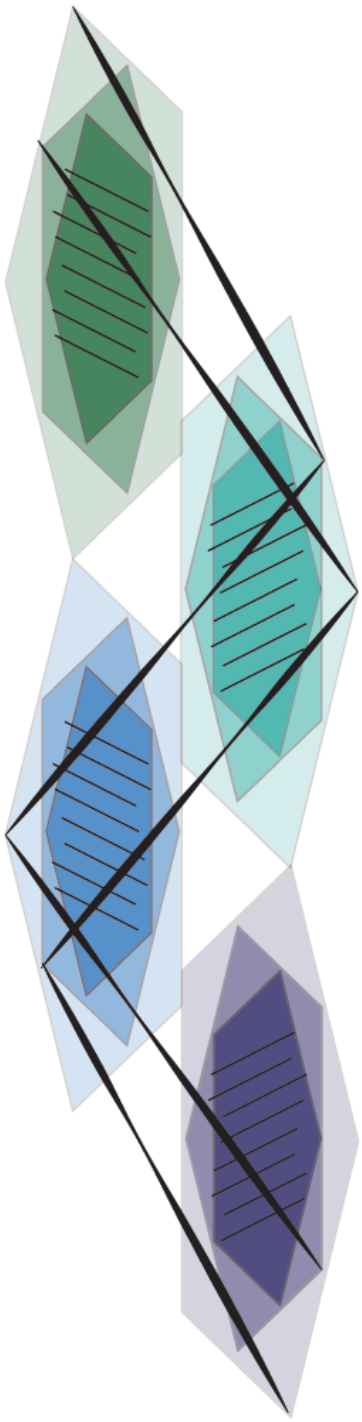

Dale J. Benos

MSRD 2016

November 4

University of Alabama at Birmingham

Submitted by: J. Paige Souder (Dale J. Benos MSRD 2016 Cover Art Winner)

MSRD 2016 JUDGES

Dr. Tolu Aduroja, Associate Professor, Psychiatry
Dr. Farrukh Afaq, Assistant Professor, Dermatology
Dr. Shaida Andrabi, Associate Professor, Pharmacology and Toxicology
Dr. Pankaj Arora, Assistant Professor, Cardiology
Dr. James Baños, Assistant Dean for Student Success, Medical Education
Dr. Anju Bansal, Assistant Professor, Med/ID
Dr. Surya Bhatt, Assistant Professor, Medicine/Pulmonary
Dr. Badari Birur, Assistant Professor, Psychiatry
Dr. Hunter Boggs, Assistant Professor, Radiation Oncology
Dr. Davide Botta, Instructor, Microbiology
Dr. Cynthia Brown, Professor, Medicine
Dr. Ayesha Bryant, Associate Professor, Anesthesia and Perioperative Medicine
Dr. Jill Butler, Instructor, Biochemistry and Molecular Genetics
Dr. Melissa Chambers, Associate Professor, Neurosurgery
Dr. Do-Yeon Cho, Assistant Professor, Otolaryngology
Dr. Laura Cotlin, Associate Professor, CDIB
Dr. Lisa Curtis, Assistant Professor, Medicine/Nephrology
Dr. Jessy Deshane, Associate Professor, Medicine
Dr. Nathan Erdmann, Instructor, Medicine
Dr. Carlos Estrada, Professor, Medicine
Dr. Ricardo Franco, Assistant Professor, Medicine
Dr. Angelo Gaffo, Associate Professor, Medicine/Rheumatology
Dr. David Galloway, Assistant Professor, Pediatrics
Dr. William Geisler, Professor, Medicine
Dr. Shawn Gilbert, Professor, Surgery, Orthopedics
Dr. Fred Goldman, Professor, Pediatrics
Dr. Jennifer Guimbellot, Assistant Professor, Pediatrics
Dr. Fadi Hage, Associate Professor, Medicine
Dr. Ganesh Halade, Assistant Professor, Medicine
Dr. Craig Hoesley, Professor, SADME, Medicine, Medical Education
Dr. Sabine Huke, Associate Professor, Medicine
Dr. Cecelia Hutto, Professor, Pediatrics
Dr. Patricia Jackson, Associate Professor, Medicine
Dr. Michael Johnson, Assistant Professor, Orthopedics
Dr. Rachel Kassel, Assistant Professor, Pediatrics
Dr. Prasanna Krishnamurthy, Associate Professor of Medicine & Engineering, Biomedical Engineering
Dr. Tejaswini Kulkarni, Instructor, Medicine
Dr. Vineet Kumar, Assistant Professor, Cardiology
Dr. Robin Lester, Professor, Neurobiology
Dr. Runhua Liu, Assistant Professor, Genetics
Dr. Clinton Martin, Assistant Professor, Child and Adolescent Psychiatry
Dr. Colin Martin, Assistant Professor, Surgery
Dr. Sadis Matalon, Professor, Anesthesiology and Perioperative Medicine
Dr. Jori May, Chief Resident, Internal Medicine
Dr. Craig Maynard, Assistant Professor, Pathology
Dr. Jonathan McConathy, Associate Professor, Radiology
Dr. Mamie McLean, Assistant Professor, OBGYN-REI
Dr. Erik Middlebrooks, Assistant Professor, Radiology, Neuroradiology
Dr. Kasturi Mitra, Assistant Professor, Genetics
Dr. Rajasekaran Namakkal Soorappan, Assistant Professor, Pathology

MSRD 2016 JUDGES

Dr. Marek Napierala, Assistant Professor, Biochemistry and Molecular Genetics
Dr. Vinay Narasimha Krishna, Instructor, Medicine/Nephrology
Dr. Ravi Paluri, Assistant Professor, Hematology Oncology
Dr. William Placzek, Assistant Professor, BMG
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Dr. Jennifer Pollock, Professor, Medicine
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Dr. Vikram Saini, Instructor, Microbiology
Dr. Emily Spangler, Assistant Professor, Surgery/Vascular
Dr. Ed Swords, Professor, Pulmonary
Dr. Linda Thompson, Assistant Professor, Emergency Medicine
Dr. Barbara Van Der Pol, Associate Professor, Medicine
Dr. Adam Wende, Assistant Professor, Pathology
Dr. Chang L Wu, Assistant Professor, Pediatrics/Hospital Medicine
Dr. Yang, Associate Professor, Pathology
Dr. Nabiha Yusuf, Assistant Professor, Dermatology
Dr. Jianhua Zhang, Associate Professor, Pathology

Dale J. Benos Medical Student Research Day
Friday, November 4, 2016
UAB Hill Student Center

Event Agenda:

1:00-2:45pm:	MSRD Poster Presentation (Ballroom A/B)
3:00-4:30pm:	MSRD Oral Presentation
	Short Term: Ballroom C/D
	Intermediate/Long: Alumni Theater
4:30-6:00pm:	Reception/Award Ceremony (Ballroom C/D)

* Denotes 1st Place Winner
** Denotes 2nd Place Winner
*** Denoters 3rd Place Winner

Dale J. Benos Medical Student Research Day
Oral Presentations
Friday, November 4, 2016
Ballroom C/D

Short Term Research

3:00 – 3:15 pm	**Sarah F. McClees, MS2*** Plumbagin Induces Apoptosis in Melanoma Cells by Inducing Endoplasmic Reticulum Stress and DNA Damage Response Signaling Mentor: Dr. Farrukh Afaq
3:15 – 3:30 pm	**Stephanie L. Donaldson**, **MS2** Overexpressing IL-8 Receptors Promotes Endothelial Cell Migration and Inhibits Inflammation in Response to IL-8 Mentor: Dr. Suzanne Oparil
3:30 – 3:45 pm	**Allison M. Montgomery, MS1** Molecular Response to Neoadjuvant Chemotherapy in High-Grade Serous Ovarian Carcinoma Mentor: Dr. Rebecca Arend
3:45 – 4:00 pm	**William Summers, MS2** Living Kidney Donor-Recipient Relationship and Development of Post-donation Comorbidities Mentor: Dr. Jayme Locke
4:00 – 4:15 pm	**Zachary H. Hughes, MS2**** Estrogen exerts anti-inflammatory effects in human macrophages in an estrogen receptor α dependent manner via modulation of macrophage polarization Mentor: Dr. Fadi Hage
4:15 – 4:30 pm	**William Riley, MS3** Neurocognitive Assessment of Emergency Department Concussions Using a Modified Sports Concussion Assessment Tool Mentor: Dr. Lauren Walter

