decreasing the efficiency of neuronal transmission.

Primary Student Presenter: Laylaa Ramos Arriaza

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Vijay Ramakrishnan

Poster Title: Response of Solitary Chemosensory Cells in the Respiratory Epithelium

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose: The upper airway has multiple mechanisms to protect against harmful agents. Chemosensors in the respiratory tract can trigger mechanical forces such as sneezing and coughing or deploy autonomic reflexes such as salivation or ciliary motility.5 Nasal solitary chemosensory cells (SCCs) reside in mouse and human airways as columnar epithelial cells and function to detect irritants in the airway surface liquid. When irritants bind to bitter taste receptors (T2R) on SCCs, a protective neurogenic reflex results in local inflammation.5 In addition to broadly tuned taste receptors, SCCs express chemotactic factors, yet their role of in the adaptive immune response remains unclear.

Proteases such as those found in house dust mite (HDM) and fungi are able to invade epithelial cells and trigger an adaptive immune response.1 Consequently, murine HDM or fungi exposure models are frequently used for study of airway type 2 allergic inflammation including diseases such as rhinosinusitis and asthma. Additionally, SCCs have been found to proliferate when stimulated by Alternaria alternata and Aspergillus fumigatus.2 We hypothesize that, when stimulated, SCCs can activate immune pathways that potentiate nasal epithelial inflammation and contribute to airway inflammation.

We will characterize the SCC-mediated inflammatory response by investigating the role of cytokines such as IL-25, which is known to contribute to airway hyperactivity and subepithelial fibrosis.4 The upper airway and sinuses are designed to filter particulates, antigens and pathogens3, and failure of a well orchestrated mechanism leads to microbial proliferation and results in chronic inflammation. Determining the role of SCCs in the immune response can provide an opportunity for novel therapies to manage irritant-induced airway inflammation.

Methods: Mice were stimulated intranasally for ten consecutive days with saline, denatonium (DEN), HDM and a combination of A. alternata, A. fumigatus, and HDM. Sinus tissue was harvested 24 hours after the final intranasal allergen stimulation. RNA was extracted from the respiratory epithelium. To characterize the profile of canonical taste transduction components we used qPCR to measure RNA expression of transient receptor potential cation channel subfamily M member 5 (TRPM5), alpha-gustducin (GUS) and doublecortin-like kinase1 (DCLK1). We also used qPCR to measure the

inflammatory response of the epithelium via thymic stromal lymphopoietin (TSLP) and interleukins 25, 33 and 6. All values have been normalized to GAPDH values and expressed as the fold change to saline exposure; fold changes greater than 1 are considered an increase of gene expression.

Results: When stimulated with HDM, a fold change greater than 1 to GAPDH was not observed for any of the genes tested in mice devoid of SCCs (Skn1aKO) or wild type mice. However, TRPM5GFP mice demonstrated increased expression of all genes tested and in TRMP5KO mice, only GUS and IL6 were increased. DEN induced fold changes for TSLP, IL25 and IL33 in Skn1aKO mice but not in TRPM5KO mice. When allergens were combined fold changes occurred in Skn1aKO mice for TSLP and IL25 but not IL33. While in TRPM5KO mice, only GUS, TSLP and IL6 were upregulated.

Conclusion: The immunological effects of SCCs in the nasal airway have not been fully elucidated. This study demonstrates the role of SCCs in the inflammatory response of the respiratory epithelium for various irritants. Gaining more knowledge about SCCs and their role in inflammation could be of aid in diseases such as chronic rhinosinusitis, allergic rhinitis, or asthma.

Primary Student Presenter: Ellen Rhodes

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jeffrey Olson

Poster Title: Intravitreal Polyacrylonitrile Complement Trap Preserves Retinal Function and Morphology in Macular Degeneration Mouse Model.

EY Rhodes, (MD, SOM), JL Morgenstern, A Strong, AA Jones and JL Olson, Department of Ophthalmology, University of Colorado Schoo

Final Category: Vision Sciences

Abstract:

Purpose: Age related macular degeneration (AMD) is currently the leading cause of blindness in the developed world. Although AMD has been extensively studied, the pathology is poorly understood. The non-exudative form, which accounts for nearly 90% of patients, has no treatment options. Elevated levels of complement factors (CF) in patients diagnosed with AMD has been previously found. However, it is unclear if increased CF is an important aspect of disease pathology or is a response to a currently unknown insult. Our lab has developed an intravitreous polyacrylonitrile (PAN) device which demonstrates a high affinity, capacity, and range for binding multiple CF. Through extensive in vitro and ex vivo studies we have shown the biocompatibility of the device and capacity to adsorb multiple CF. Here, we present an intravitreal PAN device capable of trapping CF and slowing AMD disease progression. This novel therapeutic approach could provide a treatment option for non-exudative AMD and eliminate or minimize the need for repeated injections.

