University of Colorado **Anschutz Medical Campus**

32nd ANNUAL STUDENT RESEARCH FORUM

COLLEGE OF NURSING

GRADUATE SCHOOL

SCHOOL OF DENTAL MEDICINE

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PUBLIC HEALTH

DECEMBER 12th, 2017
ANSCHUTZ MEDICAL CAMPUS
Education 2, North and South

32nd ANNUAL
UNIVERSITY OF COLORADO DENVER
ANSCHUTZ MEDICAL CAMPUS
STUDENT RESEARCH FORUM

Tuesday, December 12th, 2017

Poster Sessions
1:00-2:15 pm
2:15-3:30 pm

ANSCHUTZ MEDICAL CAMPUS
Education 2, North and South

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

Poster Session Judges

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

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

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Primary Student Presenter: Davis Aasen

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Meguid

Poster Title: *Systematic Review Of Surgical Risk Communication To And Retention By Patients*

Final Category: Surgery

Abstract:

Systematic Review Of Surgical Risk Communication To And Retention By Patients. DM Aasen, (MD, MS), K Hammermeister MD, AV Prochazka MD MSc, RA Meguid MD MPH, University of Colorado School of Medicine, Aurora, CO

Purpose

Informed consent is an ethical and legal imperative of any surgical practice. While effectively communicating procedural risks to patients is an integral component of informed consent, no recent systematic review has established how well this is executed. The goal of this systematic review is to assess what risk information surgeons provide patients during consent, what information patients desire, and how well patients retain this risk information.

Methods

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses as a guide, PubMed was systematically searched for publications on preoperative communication of risks to adult surgical patients, without date restrictions. Selected studies either provided objective evaluation of patient comprehension of risk information, examined what risk information is shared with patients in practice, or evaluated patient desires for risk information.

Results

Of 4,375 studies screened on initial literature review, 72 met inclusion criteria. Twelve studies reported that patients generally desire detailed possible risk and complication information; 18 studies used clinical observation, chart analysis, and surveys, to evaluate what risk information patients are provided. Authors repeatedly reported "inadequate and inconsistent" provision of information by providers. Forty-six studies investigating patient risk information retention found a wide variety of patient recall. For example, studies measuring recall immediately after consent had a median and interquartile range of 48% (45-61%). Of studies evaluating the effect of a communication support tool or technique on

patient recall, just over half reported statistically significant improvement, which ranged from 6-37%.

Conclusion

Based on this comprehensive review, current surgical risk communication is inadequate when compared to the ethical standard of informed consent and patient desires due to wide variance in what risk information is provided to and retained by patients. This indicates that significant opportunities exist to improve consent practice. The future development of surgical communication tools and techniques should emphasize optimizing and standardizing risk communication specifically, leading to improved risk information delivery to and retention by patients.

Primary Student Presenter: Kristina Barber

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Courtney O'Donnell

Poster Title: *Case Series: Rotationplasty for Traumatic and Significant Physeal Injuries*

Final Category: Surgery

Abstract:

CASE SERIES: ROTATIONPLASTY FOR TRUAMATIC AND SIGNIFICANT PHYSEAL INJURIES. K Barber, (M.D., SOM), C O'Donnell, T Heare. University of Colorado School of Medicine; Children's Hospital Colorado.

Though initially described for use in treatment of lower extremity tumors, the Van Ness rotationplasty preserves the ankle for use as a knee joint which provides excellent function. More reporting of cases should provide a foundation for use of this surgery in other settings. The purpose of this study is to present three cases of primary reconstruction with rotationplasty in the setting of trauma or significant physeal disturbance from infection. Another case is detailed where initial reconstruction following trauma led to deformity which was successfully reconstructed by rotationplasty.

Data were retrospectively collected from electronic medical records for four patients treated at Children's Hospital Colorado between 01/01/2000 and 12/30/2016 who presented with acute traumatic injury or significant physeal disturbance leading to lower extremity deformity. Three patients underwent rotationplasty as primary treatment and the fourth patient as a revision.

Four patients with significant physeal disturbance and leg deformity resulting from trauma or infection were reconstructed with rotationplasty. Three were initial repairs while the fourth corrected a valgus deformity following initial repair with internal and external fixation. Follow up was between 10 months and five years. Two patients had re-operations for skin necrosis or infection. The other two patients had no reported complications.

In the setting of traumatic injury or physeal disturbance leading to significant lower extremity deformity, rotationplasty should be considered as a primary surgical intervention. With the drawback of suboptimal cosmetics, this procedure leads to exceptional functionality for the patient and comparable complication rates with amputation alone.

Primary Student Presenter: Colleen Bartman

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Tobias Eckle

Poster Title: *Circadian Mechanisms in Hypoxic Metabolic Adaptation*

Final Category: Cardiovascular

Abstract:

Circadian Mechanisms in Hypoxic Metabolic Adaptation: CM Bartman, (PhD, GS), Y Oyama, and T Eckle, University of Colorado Anschutz Medical Campus Cell Biology, Stem Cells, and Development Graduate Program.

Objectives: A wide search for ischemic preconditioning mechanisms identified the circadian rhythm protein Period 2 (PER2) to be cardioprotective. Studies on cardiac metabolism found a key role for PER2 in mediating metabolic dependence on carbohydrate metabolism. We profiled PER2 dependent mechanisms of hypoxic metabolic adaptation and found a strong association of PER2 with glycolysis, the TCA cycle, or mitochondrial respiration.

Methods: We use in vitro and in vivo studies and basic molecular and cellular biology techniques including qRT-PCR, western blotting, an in-situ mouse model for cardiac ischemia and reperfusion injury, chromatin immunoprecipitation, co-immunoprecipitation, ELISA, and glycolytic or fatty acid stress tests.

Results: Studies in PER2 deficient cells revealed a critical role of PER2 in the transcriptional regulation of anaerobic glycolysis by facilitating the binding of hypoxia inducible factor (HIF1A) to the promotor of lactate dehydrogenase. We found key TCA cycle enzymes co-immunoprecipitated with PER2 and sirtuin dependent regulation of TCA enzyme activity. Metabolic studies identified PER2 as a regulator of fatty acid or mitochondrial metabolism. In fact, we identified PER2 as a transcriptional regulator of a mitochondrial complex in hypoxia. Subsequent studies on intense light mediated induction of circadian PER2 in mice or humans implicated PER2 as a therapeutic target of cellular energy metabolism.

Conclusions: Our studies show that PER2 is a key regulator of cellular energy metabolism and has the potential to optimize metabolic adaptability during hypoxia or ischemia, which suggest potential circadian targets as preventative or therapeutic strategies for myocardial ischemia.

Primary Student Presenter: Diana Clabots

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Daniel Frank

Poster Title: *Analysis of the Eukaryal Microbiome of the Lung by 18S Ribosomal RNA in Cystic Fibrosis Patients*

Final Category: Microbiology and Infectious Diseases

Abstract:

ANALYSIS OF THE EUKARYAL MICROBIOME OF THE LUNG BY 18S RIBOSOMAL RNA IN CYSTIC FIBROSIS PATIENTS

Clabots, DE, (MD, SOM).1

Holt, JW.2

Robertson, CE. 1

Zemanick, ET.1

Frank, DN.1

Harris, JK.1

1 University of Colorado School of Medicine, Denver, CO

2 Oregon Health Science University, Portland, OR

Purpose of Study Cystic fibrosis (CF) is the most frequently inherited autosomal recessive life-shortening disease in people of European descent. Recurrent lung infections and the consequent inflammatory response in the lungs result in airways damage, the leading cause of morbidity and mortality in these individuals. The bacterial microbiota of the lungs in CF have been extensively characterized by culture as well as by culture independent methodologies. In contrast, much less is known about the fungi associated with CF, which have been characterized primarily by culture-based techniques. We expect that analyzing the fungal microbiome of the lung by amplification of 18S ribosomal RNA will reveal a more diverse fungal microbiome than indicated by culture.

Methods Used Bronchoalveolar lavage samples were collected from pediatric CF patients as well as

disease control patients from 13 different institutions in the United States. DNA was extracted from the resultant lavage fluid. The fungal DNA from 90 patient samples was amplified using barcoded, broad-range 18S rRNA PCR primers. The pooled amplicons were sequenced on an Illumina MiSeq platform. Samples that produced less than 5000 sequence reads were removed from the analysis.

Summary of Results Sixty-seven eukaryal taxa were detected by sequencing, with a median of 24,035 sequence reads per sample. Sixty-six out of 89 patient samples were positive for fungal DNA by 18S rRNA PCR. Of these 66 samples, 30 (45%) of these samples were culture negative. Of the samples that were positive by both methods, an average of 5 fungal taxa per sample was detected by 18S PCR while an average of 1.3 fungal taxa per sample was detected by fungal culture.

Conclusions The fungal microbiome of the lung in cystic fibrosis patients is more diverse by 18S rRNA PCR than previously indicated by fungal culture. Our data suggests that fungal species are present in the lungs of most of these patients, yet they often go undetected by culture.

Primary Student Presenter: Chrisopher Covey

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Martin Voskuil

Poster Title: *Mycobactin inhibits clofazimine killing of mycobacteria*

Final Category: Microbiology and Infectious Diseases

Abstract:

Myocbactin inhibits clofazimine killing of mycobacteria

Mycobacteria utilize specialized mechanisms to acquire iron from their environment due to its importance in a variety of vital biological processes. The siderophore mycobactin produced by Mycobacterium tuberculosis is an essential component of virulence and is a potential target for chemotherapy. While mycobacterial growth media is typically replete with iron, which lowers the need for mycobactin, microenvironments encountered during infection vary in both their chemical properties and iron availability. The antibiotic clofazimine has been used clinically to great effect against mycobacteria such as Mycobacterium leprae and Mycobacterium abscessus and has high bactericidal activity against M. tuberculosis both in vitro and in standard mouse models. However, clofazimine performs poorly against M. tuberculosis in animal models in which extracellular bacilli exist in necrotic lesions and is thus not widely used in humans. We observed that exposing Mycobacterium smegmatis to clofazimine in low-iron medium significantly reduced aerobic killing while normal high-iron media facilitated a period of growth during clofazimine treatment that was followed by a rapid death phase eventually resulting in culture sterilization. The phenomenon was also observed in M. tuberculosis. Genome expression analysis of M. tuberculosis exposed to clofazimine revealed increased expression of iron acquisition machinery, particularly in genes related to the production and trafficking of mycobactin. Radioactive analysis using C14-labeled salicylic acid confirmed that mycobactin production correlated with clofazimine tolerance. Further, genetic inhibition of mycobactin greatly increased the timing and rate of clofazimine killing, and the effect was replicable using a commercial mycobactin inhibitor salicyl-AMS. Based on these findings, we posit that mycobactin enables protection against clofazimine.

Primary Student Presenter: Lyndsey Crump

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Traci Lyons

Poster Title: *Investigating the Role of Semaphorin 7a in Breast Cancer Progression*

Final Category: Hematology and Oncology

Abstract:

While anti-estrogen based treatments are initially effective for hormone receptor
positive (HR+) breast cancers, which express the estrogen and/or progesterone
receptor (ER/PR), these tumors often recur and metastasize, emphasizing the
need for additional therapeutic targets in ER/PR+ disease. We observe that
semaphorin 7a (SEMA7A) expression in ER/PR+ patients in the METABRIC
dataset confers significantly decreased survival rates by Kaplan-Meier analysis.
Thus, we hypothesize that SEMA7A is a potential biomarker for aggressive
disease and/or a novel therapeutic target for recurrent HR+ breast cancer.
Utilizing multiple 2D and 3D in vitro approaches with human and mouse
tumor cells, we show that shRNA-mediated knockdown (KD) of SEMA7A results
in cell growth defects and reduced invasive potential. Loss of SEMA7A also
increases apoptosis in attached and forced suspension culture conditions.
Finally, we demonstrate that expression of SEMA7A is regulated by the ovarian
hormones estrogen and progesterone in a receptor-dependent mechanism.
However, we also observe increased expression of SEMA7A with stabilization of
HIF1α, suggesting its expression may be context-dependent. Overall, these

data support SEMA7A as an important driver of multiple hallmarks of cancer in ER/PR+ breast cancer, including cell growth, invasion, and resisting death. As SEMA7A expression is low in normal breast cells, it may be a novel therapeutic target with low toxic side effects

Primary Student Presenter: Tiffany Cung

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mark Laudenslager

Poster Title: *PRETRANSPLANT DEPRESSION, STRESS, AND AXIETY IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS*

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

PRETRANSPLANT DEPRESSION, STRESS, AND AXIETY IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

T Cung, (M.D., SOM), C Natvig, T.S. Sannes, M.L. Laudenslager

University of Colorado School of Medicine, Aurora, CO

Purpose of Study Allogenic hematopoietic stem cell transplantation (Allo-HSCT) is a demanding treatment for cancer patients with hematopoietic malignancies. These patients experience significant stress, which may have an impact on the treatment and the outcomes. This study is to analyze the baseline psychological characteristics of these patients and their relationships. .

Methods Used Prior to transplant, psychological measures were collected from Allo-HSCT patients (N=159) using the Perceived Stress Scale (PSS), Center for Epidemiologic Studies Depression Scale (CESD), and State-Trait Anxiety Inventory (Stai_S). Information on their demographics was collected at baseline. Chart review information was available.

Summary of Results The mean age of the patients was 53.3 years old (SD=14.8), with 64.8% were male. The mean PSS was 21.7 (SD= 8.0), placing them in the range for moderate stress. CESD mean score was 20.4 (SD=6.7), exceeding the clinical cutoff of 16. The mean Stai_S score was 36.8 (SD=11.6), exceeding population norms for this age group. There is significant correlation between CESD and PSS (r=0.550, p=0.000), between CESD and Stai_S (r=0.529, p=0.000), and between PSS and Stai_S (r=0.686, p=0.000).

Conclusions Allo-HSCT patients at baseline have elevated PSS, Stai_S, and CESD scores. These values indicate Allo-HSCT patients prior to transplant experience stressors affecting their psychological health, which may affect their treatment outcomes. There are significant correlations between depression, perceived stress and anxiety, demonstrating that these psychological measures are often comorbid. Further studies are needed to explore how the baseline measures affect treatment outcomes.

Primary Student Presenter: Ariel Kiyomi Daoud

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Emily Stuart

Poster Title: *The Relationship Between Flexibility and Low Back Pain In Female Adolescent Gymnasts*

Final Category: Bone or Skeletal

Abstract:

The Relationship Between Flexibility and Low Back Pain in Female Adolescent Gymnasts. AK Daoud (MD, SOM), MN Potter, DR Howell, and EA Stuart, Sports Medicine Center, Children's Hospital Colorado, Aurora, CO, USA; Department of Orthopedics, University of Colorado School of Medicine, Aurora, CO, USA

   The objective of this study was to investigate the association between lower back pain, flexibility, and individual characteristics in adolescent female gymnasts. Female gymnasts ages 6-18 years competing in the USA Women's Artistic Junior Olympic Program levels 3-10 were enrolled. Subjects underwent active and passive flexibility measurements at the shoulder, hip, quadriceps, and hamstrings. They were then asked if they experienced back, shoulder, and/or hip pain in the last 12 months. Those with a history of back pain then completed a modified Micheli Functional Scale and Oswestry Low Back Pain Scale. Demographic information, clinical characteristics, and flexibility measurements were compared between gymnasts with and without back pain in the previous 12 months using t-tests and Chi square tests. A binary multivariable logistic regression model was used to assess the association between back pain in the past 12 months, flexibility, and participant characteristics. Fifty-one gymnasts participated: 19 reported back pain in the past 12 months (age= 13.3±3.3 years; BMI= 18.6±2.6) and 32 did not (age= 11.1±2.4 years; BMI= 17.5±1.9). Those with back pain reported more hours per week of gymnastics participation (22.7±6.9 vs. 18.5±5.9 hours/week; p= 0.026), and a higher proportion reported experiencing menarche (37% vs. 6%; p= 0.009) than those who did not. Passive Hookline shoulder flexion (178.6±6.1 vs. 180.0±0.0 degrees; p= 0.008) and active right prone knee flexion (131.1±9.2 vs. 132.0±5.1 degrees; p= 0.07) were lower among those who reported back pain. When considered together, having experienced menarche at the time of assessment was independently associated with presence of self-reported back pain the past 12 months (adjusted odds ratio= 7.317, 95% CI= 1.22-43.87; p= 0.029). Risk factors for back pain in adolescent female gymnasts may be more complex and multifaceted than simple flexibility measurements used in this study. While the history of low back pain and flexibility were not significantly associated, low back pain was significantly more frequent in gymnasts with history of menarche. As back pain etiology is likely related to many factors, clinicians

should consider intrinsic patient factors, such as pubertal maturation, when considering risk of future back injury.

Primary Student Presenter: Ashley Denney

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MD/PhD

Year: 5th

Mentor: Michael McMurray

Poster Title: *Impact of Folding Dynamics on the Dimerization and Dominance of Tumor-Derived p53 Mutants*

Final Category: Hematology and Oncology

Abstract:

Impact of Folding Dynamics on the Dimerization and Dominance of Tumor-Derived p53 Mutants. A Denney, (Ph.D., Grad School), M McMurray, Department of Cell and Developmental Biology, University of Colorado, Denver, CO.

   Purpose: p53 is a potent tumor suppressor widely mutated in human tumors. Mutant p53 can behave in a dominant-negative fashion resulting in mixed mutant:wild-type (WT) tetramer formation and diminished WT activity. Mutant p53 can also behave in a recessive fashion and factors that influence the degree of dominance or recessivity are not well understood. p53 folds and dimerizes rapidly during translation and understanding the kinetics of co-translational biogenesis as it impacts post-translational tetramer assembly and dominance is lacking in p53 biology.