Dale J. Benos Medical Student Research Day
Oral Presentations
Friday, November 4, 2016
Alumni Theater

Intermediate Term Research

3:00 – 3:15 pm	**Elizabeth Leader**, **MS2** Human Papillomavirus (HPV) Awareness and Vaccination Status in Female Emergency Department Patients Mentor: Dr. Lauren Walter
3:15 – 3:30 pm	**Kathryn Hudak, MS3** Screening for Sexually Transmitted Infections in Persons Living with HIV Leads to Significant Financial Losses for a Healthcare System Mentor: Dr. Ellen Eaton
3:30 – 3:45 pm	**Jeremie M. Lever, MSTP GS2*** Myeloid Cell Heme Oxygenase-1 Expression Regulates the AKI to CKD Transition Mentor: Dr. Anupam Agarwal

Long Term Research

3:45 – 4:00 pm	**Alexander Bray, MSTP GS5** Mitochondrial Genetic Background Has Minimal Impact on the Progression of Atherosclerosis Mentor: Dr. Scott Ballinger
4:00 – 4:15 pm	**Jonathan R Lockhart, MSTP GS5** Rescue of a Humanized Mouse Model of β-Thalassemia Major By Allogeneic Bone Marrow Transplantation in the Absence of Cytoreductive Conditioning Mentor: Dr. Thomas Ryan
4:15 – 4:30 pm	**Tyler R. McCaw, MSTP GS2*** Induced MHCII expression on breast cancer cells delays tumor-specific T cell exhaustion and impairs tumor growth Mentor: Dr. Troy Randall

Dale J. Benos Medical Student Research Day
Poster Presentations (All)
Friday, November 4, 2016
Ballroom A/B

Poster Group A (Cancer)

A-1 **Beomjy Kim, MS2*****
Using Nanostring to identify high-intermediate risk endometrial cancer patients at high risk for recurrence
Mentor: Dr. Rebecca Arend

A-2 **Garrett T. Dunn, MS2**
Investigating the role of elective radiation of the seminal vesicles (SVs) in men with intermediate or high risk prostate cancer
Mentor: Dr. Rojymon Jacob

A-3 **Jacob P Britt, MS2**
Characterization of Estrogen Receptor Positive/Progesterone Receptor Negative Breast Cancer
Mentor: Dr. Shi Wei

A-4 **Andrew S. McGee, MS2**
Fluorescent-labeled Cetuximab for Image-guided Soft Tissue Sarcoma Surgery
Mentor: Dr. Jason Warram

A-5 **Aditi H. Jani, MS3***
Translation of Oncologic Imaging Agents for Fluorescence-Guided Surgical Resection: A Comparison of 5-Aminolevulinic Acid and IntegriSense750
Mentor: Dr. Jason Warram

A-7 **Andrew R. Schroeder, MSTP GS1****
ST6Gal-I Serves as a Major Pro-Survival Molecule in Tumor Cells
Mentor: Dr. Susan Bellis

A-8 **Andrew Janssen, MS2**
Somatostatin Receptor Expression on Medullary Thyroid Tumors Using Histone Deacetylase Inhibitors
Mentor: Dr. Herbert Chen

A-9 **Fabio Raman, MSTP GS1**
Computational Trials: Unraveling Motility Phenotypes, Progression Patterns, and Treatment Options for Glioblastoma Multiforme.
Mentor: Dr. Hassan Fathallah-Shaykh

A-10 **Jay V. Dasigi, MS2**
How levels and causes of distress in older cancer patients vary by race
Mentor: Dr. Maria Pisu

A-11 **Stephanie L Bevans, MS3**
Fluorescence imaging to localize head and neck squamous cell carcinoma for enhanced pathological assessment
Mentor: Dr. Jason Warram

Poster Group A (Cancer)

A-12 **Carolina E. Temple, MS2**
Hospital Readmissions in Gynecologic Oncology Patients – A Target for Quality Improvement
Mentor: Dr. J. Michael Straughn

A-13 **Garrett Brinkley, MSTP GS1**
Oncometabolite L-2HG : A potential regulator of the nucleus and mitochondria in renal cancer
Mentor: Dr. Sunil Sudarshan

A-14 **Joshua D. Jackson, MS2**
Basal Interferon Stimulated Gene Expression Influences the Productive Infection of Oncolytic HSV in Malignant Peripheral Nerve Sheath Tumor Cells
Mentor: Dr. James Markert

Poster Group B (Cancer)

B-1 **Emily N. Hayward, MSTP MS1**
RNAi-mediated knockdown of tRNA modification genes *UBA4, CTU1,* or *CTU2* enhance HEK-293 cell resistance to the cancer chemotherapeutic topotecan
Mentor: Dr. Mary-Ann Bjornsti

B-2 **Chris Veale, MS2**
Neutrophil-to-Lymphocyte Ratio and White-Blood-Cell Counts as Predictors of Overall Survival in Head and Neck Cancer Patients Treated with Radiotherapy
Mentor: Dr. Hunter Boggs

B-3 **Jacelyn E Peabody, MSTP MS2**
IMMUNOMODULATION OF PD-1 IN A MURINE MODEL OF SYNGENEIC OVARIAN CANCER AND DOSE DENSE CHEMOTHERAPY
Mentor: Dr. Rebecca Arend

B-4 **Joshua A. Blackwell, MS2**
Smoking Status and Postoperative Complications Following Cardiopulmonary Bypass: A Retrospective Study
Mentor: Dr. Ayesha Bryant

B-5 **John L. Johnson, MS2***
In Vivo Fluorescence Imaging of the Pelvic Ureter During Minimally Invasive Surgery for Endometrial and Cervical Cancer
Mentor: Dr. Warner Huh

B-6 **Dewey Brooke, MSTP MS2**
Identification of PTBP1-induced aberrant splice isoforms and their impact on patient survival in glioblastoma
Mentor: Dr. Markus Bredel

B-7 **Taylor Bono, MS1**
The Effect of a Ketogenic Diet on Ovarian Cancer Angiogenesis
Mentor: Dr. Rebecca Arend

B-8 **Christian A. Mays, MS2*****
Single-Institution Examination of Patients with Primary CNS Lymphoma
Mentor: Dr. Paula Province Warren

B-9 **Robert D. Stibolt, MS2**
Aldehyde Dehydrogenase as a Stemness Marker in Ovarian Carcinoma
Mentor: Dr. Kasturi Mitra

B-10 **Mary Fok, MS2**
The role of osteocytes in multiple myeloma progression
Mentor: Dr. Yang Yang

B-11 **Ryan McMonigle, MSTP MS2**
Inhibition of Prolyl-4-Hydroxylase, Alpha Polypeptide I Slows Growth of Non-Small Cell Lung Carcinoma
Mentor: Dr. Sooryanarayana Varambally

Poster Group B (Cancer)

B-12 **Bethany Johnson, MS2**
Pre-processing Pipeline for MethylationEPIC Data
Mentor: Dr. Devin Absher

B-13 **Philip W. Dockery, MS1***
Historical bone fractures and risk of multiple myeloma
Mentor: Dr. Elizabeth Brown

B-14 **Nicholas Eustace, MSTP GS3**
The Impact of MARCKS Phosphorylation on Glioblastoma Growth and Migration
Mentor: Dr. Christopher Willey

Poster Group C (Cardiovascular and Trauma)

C-1 **Colin K. Cantrell, MS2**
The Effect of Presence of a State Trauma System on Intentional Firearm-Related Mortality Rate
Mentor: Dr. Kimberly Hendershot

C-2 **Dylan J. Nichols, MS2**
Pittsburgh Cardiac Arrest Category Severity Score is Useful Despite Poor External Validation
Mentor: Dr. Michael Kurz