Methods: PAN polymer devices were intravitreously placed in cfh-/- mice, which develop a retinal phenotype similar to non-exudative AMD in humans and have elevated vitreous CF levels. Disease progression was assessed through morphological and functional changes using H&E based histology, immunohistochemistry, and electroretinograms (ERG). The implant was left in place for 2 years and repeat ERGs were performed each month. Following interval testing, cfh-/- with PAN implant, cfh-/- with sham implant, and age matched controls were sacrificed.

Results: cfh-/- with sham implant and age-matched controls showed significant loss of a-wave and b-wave amplitude ($p<0.05$). Tissue sections showed an accumulation of C3 in the retina of age-matched controls and photoreceptor atrophy.

Conclusions: PAN complement trap preserves retinal function and morphology in cfh-/- mouse model,

supporting the role of abnormal CF in AMD disease progression.

Primary Student Presenter: Alyssa Shepherd

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Wagner

Poster Title: T-Cell Deficient Mice Demonstrate Reduced Atherosclerotic Plaque Burden

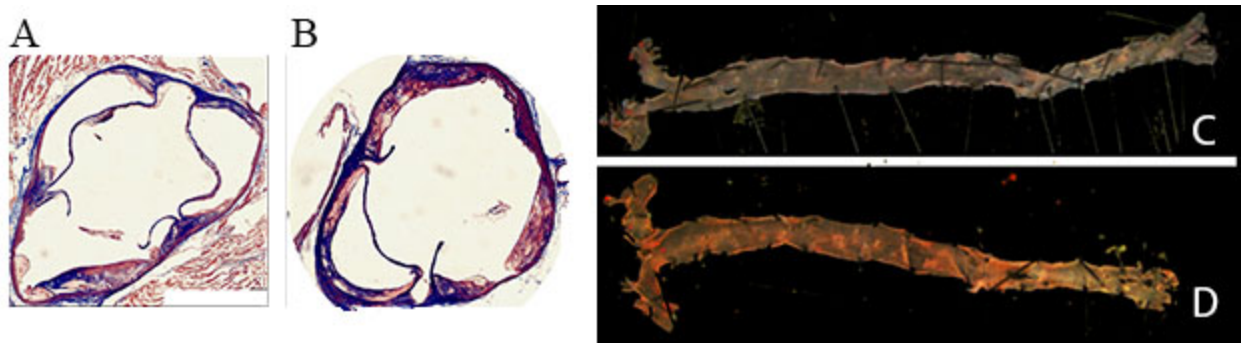
Final Category: Cardiovascular

Abstract:

PURPOSE OF STUDY: Atherosclerosis is characterized by arterial plaque deposition. The CD40-CD154 inflammatory dyad is a major driver of the auto-inflammation seen in atherosclerosis and type 1 diabetes (T1D). A sub-type of CD4+ T cells that express CD40 (Th40 cells) is increased in T1D, but has not been defined in atherosclerosis. Thus, this study seeks to explore the role of this pathogenic T-cell on plaque formation.

METHODS USED: ApoE-/- transgenic mice represent a model of atherosclerotic disease. We have generated a novel TCRα-/- ApoE-/- mouse model to investigate the role of Th40 cells. Baseline and 'add back' T cell experiments have been conducted. Mice are sacrificed at 8 months of age and then dissected to obtain the aortas and hearts. The aorta is used for en-face Sirius Red staining analysis while serial aortic valve cross sections are used to characterize the lesion in terms of area, volume, necrosis, and cellular content.

SUMMARY OF RESULTS: Trichrome-stained aortic valve cross sections show a significant reduction in overall plaque as well as ability to form advanced plaque (as determined by macrophage content) in the ApoE-/- TCRα-/- mouse model (shown in image B) as compared to its ApoE-/- counterpart (A). This reduction in plaque deposition is also shown in the Sirius Red analysis of the whole aorta. Representative samples of double KO mice show 16% plaque deposition (C) compared to 33% within ApoE-/- mice (D).



CONCLUSION: T-cell deficient ApoE-/- mouse models demonstrate a decreased plaque burden in comparison to the ApoE-/- counterparts illustrating that T-cells are implicated in atherosclerosis pathogenesis. Future studies will characterize the cell populations within the plaques.