   Methods: We are testing the hypothesis that chaperones impart a recessive phenotype to select p53 mutants by retarding nascent p53 biogenesis and hindering subsequent formation of mixed tetramers with WT. We use a bimolecular fluorescence complementation (BiFC) approach to identify chaperone interactions specific to mutant p53 in Saccharomyces cerevisiae. We also assess the functional impact of chaperone overexpression on the function of mutant p53. Further, we explore whether cycloheximide-slowed translation impacts the timing of p53 dimerization.

   Results: p53(V272M) is depleted in the nucleus at high temperature and recessive when co-expressed with WT. We have identified several cytosolic Hsp70s, a chaperonin, and a disaggregase that interact with p53(V272M) and not with WT. Select overexpression of these chaperones impairs the function of p53(V272M). Dimerization of p53 is more likely to occur co-translationally vs. post-translationally when translation speed is slowed.

   Conclusions: Our data support a model where recessive mutants are out-competed by WT during de novo tetramer assembly. Future directions include direct measurement of mixed tetramers in yeast and MCF7 cells.

Primary Student Presenter: Will Dewispelaere

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Isabelle Buard

Poster Title: *Rhythmic Enhancement of Motor Performance: Cortical Mechanisms in Healthy Older Adults and Parkinson's Disease.*

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Rhythmic Enhancement of Motor Performance: Cortical Mechanisms in Healthy Older Adults and Parkinson's Disease.

W Dewispelaere (MD, SOM), I Buard, D Rojas, P Teale, B Kluger, Department of Neurology

   Background: Parkinson Disease (PD) is a disease characterized by symptoms such as tremor, slow movement, and rigidity. Auditory rhythm can improve the motor symptoms of PD. However, the cortical mechanisms underlying rhythm processing in PD are unknown. Our objective was to elucidate the cortical regions involved in rhythm processing and how PD alters patterns of activation.

   Methods: PD patients and aged-matched healthy controls (HC) underwent magnetoencephalography (MEG) scanning during a rhythmic tapping task, during which subjects tapped a button along with an auditory rhythmic cue. Custom Matlab scripts were used to calculate reaction times for each subject. MEG data was cleaned to remove artifact and imported into SPM8 for source analysis.

   Results: 23 PD and 21 HC subjects were recruited for the study. Each group had 12 females and there no significant differences in age or handedness between groups. There were no between-group differences in reaction time. Rhythmic tapping activated a wide network of cortex in both groups. Active regions in both groups included bilateral motor cortex (M1), superior temporal gyrus (STG), supramarginal gyrus (SMG), and superior frontal gyrus (SFG). There was more activity in the left middle temporal gyrus (MTG) and right SMG in the PD group compared to the HC group.

   Conclusions: Rhythm activates large areas of cortex in HC and people with PD. However, those with PD rely on additional activation in the right MTG and SMG. The MTG is involved with sound recognition and processing, while the SMG is integral to multimodal integration. Thus, the pathophysiology of PD likely requires the brain to compensate for abnormal basal ganglia output with increased sensory processing and integration to entrain auditory and motor systems.

Primary Student Presenter: Lynn Dexter

Additional Presenter(s): Marie Free Robert Kowlaski

Presenting School: Public Health

Degree Seeking: MPH

Year: 3rd

Mentor: Kirk Bol

Poster Title: *The Role of Induction of Labor in Incidence of Acute Respiratory Dysfunction in Newborn Infants.*

Final Category: Healthcare and Public Health

Abstract:

LM Dexter, (MPH, MS), M Free, R Kowalski, Department of Epidemiology, Colorado School of Public Health, Denver, CO. Purpose of Study: Induction of labor (IoL) has more than doubled in the United States since 1990, accounts for 25% of births, and is associated with newborn complications. We sought to assess whether IoL predicted neonatal respiratory dysfunction (RD), utilizing a large, multi-year, single-state birth registry.

Methods: This retrospective cohort investigation included subjects enrolled in the Colorado Birth Certificate Registry from 2007 through 2015, meeting the following criteria: 1. Adults age ≥20 and ≤44 years, with natural delivery; 2. Neonates delivered ≥37 and ≤42 weeks of gestation, birth weights of ≥2,500 and <5,000 grams; 3. Absence of congenital anomalies. The primary outcome measure was RD, defined as immediate post-birth supplemental ventilation. Statistical comparison was performed using χ2 test and multivariable logistic regression.

Results: There were 362,161 infants born during the study period, of whom 50.5% were male and mean birth weight was 3.3 ± 0.4 kg. Of newborns, 85,946 (23.7%) were delivered following IoL, and 8,246 (2.3%) had RD. In bivariate analyses, infants born following IoL were more likely to have RD (2.9% IoL vs. 2.1% no IoL, OR 1.43, 95%CI 1.36-1.50). Independent predictors of RD were IoL (AOR 1.41, 95%CI 1.34-1.48), eclampsia (AOR 1.93, 95%CI 1.44-2.58), pre-pregnancy diabetes (AOR 1.84, 95%CI 1.41-2.39), pre-pregnancy hypertension (AOR 1.63, 95%CI 1.34-1.98), gestational hypertension (AOR 1.39, 95%CI 1.25-1.55) and asthma (AOR 1.25, 95% CI 1.13-1.38).

Conclusions: IoL independently predicted RD when controlling for other maternal and infant risk factors. Results suggest caution with elective IoL for births at early or later gestational ages.

Primary Student Presenter: Peter Doan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brian Branchford

Poster Title: *Temporal and Anatomic Relationship Between Superficial and Deep Vein Thromboses in Hospitalized Children*

Final Category: Hematology and Oncology

Abstract:

Temporal and Anatomic Relationship Between Superficial and Deep Vein Thromboses in Hospitalized Children. P Doan, (M.D., CUSOM), A Cox, E Southard, B Clark, B Wathen, K Hammett, and B Branchford, Department of Pediatric Hematology/Oncology/Bone Marrow Transplant, University of Colorado, Aurora, CO.

Recent publications have increasingly demonstrated a link between superficial-vein thrombosis (SVT) and deep-vein thrombosis (DVT) in the adult population, and have led to changes in SVT treatment considerations. A similar relationship between SVT and DVT in pediatric populations, however, is not currently well established and we seek to evaluate this relationship in pediatric inpatients. We first used a local DVT registry to retrospectively identify children admitted to Children's Hospital Colorado who developed a DVT while hospitalized. We then reviewed each patient's electronic health record for evidence of SVT to identify SVT+DVT cases and removed them from a list of patients with SVTs obtained by ICD codes to retrieve the number of isolated SVTs. Patients with SVT+DVT represent 33% of the 241 total DVT subjects and 29% of the 277 total SVT subjects. Of the total SVT subjects, 18% had simultaneous DVT and an additional 4% had a DVT diagnosed later (Table 1). Of the 12 SVT+DVT subjects in whom the SVT was diagnosed before the DVT, the subsequent DVT occurred within a mean of 6.4 days and at the same anatomic site in 6 (50%). Our results indicate a temporal and anatomic relationship between SVT and DVT in hospitalized children, particularly those with central venous catheters. The fact that 63 of the 277 SVT patients (23%) had a DVT diagnosed along with, or within about one week of, the SVT demonstrates the importance of rapid and thorough imaging studies in patients with SVT. These findings have relevance regarding pediatric hospital-acquired DVT development and suggest that SVTs in this may warrant additional consideration and treatment, similar to that of adults.

Age Groups	PICC-Related		Temporal Relationship of SVT			Anatomical Relationship of SVT	
	Yes	No	SVT Before DVT	Concurrent SVT	SVT After DVT	Same Anatomical Site	Different Anatomical Site
0 to 1 month	2	0	0	1	1	1	1
1 month to 2 years	14	0	2	10	2	11	3
2 to 12 years	21	5	3	15	8	23	3
12 to 16 years	9	6	3	11	1	14	1
16 to 21 years	17	6	4	14	5	16	7
Total	63	17	12	51	17	65	15

Table 1 Age distribution of patients with an SVT and DVT grouped by various relations

Primary Student Presenter: Jacob Feiler

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MS

Year: 2nd

Mentor: Benjamin Mullin

Poster Title: *Relationships Between Amygdala-based Resting State Functional Connectivity and Sleep Duration in Adolescents with Generalized Anxiety Disorder.*

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Relationships Between Amygdala-based Resting State Functional Connectivity and Sleep Duration in Adolescents with Generalized Anxiety Disorder. J Feiler (M.S., GS), EL Perks, DK Novins, BC Mullin, Department of Psychiatry, University of Colorado School of Medicine, Aurora, CO.

   Generalized anxiety disorder (GAD) is a common psychiatric disorder that typically onsets during adolescence and is associated with significant emotional and sleep disturbances. To date, few studies have employed resting state functional connectivity (rsFC) as a means of studying the neural basis of GAD in adolescents. In this study, we compared rsFC for 20 adolescents with GAD and 16 healthy adolescents (HA). We utilized a seed-based approach to examine correlations between bilateral amygdalae and remaining brain voxels. We also examined the relationship between rsFC and total sleep time (TST) during the week prior to scanning. GAD participants showed greater positive connectivity between the amygdala and insula relative to healthy participants and increased positive connectivity between the left amygdala and left ventrolateral prefrontal cortex when compared to HA participants. Using regression analysis to study the main effect of sleep, we found that increased TST was associated with increased rsFC between the left amygdala and the left fusiform gyrus. We then examined interactions between TST and diagnostic status on rsFC. We found that for the GAD group, TST was positively associated with connectivity between the amygdala and dorsal prefrontal and parietal cortical regions, while for the HC group the associations were negative. Taken collectively, these findings suggest that adolescents with GAD exhibit unusually high connectivity between the amygdala and regions involved in emotion processing relative to healthy peers. In addition, diminished sleep may result in a weakening of amygdala-cortical rsFC in adolescents with anxiety.

Primary Student Presenter: Andrew Flynn

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Madiha Abdel-Maksoud

Poster Title: *Strengthening urban primary care in emerging economies*

Final Category: Healthcare and Public Health

Abstract:

Strengthening urban primary care in emerging economies

Purpose

Publicly funded population-level primary care is financially feasible in emerging economies. Services should target populations with the greatest health needs. Rio de Janeiro expanded primary healthcare from 2008-2016 and public primary care utilization jumped from 3% to 60%. The initiative targeted 2.5 million residents of favelas, where life expectancy is up to 15 years lower than wealthy neighborhoods and where violence presented obstacles to service delivery. We identify strategies and factors integral to successful primary care expansion in favelas.

Methods

We reviewed national and municipal health policies, conducted 32 structured and semi-structured interviews and used participant observation of healthcare provision and promotion activities in 12 favela family clinics.

Results and conclusions

National health policy created the policy space for a universal healthcare system. The national model incorporated primary care and community health lessons from Cuba and England including public/private partnerships, accessible comprehensive primary healthcare services, local community health teams for individual neighborhoods and integration of public health and clinical medicine services. Municipal health policy planning in Rio included favela residents and local providers who favored responsive and practical policies. Partnership with the International Red Cross allowed for implementation of several lessons for providing healthcare in conflict areas. The neutrality of health services in conflicts between local groups and state agents and the willingness to treat all involved parties allowed clinics to function as safe spaces. Home visits to areas controlled by local militias increased service coverage and trust in health services. Clinics utilized local information and human

resources and maintained constant situational awareness and flexibility to ensure safety of health workers.

Primary Student Presenter: Mairelle Galanto

Additional Presenter(s): Fiona Wong

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Mei Tang

Poster Title: *Evaluation of a Mobile Pharmacy Service to Improve Medication Adherence of Long-acting Injectable Antipsychotic Therapies*

Final Category: Pharmacology and Physiology

Abstract:

Schizophrenia is a complex and challenging psychiatric disorder. Long-acting injectable antipsychotic (LAI-AP) therapies have shown superiority over oral antipsychotics in preventing hospitalization. Our objective is to assess rates of patient adherence when site of administration is at home via a mobile pharmacy service compared to the traditional clinic setting and determine the role of a specialty pharmacy in improving medication adherence.

We conducted a retrospective chart review of 184 patients who received LAI-AP over 6 months. We calculated adherence based on proportion of days covered (PDC) in two ways: interval-based PDC and prescription-based PDC. Adherence is defined as a PDC ≥ 80%. The Mann-Whitney U test was used to calculate significance (P<0.05). Primary endpoint is to determine differences in adherence based on administration sites with interval-based PDC. Secondary endpoints include assessing differences in adherence with prescription-based PDC and evaluating the benefits of a mobile pharmacy service.

Of 184 patients referred to Med Quick Pharmacy for continuation of care, 116 received ≥2 injections over six months. According to interval-based PDC, 74% receiving injections at-home were adherent compared to 69% in clinic (P=0.70). Average interval-based PDC between the groups were similar at 87%. Average prescription-based PDC between the groups were similar with 95% at-home and 94% in clinic. Overall adherence rate at Med Quick (89%) is similar to those of other studies (80-95%). Common reasons for non-adherence include: inability to contact or locate patient, lack of insurance coverage, refusal of therapy, or filled elsewhere.

In patients with schizophrenia, mobile pharmacy service providing at-home injections for LAI-AP appears to improve medication adherence. At-home patients exhibited fewer cancellations in therapy administration and demonstrated longer rates of adherence over a 6-month period. Limitations of this study include lack of study power and unmatched sample sizes. Further prospective studies are warranted to determine if mobile pharmacy services have a role in reducing healthcare costs and schizophrenia-related hospitalizations.

Primary Student Presenter: Derek George

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Benzi Kluger

Poster Title: *The Experience of Fatigue in Persons Living with Parkinson Disease*

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

PURPOSE: Parkinson Disease (PD) is the second commonest neurodegenerative disease, affecting an estimated 4.1-4.6 million people worldwide. The disease exhibits both motor and non-motor symptoms. One such symptom—fatigue—has received increased focus due to its prevalence and negative impacts on quality of life (QoL). In this study, we elicited patient perspectives on PD-related fatigue to gain a better understanding of this symptom, its personal and social impacts on patients, and to assess the ecological validity of proposed case definition criteria by evaluating their alignment with PD patient experiences.

METHODS: We recruited PD patients from the Anschutz Medical Campus. 14 participants were recruited for interviews using convenience sampling. We characterized our participant cohort with data on demographics, medications, QoL, PD severity, other non-motor symptoms of PD. Interviews were conducted using an interview guide, digitally recorded and transcribed. Transcripts were analyzed using an inductive qualitative analysis method.

RESULTS: The following themes emerged from our analysis: difficulty initiating important tasks; impact on patients' ability to be productive, limiting duration and intensity of activities performed; desire for others to understand that fatigue was due to PD; heterogeneity in patients' experience and description of fatigue; complex relationship with other non-motor symptoms; variable success of self-management strategies; and agreement with most but not all case definition criteria.

CONCLUSIONS: Fatigue influences patients' social relationships and personal fulfillment. The heterogeneity of descriptions and complex relationship with other non-motor symptoms suggest fatigue may not be a single syndrome and future research should investigate the presence of important subgroups. Patient self-management strategies also suggest avenues for therapeutic interventions.

Primary Student Presenter: Jennifer Gile

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Tobias Eckle

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

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

JG Gile, (M.D., SoM), Y Oyama, CM Bartman, B Scott, and T Eckle, University of Colorado, Denver, CO.

Delirium occurs in 30% of critically ill patients, and the risk of dying during admission doubles in those patients. Molecular mechanisms causing delirium are unknown; however, critical care units consistently disrupt patients' circadian rhythms, which is highly associated with the occurrence of delirium. Exposure to benzodiazepines (e.g. midazolam) or inflammation is a major contributor to the development of delirium. Thus, we tested the functional role of the circadian rhythm protein PER2 in a midazolam induced mouse model for delirium. All animal experiments were performed in accordance with the APS/NIH guidelines. Expression levels of Per2 were assessed by RT-PCR using midazolam. Mice were injected with midazolam 0.5 mg i.p. and 24 or 72 hours later mice underwent behavioral testing using a T-maze alternation model, open field studies, or novel recognition tests to asses a delirium phenotype.

Midazolam significantly reduced the expression of PER2 in the SCN and hippocampus of wild type mice without affecting the expression of BMAL1, the key regulator of circadian rhythm proteins. Using T-maze alternation, open field or novel object recognition tests revealed a robust phenotype for delirium at 24 or 72h after midazolam administration in wild type mice. Studies in Per2-/- mice confirmed a functional and specific role of PER2 in midazolam induced delirium. Behavioral studies indicated a critical role of hippocampal expressed PER2 in the pathogenesis of delirium. Using the recent identified small molecule nobiletin as a PER2 enhancer completely abolished midazolam-induced delirium in wild type mice. These results describe a role for Period 2 during midazolam-induced delirium, highlight the role of hippocampal expressed PER2 in the development of delirium, and suggest PER2 as a potential drug target using the PER2 enhancer nobiletin as a therapy in delirium.