C-3 **Anjali Wagle, MS2***
Performance of ECG morphologic criteria for differentiation of VT from SVT in sinus rhythm, in patients with a wide QRS at baseline
Mentor: Dr. Harish Doppalapudi

C-4 **Zachary A. Mosher, MS3**
Sinus of Valsalva Aneurysm Repair: A Historical Analysis
Mentor: Dr. David Cleveland

C-5 **Brandon M. Fox, MSTP GS4**
Acute Behavioral Stress Induces a Pressor Response via ET_A Receptor Activation by Endothelial-Derived ET-1
Mentor: Dr. Jennifer Pollock

Poster Group D (Education)

D-1 **Kristine Austriaco, MS2**
Identification of Learning Gaps in the Treatment of Children with Autism Spectrum Disorder who Present with Acute Illnesses
Mentor: Dr. Michele Kong

D-2 **Peter Sloane, MS3**
Caregiver Reception of High-fidelity Simulation –Enhanced Tracheostomy Discharge Education
Mentor: Dr. Chrystal Rutledge

D-4 **LaChaundra L. Johnson, MS4**
Reclaiming Operative Vaginal Deliveries as an Optimal Intrapartum Management Choice
Mentor: Dr. John Woods

D-5 **Georgia B. Gamble, MS4***
Simulated Artificial Rupture of Membranes with Initiation of Internal Uterine and Fetal Monitoring
Mentor: Dr. John Woods

Poster Group E (Endocrine and Metabolic Disease)

E-1 **David Hall, MS4**
Diabetes and Life-Space Mobility Decline in Older Adults
Mentor: Dr. Cynthia Brown

E-2 **Alexandra B. Khodadadi, MS2**
Assessing Community Members' Preferences of a Family-Based Diabetes Prevention Program in Rural Alabama
Mentor: Dr. Andrea Cherrington

E-3 **J. Paige Souder, MSTP GS1**
Using radiolabeled estradiol to quantify uptake in zebrafish embryos and larvae
Mentor: Dr. Daniel Gorelick

E-4 **Ryan Berry, MSTP GS4***
Differential responsiveness and sensitivity of major metabolic tissues to growth hormone
Mentor: Dr. Stuart Frank

E-5 **Katie R. Vines, MS1**
TrkA Activity is Reduced in Streptozotocin Induced Diabetes Rat Brain
Mentor: Dr. Ramesh Jeganathan

E-6 **Mark E. Pepin, MSTP GS2**
GADD45B is a novel candidate regulator of Epigenetic Reprogramming in Human Diabetic Heart Failure
Mentor: Dr. Adam Wende

Poster Group F (Genetics and Bioinformatics)

F-1 **Milza C Opper, MS2**
Replication and Confirmation of Novel Loci Identified in Systemic Lupus Erythematosus in a Genome-Wide Association Study of an Amerindian Ancestry Population
Mentor: Dr. Jeffrey Edberg

F-2 **Matthew B. Neu, MSTP GS1**
Initial Whole Genome Analysis of SFARI Phase I
Mentor: Dr. Greg Cooper

F-3 **Carly A. Cignetti, MS2**
Recognition of Neurofibromatosis Type 1 with Facial Dysmorphology Novel Analysis
Mentor: Dr. Anna Hurst

F-4 **Stephen D. Gragg, MSTP GS2**
Hypomethylation of ADORA1, SBNO2, and WIZ is associated with risk of multiple myeloma, smoldering myeloma, and monoclonal gammopathy of undetermined significance
Mentor: Dr. Elizabeth Brown

F-5 **Alex Dussaq, MSTP GS4**
HCV Genie V 2.0: A Web Platform for the Versant Hepatitis C Virus (HCV) Genotype Line Probe Assay
Mentor: Dr. Christopher Willey

F-6 **Ryne C. Ramaker, MSTP GS3***
RBRSA: A Ranked-Based Method for Two-Class RNA-seq Differential Expression Analysis
Mentor: Dr. Rick Myers

F-7 **Vincent A. Laufer, MSTP GS4**
Enabling Precision Medicine in Rheumatoid Arthritis through Prioritization of Genetic Variants
Mentor: Dr. Lou Bridges

F-8 **Andrew A. Hardigan, MSTP GS3****
Mutations in EBF3 disturb transcriptional profiles and underlie a novel syndrome of intellectual disability, ataxia and facial dysmorphism
Mentor: Dr. Richard Myers

Poster Group G (Immunology and Hematology)

G-1 **Sara E. Deas, MS2**
Psychological Stress During Pregnancy Alters Immune Function in Maternal and Neonatal Mice
Mentor: Dr. Colin Martin

G-2 **Sara Stone, MSTP GS5***
Immunity to influenza requires T-bet expression in B cells
Mentor: Dr. Frances Lund

G-3 **Daniel DiToro, MSTP GS5**
The insulin-like growth factor system is a critical regulator of the balance of Th17 and Treg CD4s in autoimmunity
Mentor: Dr. Casey Weaver

G-4 **Joseph M Ladowski, MSTP GS3**
What Does the Anti-SLA Antibody See?
Mentor: Dr. A. Joseph Tector

G-5 **Emma C. Dean, MSTP MS2**
The differential transcriptional landscape between genders during immune response
Mentor: Dr. Amy Weinmann

G-6 **Madeline M. Dills, MS2**
Altered Oxidative Stress Response in Cells with Telomere Dysfunction
Mentor: Dr. Frederick Goldman

Poster Group H (Infectious Diseases)

H-1 **Christopher A. Ray, MS3**
Killing of *Serratia marcescens* Biofilms with Chloramphenicol
Mentor: Dr. Carlos Orihuela

H-2 **Hayden Pacl, MSTP MS2**
Experimental Trial of FDA-Approved Therapeutics in a Mouse Model of Acute Infection with *Mycobacterium tuberculosis*
Mentor: Dr. Adrie Steyn

H-3 **Kristin M. Olson, MSTP GS2***
A Case for Point-of-Care Testing for Chlamydia and Gonorrhea in the Emergency Department Setting
Mentor: Dr. William Geisler

H-4 **Evida A. Dennis, MSTP GS3**
Cytomegalovirus Blocks Mucosal TGF-β-induced Inflammation Anergy by Up-regulating Macrophage MyD88-dependent NF-κB Signal Transduction and Smad7 Expression
Mentor: Dr. Phillip Smith

H-5 **Noora Siddiqui, MS3**
Virologic characteristics associated with transmission of CMV via breast milk
Mentor: Dr. Suresh Boppana

H-6 **Jeffrey Singer, MSTP GS5**
Disturbed Succession of the Microbiome in Neonates Allows Opportunists to Bloom
Mentor: Dr. Casey Weaver

Poster Group I (Neuroscience and the Brain)

I-1 **Graham D. Cochrane, MSTP MS2**
Ocular and Vestibulo-Ocular Biomarkers for Concussion in Collegiate Student Athletes
Mentor: Dr. Jennifer Braswell-Christy

I-2 **Claire E.C. Cordes, MS2**
UTILITY OF LABORATORY TESTING IN PEDIATRIC DEMYELINATING DISORDERS
Mentor: Dr. Jayne Ness

I-3 **Benjamin Echols, MS2**
Age-Related Macular Degeneration and Visualizing Cholesterol within Photoreceptors
Mentor: Dr. Christine Curcio

I-4 **Hamelmal Kassahun, MS2**
The role of lipid accumulation in the pathogenesis of acute spinal cord injury
Mentor: Dr. Candace Floyd

I-5 **Corey G. Duke, MSTP GS1****
Experience Dependent Epigenomic Reorganization in the Hippocampus
Mentor: Dr. Jeremy Day

I-6 **Morgan E. Zipperly, MSTP GS1*****
Assessment of Neuronal Activity in Reward-Associated Behavioral Circuits
Mentor: Dr. Jeremy Day

I-8 **David Figge, MSTP GS3**
DNA Methylation Regulates Levodopa-Induced Dyskinesia
Mentor: Dr. David Standaert