Primary Student Presenter: Alexander Shu

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kenneth Hunt

Poster Title: Clinical Outcome Differences Between Single and Multi-Staged Transtibial Amputations

Final Category: Bone or Skeletal

Abstract:

BACKGROUND: Transtibial amputations are currently performed as single guillotine amputations or multi-staged amputations with primary and formalization amputations. This study assessed if multi-staged amputations provide improved clinical outcomes over single stage amputations and what patient groups it may benefit.

METHODS: We queried 207 records of patients receiving transtibial amputations from January 2015 through December 2018. Patient demographics, comorbidities, preoperative factors, surgical factors, and complications were recorded. Regression modeling was utilized to compare functional outcomes and influential perioperative variables between single and multi-staged groups. After accounting for exclusion criteria, 148 patient records were analyzed.

RESULTS: From the records analyzed, 49 patients (37%) underwent multi-stage amputation. Patients with multi-stage amputations had a hazard ratio of 0.60 for complication risk (P=0.04). The most common complications were infection (n=30) and wound dehiscence (n=21). This was the case for both amputation groups. For patients who were readmitted, 72% required amputation revision. Approximately half of the patients from each amputation group were ambulatory with a prosthesis (51% for single stage and 49% for multi-stage) after one-year post-surgery. Similarly, 27% of patients in both amputation groups were ambulatory with additional assistive devices (e.g., cane, front wheel walker).

CONCLUSIONS: Based on these preliminary results, single stage and multi-stage amputation groups demonstrate similar complication rates and recovery. However, multi-stage amputations may provide a protective effect against complication risk over single-stage amputations.

Primary Student Presenter: Joshua Smith

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Swati Patel

Poster Title: Small Polyp (6-9 mm) Resection Technique: Adoption of Optimal Technique over Time

Final Category: Other

Abstract:

Incomplete resection of colorectal polyps is an important cause of post-colonoscopy cancer. Cold snare technique is the gold-standard technique for removal of small (6-9 mm) polyps to avoid incomplete resection (associated with cold biopsy resection) and bleeding/perforation complications (associated with hot snare technique). Our aim was to describe small polyp (6-9 mm) resection technique from 2012 to 2019. We conducted a single center retrospective study at an academic Veterans Affairs Medical Center including colonoscopies performed between 2012-2019 where a polyp 6-9 mm was removed. Procedures were performed by board certified gastroenterologists and surgeons and their trainees. Chart review was performed to collect patient characteristics, procedure findings, polypectomy technique and pathology results. These results are displayed overall as well as stratified by different specialties and level of experience. Monotonic trends over time were examined using the Mann-Kendall test and the resulting p-values and tau test statistics are provided. Seventeen gastroenterologists and four surgeons performed 773 procedures where a 6-9 mm polyp was removed. There was a significant increase in cold snare use from 2012-2019 overall (tau 0.86, p=0.004) and individually for both specialties (GI: tau 0.64, p=0.035; surgery: tau 0.90, p=0.007) (table). There was a sharp increase in cold snare use among gastroenterologists from 2015 (72.0%) to 2016 (97.1%) and remained over 95% thereafter. For surgeons, there was a sharp increase in cold snare use from 2016 (75.9%) to 2017 (90.9%) and remained over 90% thereafter. From 2017 and onward, zero 6-9 mm polyps were removed with a cold forceps by gastroenterologists. Trainee involvement in procedures followed similar trends of improved practice over time (figure). There was significant improvement in adoption of cold snare resection for 6-9 mm polyps by gastroenterologists and surgeons. Gastroenterologists appeared to adopt optimal practice earlier than surgeons and have had a longer standing zero-tolerance use of cold biopsy forceps for these polyps compared to surgeons. Although it is encouraging that all endoscopists are adopting the optimal technique, delayed uptake emphasizes the importance of standardized continuing education and of quality assurance across specialties.