Primary Student Presenter: Natalia Gurule

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Lynn Heasley

Poster Title: *Oncogene-targeted agents induce an interferon response in EGFR and EML4-ALK driven lung cancer*

Final Category: Hematology and Oncology

Abstract:

Immunotherapy drugs that target immune evasion, a hallmark of cancer, have significantly impacted a subset of patients with lung cancer. However, patients with EGFR mutant and EML4-ALK positive lung cancer receive little benefit from these therapies. A growing literature demonstrates that a type I interferon (IFN) response mediating T cell infiltration into the tumor microenvironment (TME) is required for immunotherapy efficacy. We observe that oncogenic EGFR and ALK cause a suppression of IFN signaling within the TME, as evidenced by an induction of interferon stimulated genes (ISGs) including STAT1, STAT2, IFIT1, IFIT3, MX2, and CXCL10 following treatment with tyrosine kinase inhibitor (TKI). We hypothesize that inhibition of EGFR or EML4-ALK upon treatment with TKIs induces a robust IFN signaling response and an increase in T cell infiltration, thus sensitizing EGFR mutant or EML4-ALK positive lung cancer tumors to immunotherapy agents. RNAseq of EGFR mutant cell lines treated with the EGFR TKI, AZD9291 reveals broad and kinetically variable transcriptional induction of IFN pathway genes. Bioinformatic analysis demonstrates enrichment in IFNα and IFNγ pathway genes with TKI treatment. In two independent lung cancer patients, RNAseq analysis of paired biopsies taken before and after a 2-week treatment with EGFR TKI reveals a similar enrichment for IFNα and IFNγ gene sets. Furthermore, multiple bioinformatic approaches support increased T cell infiltration in the EGFR TKI-treated tumors. Likewise, crizotinib treatment (2 wks) of orthotopic murine EML4-ALK tumors in syngeneic mice induced a 3.7-fold increase in CD3+ T cells. Taken together, our data demonstrate that inhibitors of oncogenic EGFR or ALK induce an IFN signaling response in cell line models as well as patient biopsies. Ongoing studies are testing the ability of TKIs to increase the responsiveness to anti-PD1/PD-L1 therapies in EGFR and EML4-ALK-drivent lung cancers.

Primary Student Presenter: Lakotah Hardie

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jay Hesselberth

Poster Title: *Multiplexed Measurement of DNA Repair Capacity for Tumor Heterogenity*

Final Category: Hematology and Oncology

Abstract:

PURPOSE OF STUDY. Mutations in DNA repair factors can lead to development of cancer, and many cancer treatments target DNA repair to cause cell death. We hypothesize that biochemical differences in DNA repair activities may underlie cellular heterogeneity in tumor and cancer pathologies. The goal of this project is to develop a novel assay to measure the DNA repair capacities of cancer cells and to apply it to individual cells in a population.

METHODS USED. The assay uses DNA hairpin substrates with different DNA damage events located to each hairpin. Individual hairpins targeting different repair pathways within the cell can be ligated to magnetic beads to test a majority of DNA repair pathways within the cell in a multiplexed fashion. To this end, bead immobilized DNA repair substrates were incubated with bulk cell lysate and products of DNA repair were recovered by bead isolation. PCR amplification and Illumina sequencing were then used to identify repair activities. Bioinformatic pipelines systematically compared differences in repair profiles across conditions in the optimization of the assay with ATP regeneration and chemotherapy pre-treated cells. Future directions will include the combination of a microfluidic platform for single cell analysis.

SUMMARY OF RESULTS. I tested whether an ATP regeneration system improves the signals in the assay. Inclusion of a creatine phosphokinase (CPK) ATP regeneration system increased capture across all repair pathways as compared to controls. We identified signification increases in Nucleotide Excision Repair (NER) and mismatch repair (MMR) that were not seen in the absence of the ATP regeneration system. Pre-treatment of cells with Temozolomide, a clinically useful DNA alkylating agent, demonstrated increased repair activities in Direct Reversal-mediated repair of methylated adducts compared to positive controls.

CONCLUSIONS: The addition of an ATP regeneration system significantly increased capture of repair events by increasing local concentrations of ATP to support cellular enzyme activities. Increases in repair activates were seen across all pathways tested. DNA damaging pretreatments indicated predictable upregulations in certain DNA repair pathways matching the type of DNA damage event generated.

Primary Student Presenter: Kellen Hirsch

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Steven Abman

Poster Title: *Stabilization of Hypoxia Inducible Factor Improves Lung Structure and Function and Prevents Pulmonary Hypertension in an Antenatal Model of Bronchopulmonary Dysplasia*

Final Category: Pulmonary and Critical Care

Abstract:

Hypoxia Inducible Factor Stabilization Prevents Bronchopulmonary Dysplasia. K Hirsch, (M.D., SOM), G Seedorf, T Nowlin, C Kim and SH Abman, Departments of Pediatrics and Surgery, University of Colorado School of Medicine, University of Colorado, Denver, CO.

Purpose: Bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity, is characterized by impaired lung structure, function, and pulmonary hypertension (PH). Hypoxia-inducible factor (HIF) regulates angiogenesis but whether enhanced HIF signaling prevents BPD is uncertain. We sought to determine if HIF stabilization preserves lung growth and function and prevents PH in a model of BPD.

Methods: Endotoxin (ETX, 10ug/sac) was administered to pregnant rats by intra-amniotic (IA) injection at embryonic day 20 (E20; term = E23), pups were delivered by c-section at E22. Dimethyloxalylglycine (DMOG) was administered to enhance HIF signaling at either E20 (antenatal, 10mgs/sac) or after birth (postnatal, 5 mg/kg IP QID). At day 14, lung tissue was assessed for radial alveolar counts (RACs); pulmonary vessel density (PVD); and right ventricular hypertrophy (RVH; RV/(LV+S) weights) as an indicator for PH. HIF and vascular endothelial growth factor (VEGF) protein contents in the lung were determined by western blot. Lung function was determined by Flexivent.

Summary: As compared to controls, IA ETX: decreased RAC 42% (p<0.01), decreased PVD 41% (p<0.01), increased RVH 70% (p<0.01), increased lung resistance 46% (p<0.01), and decreased lung compliance 41% (p<0.01). DMOG therapy restored all values to control levels except lung compliance for postnatal therapy. DMOG increased lung HIF-1 and VEGF protein expression by 4 and 3 fold above ETX alone (p<0.01).

Conclusions: DMOG improves lung structure and function and prevents RVH caused by antenatal ETX. We speculate that the beneficial effects of DMOG therapy are due to HIF stabilization and up-regulation of VEGF expression in the developing lung.

Primary Student Presenter: Anastasia Hunt

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Samuel Gubbels

Poster Title: *Outcomes of Microsurgical Resection of Vestibular Schwannoma*

Final Category: Surgery

Abstract:

OUTCOMES OF MICROSURGICAL RESECTION OF VESTIBULAR SCHWANNOMA

Anastasia A Hunt, (M.D., SOM)1; Nathan Cass, M.D.1, Adam Coughlin, M.D.2; Samuel P Gubbels, M.D.1

1University of Colorado School of Medicine, Department of Otolaryngology, Aurora, CO

2University of Wisconsin School of Medicine and Public Health, Division of Otolaryngology, Madison, WI

OBJECTIVE: To determine post-operative outcomes after microsurgical resection of vestibular schwannoma (VS).

DATA SOURCES: Systematic review of the Ovid, Cochrane, EMBASE, and Web of Science databases.

STUDY SELECTION: Inclusion criteria: full text English language articles on vestibular schwannoma resection via middle fossa or retrosigmoid approaches, describing pre- and post-treatment hearing outcomes using the AAO-HNS or Gardner-Robertson (GR) hearing scales (or an audiogram-based scoring system), with documented time to follow up. Exclusion criteria: duplicate data sets, more than 10% of patients with neurofibromatosis 2 or prior vestibular schwannoma treatment, non-surgical treatment of

vestibular schwannoma, case reports with fewer than five patients, and/or decompressive surgery without intent of tumor removal.

DATA EXTRACTION: Two authors (AH, NC) independently performed full text review to determine inclusion or exclusion of all studies. Discrepancies were settled by consensus. "Class A/B, I/II" hearing was defined as either AAO-HNS Hearing Class A or B, GR Class 1 or 2, or PTA ≤ 50db with SDS ≥ 50%.

DATA SYNTHESIS: Pooled estimates of preserved Class A/B, I/II hearing at last post-operative follow-up.

CONCLUSIONS: Of 1,323 reports identified, 18 studies met inclusion criteria providing data from 4,192 patients. Class A/B, 1/2 hearing was preserved at last follow-up in 53.4% of patients with pre-operative Class A/B, 1/2 hearing undergoing hearing-preservation microsurgical resection of vestibular schwannoma. Mean follow-up was 53.8 months (SD = 22.9). Hearing preservation is possible with microsurgical resection in many patients with VS who have class A/B, 1/2 preoperatively.

Primary Student Presenter: Matthew Hupy

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mark Petrash

Poster Title: *Aldose reductase and posterior capsular opacification in a cataract surgery mouse model*

Final Category: Vision Sciences

Abstract:

Aldose reductase and posterior capsular opacification in a cataract surgery mouse model

Background

Around two million cataract surgeries are performed each year, with posterior capsular opacification (PCO) being the most common complication reported in 15-20% of cases. This complication is a result of fibrosis pathways in which residual cells undergo epithelial-to-mesenchymal transitions (EMT), yielding cells with a myofibroblastic morphology. These cells ultimately wrinkle the capsular bag, requiring laser surgeries to clear the visual axis. Recent research has demonstrated aldose reductase (AR) to be an inducer of PCO and the associated EMT marker α Smooth Muscle Actin (αSMA). In this study, we used transgenic mice with an overexpression of AR, as well as sorbinil-mediated AR inhibition, to investigate the effects of a cataract surgery mouse model on EMT markers.

Methods

Wild-type C57BL/6 mice, as well as mice with increased expression of human AR (ARTG) in lens cells, underwent extracapsular lens extraction (ECLE). To investigate Sorbinil mediated AR inhibition, ECLE was performed on ARTG mice, followed by intraperitoneal injections of 25mg/kg sorbinil bid for 3 days. Five days after ECLE capsules were harvested for QRT-PCR to measure the EMT marker α smooth muscle actin (αSMA). Eyes were also enucleated, cryosectioned, and stained with DAPI and anti-αSMA. QRT-PCR data was analyzed using GraphPad Prism 5.0.

Results

In wildtype mice, ECLE surgery lead to increased transcription levels of EMT marker αSMA ($p < 0.01$). ECLE surgery in ARTG mice further increased transcription levels of αSMA, as compared to ARTG ($p < 0.001$) and wildtype mice ($p < 0.001$). Sorbinil-mediated inhibition of AR in ARTG mice significantly reduced transcription levels of αSMA, both without and with ECLE ($p < 0.001$ in both cases). On histology, αSMA signal was increased in ARTG mice as compared to wildtype.

Conclusions

AR has been shown to be important for the induction of EMT, ultimately resulting in PCO, the most common complication of cataract surgery. Overexpression of AR increased EMT induction with and without ECLE, while sorbinil-mediated inhibition of AR decreased EMT induction with and without ECLE, as measured by αSMA. This study supports the role of AR in PCO development in vivo with a cataract surgery moues model.

Primary Student Presenter: Beza Jobira

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Melanie Cree-Green

Poster Title: *Obese Adolescents with Polycystic Ovary Syndrome Have Decreased Diversity and Relative Abundance in the Gastrointestinal Microbiota*

Final Category: Metabolism and Endocrinology

Abstract:

Obese Adolescents with Polycystic Ovary Syndrome Have Decreased Diversity and Relative Abundance in the Gastrointestinal Microbiota. B. Jobira (MD, SOM), D. Frank, M. Kelsey, Y. Garcia-Reyes, H. Rahat, D. Ir, C. Robertson K. Nadeau, and M. Cree-Green, Children's Hospital Colorado, Pediatric Endocrinology; Infectious Disease, School of Medicine; Center for Women's Health Research

PCOS is common and associated with the metabolic syndrome. Early evidence in adults with PCOS suggests that metabolic deterioration may be related to alterations in the gut microbiota. However, this has not been studied in youth, nor in NIH-defined PCOS. Obese youth, 16 with PCOS (PCOS: 15.9 ± 0.5 years, BMI 97.8%ile) and 5 obese youth without PCOS (OB: 15.6 ± 0.7, BMI 97.6%ile) were enrolled. Participants underwent stool collection, fasting labs, oral glucose tolerance test, DXA scan, activity questionnaire and 7-day accelerometer use, and dietary intake questionnaire. The V3-V4 region of the bacterial 16S rRNA gene was amplified by PCR and bacterial Operational Taxonomic Units were generated using phylogenetic sequence analysis. Comparisons of relative abundance (RA) across groups were conducted by Wilcoxon rank sum tests and alpha diversity within groups was performed by Shannon diversity. Girls with PCOS tended to have a worse metabolic profile including HOMA-IR, presence of pre-diabetes, fasting triglycerides and alanine transferase. Diet and activity were similar between groups. PCOS had decreased alpha diversity, Shannon E (PCOS: 3.85 ± 0.09; OB: 4.16 ± 0.09, p-value = 0.034). Girls with PCOS had decreased RA of Christensenellaceae at the family level, phylum Firmicutes (PCOS: 0.30% of sequences; OB: 1.68%, p-value = 0.043), and decreased RA of Lachnospira at the genus level, phylum Firmicutes (PCOS: 0.015%; OB: 0.17%, p-value = 0.043). No difference was observed at the phylum level between the two groups. Christensenellaceae, Lachnospira, and Clostridium predicted PCOS disease status and were significantly correlated with biological markers of PCOS (e.g. free testosterone, R = -0.46, p = 0.43; R = 0.67, p - 0.001; and R = -0.44, p = 0.052). Our results suggest that alteration in the gut microbiota relate to PCOS and decreased RA in Christensenellaceae and Lachnospira are associated with PCOS and metabolic disease.

Primary Student Presenter: Jared Johnson

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jeffrey Olson

Poster Title: *PAN's Labyrinth: Using Polyacrylonitrile (PAN) To Treat Age-Related Macular Degeneration*

Final Category: Vision Sciences

Abstract:

PAN'S LABYRINTH: USING POLYACRYLONITRILE TO TREAT AGE-RELATED MACULAR DEGENERATION
Jared S Johnson (M.D., SOM)
Anthony A Jones
Jeffrey L Olson
University of Colorado School of Medicine, Aurora, CO
Department of Ophthalmology

   Purpose of Study: Age-Related Macular Degeneration (AMD) is the leading cause of vision loss in individuals over the age of 50. There are currently no available pharmaceutical or procedural options available for treating the dry type of disease. The alternative complement pathway has been implicated in AMD pathogenesis, and individuals with Complement Factor H (CFH) polymorphisms display an increased incidence of AMD. Polyacrylonitrile (PAN) fibers have been shown to adsorb complement factors D, C1q, C3, and C5 in vitro. The purpose of this study is to analyze the efficacy of PAN fibers in preventing the progression of dry AMD in vivo. Additionally, this study aims to find other proteins implicated in disease states that may be sequestered using PAN fibers.

   Methods Used: In Vivo: Six-month old CFH -/- mice (n=18) were used for in vivo models. A posterior sclerotomy was performed bilaterally, with a 4mm PAN fiber injected into the posterior chamber of the right eye, and the left eye receiving a 4mm segment of surgical suture to serve as a control. RPE thickness was determined using Optical Coherence Tomography (OCT) imaging. The eyes will be stained for complement deposition, the drusen markers, and retinal cell count.

In Vitro: 4mm segments of PAN fiber were incubated for 1 hour at 37˚C in solutions of Tau protein with concentrations varying between 2000 pg/ml and 37.5 pg/ml. Adsorption was determined by ELISA.

   Results: The in vivo portion of this study is ongoing, and results will be reported at the time of the forum. PAN fibers demonstrated adsorption of Tau when analyzed through ELISA ($p<0.001$ by two-way ANOVA).

Conclusion: We hope to conclude that PAN fibers prevent the progression of dry AMD in vivo as measured by retinal thickness and drusen deposition.

Primary Student Presenter: Alexander Jones

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jay Albright

Poster Title: *ANTERIOR CRUCIATE LIGAMENT INJURY SEVERITY AND LONG-TERM FUNCTIONAL OUTCOMES*

Final Category: Surgery

Abstract:

ANTERIOR CRUCIATE LIGAMENT INJURY SEVERITY AND LONG-TERM FUNCTIONAL OUTCOMES

A Jones (MD; SOM); A Gagliardi; JC Albright

Department of Orthopedic Surgery, Children's Hospital Colorado

Purpose: Anterior cruciate ligament (ACL) rupture is the most common injury of the internal knee in the young adult and pediatric population. While operative technique and post-operative rehabilitation protocol has dominated the discussion on ACL injuries, long-term functional outcomes remain universally unpredictable. The aim of this study was to investigate the prognostic value of the injury severity on long-term functional outcomes.

Methods: A retrospective cohort study of pediatric subjects who sustained an ACL rupture between 2013 and 2015 was conducted. The severity of the injury was defined by the occurrence of concomitant injury to the knee which was extracted from the arthroscopic findings in the operative note. The types of concomitant injury (menisci, ligament, chondral, bone) were divided into subgroups for analysis. Two validated surveys, IKDC and Lysholm, were administered to subjects with at least two years of post-reconstruction follow-up to assess functional outcomes.

Results: Of the 52 subjects who completed both surveys, 30 had sustained at least one concomitant injury. The most common concomitant injury was unilateral or bilateral damage to the menisci (83.3%). The average IKDC score of bilateral meniscus tears was 77.8 (±26.9) which was lower than the non-concomitant injury group (p<0.05). There was no difference in Lysholm score between the concomitant injury subgroups and the non-concomitant injury group.