I-9 **William M. Webb, MSTP GS3**
Memory retrieval triggers H3K4me3 in association with increased DNA hydroxymethylation activity at memory-permissive genes
Mentor: Dr. Farah Lubin

I-10 **Joshua L. Cohen, MSTP GS4**
Identification of region-specific miRNA-mRNA networks in the dorsal raphe and amygdala of high-responder/low-responder rats
Mentor: Dr. Sarah Clinton

I-11 **R M. Lockhart, MS1**
Effect of O-linked ß-N-acetyl-glucosamine post-traumatic brain injury
Mentor: Dr. Candace Floyd

Poster Group I

I-12 **Lindsay E Stoyka, MSTP GS1***
Reduction in Tau as a Therapeutic Intervention for Nonmotor Manifestations of Parkinson's Disease
Mentor: Dr. David Standaert

I-13 **Kelsey C. Patterson, MSTP GS3**
MeCP2 Deficiency Results in Robust Rett-like Behavioral and Motor Deficits in Male and Female Rats
Mentor: Dr. Michelle Olsen

Poster Group J (Other)

J-1 **David Osula, MS2**
TWEAK as a Marker for Muscle Inflammation Susceptibility in Total Hip and Total Knee Arthroplasty Patients
Mentor: Dr. Marcas Bamman

J-2 **Joseph W. Granade, MS2**
Unbiased, comparative proteomic and genomic analysis of differentially regulated canonical pathways i hyperoxia-induced lung injury in newborn mice
Mentor: Dr. Namasivayam Ambalavanan

J-3 **Jarvis J. Johnson, MS2**
Measurement and validation of step-length asymmetry using a novel clinical gait measurement tool
Mentor: Dr. David Brown

J-4 **Zachary L. Whaley, MS2**
Intraluminal Thrombus Incidence in Clinically Significant Abdominal Aortic Aneurysm Patients is Markedly Higher Than the Currently Expected Rate
Mentor: Dr. Benjamin Pearce

J-5 **Michael A. Coker, MS2**
Rehabilitation Referral for Patients with Irreversible Vision Impairment in a Publicly Funded County Clinic
Mentor: Dr. Cynthia Owsley

J-6 **Asher M. Krell, MSTP MS2***
Determination of Optimal Seeding Conditions of Fibroblasts in a Peptide Amphiphile Gel
Mentor: Dr. Ho Wook Jun

J-7 **R Wilson King, MS2**
Extubation to noninvasive ventilation versus supplemental oxygen after cardiopulmonary bypass in a pediatric cardiac intensive care unit
Mentor: Dr. Santiago Borasino

J-8 **Jeffrey Z Shen, MS2**
Optimization of Laboratory Utilization Practices at UAB Hospital
Mentor: Dr. Robin Lorenz

J-9 **Daniel P. McNeill, MS1**
Self-Compassion Scores in Post-Stroke Patients
Mentor: Dr. Victor Mark

J-10 **Ashley B. Steffens, MS2**
Evaluation of neurodevelopmental disabilities in children with complex congenital heart defects
Dr. Myriam Peralta-Carcelen

J-11 **Gobind Gill, MS2**
THE ROLE OF NITRIC OXIDE IN CHRONIC RHINOSINUSITIS
Mentor: Dr. Do-Yeon Cho

Poster Group J

J-12 **Hunter B. Dean, MSTP MS1****
Pathways toward Stopped-Flow Analysis of RNA Polymerase I Translocation
Mentor: Dr. Aaron Lucius

J-13 **Lucas D. McGee, MS2**
Surveying Physicians on the Advice Given to Women Regarding Exercise During Pregnancy
Mentor: Dr. Sara Gould

J-14 **Benjamin K. Walters, MS3**
Interventions to decrease youth injury risk: a literature review
Mentor: Dr. Reed Estes

J-15 **W. Blake Holloway, MS2*****
Enhancing Diagnostic Efficacy in Patients with suspected Concussion:
An Elucidation of Symptom Trends seen in the Emergency Department
Mentor: Dr. Lauren Walter

J-16 **Muhan Hu, MSTP GS2**
TGFβ and Prostaglandin Synthesis in *C. elegans*: Linking Environmental Cues to Sperm Motility Function
Mentor: Dr. Amy Weinmann

Poster Group K (Public Health Outcomes and Quality Improvement)

K-1 **Catherine E. Lumb, MS2**
Timeliness of Therapies for Septic Shock in the Pediatric Emergency Department
Mentor: Dr. Christopher Pruitt

K-2 **Joann Hsu, MS2**
Aspirin Use and Long-Term Rates of Sepsis: A Population-Based Cohort Study
Mentor: Dr. Henry Wang

K-3 **Matthew C. Hess, MS3****
Injury Rates and Characteristics in the American Ultimate Disc League
Mentor: Dr. Eugene Brabston

K-4 **Benjamin Palmer, MS2**
Development of a Septic Shock Algorithm in the Pediatric ICU
Mentor: Dr. Leslie Hayes

K-5 **Keri A. Mallicoat, MS2**
Characterization of Young Children Presenting to the Emergency Department for Mental Health Complaints
Mentor: Dr. Kathy Monroe

K-6 **Madeline I Bender, MS2**
Characterization of Pediatric Patients Identified by Septic Shock Pathway
Mentor: Dr. Christopher Pruitt

K-7 **Shenila B. Lallani, MS2**
MSEP Experience in Granada, Nicaragua
Mentor: Dr. Majd Zayzafoon

K-8 **Timothy I. Kennell Jr, MSTP GS2**
The Almighty, Overridden Clinical Decision Support Alert
Mentor: Dr. James Cimino

K-9 **Anna Joy Rogers, MSTP GS4***
Missed Opportunities for Repeat HIV Testing and Early ART Initiation during Pregnancy in Southwestern Kenya
Mentor: Dr. Janet Turan

Poster Group L (Pulmonary)

L-1 **Tarek Abdalla, MS2**
Exosomes from activated human neutrophils produce COPD-like disease in mice
Mentor: Dr. J. Edwin Blalock

L-2 **Lydia L. McCormick, MS2***
The Effect of Maternal Smoking on CFTR Function of the Neonate
Mentor: Dr. Steven Rowe

L-3 **Garrett A. Nix, MS2**
Potential role for IL-7 immune complex therapy for the treatment of invasive fungal infection
Mentor: Dr. Chad Steele

L-4 **Bria N. Williams, MS2****
The Effects of Oxygen Exposure in Combination with Retinoic Acid on the Oxidant/Antioxidant Balance in Human Bronchial Epithelial Cells
Mentor: Dr. Trent Tipple

L-5 **Alexandra Simpson, MS2**
Role of Pulmonary Microbiome Induced Inflammation in Bronchopulmonary Dysplasia
Mentor: Dr. Chariharth Vivek

L-6 **Chandler S. Stisher, MS2**
Electrophysiological characterization of sweat gland cultures for the study of cystic fibrosis
Mentor: Dr. Carmel McNicholas

L-7 Morgan L. Locy, MSTP GS3
Dityrosine Cross-linking of Fibronectin is Increased in Plasma of Human Subjects with Interstitial Lung Disease
Mentor: Dr. Victor Thannickal

Poster Group M (Combined Gastrointestinal and Renal)

M-1 **Patrick A. Molina, MSTP MS2**
Ho-1 Regulates Lymphatic Endothelial Cell Proliferation Following Hypoxia-Induced Inflammation
Mentor: Dr. Anupam Agarwal

M-2 **Brendon R. Herring, MS1***
DIFFERENT CULTURE CONDITIONS ALTER GROWTH AND VIABILITY OF MESENCHYMAL STEM CELLS
Mentor: Dr. Lisa Curtis

M-3 **Goetsch MR, MS2**
Short Term Effects of Hepatitis C Virus Clearance Using Direct Acting Antivirals on Markers of Glomerular Damage in Kidney Transplant Patients
Mentor: Dr. Ricardo Franco

M-4 **Macie A. Enman, MS2**
Key Determinants for Achieving Enteral Autonomy in Pediatric Intestinal Failure
Mentor: Dr. David Galloway

Poster Group N (Surgery and Anesthesiology)