Primary Student Presenter: Kelly Stanek

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Shideh Majidi

Poster Title: Psychological Resource Use in Patients With Type 1 Diabetes who Endorsed Depressive Symptoms or Suicidal Ideation

Final Category: Metabolism and Endocrinology

Abstract:

Studies have shown higher depression rates in youth with type 1 diabetes (T1D) compared to the general population. Literature on suicidal ideation in T1D and how to provide appropriate follow-up for youth with depression or suicidal ideation is sparse. The objectives of this study were to evaluate the psychological resource use in adolescents with T1D after initial endorsement of depressive symptoms and/or suicidal ideation (SI), and to compare T1D and psychological characteristics between those who utilized resources versus those who did not. Patients at the Barbara Davis Center who scored positive for depressive symptoms or endorsed SI using the Patient Health Questionnaire 9 (PHQ-9) were identified by retrospective chart review. At time of PHQ-9 screening, patients with positive scores met with a provider or psychologist and were provided psychological resources for follow-up. T1D characteristics and use of psychological resources before and after the initial screen were recorded. Chi-square, t-tests, and descriptive analyses were used for data analysis. Of 1376 screened, 200 patients were identified with positive depressive symptoms (n=169) and/or positive SI (n=101). Of those identified, 52% (n=104) utilized psychological resources; specifically, 30% therapy, 5% psychiatric medications, and 17% both. Those who utilized resources had a higher initial PHQ-9 score (13.6 vs. 12.0, p=0.02), were female (53.2% vs. 37.5%, p=0.03), and utilized a continuous glucose monitor less often (22.1% vs. 34.4%, p=0.01). There was no difference between groups in race, age, T1D duration, insulin pump use, average follow-up PHQ-9 score, SI at initial screen or follow-up, or HbA1c. Although depressive symptoms and SI is common in the pediatric T1D population, only half those who have a positive screen utilize the resources given, indicating additional education and follow-up are needed to help patients obtain the appropriate counseling needed. While no changes in glycemic management were seen in those who utilized resources, HbA1c changes are gradual; thus, a longer interval may be needed to determine if HbA1c does improve. Future studies should investigate how to improve utilization of resources in youth with depressive symptoms or SI, particularly in males.

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-based identification of novel, small molecule inducers of phosphatase and tensin homolog (PTEN) upregulation in smooth muscle cells

Final Category: Cardiovascular

Abstract:

PTEN is known to antagonize PI3K/Akt signaling and our recent work shows that it also 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. In mice, PTEN overexpression reduced plaque area and preserved SMC contractile protein expression in intimal SMCs in the PCSK9 atherosclerosis model. PTEN overexpression also blunted 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 a high-throughput screen using a fluorescence based PTEN promoter-reporter system. We generated a lentiviral 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. We screened ~3400 compounds dosed at 10 uM using mCherry induction as a readout for PTEN expression. These were narrowed to 11 final compounds based on their level of mCherry induction and mechanism of action. Following in vitro testing of these 11 compounds, we focused on the DNMT1 inhibitor, 5-azacytidine (5-aza), due to its ability to induce PTEN expression in SMCs. We found that in addition to PTEN upregulation, 5-aza treatment increased basal expression of genes associated with a mature, contractile SMC phenotype such as SM-MHC, aSMA, Cnn1, and Tet2. Treatment with 5-aza also maintained contractile gene expression and reduced inflammatory cytokine expression after PDGF stimulation, suggesting that 5-aza is able to inhibit PDGF-induced SMC de-differentiation. However, the protective effects of 5-aza were lost in PTEN knockdown SMCs. These findings were confirmed in vivo using a tamoxifen-inducible, SMC-specific PTEN knockout mouse model (PTEN iKO) by performing carotid ligation injuries then treating with 5-aza for 3 weeks post injury. In WT controls, 5-aza treatment reduced neointimal formation and cell proliferation while maintaining contractile protein expression in SMCs. In contrast, 5-aza treatment was ineffective in PTEN iKO mice, suggesting that the protective effects of 5-aza are mediated through PTEN upregulation. Our data indicate that 5-aza is able to upregulate PTEN expression in SMCs, maintain SMC differentiation, and reduce in vivo pathological

vascular remodeling via PTEN induction.

Primary Student Presenter: Andrew Tannous

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Ethan Cumbler

Poster Title: Pseudohyponatremia: A case-study of a Multiple Myeloma Patient

Final Category: Hematology and Oncology

Abstract:

Hyponatremia is most common electrolyte disorder diagnosed in the hospital [1]. Untreated acute hyponatremia can lead to substantial morbidity and mortality as a result of osmotically induced cerebral edema, and rapid correction of chronic hyponatremia can cause severe neurologic impairment and death as a result of osmotic demyelination [2]. The risks implicated with managing hyponatremia emphasize the need for ruling out other factors before treatment occurs. With the availability of direct sodium-selective electrodes, it is easier to recognize pseudohyponatremia [3]. This case report highlights the importance of considering pseudohyponatremia and how deductive analysis of the etiology of low sodium readings can provide cues to reveal an ambiguous disease state.