Conclusions: Bilateral meniscus tears may be trending towards worse functional outcomes at least 2 years after ACL reconstruction. There is a trend towards any kind of concomitant injury having lower functional scores than non-concomitant injuries. Recruiting more subjects into the study will increase

the likelihood of observing a meaningful difference.

Primary Student Presenter: Megan Kalata

Additional Presenter(s): Kathryn Kalata Taylor Davis

Presenting School: Medicine

Degree Seeking: MD

Year: Other

Mentor: Janet Meredith

Poster Title: *Addressing Racial Disparity in Infant Mortality*

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

ADDRESSING RACIAL DISPARITY IN INFANT MORTALITY. M Kalata, K Kalata, T Davis, S Bardwell, H Yen, J Thai, A Khorshid, T Nelson, L Escobedo, L Kellogg, M Thayer, J Meredith, University of Colorado School of Medicine, Aurora, CO.

Purpose: The infant mortality rate in the United States is higher than that of most other developed countries, with the gap being greatest among infants born to African American women. Previous research suggests that this is not due to education or socioeconomic status alone as an educated, middle class African American woman has a greater likelihood of her baby not surviving their first year of life than a baby born to a White woman with less than a high school education living below the federal poverty line.

Methods: Key Informant interviews (8) and focus groups (6) were conducted with eight professionals and 27 community members, respectively. Both used a semi-structure interview format. Focus group participants included self-identified African American women ages 18-80 who had been pregnant to 20+ weeks gestation at least once. Data was transcribed via professional transcription software services and researchers conducted qualitative data analysis.

Results: Several common themes emerged through conversations with researchers, physicians, community partners, and community members. They agreed that the highest risk women, and thus those who should be targeted for future research and interventions, include young, African American, first time mothers. Key themes that emerged, and which require further exploration, include biases and miscommunications with healthcare providers, such as assumptions made about patients and lack of cultural awareness, lack of resources for first time mothers, and lack of patient empowerment to voice their values and concerns.

Conclusions: Our focus is to understand the effects of stress caused by systemic racism and lack of support from the healthcare community on pregnancy outcomes for African American women. A community based participatory research (CBPR) approach may provide new insights into how to address

this issue through collaboration between African American women, community partners, and future healthcare professionals. Interviews and focus groups suggested a crucial role of patient-provider relationships as well as race and implicit bias impacting this inequity. Once formed, a Community Advisory Board can collaboratively address how to change women's experiences with prenatal care in the clinic setting to serve the needs of this target population.

Primary Student Presenter: Peter Klauck

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Todd Pitts

Poster Title: *Metabolic Reprogramming to Enhance the Efficacy of mTOR Inhibition in Colorectal Cancer*

Final Category: Hematology and Oncology

Abstract:

METABOLIC REPROGRAMMING TO ENHANCE THE EFFICACY OF MTOR INHIBITION IN COLORECTAL CANCER

Klauck PJ1 (MD, SOM), Weber M1, Pitts TM1

1University of Colorado School of Medicine, Aurora, CO.

Purpose of Study:

   PI3K/mTOR pathway is mutated in 10-20% of colorectal cancer (CRC) specimens and has been associated with poor survival. In this study, we found diacylglycerol kinase (DGK), involved in lipid signaling, to be synthetically lethal in mTOR inhibitor resistant CRC. We evaluated the antiproliferative and pharmacodynamic effects of dual inhibition with an mTOR (TAK-228) and DGK (ritanserin and R59022) inhibitors.

Methods:

   A synthetic lethal screen was performed with two TAK-228 resistant colorectal cancer cell lines (HCT116 and SW620). Subsequent experiments were performed with one TAK-228 sensitive (DLD1) and one resistant (HCT116) CRC cell lines. Efficacy of TAK-228 + Ritanserin and TAK-228 + R59022 combination therapy was evaluated by CellTiter-Glo cell viability and clonogenic colony formation assays. Pharmacologic DGK inhibition was phenocopied using lentiviral shRNA knockdown of two DGK isoforms (DGKα and DGKζ). Immunoblotting was performed to evaluate mechanism of action of TAK-228 combination therapy.

Summary of Results:

   TAK-228 combined with ritanserin and R59022 displayed decreased cell viability and colony formation as compared to either single agent. Lentiviral shRNA transduction resulted in DGKα and DGKζ knockdown as evaluated by RT-PCR and immunoblotting. Phenocopy combination therapy with TAK-

228 and DGKα resulted in an increased sensitivity to mTOR inhibition compared to mock transduced control. Immunoblotting confirmed TAK-228 abrogates PI3K/mTOR pathway activity. DGK inhibition alone resulted in a reciprocal increase in mTOR pathway activation, indicating the need for combination therapy.

Conclusions:

   Pharmacologic and shRNA knockdown inhibition of DGK in combination with mTOR inhibition resulted in decreased cancer cell viability as well as decreased colony formation. These results suggest a therapeutic anticancer advantage of targeting lipid metabolism simultaneously with mTOR inhibition. Recently, DGK inhibition has been implicated as an immunomodulator and could be beneficial in potentiating the effects of immune checkpoint inhibition. The rational combination of DGK and mTOR inhibition is promising both as a targeted anti-cancer therapy as well as the possible effect to modulate immune system response.

Primary Student Presenter: Iain Konigsberg

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Ivana Yang

Poster Title: *DNA Methylation Changes in Bronchoalveolar Lavage Associated with Chronic Beryllium Disease*

Final Category: Pulmonary and Critical Care

Abstract:

Rationale

Chronic beryllium disease (CBD) is an occupational/environmental lung disease characterized by granulomatous inflammation that can lead to reduced lung function and fibrosis. Individuals are first sensitized upon exposure to beryllium (BeS). At least half of individuals go on to develop disease, for which there is no cure, with treatments focusing on life-long symptom management. Many features of CBD, including variable susceptibility and exposure relationships, implicate epigenetic mechanisms as potential drivers of disease. We profiled DNA methylation and gene expression in CBD patient lungs to elucidate functional differences in diseased cells in the affected organ.

Methods

We obtained bronchoalveolar lavage (BAL) cells from 8 CBD and 8 BeS individuals without disease as well as fresh and Be-stimulated BAL CD4+ T cells from additional 30 CBD, 30 BeS, and 12 control individuals. DNA from all BAL cells or isolated CD4+ T cells was bisulfite-converted and hybridized to Illumina Infinium Human Methylation 450k or EPIC BeadChips. Pyrosequencing was performed to validate methylation changes in genes and regions of interest. Gene expression of RNA extracted from the same cells was analyzed on Affymetrix Human U133 Arrays or by RNA-seq. Mixed effects linear modelling was used to detect statistically significant differentially methylated/ expressed genes (p <0.005, FDR <0.05). NetworkAnalyst and Ingenuity Pathway Analysis were used to identify enriched gene and protein interactions.

Results

52,860 CpGs were differentially methylated in CBD compared to BeS in all BAL cells. 2,726 probes showed absolute methylation changes >25%, mapping to 1,944 unique genes. Pathway analysis of these genes showed enrichment in immune pathways such as cytokine-cytokine interactions, T-cell receptor signaling, and Jak-STAT signaling. Gene expression data supports this, with 69% of differentially

methylated genes showing significant differential expression. Correlating methylation and expression reveal multiple genes with large effect sizes. Many of these genes are involved in Th1 cell differentiation (TBET, IFNG), chemokine signaling (CCR5, CXCR6, CCL5), and immunity (LTA, IL26). Most of the same immune pathways were also enriched in fresh CD4+ cells. The analysis of Be-stimulated CD4+ cells is ongoing.

Conclusions

Substantial genomic alterations in DNA methylation are observed in patients with CBD compared to BeS. Changes in gene expression correlated to differential methylation implicate a functional role for DNA methylation in transcriptional regulation in CBD. Multiple genes and pathways that are dysregulated in CBD have been identified and offer future potential targets for biomarker development, therapies, and further study.

Primary Student Presenter: Jaclyn Kurttila

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Tien Nguyen

Poster Title: *Updates on antibiotic and biologic treatments for hidradenitis suppurativa*

Final Category: Other

Abstract:

Updates on antibiotic and biologic treatments for hidradenitis suppurativa

Jaclyn Kurttlia, BS, Tien V. Nguyen, MD

School of Medicine and Department of Dermatology, University of Colorado

Introduction: Hidradenitis suppurativa (HS) is a debilitating chronic inflammatory disease of the intertriginous areas of the body, most commonly affecting the axilla, groin and perianal regions. Disease presentation is on a spectrum, ranging from double and triple-comedones and small inflammatory nodules to deep abscesses with suppurating interconnected sinus tracks. For moderate-to-severe disease, which is most often determined via the Hurley Staging System, treatment options consist of topical antibiotics, injectable corticosteroids, deroofing procedures, oral antibiotics, oral retinoids, hormonal therapies, surgery, biologic agents, and most recently, liraglutide. Many antibiotic combinations and biologics, including but not limited to TNF-alpha, IL-17 and IL-12/23 inhibitors, have been reported to show promising results. This poster aims to review, summarize, and present traditional as well as novel treatments in the areas of systemic antibiotic and biologic therapies for HS.

Methods: Articles for review were found using Google scholar, Medline, PubMed, Cochrane review and the University of Colorado Anschutz library database. Review articles were inspected for relevant research studies relating to currently accepted treatments as well as for innovative therapeutic approaches. 48 articles related to antibiotic and biologic treatments for HS from 24 different indexed journals were analyzed. Research studies include case studies, prospective, retrospective cohorts and randomized control trials (RCT).

Results: See attached excel document.

Conclusion: Review articles suggest that long-term broad-spectrum antibiotic treatment seems to be more efficacious than single antibiotic treatment alone. Severity of HS determined by Hurley staging can provide insight for treatment length, with more severe cases requiring longer treatment regimens.

IV Ertapenem is emerging as an important player in controlling the degree of inflammation in lesional skin. In terms of biologic therapy, adalimumab is the only FDA-approved drug for HS; and, it provides greater than 50% Hidradenitis Suppurativa Clinical Response (HiSCR) efficacy, based on data from the PIONEER I and PIONEER II randomized clinical trials. Secukinumab, an IL-17 inhibitor, and Ustekinumab, an anti-p40 antibody, show promise as well in case studies, but more systematic research needs to be performed to confirm efficacy of these biologics. Anakinra, an IL-1 inhibitor, may be effective therapy for HS, as well as a novel IL-1alpha antibody, MABp1. As the field of biologic therapy is changing rapidly, we will hopefully see more emerging agents with better clinical outcomes for HS.

Primary Student Presenter: Eric Lakey

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kenneth Hunt

Poster Title: *Application of PROMIS Instruments to Sub-Populations of Interest*

Final Category: Healthcare and Public Health

Abstract:

APPLICATION OF PROMIS INSTRUMENTS TO SUB-POPULATIONS OF INTEREST

Lakey EJ (MD, SOM); Anderson S; Kumparatana P, MSW, MPH; Roberts J, MD; Hunt KJ, MD

Purpose: The Patient-Reported Outcomes Measurement Information System (PROMIS) is a series of metrics developed by the NIH. PROMIS data are reported separately for each domain on a scale of 0 to 100, with a mean of 50. PROMIS scores were calibrated from Medicare and disability databases and it is unknown if these scores are representative of sub-populations of interest. This study aims to test the hypothesis that mean PROMIS scores for these sub-populations will not differ from NIH population mean values.

Methods: Participants from two state university institutions were recruited to complete a voluntary survey administered through REDCap. The survey included the following PROMIS domains: Pain Interference, Physical Function, Mobility, Social Functioning, Depression, and Global Health. Respondents were grouped into one of three categories: (1) Elite Athletes on an NCAA Division 1 roster (N=38); (2) Medical Students (N=15); and (3) Residents/Fellows (N=76). Data were analyzed using SAS 9.4 using ANOVA with Tukey-Kramer pairwise comparisons and one-sample t-tests. A p-value < 0.05 was considered statistically significant.

Results: Mean PROMIS scores for both Elite Athletes and Residents/Fellows differed from the population mean across all PROMIS domains (p < 0.01). Mean PROMIS scores for Medical Students differed from the population mean for Physical Functioning, Pain Interference, Mobility, Social Functioning, and Global Health (Physical) (p < 0.01). Mean PROMIS scores for Medical Students did not differ from the population mean for Depression (p = 0.4780) or Global Health (Mental) (p = 0.6623).

Conclusions: These data suggest that NIH mean PROMIS domain scores may not be generalizable to sub-populations of interest. This demonstrates the importance of caution with PROMIS score interpretation in the clinical setting.

Primary Student Presenter: Melissa Laughter

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Daewon Park

Poster Title: *Engineering an injectable microenvironment for RGC transplantation.*

Final Category: Vision Sciences

Abstract:

Worldwide, glaucoma is considered the second leading cause of blindness and one without a known cure. Glaucoma is broadly defined as a group of eye diseases that are characterized by the neurodegeneration of retinal ganglion cells (RGCs), the projection neurons located in the retina with axons extending through the optic nerve. These cells play a crucial role in vision by transmitting signals and visual information from bipolar, amacrine, and interplexiform cells to the cortex of the brain. Glaucoma was originally considered to be directly linked to and increase in intraocular pressure (IOP), which was causing the damage to the RGCs and subsequent vision loss. However, it is now known that Glaucoma can develop under normal IOP conditions. Furthermore, in cases where IOP is in fact increased and met with early detection and vigilant preventative measures to lower IOP, RGC death and the subsequent vision loss can still occur. Due to the inability of these cells to regenerate in unaltered disease conditions, the loss of these cells is permanent meaning the vision that is lost is not regained. To regain function and restore the quality of life for these patients, glaucoma treatments must include methods to prevent further damage as well as methods to facilitate the survival and regeneration of RGCs. We aim to create an injectable biomaterial that can protect RGCs from apoptotic death and encourage RGC axons regeneration to recover lost vision. To do this we synthesized an injectable biomimetic polymer conjugated with cell adhesive biomolecules. Preliminary studies were performed to transplant RGCs encapsulated in the polymer into the subretinal space of a healthy rat. We were able to show survival and incorporation of these cells into the RGC layer. Furthermore, to test the regenerative capacity of this polymer in vivo, we have established a glaucoma animal model by performing an optic nerve crush in a rat. Future studies will include the injection of the transplanted cells within the polymer scaffold following optic nerve crush surgery. A power study will be performed to determine the appropriate study size to show efficacy of the transplantation.

Primary Student Presenter: Peter Lawson

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Trevor Nydam

Poster Title: *Viscoelastic Clot Strength Correlates to Hypercoagulable Conditions Under Flow Model of Hemostasis*

Final Category: Hematology and Oncology

Abstract:

Viscoelastic Clot Strength Correlates to Hypercoagulable Conditions Under Flow Model of Hemostasis.

PJ Lawson (MD, CUSOM), HB Moore MD, EE Moore MD, ME Gerich MD, GR Stettler MD, A Banerjee PhD, JA Schoen MD, RD Schulick MD/MBA, TL Nydam MD. Dept. of Surgery, University of Colorado, Denver, CO.

   Elevated clot strength (MA) measured by thrombelastography (TEG) is associated with thrombotic complications. It remains unclear how MA translates to thrombotic risks, as this measurement is independent of blood flow. Total Thrombus-formation Analysis System (T-TAS) analyzes clot formation under flow conditions. We hypothesize that under flow conditions, increased clot strength correlates to time dependent measurements of coagulation.

   Patients at high risk of thrombotic complications were analyzed with TEG and T-TAS. TEG hypercoagulability was defined as an R<11.2min, Angle>49, MA>60 or LY30<0.9% (healthy control data, n=160). The T-TAS platelet chip (PL) measured clotting at arterial shear rates. PL measurements include: occlusion time (OT), occlusion speed (OSp), and total clot generation [area under the curve (AUC)]. These measurements were correlated to TEG indices.

   Thirty patients were analyzed. 56% had TEG detected hypercoagulability based on R, 63% angle, 73% MA, and 64% LY30. When correlated to PL output, only the MA significantly correlated to OT (Rho -0.418 p=0.022), OSp (Rho 0.446 p=0.014), and AUC (Rho 0.439 p=0.015). Hypercoagulability defined by MA was associated with significantly decreased OT (4:06 min vs 6:42 p=0.016), faster OSp (21 kPA/min vs 11 p=0.014), and increased clot generation (AUC 430 kPA*min vs 350 p=0.035).

   Clot strength measured by TEG correlates to flow measured coagulation changes, and is consistent with clinical data implicating MA with thrombotic events. This in vitro data supports feasibly using MA or T-TAS PL to guide the treatment of hypercoagulability with antiplatelet medication, and warrants prospective evaluation.

Primary Student Presenter: Pierce Lewien

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Moshe Levi

Poster Title: *NAD+-Dependent Deacetylase SIRT3 Activation Inhibits Diabetic Kidney Disease*

Final Category: Metabolism and Endocrinology

Abstract:

PM Lewien (MD, CU SOM), X Wang, K Myakala, D Wang, Y Luo, M Levi

University of Colorado School of MedicinePurpose of Study: Despite interventions for diabetes that seem to have some clinical benefit such as tight glucose and blood pressure control, kidney disease continues to be a problem. Recently mitochondrial dysfunction has been found to play an important role in the pathogenesis of kidney disease. We aimed to test the influence of Sirtuin 3 (SIRT3) as a potential target for therapy in patients with chronic kidney disease.