N-1 **Ilya M. Gutman, MS2**
Slipped Capital Femoral Epiphysis Trends In Treatment: Analysis Of 11,002 Patients From 1997 To 2012
Mentor: Dr. Shawn Gilbert

N-2 **William T. Davis, MS2**
Methicillin-resistant vs. methicillin-susceptible *Staphylococcus aureus* pediatric osteomyeltis: a retrospective analysis of the Kid's Inpatient Database (KID)
Mentor: Dr. Shawn Gilbert

N-3 **Alexia J. Powers, MS2****
Modifiable factors that impact long-term Quality of Life and development of chronic pain after pulmonary resection (an interim analysis)
Mentor: Dr. Ayesha Bryant

N-4 **Robert A. Esposito, MS2**
The value of post-operative chest radiography immediately following posterior spinal instrumentation and fusion in adolescent idiopathic scoliosis cases
Mentor: Dr. Michael Conklin

N-5 **Kevin S. Shrestha, MS1****
A comparison of post-operative MI rates based on the universal 2012 and NSQIP definitions
Mentor: Dr. Melanie Morris

N-6 **Mary Smithson, MS3**
A Formula for Planning and Predicting Post-Operative Mammoplasty Results
Mentor: Dr. Sherry Collawn

N-7 **Rohan Prabhu, MS2**
Total Intravenous Anesthesia (TIVA) compared to Inhalation Anesthesia: Which One Is Better for the Brain? A systematic review
Mentor: Dr. Lee Ann Riesenberg

N-8 **Nicholas Laskay, MS3**
How applicable are MOMS Trial results? A comparison of a single-institution cohort to the results from the randomized trial
Mentor: Dr. Brandon Rocque

N-9 **Caleb Jones, MS3**
A Retrospective Case Series of Carbon Fiber Plate Fixation of Ankle Fractures
Mentor: Dr. Ashish Shah

N-10 **Caleb Jones, MS3**
Retrospective Case Series of Tibiotalocalcaneal Arthrodesis (TTCA) Using a Carbon Fiber Intramedullary Nail
Mentor: Dr. Ashish Shah

N-11 **Ashlyn M Alongi, MS2***
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N-12 **Adam T. Archie, MS2**
Patient-declared Sternoclavicular Joint Pain: The Shoulder's Waddell's Sign?
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Thoracic Outlet Syndrome Decompression in Adolescents
Mentor: Dr. Brent Ponce

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Telemedicine with mobile devices using merged-reality for early postoperative care: A feasibility study
Mentor: Dr. Barton Guthrie

N-15 **Shelby L. Bergstresser, MS2**
Which hepatocellular carcinoma staging system has the highest predictive value?
Mentor: Dr. Derek DuBay

Short Term Oral:

Plumbagin Induces Apoptosis in Melanoma Cells by Inducing Endoplasmic Reticulum Stress and DNA Damage Response Signaling

Sarah F. McClees[1], B.S., Harish Chandra Pal[1], Ph.D., *Farrukh Afaq*[1,2], *Ph.D.*

[1]Department of Dermatology, University of Alabama at Birmingham, Birmingham, AL; [2]Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL

Introduction: Melanoma is the deadliest form of skin cancer due to its propensity to aggressively metastasize. Despite advances in therapy options, melanoma patients with distal metastasis often develop resistance to treatment and have a median survival of six months. Recently, interest has risen in utilizing phytochemicals as potential adjuvant or chemotherapeutic agents. Plumbagin, a phytochemical found in flowers and roots of the Plumbaginaceae family, exhibits anti-proliferative and anti-tumorigenic properties.

Objective: This study aimed to determine the effect of plumbagin on cell proliferation and apoptosis by targeting endoplasmic reticulum (ER) stress and DNA damage response (DDR) signaling pathways in melanoma cells from different genetic backgrounds.

Methods: The effects of plumbagin on melanoma cell proliferation were determined using MTT and colony assays. Melanoma cell apoptosis was analyzed using flow cytometry. Reactive oxygen species (ROS) generation was determined by using 2′,7′-dichlorodihydrofluorescein diacetate. Western blotting was used to evaluate ER stress and DDR signaling.

Results: Treatment of melanoma cells with plumbagin resulted in dose-dependent reduction of cell proliferation, increased production of ROS, and induction of apoptosis. Furthermore, treatment of melanoma cells with plumbagin induced ER stress, evidenced by increased (i) protein expression of ATF4, GRP78, PERK, and eIF2α, (ii) phosphorylation of PERK and eIF2α, and (iii) protein expression of CHOP, a key protein involved in ER-mediated apoptosis. In addition, plumbagin treatment induced DDR in melanoma cells as shown by increased phosphorylation of ATM, ATR, CHK-2, and γ-H2AX. Moreover, N-acetyl-L-cysteine treatment inhibited the apoptotic effects of plumbagin.

Conclusion: We conclude that plumbagin reduces proliferation and induces apoptosis of melanoma cells by triggering ER stress and DDR signaling pathways through increased production of ROS. Based on these observations, we suggest that plumbagin, alone or as an adjuvant to current therapies, could be used for the management of melanoma.

Short Term Oral:

Overexpressing IL-8 Receptors Promotes Endothelial Cell Migration and Inhibits Inflammation in Response to IL-8

Stephanie L. Donaldson. *Dongqi Xing, MD PhD. Suzanne Oparil, MD.*

Vascular Biology and Hypertension Program, Department of Medicine, University of Alabama at Birmingham, Birmingham, Alabama.

INTRODUCTION: Neutrophils are the main leukocyte subset that interacts with damaged endothelial cells (ECs), triggers the initial pro-inflammatory response, and facilitates the influx of other classes of inflammatory cells in a variety of vascular diseases. Interleukin-8 receptors A and B (IL8RA/B) mediate neutrophil migration in response to IL-8. We previously demonstrated that systemic administration of ECs overexpressing IL8RA/B (IL8RA/B-ECs) inhibits inflammation and injury response in acute vascular injury models, including balloon injury of rat carotid artery.

OBJECTIVES: We tested the hypothesis that overexpressing IL8RA/B promotes EC migration in response to IL-8 without triggering expression of inflammatory mediators by ECs.

METHODS: Cultured rat aortic ECs (RAECs) were transduced with adenovirus containing IL8RA/B vectors or Ad-null control vectors. Untransfected RAECS are controls. EC migration in response to IL-8 was assessed in a 96-well modified Boyden chamber. Actin polymerization, a precursor to migration, was assessed by immunofluorescent staining of F-actin. Inflammatory mediator mRNA expression was analyzed by real-time RT-PCR.

RESULTS: IL-8 dose dependently (20–500 ng/ml) enhanced migration of untransfected-, AdNull- and IL8RA/B ECs. IL8-stimulated cell migration was significantly greater in IL8RA/B-ECs (2 way ANOVA, $p<0.05$) compared to the other 2 experimental groups. IL-8 (100 ng/ml) induced greater F-actin polymerization in IL8RA/B-RAECs compared to other groups. In response to IL-8, expression of adhesion molecules intercellular adhesion molecule (ICAM)-1, P-selectin, and chemokine monocyte chemoattractant protein (MCP)-1 were significantly reduced in IL8RA/B-RAECs compared to other groups.

CONCLUSION: In contrast to neutrophils, which are activated and promote inflammation in response to IL-8, ECs overexpressing IL8RA/B exhibit enhanced migratory activity and attenuated inflammatory response to IL-8 treatment.