Primary Student Presenter: Kumar Thurimella

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Cathy Lozupone

Poster Title: Employing Metabolomics and Microbiome Data to Build Algorithms for Interrogating Host-Microbe Interactions

Final Category: Metabolism and Endocrinology

Abstract:

The microbiome has been linked to the pathogenesis and salubrious states in the human body. However, much of the recent research has been driven by correlative studies, linking an unfavorable disease state to certain microbes. The push towards uncovering causative mechanisms between these interactions could yield a new era of therapeutics to ameliorate certain disease states. Untargeted metabolomics approaches have yielded an abundance of datasets but the complexity of the data interpretation remains. We introduce AMON: Annotation of Metabolite Origins via Networks and SCNIC: Sparse Cooccurence Network Investigation for Compositional data as tools to help address these issues. Both are open source software tools used to label compound origins of certain metabolites, from microbe to host or both to then build a higher level picture of groups of microbes that co-exist together. We illustrate the utility of AMON and SCNIC using a dataset (16s rRNA) from the gut microbiome and blood metabolome (LC/MS) of HIV positive individuals. This validation was part of a larger study of differences in fecal microbiomes in HIV and non-HIV populations. AMON uses KEGG Orthology to generate pathway enrichment and a hypergeometric test to verify the prediction of metabolites and their origin. SCNIC uses a microbiome table to build a correlation network to and groups of microbes are clustered together and collapsed into a smaller microbiome table. After benchmarking SCNIC, the optimal parameter values were an R-value above 0.5 for the SMD algorithm and for a gamma value above 0.1 for the LMM algorithm. With AMON applied to the data, 40 compounds were produced by bacteria alone, 58 by the host alone and 91 by both. Together, these analyses show that AMON can be used to predict the putative origin of compounds detected in a complex metabolome and SCNIC can help understand microbial dynamics.

Primary Student Presenter: Ivan Trang

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Samantha Holden

Poster Title: Prognostic Value of the UCSD Performance-Based Skills Assessment for Cognitive Decline in Parkinson's Disease

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Purpose of study: In Parkinson's disease (PD), functional impairments in cognitively demanding activities of daily living (ADLs) (e.g. paying bills, planning activities) can precede cognitive changes detectable by neuropsychological testing by up to 10 years. However, current screening protocols for cognitive decline do not objectively assess ADLs. The UCSD Performance-Based Skills Assessment (UPSA) is a 30-minute test for assessing ADLs that we recently validated in PD. We now examine the UPSA's potential to predict cognitive decline at an earlier time point than standard cognitive screening tests.

Methods: 47 non-demented PD participants (Table 1) completed the UPSA, neuropsychological battery, motor exam, and mood and quality of life scales at baseline and one year. Z-scores from neuropsychological tests were averaged into composite cognitive scores. Cognitive classifications were assigned by expert consensus conference.

Results: 11/47 (23.4%) PD participants converted to a more impaired cognitive class during the one-year follow-up. Baseline UPSA scores were not significantly different ($p=0.16$) between converters ($x=79.4$, SD 9.4) and non-converters ($x=83.6$, SD 7.8) and did not predict conversion (OR 0.95, $p=0.24$). However, lower baseline UPSA score predicted more rapid decline in the composite cognitive score in converters compared to non-converters ($F(1,9)=10.1$, $p=0.01$).

Conclusion: The UPSA may identify those at risk of more rapid cognitive decline in PD. Our cohort will continue to be followed over time to allow for more robust exploration of cognitive functional decline in PD.

Primary Student Presenter: Anastasiya Trizno

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jason Stoneback

Poster Title: Optimal Nail Diameter to Medullary Canal Ratio in Diaphyseal Tibia Fractures

Treated With Intramedullary Nailing

Final Category: Bone or Skeletal

Abstract:

Purpose: Most patients with diaphyseal tibia fractures achieve excellent outcomes with intramedullary nailing; however, up to 17% develop delayed union or nonunion. The goal of our study was to assess potential risk factors that may influence fracture healing in these patients with an emphasis on the nail dimeter to medullary canal (ND/MCD) ratio.

Methods: Adult patients that underwent intramedullary nailing of tibia fractures over a 10-year period were retrospectively reviewed. Exclusion criteria were inadequate follow-up (<12 months), additional lower extremity fractures and hardware, non-diaphyseal and pathologic fractures. ND/MCD ratio was measured in PACS Web with a digital caliper. Multi-variable logistic regression analyses were used to identify variables associated with complications. A receiver operating curve analysis was used to identify the ND/MCD ratio that best differentiated between subjects who developed a nonunion and those who did not.