Methods Used: We used kidney biopsies from human patients with and without diabetic nephropathy or glomerulopathy to measure for SIRT3 expression and activity. To test the effect of SIRT3 on the prevention of diabetic kidney disease, we conducted a study comparing three groups of mice: A control group, a diabetic group, and a diabetic group treated with an agonist for SIRT3, nicotinamide riboside (NR). We performed histopathology and immunofluorescence microscopy to visually assess the health of the kidney which included mesangial expansion, glomeruli area, collagen IV expression, and synaptopodin. We also measured for albuminuria, serum triglycerides, SOD2, acetylated lysine, and 4-HNE, all of which are markers for kidney disease progression.

Summary of Results: SIRT3 expression and activity decreased in human glomeruli and tubules in diabetic patients compared to controls. This result was also shown in diabetic mice compared to controls. Treatment with NR in diabetic mice decreased mesangial expansion, glomeruli area, albuminuria, serum triglycerides, acetylated lysine, SOD2, and 4-HNE compared to control.

Conclusions: SIRT3 plays an important role in the progression of diabetic kidney disease. In human renal biopsies SIRT3 expression and activity was decreased in diabetic patients with similar findings in in mice as well. Furthermore, markers of kidney disease decreased in treated diabetic mice compared to the untreated diabetic mice. The results of this study show promising results about a potential pharmaceutical target to help prevent the progression of diabetic kidney disease.

Primary Student Presenter: Colleen Long

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Ayelet Talmi

Poster Title: *Pediatric Obesity and Exposure to Environmental Adversity*

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

Background:

Exposure to 4 or more environmental adversity factors in childhood is associated with a 1.4-1.6 fold increase in obesity and myocardial infarction in adulthood and a 1.4 increase in coronary artery disease and stroke. Specifically, experiencing sexual abuse in childhood is associated with an elevated risk of being obese in adulthood. However, few studies have investigated adversity exposure and elevated weight in childhood. The aim of this study is to characterize the relationship between environmental adversity, pediatric obesity, and cardiovascular risk factor diagnoses.

Methods:

A retrospective medical review of electronic medical records of 295 children aged 1 to 17 years old with elevated BMI was conducted. Records were obtained from Child Health Clinic at Children's Hospital Colorado, selecting for patients who received a mental health consultation following a weight measurement of BMI greater than the 85th percentile. Data collected included: demographics, cardiovascular risk related diagnosis, BMI and behavioral health flowsheets. Following EHR abstraction encounter data were manually coded for adversity using ATLAS.ti.

Results:

The sample was predominately Latino/Hispanic (67.7%) and publicly insured (85.7%) patients. There were equal percentages of males and females (50.5% and 49.5%, respectively). On average, there were 1.5 adversity factors reported per child with 72.5% of patients reporting at least one adverse experience. The most common adversity factor reported was family separation (38%) followed by abuse (15%). Weight diagnoses were evenly distributed between overweight (25.8%), obese (40.3%), and morbidly obese (33.9%). There were 38 patients with cardiovascular risk factor diagnoses including: essential hypertension, hyperglycemia, hypertriglyceridemia, and dyslipidemia. After correcting for age, race, gender, insurance, and financial factors families who reported housing instability were more likely (p=0.002) to have children who were morbidly obese (61.3%) than families who did not report housing

instability (30.7%).

Conclusion:

This study demonstrated a high percentage of Latino/Hispanic and publically insured children had elevated BMI relative to the given patient population. Additionally, the most common environmental adversity factor in the overweight or obese pediatric population was family separation. Finally, it demonstrated a dose dependent relationship between elevated weight in childhood and housing instability.

Primary Student Presenter: Bailey Loving

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Robert Eckel

Poster Title: *Lipoprotein Lipase: Exploring a novel microglial phenotype that supports remyelination in the CNS*

Final Category: Metabolism and Endocrinology

Abstract:

Purpose of Study: Multiple Sclerosis (MS) is a severe demyelinating disorder of the central nervous system (CNS) that affects 2.5 million people worldwide. It has been suggested that microglia modulate the de- and re-myelination processes through polarization into either a pro-inflammatory — associated with increased glycolysis and reduced fatty acid oxidation (FAO) — or anti-inflammatory reparative phenotype. We have previously shown that Lipoprotein Lipase (LPL), the rate-limiting enzyme in the hydrolysis of triglyceride-rich lipoproteins, is expressed in the peripheral nervous system and is elevated following nerve crush injury. Thus, we hypothesize that LPL may scavenge and reutilize myelin-derived lipids to aid remyelination in the CNS. The purpose of this study is to determine the role of microglial LPL in inflammation and lipid-processing.

Methods Used: We generated BV-2 murine microglial cell lines with either depleted (LPL KO) or endogenous (WT) levels of LPL. mRNA was isolated, and cDNA generated for qtPCR to quantify the expression of genes associated with inflammation and cellular lipid processing. Cells and media from both LPL KO and WT BV-2 microglia were then processed for metabolomics analysis. Summary of Results: Compared to WT, LPL KO cells showed decreased expression of lipid scavenger protein SR-B1(-6 fold, $p<0.001$) as well as decreased expression of nuclear lipid sensor/transcription regulator protein PPARδ (-4 fold $p<0.05$). LPL deficient cells exhibited an increased expression of pro-inflammatory marker iNOS ($+53$ fold, $p<0.001$) and decrease in anti-inflammatory marker Arg1 (-265 fold, $p<0.001$). Metabolomic analysis revealed multiple increased intracellular glycolytic metabolites, such as D-Fructose 1-6BP ($+3$ fold, $p<0.0005$) and decreased FAO

metabolite L-Carnitine (-2 fold, $p<0.00005$).

Conclusions: In summary, LPL KO cells showed increased glycolytic metabolites and decreased FAO metabolites, along with decreased lipid processing gene expression. These data suggest that LPL is needed to prioritize fatty acid oxidative metabolism over glucose metabolism. LPL KO cells also exhibited increased iNOS and decreased Arg1, suggesting that LPL supports an anti-inflammatory microglial

phenotype. Taken together, LPL is a key feature of a reparative microglial phenotype that prioritizes lipid-processing.

Primary Student Presenter: A. Itzam Marin

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kristen Demoruelle

Poster Title: *Rheumatoid Arthritis Antibodies in Idiopathic Pulmonary Fibrosis*

Final Category: Immunology and Autoimmune Diseases

Abstract:

RHEUMATOID ARTHRITIS ANTIBODIES IN IDIOPATHIC PULMONARY FIBROSIS. AI Marin, MK (MD, SOM), JJ Solomon, S Matson S, KD Deane, J Swigris, MK Demoruelle, Department of Medicine, University of Colorado, Denver, CO.

Rheumatoid arthritis (RA) is characterized by inflammatory arthritis, but many RA patients also develop interstitial lung disease (ILD). Idiopathic pulmonary fibrosis (IPF) is the most common type of ILD, and it is of interest that RA-ILD and IPF have similar pathological and radiological features. While the etiology of IPF is unknown, because of their shared features, we hypothesize that IPF patients will have RA-related autoantibodies that can provide insight into the etiology of IPF. From the National Jewish Health Biorepository, we tested serum from 56 RA-ILD and 80 IPF patients using commercial anti-cyclic citrullinated peptide (CCP) ELISAs: CCP3 (IgG) and CCP3.1 (IgG/IgA). From the COPDGene study, we also tested serum from 112 COPD patients. In IPF, lung disease progression was determined by pulmonary function tests (PFT) at baseline and 12-24 months later. We compared anti-CCP positivity between groups (Chi-square/Fisher's exact) and within groups (McNemar's). Non-parametric testing compared change in PFT forced vital capacity (FVC) per year. Our results found that anti-CCP3 and CCP3.1 positivity were more prevalent in RA-ILD compared to IPF or COPD (p<0.01). However, anti-CCP3.1 was significantly more prevalent in IPF compared to COPD patients (29 v. 13%, p<0.01). Within IPF, anti-CCP3.1 was more prevalent than anti-CCP3 (29 v. 8%, p<0.01). Furthermore, in IPF, anti-CCP3.1 but not anti-CCP3 positivity associated with greater decrease in FVC/year (p=0.02). In conclusion, anti-CCP3.1 (IgG/IgA) but not anti-CCP3 (IgG) was significantly associated with IPF and was associated with worse lung disease prognosis. These data support a potential pathogenic role for anti-CCP-IgA in IPF, although future prospective studies are needed to validate these findings.

Primary Student Presenter: Aaron Mauner

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Eoin McNamee

Poster Title: *Morphometric and Cytologic Characterization of Ectopic Lymphoid Tissue in resected bowel of patients with Diverticulitis, Ulcerative Colitis, and Crohn's Disease*

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose of Study Recent reports state that over 23 million Americans suffer from an autoimmune disorder. Implicated in many of these diseases is the development of Ectopic Lymphoid Tissues (ELT) in their pathogenesis. The present study aims to define the morphological and cytologic characteristics of ELTs in Crohn's disease, Ulcerative Colitis, and Diverticulitis with the goal improving treatment modalities and outcomes.

Methods Used Resected bowel tissue was collected from 29 patients; 10 with Diverticulitis, 10 with Crohn's Disease and 9 with Ulcerative Colitis. Samples were formalin fixed, paraffin embedded, serially sectioned, and subsequently stained with immunohistochemical markers. Morphometric analysis was done using Olympus CellSens software and PerkinElmer Vectra 3.0 Automated Quantitative Pathology Imaging System. Cytologic analysis was done by isolating mRNA from FFPE tissues using the Ambion RecoverAll Kit and subsequent qPCR analysis. Statistical and Nearest Neighbor Analysis were performed using R Statistical Software.

Summary of Results This study is still in progress. Preliminary results indicate that the number and size of B-cell aggregates differ between disease states as well as where in the bowel wall they organize. There is also a cross-sectional area cutoff in which larger follicles develop into Tertiary Lymphoid Tissues (TLT) which have organized germinal centers. Cytological analysis suggests that there are distinct differences in chemokine profiles with Diverticulitis having a more T-cell driven profile, Ulcerative Colitis having a more B-cell driven profile. Fibrostenotic Crohn's samples showing lower expression of specific T (CCL19 & CCL21) and B-cell (CXCL12 & CXCL13) chemokines in comparison.

Conclusions Defining the composition of ELTs is an important first step in developing treatments for these disease states. The present study indicates that despite ELTs being implicated in all of these disease states their development and life cycles differ. This information should guide the development of future therapeutics and give more insight into how and why ELT development in various tissues.

Primary Student Presenter: Martha Meyer

Additional Presenter(s):

Presenting School: Other

Degree Seeking: PhD

Year: 5th

Mentor: Adam Atherly

Poster Title: *Understanding the mechanisms by which Colorado Medicaid reduced 30-day hospital readmission: did financial incentives alter post-discharge care?*

Final Category: Healthcare and Public Health

Abstract:

Mechanism for 30-day hospital readmission reduction in Colorado Medicaid

ML MEYER (Ph.D., CSPH), A. Atherly, C. Battaglia, L. Argys, G. Grunwald, H. Wald. Colorado School of Public Health, University of Colorado, Aurora, CO

Colorado Medicaid, Accountable Care Collaborative (ACC) program successfully reduced 30-day readmissions between 13-25% 2011-2014. Readmission within 30-days of discharge is considered an indicator of care quality and The Centers for Medicare & Medicaid (CMS) have focused Medicare programs and policies at reducing 30-day readmission. As such, much of what is known about preventing 30-day readmission is among patients over 65 years. Much less is known about 30-day readmissions among the Medicaid population. The purpose of this study was to understand the causal mechanism whereby the 30-day readmission rate was reduced among ACC members.

The study analyzed Medicaid and commercial claims data for the years 2009 to 2015 from Colorado's All Payers Claims Database. A probit model was used to estimate the probability that discharged patients was readmitted within 30-day. A difference-in-differences model was used to separate out the effect of the ACC program and other factors.

ACC members had a statistically significant lower probability of 30-day readmission (1.57 percentage points lower). The effect was greatest among maternal and delivery related hospitalizations (-1.13, p<.0001) and insignificant among those with a Medicare target condition (-.03, p=.857), suggesting an ACC effect and not a Medicare spillover. The results were robust to a number of different sensitivity tests.

The ACC care delivery model led to reduced readmissions without increasing post-discharge care utilization. The main effect was in maternity care. The program reduced 30-day readmission risk among the largest Medicaid population. This represents a substantial savings for the program as a recent HCUP Statistical Brief found on average Medicaid maternal readmission cost approximately $6400 in 2013.

Further, 43% of all Colorado births are covered by Medicaid in 2014. Because the majority of Medicaid members continue to be female even after the 2014 Medicaid expansion, this analysis will help to inform Colorado and other state Medicaid program care delivery system redesign.

Primary Student Presenter: Matthew Miller

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 3rd

Mentor: Cory Christiansen

Poster Title: *Factors Influencing Participation in Physical Activity after Dysvascular Amputation: a Qualitative Meta-Synthesis.*

Final Category: Healthcare and Public Health

Abstract:

MJ Miller, (Ph.D., GS), J Jones, College of Nursing, University of Colorado, CB Anderson, (Ph.D., GS), and Cory L Christiansen, Physical Therapy Program, School of Medicine, University of Colorado. Purpose: Identifying psychosocial factors associated with physical activity after dysvascular lower limb amputation (LLA) could provide potential targets for improving rehabilitation outcomes. The purpose of this qualitative meta-synthesis was to identify modifiable factors that influence participation in physical activity after dysvascular LLA, a condition characterized by amputation in the setting of older age, diabetes mellitus (DM) and/or peripheral artery disease (PAD).

Methods: A systematic search of the literature identified qualitative studies exploring the perceptions of physical activity in people with LLA, older age, DM, or PAD. The qualitative rigor of the included studies was assessed using the McMaster University's Guidelines for Qualitative Review. Thematic analysis was undertaken to synthesize the findings within and across the studies.

Results: Fourteen studies were included for analysis, and methodological quality of studies was variable. Three overarching factors influencing physical activity in the presence of LLA, older age, DM, or PAD emerged: 1) educational experiences and motivation, 2) support and self-efficacy, and 3) special concerns after LLA.

Conclusions: Physical activity after dysvascular LLA is influenced by complex relationships among health understanding, motivation, support and self-efficacy in the presence of severe physical disability. These findings can be used to develop and test behavior-based interventions targeting improved physical activity after dysvascular LLA.

Primary Student Presenter: Katie Mishall

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Rebecca Schweppe

Poster Title: *IL-1beta promotes invasion through the FAK>p130Cas>c-Jun signaling axis in thyroid cancer*

Final Category: Hematology and Oncology

Abstract:

Anaplastic thyroid cancer (ATC) is one of the most deadly cancers, with most patients succumbing to the disease less than one year after diagnosis. Our lab has shown Src is a key mediator of tumorigenesis in thyroid cancer. However, Src inhibitors have limited efficacy in the clinic. To more effectively target Src, our lab generated 4 thyroid cancer cell lines resistant to the Src inhibitor, dasatinib using a dose escalation approach (Beadnell, 2016). We have shown the dasatinib-resistant cells have undergone a phenotype switch and are now more reliant on the IL-1β>FAK>p130Cas>c-Jun signaling axis to regulate cell growth and invasion. We hypothesized IL-1β plays an important role in the early reprogramming of this switch by signaling through the FAK>p130Cas>c-Jun pathway. In support of this, we have shown IL-1β treatment increases invasion in a panel of thyroid cancer cell lines 1.5-3 fold ($p<0.05$, 3/5), but has no effect on cell growth. We have also shown that acute IL-1β treatment induces c-Jun expression and phosphorylation by 2-4 fold ($p<0.05$ 2/4 cell lines), suggesting c-Jun may be playing a role in the increased invasive potential of thyroid cancer cells upon IL-1β stimulation. Accordingly, we have shown that inhibition of c-Jun using a pharmacological inhibitor, JNK-IN-8, prevents IL-1β mediated invasion ($p<0.01$). Interestingly, we do not observe changes in FAK or p130Cas phosphorylation in response to IL-1β stimulation. Thus, changes in protein-protein interactions or localization may be important. Overall, these studies have identified an important role for c-Jun in mediating IL-1β induced invasion, which has important implications for ATC, due to the high infiltration of immune cells in these tumors. Furthermore, our studies provide an important step to begin to understand the complex molecular environment ATC tumors have to help improve patient outcomes.

Primary Student Presenter: Danielle Ostendorf

Additional Presenter(s):

Presenting School: Public Health

Degree Seeking: PhD

Year: 5th

Mentor: Victoria Catenacci

Poster Title: *Doubly-Labeled Water Assessment of Total Energy Expenditure in Successful Weight Loss Maintainers*

Final Category: Metabolism and Endocrinology

Abstract:

Doubly-Labeled Water Assessment of Total Energy Expenditure in Successful Weight Loss Maintainers. DM Ostendorf, (PhD, CSPH), AE Caldwell, SA Creasy, Z Pan, K Lyden, HR Wyatt, A Bergouignan, JO Hill, EL Melanson, and VA Catenacci, Department of Medicine, Anschutz Health and Wellness Center, University of Colorado Anschutz Medical Campus, Aurora, CO, USA.