Short Term Oral:

Molecular Response to Neoadjuvant Chemotherapy in High-Grade Serous Ovarian Carcinoma

Allison M. Montgomery[2]; David Crossman, PhD[3]; Eddy Yang, MD[4], PhD; Angelina Londono, PhD[4]; Ronald D. Alvarez, MD[1]; Warner K. Huh, MD[1]; Kerri S. Bevis, MD, MSPH[1]; J. Michael Straughn, Jr., MD[1]; Charles A. Leath III, MD[1]; Rebecca C. Arend, MD[1]
[1]Division of Gynecologic Oncology, Department of Obstetrics & Gynecology; [2]School of Medicine; [3]Department of Biostatistics; [4]Department of Radiation Oncology; University of Alabama at Birmingham; Birmingham, Alabama

PURPOSE: Most ovarian cancer will recur and become resistant to chemotherapy. Oncogenesis has been attributed to molecular variations, leading to altered gene expression and cellular dysregulation.
OBJECTIVES: To evaluate genetic variation in high-grade serous carcinoma (HGSC) pre- and post-neoadjuvant chemotherapy (NACT), observe how gene expression affects specific pathways, and assess the utility of using cell-free DNA (cfDNA) to molecularly profile patients.
METHODS: Plasma and tumor specimens were collected from 19 patients with a median age of 74 years (47–85). 70% were identified as Stage IIIC. Genetic sequencing was conducted on matched samples using the NanoString® PanCancer Pathways Panel. Analysis was performed using Ingenuity Pathway Analysis and nSolver Advanced Analysis. Next generation sequencing (NGS) was performed on plasma cfDNA and tumor DNA from 14 patients. Mutations were compared using standard statistical tests.
RESULTS: The top 3 pathways affected by NACT were Immune Signaling (P=1.30E-09), Cell Proliferation (P=5.03E-08), and Cell-To-Cell Signaling (P=7.49E-06). The top 5 upregulated genes were NR4A3, NR4A1, DUSP5, FOS, and FOSL1. NGS cfDNA analysis detected more mutations in cancer-related genes than tumor DNA. The cfDNA pre-NACT contained 19 mutated genes with 57 specific mutations; the tumor contained 6 mutated genes with 38 specific mutations. Similar findings were revealed when comparing post-NACT mutations. cfDNA demonstrated more genetic diversity after NACT. Of the 57 mutations in the plasma pre-NACT, only 6 persisted, whereas 33 of 38 mutations in the tumor remained unchanged.
CONCLUSION: Analysis of matched tumors showed significant alterations in cell cycle, DNA damage, chromatin modification, Wnt, TGFB, and JAK-STAT signaling. These changes reflect tumor dysregulation caused by NACT. Furthermore, plasma cfDNA detects more mutations than DNA extracted from solid tumor and may better capture clonal evolution.

Short Term Oral

Living Kidney Donor-Recipient Relationship and Development of Post-donation Comorbidities

J. McLeod[1] , C. Carroll[1] , **W. Summers[1]** , C. Baxter[1] , R. Deierhoi[1] , P. MacLennan[1] , *J.E. Locke[1]* ; [1]University Of Alabama, Birmingham, Alabama, USA

Introduction: Living donor selection practices aim to quantify lifetime risk of comorbid disease development (e.g. hypertension, diabetes, kidney disease) based on candidate's pre-donation demographic and health characteristics at the time of evaluation. Studies aimed at predicting this risk have been limited by lack of information on donor relationship or family history. The goal of this study was to better understand the relationship between donor-recipient relationship and risk for post-donation comorbid disease development.

Methods: Participants enrolled in an IRB approved study agreed to survey examination and consented for medical record abstraction, allowing for capture of baseline health characteristics and post-donation outcomes. We used descriptive statistics and logistic regression to examine the odds of comorbid disease by donor-recipient relationship (adjusted for age, ethnicity, gender).

Results:59 adult living kidney donors were studied; median age at donation 43.3 (IQR: 38.9-56.7); median age at survey 64.5 (IQR: 51.2-69.7); 54 European American and 5 African American; with median follow-up of 6.6 years (IQR: 4.3-29.2). More than half of the cohort was related to their recipient (Related: 67% vs. Unrelated: 33%). Twenty living kidney donors developed comorbid disease over the course of the study. Hypertension was the most common post-donation comorbidity. Interestingly, 19 of 20 post-donation comorbidities developed in related donors. Related donors had a 17-fold higher odds of developing a post-donation comorbidity compared to their unrelated donor counterparts (adjusted odds ratio: 17.00, 95%CI: 1.84-157.08, p=0.01).

Conclusion: Donor-recipient relationship was strongly correlated with development of post-donation comorbidities. This finding suggests the potential for some underlying genetic susceptibility carried by family members and warrants further study.

Short Term Oral

Estrogen exerts anti-inflammatory effects in human macrophages in an estrogen receptor α dependent manner via modulation of macrophage polarization

Zachary H. Hughes, Christopher Ives, Samantha S Giordano PhD, Yuanyuan Guo PhD, Yiu-Fai Chen PhD, Dongqi Xing PhD, *Suzanne Oparil MD, Fadi G Hage MD.*
Vascular Biology and Hypertension Program, University of Alabama at Birmingham, Birmingham, Alabama, USA.

Introduction: Inflammation plays a critical role in the pathogenesis of vascular disease. The increased risk of cardiovascular disease (CVD) in postmenopausal women compared to premenopausal women has been partially attributed to decreased plasma estrogen (E2) levels after menopause. Macrophages play a crucial role in the inflammatory response seen in induced vascular injury through several potential mechanisms. Macrophages are able to express different functional phenotypes that can be pro-inflammatory (M1) or anti-inflammatory (M2) in response to different signals. We have previously shown that E2 can attenuate the inflammatory response seen in vascular injury of young mice but exhibit no effect or paradoxically exacerbates the inflammatory response in aged mice.
Objective: We tested the hypothesis that menopausal status and treatment with menopausal hormone therapy (MHT) will alter macrophage phenotype such that postmenopausal women will have a predominately pro-inflammatory macrophage phenotype compared to premenopausal women and that MHT will attenuate this polarization shift.
Methods: Mononuclear cells isolated from peripheral blood phlebotomy samples were differentiated ex vivo into macrophages from 3 groups of women: 1) premenopausal women aged 20-40 with regular menstrual cycles, 2) postmenopausal women aged >55 years with no menses >12 months, and 3) postmenopausal women aged >55 years who have received MHT since menopause. To test the anti-inflammatory effects of E2, macrophages from the 3 groups were treated with vehicle or CRP with or without E2 pretreatment. RT-PCR was used to determine the expression of markers of macrophage polarization. The relative prevalence of M1 to M2 phenotypes were confirmed using flow cytometry.
Results: Pending.
Conclusion: This study will provide insight on the anti-inflammatory effects of E2 in human macrophages and the mechanism(s) by which E2 loses these effects in postmenopausal women. These results will help explain the contradictory findings from clinical trials that tested the vascular effects of E2 in postmenopausal women.

Short Term Oral

William Riley, MS
Faculty Advisor – *Lauren Walter, MD* – UAB Department of Emergency Medicine

Neurocognitive Assessment of Emergency Department Concussions Using a Modified Sports Concussion Assessment Tool

INTRODUCTION: In the US, an estimated 1.7 million concussions occur annually and over 80% of these present to emergency departments (ED). The Sport Concussion Assessment Tool -2 (SCAT-2) is a well-validated standardized examination that is frequently used to diagnose and measure the acute effects of sports related concussion on athletic sidelines. SCAT-2 is limited in its practical application in the ED setting however due to its length as well as exam components which are less appropriate to the ED environment.

OBJECTIVE: The objective of this study was to develop a novel instrument which could be more practically applied in the ED setting to accurately identify patients with concussions.

METHODS: We recruited head injury patients at risk for concussion to non-head-injury patients who presented to the University ED. A modified SCAT-2 was administered to evaluate the neurocognitive status of participants, including evaluation of associated symptom severity and cognitive status. The subsections were graded individually and compared to factors that best stratified patients. From this comparison, the subsequent SCAT-ED, a novel tool for ED concussion diagnosis tool, was developed.

RESULTS: 28 patients with head injuries and 28 negative controls were enrolled. Using the modified SCAT-2 instrument, 'concussion' participants and non-concussion patients scored an average of 57 and 51 out of 71, respectively, with lower being indicative of worse impairment. The SCAT-ED tool was minimized to a symptom score, total number of symptoms and physical signs totaling a possible 86 points, with *higher* scores being more indicative of a concussion. Using this SCAT-ED assessment, concussion patients scored an average of 34 out of 86 and controls scored an average of 19.