Results: The odds of a complication among open fractures were 10.1 times [95% CI: 3.2 to 32.1, $p<0.0001$] times the odds of a complication among closed fractures. Age, sex, ND/MCD ratio, and presence of an open fracture were used to build a logistic model to predict nonunion (AUC=0.83; 95% CI: 0.71 to 0.96]. ND/MCD ratio cutoff of 85% was associated with the highest AUC value in an exploratory analysis differentiating between the subjects that developed nonunion and the ones that did not.

Conclusions: Presence of an open fracture is strongly associated with increased complication rates among patients undergoing intramedullary nailing of tibia fractures. ND/MCD ratio of <85% should be avoided as it may lead to nonunion development.

Primary Student Presenter: Brittany Truong

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Kristin Artinger

Poster Title: Loss of Neural Crest Cell Regulator PRDM1 Accelerates Melanoma Onset and Progression

Final Category: Hematology and Oncology

Abstract:

Melanoma is an aggressive, deadly skin cancer derived from melanocytes, a neural crest cell derivative. Melanoma cells mirror neural crest cells in that they exhibit the same gene expression patterns and utilize similar cellular mechanisms for their development. Here we studied the role of neural crest regulator PRDM1 in melanoma onset and progression. We found that high PRDM1 expression in human melanoma is correlated with better patient survival. When we lose one copy of prdm1a in a zebrafish model (Tg[mitfa:BRAFV600E];p53-/-;prdm1a+/-), melanoma onset occurs more quickly and the resulting tumors are more invasive, suggesting that PRDM1 normally acts as a tumor suppressor. To determine the mechanism by which this occurs, we studied PRDM1's role in normal melanocyte development in zebrafish embryos. We found that Prdm1a is required for melanocyte differentiation and its loss results in an increase in expression of SOX10, a melanocyte stem cell marker and melanoma marker. This same trend is observed in our zebrafish adult tumors and when we knockdown PRDM1 in melanoma cell lines. Therefore, we demonstrate that PRDM1 functions as a tumor suppressor in melanoma through regulation of SOX10 expression.

Primary Student Presenter: Logan Tyler

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Robert Doebele

Poster Title: MET-mediated acquired resistance to tyrosine kinase inhibitor in ROS1 fusion positive non-small cell lung cancer

Final Category: Pharmacology and Physiology

Abstract:

ROS1 gene fusions have been identified in numerous cancer types, but is predominantly found in non-small cell lung cancer (NSCLC). ROS1 gene fusions are the product of chromosomal rearrangements which generate constitutive expression and activation of the ROS1 kinase domain, and subsequent aberrant downstream proliferative and survival signaling pathways. Currently, there are two ROS1 kinase inhibitors, which are US FDA approved, crizotinib and entrectinib, both of which generate tumor response rates in excess of 70% and demonstrate prolonged disease control. However, acquired resistance to TKIs is inevitable, and has been reported in ROS1 fusion-positive NSCLC tumors by our group and others. Herein, using a patient-derived NSCLC cancer cell line (CUTO28) harboring a TPM3-ROS1 fusion, we derived an entrectinib-resistant cell line, CUTO28-ER through in vitro culture under drug selection. Utilizing western blotting, polymerase chain reaction (PCR) assays, next-generation sequencing (NGS), fluorescence in situ hybridization (FISH) imaging, and proximity ligation assay (PLA) imaging, we identified: (1) MET-mediated bypass signaling as an acquired resistance mechanism to entrectinib, (2) upregulation of MET signaling is accomplished via MET gene amplification, and (3) resistance could be overcome by the dual ROS1/MET inhibitor crizotinib. To our knowledge, this is the first reported case of MET-mediated acquired resistance in a ROS1 fusion-positive cancer. This finding is supported by another primary, patient-derived cell line (CUTO38) harboring a CD74-ROS1 fusion, which was derived following acquired resistance to a ROS1 TKI in clinic and displays elevated MET expression and dependence on MET for cell proliferation and survival. This finding may allow prediction of future TKI resistance in ROS1 positive NSCLC patients who experience disease progression on entrectinib or other ROS1 TKIs which do not inhibit MET.