   Total daily energy expenditure (TDEE) declines with weight loss due to decreases in resting energy expenditure (REE) and physical activity energy expenditure (PAEE) that results primarily from the reduction in body mass, as well as due to additional metabolic adaptations that occur with weight loss. Successful weight loss maintainers (WLM) report high levels of physical activity (PA), however, the mechanisms through which PA promotes weight loss maintenance are unclear. Therefore, we compared TDEE, REE, and PAEE (TDEE-REE-.1*TDEE) in successful WLM (n=25, maintaining ≥13.6 kg weight loss for ≥1 year), normal weight controls (NC, n=27, BMI matched to current BMI of WLM), and controls with overweight/obesity (OC, n=28, BMI matched to pre-weight loss maximum BMI of WLM). TDEE was measured with doubly labeled water over 7 days, and REE with indirect calorimetry. Results are mean (95% CI). TDEE in WLM and OC was significantly higher than NC (WLM: 2470.0 (2302.3-2649.8), NC: 2142.6 (2002.5-2292.5), OC: 2543.5 (2380.1-2718.1) kcal/d; p<0.05). REE in OC was significantly higher than WLM and NC (WLM: 1408.1 (1336.8-1509.6), NC: 1345.7 (1268.1-1428.2), OC: 1660.0 (1562.4-1763.8) kcal/d; p<0.05), as expected given the higher body mass. PAEE was significantly higher in WLM compared to OC and NC (WLM: 812.2 (702.6-921.7), NC: 620.6 (513.2-728.0), OC: 637.1 (527.6-746.7) kcal/d; p<0.05). Thus, weight loss maintainers are successfully achieving energy balance at a reduced body weight through higher levels of PAEE, while maintaining a TDEE level similar to that of controls with overweight/obesity.

Primary Student Presenter: Nuria Padilla Just

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 6th

Mentor: Carol Sartorius

Poster Title: *Molecular determinants of ER+ breast cancer organ-specific metastasis*

Final Category: Hematology and Oncology

Abstract:

Over half of all deaths from breast cancer are due to metastatic estrogen receptor (ER+) disease. Patients with ER+ breast cancer are at chronic and prolonged risk of relapse; overall survival upon detection of distal metastasis is less than 2 years. The most frequent sites of ER+ breast cancer metastasis are in relative order bone, liver, lung, and brain, with individual tumors preferring one or more sites. The underlying mechanisms of site-specific metastasis are poorly understood and are critical for prevention and treatment of metastatic disease. A prevailing theory is that tumor cells seed early and often, but only rare cancer stem cells (CSCs) allow survival and expansion at distal sites. We hypothesize that hormone signaling influences CSCs and metastatic organ specific survival. To test this, our group has developed ER+ patient-derived xenografts (PDX) labeled with constitutive luciferase-GFP. Using intracardiac dispersal as a measure of late stage metastasis, we have indeed observed organ homing preference of ER+ PDX. Two highly ER+PR+ tumors spread to bone and brain, but not liver or lung, whereas an ERlowPR− tumor spreads ubiquitously to liver and lung, but never bone or brain. Single cell RNA sequencing of the ER+PR+ PDX-derived brain metastatic cells and ERlowPR− PDX-derived liver metastatic cells compared to their cognate primary tumors revealed significantly different patterns. The brain metastatic cells had elevated PR expression and progesterone (P4) signaling, including several previously defined P4-regulated CSC genes. By contrast, the liver metastatic cells showed no evidence of hormone programming and a basal/CSC gene program. We conclude that ER+ tumors have diverse CSC populations that may dictate their organ homing preference and survival; ER+PR+ tumors retain hormone signaling that may direct CSCs to seed to bone and brain, while loss of estrogen responsiveness may enrich for more basal/CSCs that preferentially land and expand in liver and lung. Our long term goal is to identify key patterns and vulnerabilities of ER+ breast cancer cells driven to more lethal (brain, liver) vs. static (bone) metastatic sites to identify at-risk patients and reduce acquisition of lethal metastatic ER+ breast cancer.

Primary Student Presenter: Adam Panzer

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jim Costello

Poster Title: *Using Ancestry to Find Hidden Disease Variants in The Cancer Genome Atlas*

Final Category: Hematology and Oncology

Abstract:

Using Ancestry to Find Hidden Disease Variants in The Cancer Genome Atlas. AA Panzer, (MD, SOM) and J Costello, Department of Pharmacology, University of Colorado, Aurora, CO.

Genomic studies like The Cancer Genome Atlas (TCGA) are enabling understanding of cancer through identification of driver mutations. However, driver genotypes alone often do not predict disease development or course. Modifier genotypes in the genetic background determine the ultimate effect of primary genetic insults. When modifiers are subgroup-specific, discovery may require a sample stratification strategy that enables local enrichment of rare variants in downstream analysis. Self-reported race has been used for this purpose, but with limited success as crude racial categories poorly represent underlying genetic diversity. We hypothesize that ancestry inference algorithms, which infer relatedness directly from genetic data, will offer a superior stratification strategy.

We used Genome Analysis Toolkit to call variants from TCGA sequence data. These variants were input to ancestry inference programs, including ADMIXTURE, LASER and DietNet, for clustering of patients according to their genetic similarity with one another (unsupervised) or to 1000 Genome global SNP profiles (supervised) based on genomewide allele frequencies. Using these groupings, we recapitulated the genetic association and differential expression analyses in the TCGA data pipeline.

Our clustering of TCGA revealed demographics beyond that found by self-reported ethnicity, implicated previously discovered and novel disease variants, and suggested associations between particular racial/ethnic groups and different driving alterations that may underlie observed disparities in cancer burden.

In addition to yielding additional insight on the genetic etiology of various cancers, these results suggest that ancestry-based clustering may be a useful technical innovation applicable to almost all large human genomics projects.

Primary Student Presenter: Rupa Parikh

Additional Presenter(s): Melissa Gamble, Carol Stamm, Rachel Johnson, and Leanne Rupp

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Laura Borgelt

Poster Title: *Barriers Remain For Access To Emergency Contraception In Arizona and Utah*

Final Category: Healthcare and Public Health

Abstract:

Background: Emergency contraception (EC) is a form of birth control that is used to prevent unintended pregnancy after unprotected sexual intercourse has occurred. This study aimed to determine whether young women who sought EC encountered access barriers at pharmacies in Arizona and Utah. Additionally, knowledge of pharmacists regarding weight and EC effectiveness was assessed.

Methods: Mystery caller survey of 1,008 outpatient pharmacies in Utah and Arizona. Two female researchers poses as "mystery shoppers" seeking EC using telephone call during days, evenings, weekends and holidays. . All of the pharmacies called were found in The Little Blue Book 2015 and serve the general public as outpatient pharmacies. The predetermined script included questions about brand and generic availability (in-stock), location of product, anything else needed to obtain EC such as identification cost, and effectiveness of EC with weight. Comments reflecting willingness of pharmacy staff to offer alternatives if EC was out-of-stock or if patient was overweight were recorded.

Results: Overall, 833/1,008 (82.6%) pharmacies had EC in stock; however, only 672/833 (80.7%) said that it was available on the shelf to pick up now, and 638/838 (76.6%) correctly identified that the caller wouldn't face an artificial barrier, such as providing an ID, when purchasing the EC. When examining the question regarding weight and effectiveness, pharmacists were much more likely than pharmacy technicians to correctly answer "Yes", that weight can affect effectiveness of EC (p=0.033).

Conclusion: Although most pharmacies claimed to have EC in stock, a significant number of pharmacies posed access barriers to women who aimed to seek EC. Additionally, incorrect information regarding weight and EC effectiveness was conveyed and was dependent on the type of pharmacy and employee level. These data indicate education of pharmacy staff is needed regarding accessibility and effectiveness of EC.

Primary Student Presenter: Harin Parikh

Additional Presenter(s): Harin Parikh

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Dr. Tessa Mandler

Poster Title: *Comparing the efficacy of print versus media based patient education materials in OnQ peripheral nerve catheter education for caregivers*

Final Category: Education

Abstract:

Title: Comparing the efficacy of print versus media based patient education materials in OnQ peripheral nerve catheter education for caregivers

Purpose: The purpose of this study is to verify the efficacy of patient-education materials (PEM), determine whether print-based PEMs or media-based PEMs are more efficacious in providing caregiver education, and assess caregiver preference for one PEM mode over another.

Methods: This prospective, randomized study includes caregivers of pediatric patients undergoing ACL Reconstruction surgery performed by a single sports medicine orthopedic surgeon at Children's Hospital Colorado. Subjects were assigned to review either a handout (print-based PEM) or a three-minute video (media-based PEM) on the OnQ peripheral nerve catheter, a device used to control postoperative pain. Both PEMs contain exactly the same information regarding OnQ catheter management and removal. The caregiver subsequently completed a standardized assessment of their knowledge in managing the catheter at home and a survey 24 hours postoperatively to assess caregiver satisfaction and preference with the assigned PEM.

Results: Standardized assessment results indicate an average of 9.25 and 9.5 (out of 10) for caregivers in the print-based and media-based groups, respectively. Preliminary results show 76% of caregivers (16/21) preferred the media-based PEM in initial education. We are continuing data collection and expect to include thirty patients within the next two months.

Conclusion: Preliminary data suggests no apparent difference in efficacy between the media-based PEM and the print-based PEM. However, these preliminary results suggest that media-based PEMs may result in better caregiver satisfaction, as 72% stated that the video PEM was more helpful to them in understanding how to managing their child's OnQ peripheral nerve catheter at home.

Primary Student Presenter: Megan Perez

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Granville Lloyd

Poster Title: *A Preoperative Mathematical Model to Estimate Available Tissue Length for Ureteral Reimplantation by Different Methods of Bladder Mobilization*

Final Category: Surgery

Abstract:

A PREOPERATIVE MATHEMATICAL MODEL TO ESTIMATE AVAILABLE TISSUE LENGTH FOR URETERAL REIMPLANTATION BY DIFFERENT METHODS OF BLADDER MOBILIZATION

Presenting Author: Megan A. Perez, MD candidate in the University of Colorado School of Medicine

Author: Granville Lloyd – Assistant Professor, Denver VA/ University of Colorado Department of Surgery- Urology

Introduction & Objective

   Ureteral injury occurs after pelvic surgery at a rate that has been estimated to range from 0.2-9% of cases; other causes of iatrogenic ureteral obstruction include endoscopic surgery, malignancy, radiation and external trauma. These injuries are commonly reconstructed with ureteral reimplantation; depending on the level of injury more complex reconstructions of the bladder may be required, such as Boari flap, to bridge distances to viable proximal ureter. Accurate preoperative estimate of the amount of ureteral length available after bladder mobilization, with or without advancement flap, is desirable. We sought to create a graphical tool to estimate the distance that can be generated from the base of the bladder after maximal mobilization toward ureteral reimplantation, based on bladder volume.

Methods

Starting assumptions include:

1. A fully mobilized bladder conformationally represents a sphere.
2. A maximally mobilized bladder would yield a length for simple direct reimplantation equivalent to ½ circumference.
3. Boari flap was designed as commonly cited with a base-width to length ratio of 1:1 with a 4cm wide base and thus would optimally add 4 cm to the length generated from a mobilized bladder.

A curve was generated by solving $v = 4/3\, \pi(c/2\pi)^3$ for ½ circumference from bladder volume (Fig 1).

Results

    Figure 1 demonstrates the relationship between bladder volume and available length for simple direct reimplantation. Boari flap reimplantation adds 4 cm of additional length at the cost of approximately 8 cm worth of sutured repair of the bladder.
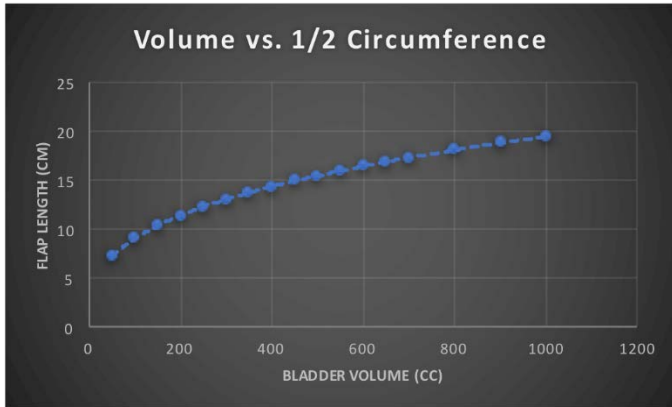

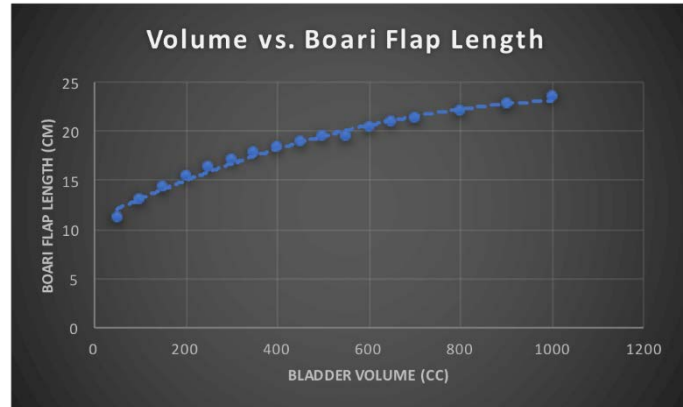Figure 1. Volume vs. ½ Circumference to predict simple reimplantation.

Figure 2. Volume vs. Boari Flap reach, solving for 1/2 C then adding an additional 4 cm to each based on a 4 cm wide flap base and length.

Conclusions

    We present a mathematical model for the estimation of maximal generated length from bladder for ureteral reimplantation in the setting of distal ureteral loss. We believe that knowledge and usage of this model will prove beneficial in difficult reconstructions for accurate surgical planning. This mathematical model awaits validation *in vivo*, and suffers from limitations including the inability to estimate additional length from bladder compliance, as well as limitation of mobilization from fixation at the contralateral vascular pedicle. Despite these limitations, we have found that bladder volume provides a useful estimate of available tissue length for preoperative planning in the setting of complex ureteral reconstructions.

Primary Student Presenter: Erik Polsdofer

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Bolin Liu

Poster Title: *Treatment With Metformin Enhances TRAIL Upregulation and TRAIL-Mediated Apoptosis In Triple Negative Breast Cancer Cell Lines*

Final Category: Hematology and Oncology

Abstract:

Erik V. Polsdofer

Hui Lyu

Bolin Liu

University of Colorado Anschutz Medical Campus, Aurora, CO

Department of Pathology

Purpose of Study: Triple negative breast cancer (TNBC) does not respond to conventional targeted therapy, necessitating novel treatment options. Metformin has shown evidence of possessing anti-proliferative and pro-apoptotic properties in TNBC, but it's mechanism of action is incompletely understood. Our experiments aim to examine TRAIL signaling pathway's involvement in Metformin's effects on TNBC.

Methods Used: In Vitro – TNBC cell lines BT549, HCC1806, MDA231, and MDA468 were cultured. Cell survivability was assessed by MTS assay. Changes in protein levels of pro-caspase 8, pro-caspase 3, PARP and TRAIL were assessed by Western Blot analysis.

Summary of Results: Cell survivability decreased after Metformin treatment in a dose dependent manner by MTS assay in MDA231 and HCC1806 cell lines. BT549, HCC1806, MDA231, and MDA468 cell lines demonstrated increased apoptosis after Metformin treatment through evidence of decreased pro-caspase 8, pro-caspase-3, and increased PARP cleavage on Western Blot as compared to control. MDA231 cell line demonstrated increased TRAIL expression with Metformin treatment in a dose- and time- dependent manner on Western Blot as compared to control.

Conclusion: TNBC cell lines demonstrate increased apoptosis and levels of TRAIL protein after treatment with Metformin. If our future experiments targeting the blockade of TRAIL signaling demonstrate an

attenuation of apoptosis in TNBC cell lines after Metformin treatment we can conclude that the TRAIL signaling pathway plays a critical role in Metformin's apoptotic effect.

Primary Student Presenter: Howe Qiu

Additional Presenter(s): Nathan A. Fischer

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Emily McCourt

Poster Title: *Frequency of Pediatric Traumatic Cataract Complicated by Retinal Detachment*

Final Category: Vision Sciences

Abstract:

H Qiu, (MS, SOM), NA Fischer, JL Patnaik, JK Singh, and EA McCourt, Department of Ophthalmology, University of Colorado School of Medicine, Aurora, CO.

Purpose: Traumatic cataract in the pediatric population is a treatable cause of vision loss. However, in cases of simultaneous retinal detachment, the surgical approach may be different and the prognosis for visual recovery is poor. Thus, understanding which eyes with traumatic cataract are at risk for concurrent retinal detachment is important for both surgical planning and patient counseling. Our study investigates comorbid traumatic cataract and retinal detachment with the goal of better understanding risk factors for retinal detachment in these patients.

Methods: A retrospective review of patients diagnosed with traumatic cataract at Children's Hospital Colorado between 2005 and 2014 was conducted and demographics, mechanism and type of injury, and incidence of retinal detachment were recorded. Fischer's and chi-square tests were used for statistical analysis.

Results: Of 64 total eyes with traumatic cataract, 54 eyes presented unilaterally and 10 presented bilaterally. Mean patient age was 8.0 years (range 0 to 16) with 80% of patients identified as male. A total of 16% of eyes were found to have a comorbid retinal detachment. Of the eyes with retinal detachment, 60% (n = 6) were identified as having self-injurious behavior and all were above the age of 5 years.

Conclusion: Patients who display self-injurious behavior and present with traumatic cataract are at five-fold risk for concurrent retinal detachment. Such patients are often difficult to examine in the office and B scan ultrasound is often not done until the patient is in the operating room. The ophthalmologists should council the families of these high risk patients and consider involvement of a retina specialist in surgical planning. Patients without self-injurious behaviors are unlikely to have comorbid retinal detachment.