CONCLUSION: The equally stratified results show the SCAT-ED serves to identify concussions equally as well as the modified SCAT-2 assessment tool, while being much more applicable to the emergency setting.

Intermediate Term Oral:

Title: Human Papillomavirus (HPV) Awareness and Vaccination Status in Female Emergency Department Patients

Authors: Elizabeth D. Leader; *Lauren A. Walter, MD*

Introduction: Human Papillomavirus (HPV) is the most common sexually transmitted infection and the leading cause of cervical cancer in the United States. Racial minorities, rural patients, and patients in poverty comprise a high-risk population, representing more than 60% of cervical cancer cases in the US.

Objective: This study sought to gather information pertaining to awareness of HPV and the HPV vaccine in female patients presenting to the ED to determine the presence of any high-risk ED populations that might benefit from further health resources and/or interventions.

Method: Face-to-face surveys were obtained of 200 female patients aged 18-65 presenting to the ED at University of Alabama at Birmingham, an urban tertiary care center. Demographic information obtained included patient age, race/ethnicity, income, insurance status, primary care provider status, and known cervical cancer risk factors. Subsequent survey questions explored respondents' knowledge, familiarity, and attitudes regarding HPV, cervical cancer, and the HPV vaccine.

Results: Respondents included Black or African American, White or Caucasian, and Hispanic women (56%, 42.5%, and 1.5% respectively). Medicaid and self-pay patients represented 30.7% and 23.1% of respondents respectively and 45% reported income below the federal poverty level. Nearly a quarter of respondents had not heard of HPV and more than a third were unaware that HPV was the primary cause of cervical cancer. Likewise, more than a third were also unaware of an HPV vaccine. Of the subset of respondents less than 33 years of age (HPV vaccine first available in 2008), more than half reported that they had never been offered the HPV vaccine and fewer than a quarter had actually completed the vaccine series.

Conclusion: The respondents in this study constituted a higher than average proportion of high risk patients as compared to the general population and reported relatively low awareness of HPV and the HPV vaccine.

Intermediate Term Oral:

Title: Screening for Sexually Transmitted Infections in Persons Living with HIV Leads to Significant Financial Losses for a Healthcare System

Authors: **Kathryn Hudak, BS**[1], Christina Muzny, MD[2], Jane Schwebke, MD[2] and *Ellen Eaton*, MD[2], (1)University of Alabama School of Medicine, Birmingham, AL, (2)Division of Infectious Disease, University of Alabama at Birmingham, Birmingham, AL

Introduction: Sexually transmitted infections (STIs) are common in persons living with HIV (PLWH) and can facilitate the transmission of HIV. The current CDC guidelines recommend annual screening of all PLWH for *Neisseria gonorrhea (GC), Chlamydia trachomatis (CT),* and *Treponema pallidum (Syphilis),* and screening for *Trichomonas vaginalis (TV)* in HIV-positive women.

Objective: The objective of this study was to understand the financial implications of recommended STI screening in PLWH.

Methods: We estimated the costs of providing recommended STI screening tests annually to all eligible patients at an academically affiliated HIV clinic in Birmingham, AL from August 2014- August 2015. Expenditures for GC, CT, TV and Syphilis *s*creening were calculated using lab charges (Table 1). Revenue was calculated using reimbursement data for the above tests based on insurer. Commercial insurance reimbursement was based on data from Blue Cross Blue Shield of Alabama, the largest commercial insurer in our population. Uninsured patients were assumed to have commercial insurance under the provisions of the Affordable Care Act (ACA).

Results: 3,163 patients (27% Medicare, 13% Medicaid, 26% Commercial, 34% Uninsured/ACA) met study inclusion criteria. Net yield, defined as reimbursements minus charges, was calculated for each test. Providing recommended STI screening annually to all eligible patients would result in a clinic net yield of -$783,834.76.

Conclusion: Providing PLWH with recommended annual STI screening tests would potentially result in approximately $790,000 of uncompensated expenditures for this healthcare system. Policy makers should address this lack of compensation to ensure sustainability and compliance with recommended STI screening in PLWH. Caring for uninsured patients will lead to greater losses.

Intermediate Term Oral:

Myeloid Cell Heme Oxygenase-1 Expression Regulates the AKI to CKD Transition

Jeremie M. Lever, BS[1], Bo Chen, MD[2], Ravindra Boddu, PhD[1], Oreoluwa O. Adedoyin, PhD[1], *James F. George, PhD*[1,3], *Anupam Agarwal, MD*[1,3]

[1]Department of Medicine, [2]Department of Pathology, [3]Department of Surgery, University of Alabama at Birmingham, [3]Birmingham VA Medical Center, Birmingham, AL

INTRODUCTION: Acute kidney injury (AKI) is a major public health concern accounting for up to 3% of hospitalized patients. Those who experience AKI requiring dialysis are at a 28-fold increased risk of chronic kidney disease (CKD). Heme oxygenase-1 (HO-1) is an inducible, cytoprotective enzyme that catabolizes heme, and its induction is protective in animal models of AKI. Previous studies have demonstrated that myeloid cell HO-1 mitigates damage following renal ischemia-reperfusion injury (IRI).

OBJECTIVES: Our objective was to test the role of myeloid cell-specific expression of HO-1 in the AKI to CKD transition. Given the importance of macrophages (MΦs) in regulating kidney damage after AKI, we *hypothesized* that HO-1 deficiency in myeloid cells would lead to worse outcomes in this model.

METHODS: We modeled the AKI to CKD transition in mice using unilateral IRI, and followed the animals for 3 weeks. We used cre-lox mice in which HO-1 is selectively deleted in myeloid cell populations (LysM-HO-$1^{-/-}$).

RESULTS: Interestingly, we found LysM-HO-$1^{-/-}$ mice exhibited a trend toward less atrophy and renal fibrosis, when compared with flanking loxP control mice (LysM-HO-$1^{+/+}$). In addition, greater absolute numbers of bone marrow-derived MΦs (F4/80^{low}CD11b^{hi}, $7.22x10^6 \pm 6x10^5$ vs $4.90x10^6 \pm 6x10^5$, $p = 0.03$) and NK cells (NK1.1^+, $4.51x10^6 \pm 6x10^5$ vs $2.44x10^6 \pm 5x10^5$, $p = 0.02$) were observed in injured kidneys from LysM-HO-$1^{-/-}$ mice, indicating these cell types may play a protective role in this model. Further, myeloid cell HO-1 deficiency resulted in a trend toward lower proportions of pro-fibrotic tissue-resident MΦs (F4/80^{hi}CD11b^{low}, 12.14 ± 1.3% versus 16.56 ± 1.6%, $p = 0.07$). **CONCLUSION:** These studies demonstrate that HO-1 expression in myeloid cells regulates progressive kidney disease in the AKI to CKD model, having potential implications for developing cell-based therapy or strategies involving modulation of HO-1 expression in the AKI to CKD transition.

Long Term Oral:

Mitochondrial Genetic Background Has Minimal Impact on the Progression of Atherosclerosis

Alexander W. Bray, Jessica L. Fetterman, David G. Westbrook, Kimberly J. Dunham-Snary, Scott W. Ballinger

University of Alabama at Birmingham, Department of Pathology

Cardiovascular disease (CVD) is the leading cause of mortality in the United States, and the majority of cases are due to atherosclerosis. Despite the widespread prevalence of this disorder, the contribution of inherited genetics to CVD susceptibility remains poorly understood. Furthermore, the cellular mechanisms through which defined CVD risk factors such as age, ethnicity, family history, hypercholesterolemia, and tobacco smoke converge to stimulate atherogenesis have yet to be clearly articulated. Mitochondria are multifunctional organelles that sustain oxidant-mediated damage following chronic exposure to these CVD risk factors. In addition, mitochondria possess their own maternally inherited genome that reflects maternal geographic origins and contains polymorphisms capable of influencing mitochondrial and cellular function. In the following study, we directly assessed the causal role mitochondrial genetics and function play in the pathogenesis of atherosclerosis. Utilizing novel Mitochondrial-Nuclear eXchange (MNX) mouse technology developed in the our laboratory, apoE$^{-/-}$ WT (apoE$^{-/-}$ C57^{n}:C57^{mt}) and MNX (apoE$^{-/-}$ C57^{n}:C3H^{mt}) mice were generated in order to test the hypothesis that altering a mouse's mitochondrial genetic background would influence atherogenesis in this setting of genetically driven hypercholesterolemia. Interestingly, apoE$^{-/-}$ C57^{n}:C57^{mt}) and apoE$^{-/-}$ C57^{n}:C3H^{mt} animals displayed differences in vascular function and bioenergetics as early as 8 weeks of age. However, these differences did not appear to influence atherogenesis as both animals displayed equal plaque burden at 16 and 20 weeks of age. Moreover, studies performed on aortic tissue isolated from 12 and 16 week old apoE$^{-/-}$ C57^{n}:C57^{mt} and apoE$^{-/-}$ C57^{n}:C3H^{mt} mice revealed no differences in accumulation of mtDNA damage or aconitase activity, a surrogate marker of mitochondrial oxidative stress. Together, these data indicate that although mitochondrial DNA background appears to modulate certain aspects of vascular mitochondrial function, it has minimal effect on the progression of atherosclerosis in this mouse model of the disease.