Primary Student Presenter: Brett Wiesen

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Granville Lloyd

Poster Title: Association of C-Reactive Protein Levels and Lower Urinary Tract Symptoms in Men and Women

Final Category: Surgery

Abstract:

Lower urinary tract symptoms (LUTS) are highly prevalent among aging men and women. The etiology of this process remains unclear. C-reactive protein (CRP) is an acute-phase protein associated with systemic inflammation and may predict voiding symptoms. Our goal was to explore and compare this relationship in men and women.

Cohorts of 1,025,645 men (398,526 ≥ age of 45 at time of sampling) and 1,117,264 women (524,685 ≥ age of 45 at time of sampling) were analyzed and patients with only a single visit excluded. Of these, 27,228 men and 53,294 women had at least one documented CRP value. Analysis of these patients was performed to correlate LUTS treatment to serum CRP levels. All reported Odds Ratios were calculated and subsequently adjusted for race/ethnicity, age, hypertension, diabetes mellitus, depression, and obesity/metabolic syndrome.

A statistically significant association was observed between CRP levels >10mg/L and treatment for LUTS among both men and women (Table 1).

We observe an association between elevated CRP levels and likelihood of LUTS treatment in both men and women. CRP level was statistically significant as a continuous variable, and also discriminatory at levels >10mg/L but not in 3mg/l - 10mg/L. The role and significance of CRP in LUTS is unknown, but these findings suggest that voiding symptoms associated with elevated CRP regardless of gender.

	CRP (mg/L)	Unadjusted Odds Ratio (95% CI)	P-value	Adjusted Odds Ratio (95% CI)	P-value
Women (n=53,294)	< 3 (33.8%)	1.00	--	1.00	--
	3 – 10 (31.8%)	1.15 (1.03 – 1.29)	0.014	1.08 (0.98 –1.18)	0.11

	> 10	1.54 (1.39 – 1.69)	< 0.001	1.23 (1.13 –1.34)	< 0.001
	Log (CRP)	1.13 (1.11 – 1.15)	< 0.001	1.06 (1.03 –1.08)	< 0.001
Men (n=27,228)	< 3 (30.4%)	1.00	--	1.00	--
	3 – 10 (27.2%)	1.22 (1.12 – 1.32)	< 0.001	1.11 (1.00 –1.23)	0.051
	> 10 (42.4%)	1.53 (1.42 – 1.64)	< 0.001	1.28 (1.17 –1.40)	< 0.001
	Log (CRP)	1.12 (1.10 – 1.13)	< 0.001	1.07 (1.04 –1.09)	< 0.001

Primary Student Presenter: Sophia Wolfe

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Liron Caplan

Poster Title: Cessation of Tumor Necrosis Factor Inhibitors in Psoriatic Arthritis and Psoriasis

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose of Study: Psoriatic arthritis (PsA) is a chronic inflammatory disease of the joints and skin that affects 1/1000 people in the US. Tumor necrosis factor inhibitors (TNFi) are used when symptoms are severe. However, current research describing TNFi persistence rates, defined as time from initiation to discontinuation of the drug, is inconsistent and incomplete. This study examined characteristics associated with persistence of TNFi and reasons for discontinuation.

Methods Used: US veterans enrolled in the Program to Understand the Longterm Outcomes in Spondyloarthritis from 2007 – 2017 who 1) were diagnosed with PsA or psoriasis and 2) had been treated with a TNFi were included in the study. Stata was used to conduct time-to-event analyses and multivariate analyses.

Summary of Results: 321 individuals with 931 TNFi courses were included in the study. The mean age was 55.4 years, and 83.8% of the cohort continued at least one TNFi course at one year. TNFi course order (HR 1.096, $p<0.001$), former smoker (HR = 0.827, $p=0.037$), and PsA duration in years (HR 0.991, $p<0.001$) were significantly correlated with discontinuation of a TNFi. Other demographics were not independent predictors of discontinuation. The most commonly cited reason for discontinuing TNFi treatment was secondary failure (33%), defined as a loss of prior efficacy after >6 months of treatment.

Conclusions: This study found that most clinical characteristics did not affect persistence on a TNFi, suggesting that persistence is difficult to anticipate. Since persistence is suboptimal, further research should study possible mechanisms to explain loss of efficacy, including the immunogenicity of TNFi, in an effort to improve treatment outcomes.

Primary Student Presenter: Jerry Yang

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Sarah Tevis

Poster Title: Delays in Breast Cancer Diagnoses: Do Patients Have Higher Distress?