Primary Student Presenter: Bill Quach

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Jennifer Kwak

Poster Title: *Confounding bone marrow findings in lymphoma patients due to granulocyte colony stimulating factor on FDG PET/CT*

Final Category: Hematology and Oncology

Abstract:

FDG PET/CT imaging is essential for evaluating chemotherapy response in lymphoma patients. Unfortunately, drugs used to treat chemotherapy associated neutropenia, i.e. granulocyte colony stimulating factors (G-CSF), stimulate hematopoiesis that cause elevated FDG uptake in the bone marrow (BM) which confound FDG PET/CT interpretations. Few small studies that have investigated the optimal wait time after G-CSF administration reported widely differing recommendations. We sought to bridge this knowledge gap by performing a retrospective study of 177 lymphoma PET/CT cases. FDG uptake in the bone marrow was measured quantitatively with standardized uptake value (SUV) measurements and qualitatively by visual assessment of FDG uptake in the bone marrow compared to liver and blood pool. In the longer acting G-CSF group, bone marrow SUV reached control levels at 27 days and the probability of BM uptake being less than liver uptake was 60% at 30 days suggesting an optimal wait time of 27 to 30 days. In the shorter acting G-CSF group, SUV reached control levels at 37 days but the probability of BM uptake being less than liver uptake was 75% at 10 days. Interreader agreement was good (ICC = 0.83). Primary factors affecting BM FDG uptake were age and number of days since G-CSF administration while WBC count (0.44), ANC (0.50), hematocrit (0.75) and platelet count (0.99) had no correlation. Our data advocate for a longer waiting period prior to FDG PET/CT for lymphoma patients receiving G-CSF as imaging data may be confounded by G-CSF stimulation of the BM.

Primary Student Presenter: Bradley Reeves

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Francisco Rodriguez-Fontan

Poster Title: *Strap Stabilization Use in Posterior Instrumented Spinal Fusion for Proximal Junctional Kyphosis Prevention: A Retrospective Cohort Study*

Final Category: Bone or Skeletal

Abstract:

The use of posterior instrumented fusion (PIF) with pedicle screws is a standard approach for surgical correction of adult spinal deformity (ASD). Following PIF, a change in biomechanical properties secondary to increased loading of uppermost instrumented vertebra (UIV) may lead to proximal junctional kyphosis (PJK) and the more severe manifestation, proximal junctional failure (PJF). These complications manifest as a post-operative proximal junctional sagittal Cobb angle ⬚ 10° and PJF is associated with proximal symptomatic vertebral fracture, hardware failure, spondylolisthesis and increased risk of neurologic injury. The incidence of PJK and PJK is variable, ranging from 5.6% to 41% and 1.4% to 35% respectively with up to 47% of PJF cases requiring reoperation. Many previous attempts have been made to maintain normal spinal biomechanics and reduce the incidence of PJK, but none have proven effective. A retrospective cohort study was conducted to evaluate potential risk factors of PJK and the association between use of Mersilene-tape stabilization and risk of PJK in patients undergoing thoracolumbar PIF for correction of ASD at UC Hospital between 2006 and 2014. Fifty-nine patients were included: 15 cases, and 44 controls. The cumulative rate of PJK>10° at 2-year follow-up was 20% in cases versus 43.1% of controls (OR=0.33, P=0.09) with higher latent period in cases, P=0.045. Mersilene-tape significantly decreased risk of PJK in the following conditions: age ≥55 years-old (OR=0.2, P=0.04); BMI, ≥27 kg/m2 (OR=0.2, P=0.04); UIV, T1-T12 (OR=0.2, P=0.05); post-operative versus pre-operative PI difference ≥11° (OR=0.04, P=0.04); and no transforaminal-LIF (OR=0.16, P=0.04). We concluded that Mersilene-tape stabilization of the spine at UIV and 1-2 supra-adjacent levels decreases the risk of PJK after correction of ASD by long PIF.

Primary Student Presenter: Kelsey Repine

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: John Repine

Poster Title: *UNIQUE NEONATAL RATS HAVE DECREASED ACUTE LUNG INJURY FOLLOWING HYPEROXIA*

Final Category: Pulmonary and Critical Care

Abstract:

UNIQUE NEONATAL RATS HAVE DECREASED ACUTE LUNG INJURY FOLLOWING HYPEROXIA

K.M. Repine, P. V. Wilson, D. Pinto Payares, T. Toni, B. Florence, K. Baer, Q. He, A. Fernandez-Bustamante, B. W. Saccomano, J. E. Repine, Webb-Waring Center, Department of Medicine and Pediatrics, University of Colorado, Aurora CO.

High oxygen concentrations (hyperoxia) are often used to treat hypoxemia in hospitalized neonates. The exact effects of hyperoxia are unknown but prolonged hyperoxia is associated with Bronchopulmonary Dysplasia (BPD). While studying Acute Respiratory Distress Syndrome, we serendipitously created a novel strain of hyperoxia tolerant rats by repeatedly breeding a single naturally hyperoxia tolerant rat and its tolerant offspring. Adult tolerant rats survive indefinitely while all control rats die in hyperoxia. After hyperoxia, adult tolerant rats also develop less acute lung injury and inflammation and have bone marrow mononuclear cells (BMM) with higher levels of heme oxygenase-1 (HO-1)—an anti-inflammatory antioxidant—than adult control rats. To determine if this novel genetic tolerance disposition is also protective during the neonatal period (0-21 days of life), we evaluated acute lung injury and BMM HO-1 levels in neonatal control and tolerant rats before and after hyperoxia.

Methods: Acute lung injury (lung lavage LDH and protein levels) and lung inflammation (lung lavage neutrophils) of male neonatal (~21-day-old) unexposed and hyperoxia exposed (~52 hr) control and tolerant rats were measured. Femoral BMM of neonatal rats was harvested, counted, and analyzed (ELISA) for HO-1 expression.

Results: After hyperoxia, neonatal tolerant rats have less LDH ($p<0.005$) and protein ($p<0.05$), but the same ($p>0.05$) neutrophils, and higher ($p<0.005$) BMM HO-1 levels compared to neonatal control rats. Although before hyperoxia, neonatal control rats have higher ($p<0.05$) BMM HO-1 levels than neonatal tolerant rats, after hyperoxia, BMM HO-1 levels from neonatal control rats decrease ($p<0.005$) to below pre-hyperoxia baseline levels while BMM HO-1 levels of neonatal tolerant rats triple ($p<0.05$).

Conclusion: BMM HO-1 increases may decrease acute lung injury in BPD related to hyperoxia.

Primary Student Presenter: Thomas Ryan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Brett Reece

Poster Title: *Neuronal Supplement Deprivation Decreases Erythropoietin Receptor Expression in Mouse Brain and Spinal Cord Neurons in-vitro*

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Neuronal Supplement Deprivation Decreases Erythropoietin Receptor Expression in Mouse Brain and Spinal Cord Neurons in-vitro. TJ Ryan (MD, SOM), M Eldeiry, M Aftab, D Fullerton, TB Reece, Department of Cardiothoracic Surgery, University of Colorado, Denver, CO.

Purpose: The tissue protective receptor (TPR), a heterodimer of β-common receptor (BCR) and erythropoietin receptor (EpoR), triggers a tissue protective mechanism in neurons. An in-vitro model of neuronal ischemia requires oxygen and glucose deprivation (OGD). OGD experiments on neurons revealed a large decrease in EpoR. Serum free neuronal culture commonly uses neuronal supplement (NS) B27. It is not present in OGD media to avoid alteration of ischemic damage. We hypothesize that NS deprivation independently reduces EpoR present on the neuronal cell membrane.

Methods: Neuronal tissue was collected from neonatal mice, then digested by papain and trituration. Neurons were isolated by centrifugation. They were cultured at 200k-250k cells/cm2 for 1 week on PDL coated plates in Neurobasal-A Medium with 2% (v/v) B27 NS (Gibco). The cells were then treated with B27 deprived media or media with 2% B27. After 1-2 hours, a Western blot for BCR and EpoR was performed.

Results: NS deprived neurons showed undetectable EpoR expression relative to neurons given 2% B27 (brain: 0.0 vs. 0.39±0.055, p<0.01; spinal cord: 0.0 vs. 0.33±0.056, p<0.01). BCR was not significantly different in neurons deprived of NS versus neurons given 2% B27 (brain: 0.45±0.046 vs. 0.46±0.044, p=0.91; spinal cord: 0.35±0.056 vs. 0.32±0.051, p=0.74).

Conclusions: NS deprivation reduces the amount of EpoR present on neurons, and has no effect on BCR. This may imply that EpoR is required at some ratio to facilitate BCR's protection mechanism. Future study aims to better define the relationship between EpoR and BCR, and their tissue protective mechanism. In addition, effects of a decrease in TPR should be considered when using this in-vitro model.

Primary Student Presenter: Weston Ryan

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Todd Baldini

Poster Title: *The Effects And Evaluation Of Pre-Contoured Plate Fixation On Transverse Acetabular Fractures*

Final Category: Bone or Skeletal

Abstract:

Background and Objective

Operative reduction and internal fixation of acetabular fractures is the gold standard for complex cases. Conservative management or insufficient fixation of these fractures leads to arthrosis and has a high incidence of pain. This study aims to characterize the relationship between reduction and fixation method by utilizing traditional reconstruction plates and quadrilateral surface (Matta) plates post-fixation and evaluating their mechanical properties.

Methods

18 synthetic hemipelvises were used in this investigation. A transverse acetabular fracture was created through the lunate surface and reduced in one of three ways: (1) lag and positional screws then a Matta plate; (2) reduction with K-wires then a Matta plate; (3) lag and positional screws then reconstruction plates. Fracture displacement was measured pre and post fixation. Specimens were cyclically loaded in to 42,000 cycles, then to failure.

Results

Simulated transverse acetabular fractures fixated with Matta plates but no supporting screws developed fracture surface displacement greater other groups, particularly across the anterior column and acetabular surface. The Matta plate-only samples also failed at a lower cycle number at 7BW than both other groups.

Discussion

The fracture displacement of the plate-only group suggests that optimal fracture fixation may require additional support such as lag or positional screws. Temporary wire reduction allows anatomic reconstruction, however is susceptible to plastic deformation forces exerted by the plate. Although

initial displacement of fractures may exist, loading of the fixated joint favors fracture compression at even low loads, acting in a 3-point bend. All samples demonstrated adequate ultimate strength for limited weight bearing loads, however secondary fixation bolsters the constructs strength allowing for more dependable fixation and recovery with potentially greater mobility in the post-operative period.

Primary Student Presenter: Jenny Mae Samson

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Mayumi Fujita

Poster Title: *Stress-induced NLRP1 contributes to resistance to drug therapy in human melanoma*

Final Category: Hematology and Oncology

Abstract:

Metastatic melanoma remains a challenging disease due to the development of resistance against available therapies. We have demonstrated that the NLR sensor NLRP1 promotes melanomagenesis through activation of IL-1-mediated inflammation and inhibition of apoptosis. Here we investigate a potential role of NLRP1 in the development of drug resistance in human melanoma cells. Pharmacologically relevant doses of temozolomide (TMZ), vemurafenib (VEM), and trametinib (TRA) significantly increase expression of NLRP1 in metastatic melanoma cells. However, NLRP1 induction had no concurrent increase in IL-1b synthesis or secretion, suggesting that NLRP1 induction is uncoupled from its inflammatory role. To understand the role of upregulated NLRP1 in drug resistance, we generated TMZ-resistant 1205Lu and HS294T, VEM-resistant A375 and 1205Lu, and TRA-resistant Sk-mel-28 and HS294T cells. All of these cells show elevated expression of NLRP1 without subsequent induction of IL-1b synthesis or secretion, supporting an inflammasome-independent role of NLRP1 in drug resistance. Drug treatment activates ER stress pathways, of which PERK-eIFa-ATF4 may transcriptionally regulate NLRP1. We observed increased expression of ATF4 in drug-treated parental and drug-resistant cells consistent with NLRP1 induction. Further, silencing of ATF4 reduced NLRP1 expression, supporting ATF4 as a transcriptional regulator of NLRP1. These observations support the possibility that melanoma cells use ER stress mechanisms to overcome treatment and develop resistance. By inhibiting ER stress response, we observed reduced viability, increased caspase-3 activity, and increased apoptosis in our models. These data suggest a novel role of stress-induced NLRP1 in melanoma drug resistance that may be associated with its anti-apoptotic function, independent from its inflammasome-related activities. The roles of NLRP1 and upstream ATF4 in ER stress, cell death, and drug resistance are under active investigation.

Primary Student Presenter: Colton Sauer

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Jim Carollo

Poster Title: *Comparison of Rotational and Clinical Outcomes in Femoral Derotation Osteotomies Between Blade Plate and Intramedullary Nail Fixation*

Final Category: Surgery

Abstract:

COMPARISON OF ROTATIONAL AND CLINICAL OUTCOMES IN FEMORAL DEROTATION OSTEOTOMIES BETWEEN BLADE PLATE AND INTRAMEDULLARY NAIL FIXATION
CD Sauer, JJ Carollo, JT Rhodes

Femoral derotational osteotomies (FDROs) are an orthopedic intervention to correct transverse plane deformities and improve biomechanical function. Blade plates (BP) and trochanteric intramedullary nails (IMN) are two fixation techniques compared in this study. The goal of this study is to test equivalence between the two fixation methods regarding accuracy of rotational correction and clinical or surgical metrics.

After IRB approval, retrospective gait analysis data were collected on 89 subjects receiving FDROs, including pre- and post-operative measurements of hip internal and external rotation, average pelvic and hip rotation, medical diagnoses, fixation method, and concurrent surgeries. Hip internal and external rotation were averaged to estimate femoral anteversion. Pelvic and hip rotations were calculated as averages over complete gait cycles using 3D kinematics. To test rotation accuracy, subjects diagnosed with cerebral palsy (N = 29) were separated into groups receiving IMN and BP fixation. Changes in hip kinematics, and internal/external hip rotation were compared pre- and post-operatively using Student's t test. To account for single event multilevel surgeries while investigating differences in clinical and surgical metrics, BP and IMN subjects were optimally matched (N = 26) using MatchIt R statistical package and compared using Fisher's exact test.

The IMN and BP groups had no statistically significant differences except for time to weight bear, which was 11.9 days sooner for individuals that received IMNs when compared to BPs. Note that values for each measurement were subtracted between BP and IMN groups, where a positive number represents BP > IMN.

Measurement	BP vs. IMN	P-Value (α = 0.05)
Difference in Hip Int/Ext Rotation	0.7°	0.9181
Difference in Hip Kinematics	6.8°	0.3982
Time to Weight Bear	11.9 days	0.0311

There were no significant differences between BP and IMN groups regarding rotational outcomes of the FDROs. The surgical and clinical metrics between the two fixation methods were nearly identical as well, with the exception of time to weight bear. This study suggests use of IMN for isolated FDROs to treat femoral anteversion because IMNs have shorter times to weight bear while being equivalent to BPs in all other variables investigated in this study.

References

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[2] Ho DE, Imai K, King G, Stuart EA. MatchIt: nonparametric preprocessing for parametric causal inference. *Journal of Statistical Software.* 2011;42(8):1-28.

Primary Student Presenter: Alexander Schulick

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Schwartz

Poster Title: *Expression of MUC5B and Markers of Endoplasmic Reticulum Stress are Jointly Expressed in Idiopathic Pulmonary Fibrosis.*

Final Category: Pulmonary and Critical Care

Abstract:

Purpose of Study: Idiopathic Pulmonary Fibrosis (IPF) is a progressive, incurable fibrotic disease that is restricted to the lung. We have identified a gain-of-function variant in the promoter of the lung gel-forming mucin gene MUC5B that is the strongest risk factor for developing IPF. Since MUC5B is a large glycoprotein that requires substantial post-translational modification and markers of Endoplasmic Reticulum (ER) stress have previously been associated with IPF, we hypothesized that the MUC5B gain-of-function variant is associated with ER stress in the IPF lung.

Methods: Samples for immunohistochemistry were selected based on disease (n = 19) vs. normal (n = 24), and presence of the MUC5B promotor variant. Quantitative polymerase chain reactions (qPCR) were run from whole tissue extracted mRNA for ER stress genes. The ER stress genes were also studied in a larger sample size using microarray techniques (disease n = 230, normal n = 89).

Summary of Results: The qPCR experiment demonstrated that IPF in comparison to controls is most associated with enhanced ER stress gene expression for XBP1 and ERN1. More rigorous analysis did not show ER stress expression levels correlated with expression of MUC5B. However, the microarray study conducted on the larger sample size did show that ER stress genes ERN2 and XBP1 were correlated with MUC5B expression.

Conclusions: Our results confirm the previous studies that have demonstrated that IPF is associated with increased expression of ER stress genes. Moreover, through the larger array study, we have found that expression of some ER stress genes is associated with expression of MUC5B among patients with IPF, suggesting that MUC5B may be driving cell stress in IPF. In aggregate, our findings indicate a potentially important relationship between expression of MUC5B and markers of ER stress in IPF.

Primary Student Presenter: Sara Schuster

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Carol Stamm

Poster Title: *Unprotected Sex while Visiting Denver: Emergency Contraception Access in Colorado Pharmacies*

Final Category: Healthcare and Public Health

Abstract:

Unprotected Sex while Visiting Denver: Emergency Contraception Access in Colorado Pharmacies. SM Schuster (MD candidate in the School of Medicine), H Yi, CA Stamm (MD, FACOG), L Borgelt (PharmD), K Cleland (MPA, MPH).

   Background: Plan B One-Step has been available over the counter for women of all ages since 2013, and generic forms were made available in 2014. There are no federally imposed restrictions on who can purchase emergency contraception and it can be sold on store shelves in no security packaging. However, the actual access for emergency contraception in pharmacies is dependent on each store's individual policies. Given this potential for variability, someone seeking emergency contraception can have a very different experience depending on which store they select.

Objective: The goal of this project was to obtain an overview of what buying emergency contraception is like in pharmacies in highly trafficked areas of Denver, Boulder, and Colorado Springs.

 Methods: To simulate a casual visitor, two students visited pharmacies based on their location near major roads and popular tourist destinations, and how easily they could be found on internet search of "pharmacy" on default smartphone navigation apps and Google Maps. Each pharmacy was then surveyed in person to determine if emergency contraception was available on shelves, where in the store it was located, and any additional restrictions on purchase. Stores were also subjectively assessed for ease of locating emergency contraception by the students.

Results: 37 pharmacies were surveyed. In 25% [9/37] of stores, emergency contraception was available on store shelves and not locked in any container or placement. In 35% [13/37] of stores, emergency contraception was on the shelf locked in a container requiring employee assistance, and 5% [2/37] had a place for emergency contraception on shelves but were out of stock. Of the 24 stores carrying emergency contraception on shelves, the family planning (75%), and feminine care (21%) aisles were the most common locations. 19% of stores had an age restriction, and in 3% of stores men were not able to

purchase emergency contraception. In 22% of stores an ID was required for purchase of emergency contraception regardless of age or location in store. Locating emergency contraception was "very difficult" in 3% of stores, "somewhat difficult" in 26%, "somewhat easy" in 22%, and "very easy" in 49%. Stores providing emergency contraception on the shelf compared to behind a counter, stores providing emergency contraception on the shelf most often rated "very easy" [18/24], while stores with emergency contraception behind the counter most frequently were rated as "somewhat difficult" [7/13].

Conclusion: Overall, approximately one- third of stores did not have emergency contraception on store shelves and one-fifth had a minimum age restriction. Surveyors perceived stores in which emergency contraception was available on the shelves as providing an easier and more comfortable experience for purchase. Colorado visitors may not have an easy time accessing emergency contraception if needed while visiting this state.

Primary Student Presenter: Elizabeth Terhune

Additional Presenter(s):

Presenting School: Graduate

Degree Seeking: MS

Year: 3rd

Mentor: Karen King

Poster Title: *Age Affects Bone Response to Chronic Kidney Disease in a Murine 5/6 Nephrectomy Model*

Final Category: Bone or Skeletal

Abstract:

AGE AFFECTS BONE RESPONSE TO CHRONIC KIDNEY DISEASE IN A MURINE 5/6 NEPHRECTOMY MODEL

E.A. Terhune (M.S., GS), R.C. Clark, W.G. Schroeder, K.B. King, Department of Orthopedics, University of Colorado Anschutz Medical Campus, Aurora, CO

Chronic kidney disease (CKD) is defined by a decrease in glomerular filtration rate (GFR) that affects 1 in 7 Americans and half of those over age 65. Elderly dialysis patients experience a 4-fold increase in hip fracture and a 3-fold increase in one-year mortality over those with normal kidney function. Advanced stages of CKD can lead to disruptions in mineral homeostasis, which can lead to low bone density, vascular calcifications, and increased fracture risk. Although murine models are frequently used for CKD research, few studies have investigated CKD in older mice, despite CKD risk strongly correlating with increased age in humans. Here, we use a 5/6 nephrectomy model to induce CKD in young (3 months, n= 7), middle-aged (15 months, n= 10) and geriatric (21 months, n= 8) male C57Bl/6J mice, with similar numbers used for sham controls. 12 weeks after nephrectomy, mice were euthanized, and blood and femurs were collected for protein and gene expression analysis.

Mice were confirmed to have moderate CKD by increased serum blood urea nitrogen (BUN) levels. Serum concentrations of type I collagen propeptides (PINP) and fragments (CTX-I) revealed that all age groups with CKD had increased rates of bone turnover, although this was only statistically significant in geriatric mice (p= 0.012 for PINP, p= 0.035 for CTX-I). Geriatric CKD mice also showed decreased expression of several bone mineralization genes, including Sost (p= 0.005), Bglap (p= 0.008), and Sox9 (p= 0.010). Our results suggest that the bone of geriatric individuals may respond distinctly to CKD. Understanding the mechanisms controlling the bone's response to CKD represents a crucial step towards the development of clinical treatments for CKD-associated osteoporosis.

Primary Student Presenter: Eline van den Broek-Altenburg

Additional Presenter(s):

Presenting School: Public Health

Degree Seeking: PhD

Year: 4th

Mentor: Adam Atherly

Poster Title: *Using Twitter to Analyze Consumers Sentiments Toward Healthcare Provider Networks*

Final Category: Developmental Neuroscience and Brain and Behavior - Child

Abstract:

USING TWITTER TO ANALYZE CONSUMERS SENTIMENTS TOWARD HEALTHCARE PROVIDER NETWORKS

Millions of people buying health insurance during enrollment season prioritize one plan attribute: how little they can pay in premiums. However, studies of health insurance choice often do not tell us the complete story regarding the attributes that are being considered, such as the network of providers the plan covers.

Purpose of Study: to understand consumers' attitudes toward the health provider network of their insurance plan, to assess the trade-offs that they consider in choosing their health plan in the ACA exchanges and to examine the relationship between consumer attitudes and individual marketplace characteristics.

Methods Used: In this study, we gathered and analyzed text data from Twitter to answer the questions: "Are concerns about provider networks associated with considering health plan switching? What particular sentiments do people have regarding provider choice?" Using an Application Programming Interface, we gathered all text from Twitter with the words "health insurance" or "health plan" during open enrollment season from November 1st, 2016 until January 31st, 2017. We preprocessed the tweets, so that text was represented as lemmatized plain words. We then used machine learning techniques to find associations between words indicating provider network and words expressing an intention to perform a behavior on the insurance market, such as switching a plan. We also analyzed sentiments consumers expressed regarding provider networks.

Summary of Results: The sample includes individuals between the ages of 18 and 64 who posted a "tweet" about health insurance during the open enrollment period. Twitter has 66 million monthly active users in the U.S. "Health insurance" or "health plan" generates approximately 1 tweet every 3 seconds, which corresponds to 20 per minute, and almost 3 million tweets during ACA enrollment season. We identified that provider networks, prescription drug benefits, political preference, particular sentiments, and norms of others matter. We also found that provider networks are associated with

health plan switching and that consumers trust their medical providers but they fear unexpected healthcare expenses their plan will not cover.

Conclusions Reached: Text mining exposes some of the previously unobserved preferences of consumers in the health insurance market. The study highlights that new methods in Health Services Research and behavioral economics help identify additional factors researchers should include in their studies. With text mining and machine learning techniques, we determined the expressed intent of consumers that they may not have expressed in surveys. The study's conclusions directly relate to recent reports about narrow networks being a popular choice in the ACA exchanges. Our study is hypothesis generating: gaining insights into the decision-making processes of consumers when making insurance enrollment decisions will lead to better informed decision theory in health plan choice. This study is therefore relevant to policy makers who are interested in more realistic decision models for predicting market shares and to insurance companies interested in optimizing underwriting processes and marketing actions or by changing benefit structures accordingly. We recommend including some of the factors we found in future studies to create more realistic decision models for predicting consumer choice.

Primary Student Presenter: Malvin Vien

Additional Presenter(s):

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Xiao Jing Wang

Poster Title: *Investigating Mechanisms of PI3K Inhibitor Resistance in Head and Neck Squamous Cell Carcinoma.*

Final Category: Hematology and Oncology

Abstract:

Investigating Mechanisms of PI3K Inhibitor Resistance in Head and Neck Squamous Cell Carcinoma.

Malvin Vien

Christian D. Young

Xiao-Jing Wang

University of Colorado School of Medicine, Denver, CO

Purpose of Study:

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common type of cancer worldwide and with a 5 year survival rate of 40-50%, the morbidity associated with HNSCC remains high. Phosphoinositide 3 Kinase (PI3K) is a pro-survival molecule associated with tumorigenesis and tumor progression in many types of cancer, including HNSCC. BKM120 (Buparlisib) is a PI3K inhibitor currently in clinical trials for treatment of HNSCC. This study aims to investigate the potential mechanisms by which HNSCC may acquire resistance to BKM120 so superior treatment strategies can be devised for the benefit of HNSCC patients.

Methods Used:

BKM120-sensitive human HNSCC cell lines (Cal27 and UMSCC1) were made resistant to BKM120 by gradually increasing BKM120 concentration in a stepwise manner over time. Parental and BKM120-resistant HNSCC cells were evaluated for proliferation, receptor tyrosine kinase (RTK) activation, downstream signaling activation, and drug sensitivity in cell culture models of HNSCC.

Summary of Results:

Sulphorhadamine B (SRB) viability assay confirmed that BKM120-resistant Cal27 and UMSCC1 cells were less sensitive to BKM120 than parental cells. Cell lysates from parental and BKM120-resistant cells were applied to a receptor tyrosine kinase (RTK) antibody array to determine potential RTKs that may be activated in BKM120 resistant cells. P-Met was identified as being upregulated in the Cal27 BKM120-resistant cells compared to parental Cal27 cells. This P-Met upregulation was verified via Western Blot. To determine whether changes in Met activity were causally related to BKM120 resistance, we tested proliferation of cells treated +/- BKM120 and +/- Met inhibitor, Tivantinib. Cal27 and UMSCC BKM120-resistant cells demonstrated increased P-Met activity in the presence of BKM120 as verified by Western Blot. Co-treatment with BKM120 and Tivantinib demonstrated a reduction in P-Met levels and superior growth inhibition in the BKM120-resistant UMSCC1 cells.

Conclusions:

This study is ongoing. At present, our data indicate that Met/HGF signaling plays a causal role in HNSCC cell BKM120 resistance. These findings have important implications for both patient selection and the development of strategies to overcome resistance.

Primary Student Presenter: Nemanja Vukovic

Additional Presenter(s): Ashley Quick Bear, Paola Casillas

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Janet Meredith

Poster Title: *Engaging Teenagers In Positive Conversations About Body Weight*

Final Category: Healthcare and Public Health

Abstract:

Engaging Teenagers In Positive Conversations About Body Weight

N Vukovic, (M.D., SOM), A Angstadt, C Ard, P Casillas, J Meredith, A Prasad, A Quick Bear, T Reinking, N Riechers, K Tran, and E Webster, Department of Medicine, University of Colorado, Denver, CO.

Adolescent obesity rates have quadrupled since 1980, with 20% of adolescents being considered obese today. Knowing that conversations between providers and patients can have significant impacts on weight loss and management, "Working to End Teen Obesity" examines whether improvements in the quality of these conversations can translate into improvements in weight management.

Teenagers were recruited for focus groups from high schools in Denver and Aurora, Colorado to discuss weight, body image, and their experiences with providers. To evaluate provider input, surveys were distributed by hand and via REDCap to local hospitals and practices that serve teenage patients. Qualitative analysis of the provider surveys and transcribed discussions from teen focus groups was performed.

Six focus groups with 47 multi-racial, Latino(a), and black teenagers were completed. Teens recommend that providers get to know them before discussing sensitive topics, avoid body mass index (BMI)-centric conversations, and focus on individual goals and motivations with realistic expectations. Providers, although they report good confidence in initiating conversations about weight, report consistent use of BMI in their discussions, and self-rate their conversations with teenagers about weight loss as ineffective.

Although both providers and teens view conversations about body image and weight management as important, providers often feel as if their approaches are ineffective, while teenagers are able to provide specific and relevant recommendations for improvement. Programs aimed at updating providers on the most recent and direct recommendations from teenagers should be developed, tested, and implemented if successful.

Primary Student Presenter: Katie Yamamura

Additional Presenter(s): Christopher Erickson, Nicole Shaw

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Karin Payne

Poster Title: *Evaluation of Kartogenin, a Chondrogenic Small Molecule, in Cartilage Regeneration for Growth Plate Injuries*

Final Category: Bone or Skeletal

Abstract:

EVALUATION OF KARTOGENIN, A CHONDROGENIC SMALL MOLECULE, IN CARTILAGE REGENERATION FOR GROWTH PLATE INJURIES. MK Yamamura (MD, SOM), C Erickson, N Shaw, K Payne, Department of Orthopedics, University of Colorado School of Medicine, Aurora, Colorado.

Purpose of the Study: A significant proportion of pediatric fractures involves the physis (cartilaginous growth plate). Damaged cartilage within the physis is often replaced by unwanted bony repair tissue, forming a "bony bar". This can cause joint deformities or halt longitudinal bone growth. Current treatments are limited to largely unsuccessful surgical interventions. Thus, there is a need for therapy to prevent bony bar formation and regenerate healthy cartilage. This study investigated whether kartogenin (KGN), a chondrogenic and chondroprotective small molecule, can reduce bony bar formation and promote cartilage formation in a rat model of growth plate injury.

Methods Used: All animal studies were approved by the University of Colorado IACUC. A drill hole injury in the proximal tibial growth plate of 6-week old Sprague-Dawley rats was created. Injury sites received either no treatment, fibrin glue, fibrin glue + KGN, or fibrin glue + KGN + rat bone marrow mesenchymal stem cells (MSCs). There were 8 limbs per experimental group. 28 days post-treatment micro CT was performed, rats were sacrificed, and their tibias were harvested for histological analysis. Using Bone J software, we measured tibial length and bone to total tissue ratio at the growth plate. Samples were processed with either Alcian Blue Hematoxylin staining or immunostaining for collagen II and examined by light microscopy.

Summary of Results: All groups developed bony bars, with no statistically significant differences between the groups in either micro CT analysis or Alcian Blue Hematoxylin staining. However, a subset of limbs that received KGN and MSCs led to increased fibrogenic and chondrogenic-like tissue expressing collagen II.

Conclusion: These data suggest that KGN may have a positive effect on cartilage regeneration in rat

tibial physeal injuries if delivered in conjunction with rat MSCs. Limitations of the study include a lack of fibrin glue + MSC cohort and that KGN release was not optimized. Next steps include a release study to optimize fibrin glue concentration for sustained KGN release and a repeat experiment with the aforementioned cohort. Additionally, we plan to pair KGN with known chondrogenic growth factors (ex. TGF) to investigate their synergistic potential.

Primary Student Presenter: Eric Yang

Additional Presenter(s): Fiona Wong

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Matthew Miller

Poster Title: *Evaluation of an Oral Ribavirin (RBV) Protocol for Treating Community Acquired Respiratory Virus (CARV) Infections in Patients with Hematologic Malignancy*

Final Category: Microbiology and Infectious Diseases

Abstract:

Evaluation of an Oral Ribavirin (RBV) Protocol for Treating Community Acquired Respiratory Virus (CARV) Infections in Patients with Hematologic Malignancy. E Yang, (Pharm.D., PS), F Wong, Miller M, Barber G, Smith P, Kaiser J, Tobin J, Levi M, Gutman J, Department of Pharmacy, University of Colorado Hospital, Aurora, CO.

Purpose:

Treatment of respiratory syncytial virus (RSV) in patients with hematologic malignancy (HM) and hematopoietic stem cell transplantation (HSCT) has relied on nebulized ribavirin (nRBV) administration. Recent price increases for nRBV makes the option less attractive at 24,000 dollars per day. Reports have suggested comparable activity with oral ribavirin (poRBV). The purpose of this project is to retrospectively assess the impact of a quality improvement initiative on the management of CARV infections following implementation of a treatment protocol utilizing poRBV preferentially.

Methods:

Retrospective chart review of patients identified through the EPIC database with diagnosed CARV infection confirmed by positive multiplex PCR (polymerase chain reaction) of respiratory syncytial virus (RSV), human metapneumovirus (HMPV), or human parainfluenza virus (HPIV) who received treatment with oral and nebulized ribavirin. Mann-Whitney U test was used to calculate significance (P < 0.05 is significant). Primary endpoints: improvement in quality of life (decreased inpatient admissions, decreased length of inpatient stay). Secondary endpoints: direct and indirect cost savings.

Results:

Five patients were treated with nRBV in the months preceding protocol implementation and 39 patients received poRBV. Of those, 80 percent (4 of 5) and 95 percent (37 of 39) tested positive for RSV with lower respiratory tract (LRT) involvement at presentation in 60 percent (3 of 5) and 15 percent (6 of 39)

of the nRBV and poRBV patients, respectively. HSCT was present in 80 percent (4 of 5) nRBV and 51 percent (20 of 39) poRBV recipients, with graft-versus-host disease present in 20 percent (1 of 5) and 31 percent (12 of 39), respectively. No RSV-related mortality or adverse drug events were noted in either group due to poRBV, and 5 patients deceased due to respiratory complications and congestive heart failure. 100 (5 of 5) percent of nRBV patients were admitted to the hospital whereas only 38 percent (15 of 39) required admission in the poRBV group (P less than 0.05); mean length of stay 10 days versus 5 days for nRBV and poRBV, respectively (P less than 0.05). Direct cost savings estimated to be 5,496,000 dollars over two flu seasons.

Conclusion:

The selective and preferential use of weight-based oral ribavirin among higher-risk HM patients and recipients of HSCT presenting with non-severe symptoms of RSV infection has shown to be an economical alternative to nebulized ribavirin with similar outcomes and reduced need for hospitalization at our center. Nebulized ribavirin is reserved for those with severe infection requiring mechanical ventilation at our center. This quality improvement project has demonstrated: decreased inpatient admission requirements, decreased length of stay and substantial institutional savings, estimated cost avoidance of $5.5 million