Final Category: Surgery

Abstract:

Background: There is no current standard of care for timing between abnormal mammogram and breast biopsy. For many patients undergoing workup of a new mammographic finding, the time to definitive diagnosis is full of uncertainty, anxiety, and stress. We sought to evaluate the relationship between time from mammogram to biopsy and distress in patients newly diagnosed with breast cancer.

Method: Newly diagnosed breast cancer patients who completed a distress screening tool at their initial multidisciplinary clinic visit at an academic institution between 2016 and 2019 were retrospectively evaluated. The distress screen asked patients to rate their distress level in emotional, social, health and practical domains on a scale of 0-10. A score >5 was defined as "high distress" based on current clinical practice guidelines at this institution. Delay from mammogram to biopsy was defined as $\geq$ 31 days, or the fourth quartile within the study population. Wilcoxon two-sample test and Wilcoxon rank sum test were used for statistical analysis.

Results: Two hundred fifty-eight patients completed the distress screen. The median time between mammogram and biopsy was significantly longer for patients 50 years or older (11 days) compared to patients 49 and younger (6 days) (P = 0.003). Median distress scores in each domain were: emotional 7 (IQR = 5-8), social 3 (IQR = 0-6), health 7 (IQR = 6-8), and practical 4 (IQR = 1-6) (Table 1). Interestingly, patients in the non-delayed group reported higher health related distress (7) compared to patients in the delayed group (6, p=0.04). No difference in distress level were found for emotional, social, and practical distress between the delayed and non-delayed groups (p >0.05 for all).

Conclusion: Longer time from abnormal mammogram to definitive diagnosis of breast cancer was generally not associated with higher levels of distress in our study population. These findings may be specific to our patient population where patients can typically schedule a biopsy within few days of an abnormal imaging finding. Therefore, patients with higher distress or anxiety may seek out earlier biopsy appointments than patients with less distress. As time elapses, patients may also engage in coping behaviors such as online education, peer support, and spiritual practices and thereby decrease distress levels.

Table 1. Relationship between Timing to Definitive Diagnosis of Breast Cancer and Patient Distress

Distress Domain	Overall (n=258) Median (IQR)	Delay (n=240) Median (IQR)	No Delay (n=18) Median (IQR)	P value
Emotional	7 (5-8)	7 (5-8)	6 (4-7)	.13
Social	3 (0-6)	2.5 (0-6)	3 (0-4)	.75
Health	7 (6-8)	7 (6-8)	6 (5-7)	**.04**
Practical	4 (1-6)	4 (1.5-6)	3 (1-6)	.69

Primary Student Presenter: Tessa Zangara

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Lisa Ferrigno

Poster Title: Missed Chemoprophylaxis Doses Matter: A Multicenter Analysis of Venous Thromboembolism Chemoprophylaxis in Traumatic Brain Injury Patients

Final Category: Surgery

Abstract:

Purpose: Traumatic brain injury (TBI) is associated with morbidity/mortality in trauma patients. Concern for intracranial hemorrhage leads to delayed/missed doses of venous thromboembolism (VTE) chemoprophylaxis (VTE-C) and higher risk of thrombosis. There is no consensus about use of VTE-C in TBI patients (TBI-P) and we hypothesize late/missed VTE-C in TBI-P increases VTE.

Methods: A two-year multicenter study of adults with head abbreviated injury scale ≥2, ≥2 head CTs, and LOS ≥72h comparing early v late (48h) VTE-C initiation and proportion with missed v those without missed doses.

Results: Of 1,803, 8% developed VTE. Median age was 55, 69% were male and 95% had blunt injury. Median time to VTE-C initiation was 63h. VTE-C was not given in 29%; late in 47%; given within 48h in 25%; and given within 24h in 3%. Of 1,288 receiving VTE-C, 1,092 missed no doses. In patients with missed doses (196), there was longer time to initiation (57 v 63h, p=0.02) and they were more severely injured (ISS 27 v 22, p<0.001). They had more polytrauma (22% v 9%, p<0.001), higher rates of VTE (20% v 8%, p<0.001), longer hospital LOS (17 v 8 days), and longer ICU LOS (12 v 4d), (both p<0.0001). There was no significant reduction in VTE with early VTE-C for the group, however, among TBI-P who underwent delayed neurosurgery, early VTE-C was protective against VTE (HR 0.81, 95% CI 0.73–0.91). After multivariable regression, missed VTE-C doses significantly predicted development of VTE (HR 1.03, p=0.01).

Conclusions: VTE-C is often delayed >48 h or held in TBI-P, predicting higher VTE risk. Future studies are needed to examine the safety of early and perioperative VTE-C.