Long Term Oral:

Rescue of a Humanized Mouse Model of β-Thalassemia Major By Allogeneic Bone Marrow Transplantation in the Absence of Cytoreductive Conditioning

Jonathan R Lockhart[1], Yongliang Huo PhD[1], Shanrun Liu PhD[1], Suean D Fontenard[1], Michael Berlett[1], and *Thomas M Ryan, PhD*[1]

[1]Department of Biochemistry and Molecular Genetics, University of Alabama at Birmingham, Birmingham, A

INTRODUCTION: β-thalassemia major, or Cooley's anemia (CA), is a genetic disease that results in a complete absence of β-globin chains and thus the major adult hemoglobin (HbA) in erythroid cells. Allogeneic bone marrow transplantation (BMT) can cure CA patients; however, there are many dangerous obstacles to overcome before and after treatment.

OBJECTIVE: The primary goal of this study is to test a novel treatment for Cooley's anemia in a humanized mouse model.

METHODS: Newborn CA mice received anti-CD122 antibody on the second day of life and single intravenous injection of bone marrow cells on the third day of life. Animals were bled periodically to monitor donor red blood cell (RBC) chimerism by flow cytometry. After at least 5 months, animals were sacrificed for analysis of donor hematopoietic stem and progenitor (HSPC) chimerism as well as disease and treatment related pathology.

RESULTS: A single injection of bone marrow cells into CA pups results in stable, long-term hematopoietic chimerism that is capable of reconstituting greater than 90% of RBCs. Interestingly, at the HSPC level, donor chimerism was determined to be much lower with a range of <1% to 15%. This suggests there is a tremendous survival advantage of donor erythroid cells over those derived from the recipient. Transplanted animals are transfusion independent, fertile, and exhibit no evidenced of graft-versus-host disease.

CONCLUSIONS: In conclusion, we have demonstrated rescue of CA mice from lethal anemia by allogeneic BMT in the absence of cytoreductive conditioning. This suggests that exploitation of the naivety of the newborn immune system provides a means to circumvent the need for toxic cyto-reductive conditioning. Based on the success of these studies, we are testing the hypothesis that perinatal BMT without cyto-reductive conditioning is capable of overcoming MHC-mismatch between graft and host. These studies pave the way for safer transplantation strategies in children with Cooley's anemia.

Long Term Oral:

Induced MHCII expression on breast cancer cells delays tumor-specific T cell exhaustion and impairs tumor growth

Tyler R. McCaw[1]; Selene Meza-Perez, PhD[1]; Mei Li[2]; Donald J. Buchsbaum, PhD[2]; *Troy D. Randall, PhD*[1]

1. Department of Medicine, University of Alabama at Birmingham, Birmingham, AL

2. Department of Radiation Oncology, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: We recently reported that aberrant expression of Major Histocompatibility Class II (MHCII) molecules on human triple negative breast tumors correlates with patients' prolonged progression-free survival and increased tumor infiltrating lymphocytes.

OBJECTIVES: This study aimed to determine if MHCII-expressing tumors increase the intratumoral activation of CD4+ T cells and whether this leads to enhanced tumor killing by CD8+ T cells over time.

METHODS: We created MHCII-expressing tumor cells by transfecting murine breast cancer (TS/A) cells with the human MHCII transcriptional activator (hCIITA). Transfected cells were then injected into BALB/c mice and the resulting immune response was analyzed by flow cytometry at several time points.

RESULTS: hCIITA-expressing tumors grew slower than control tumors in immunocompetent recipients, but this difference was abrogated in both immunocompromised mice and CD4+ T cell depleted mice. CD4+ T cells isolated from hCIITA-transfected tumors produced more cytokines associated with anti-tumor immunity (e.g. IFNγ) for longer times than their counterparts in control tumors. Similarly, CD8+ T cells isolated from hCIITA-transfected tumors displayed a more activated phenotype and produced more cytotoxic cytokines for longer times. Nevertheless, CD4+ and CD8+ T cells eventually became exhausted in both groups. Interestingly, hCIITA-expressing tumors harbored significantly more regulatory T cells (Tregs) with more suppressive phenotypes than Tregs from control tumors. Finally, we showed that histone deacetylase inhibitors (HDACis) are capable of inducing tumor MHCII expression in vivo.

CONCLUSION: These results suggest that expression of MHCII on tumor cells promotes intratumoral CD4+ T cell activation, which enhances CD8+ T cell anti-tumor responses and delays T cell exhaustion. Thus, epigenetic modifying drugs, specifically HDACis, are clinically viable approaches for enhancing tumor cell expression of MHCII and boosting the anti-tumor immune response in vivo. These effects may be magnified by combinatorial therapy with checkpoint inhibitors to promote durable anti-tumor immunity.

Project Length: Short
A-1

Beomjy Kim[2]; Zachary Dobbin, MD, PHD[2]; Nuget A. Nugyen[1]; Emily Landers, MD[2]; Jonathan Boone, MD[1]; David Crossman, PhD[3]; Todd M. Stevens, MD[5]; Dezhi Wang[5]; Eddy Yang, MD[4], PhD; Angelina Londono, PhD[4]; Ronald D. Alvarez, MD[1]; Warner K. Huh, MD[1]; Kerri S. Bevis, MD, MSPH[1]; J. Michael Straughn, Jr., MD[1]; Charles A. Leath III, MD[1]; Rebecca C. Arend, MD[1]

[1]Division of Gynecologic Oncology, Department of Obstetrics & Gynecology; [2]School of Medicine; [3]Department of Biostatistics; [4]Department of Radiation Oncology; [5]Department of Pathology; University of Alabama at Birmingham; Birmingham, Alabama

Title: Using Nanostring to identify high-intermediate risk endometrial cancer patients at high risk for recurrence

Purpose: Approximately 20% of patients with high-intermediate risk (HIR) endometrial cancer (EMCA) will have recurrence of disease after surgery. The use of adjuvant therapy in patient with H-IR EMCA is controversial. Adjuvant treatment could increase progression free survival but has limited data on impact in overall survival.

Objectives: To develop a genetic signature that identifies which H-IR endometrial cancer patients are at high risk for recurrence.

Methods: UAB patient cohort included H-IR EMCA patients diagnosed between 2000-2010 without adjuvant treatment. Thirteen recurred patients were matched with thirteen patients without recurrence. All patients met criteria for HIR EMCA: presence of 1-3 pathologic risk factors based on age according to GOG 99. Matches were based on stage, grade, race, age of diagnosis, presence or absence of LVSI, depth of invasion, and size of tumor. Molecular profiles of the two groups were compared using the Nanostring nCounter® PanCancer Pathways Panel. Pathway analysis was performed with Ingenuity Pathway and nSolver Analysis Software. Genes were evaluated using a fold change of $\geq +/- 1.5$ and a p-value of < 0.05.

Results: There were 10 genes that had greater than 2-fold (range 2.07 – 4.13) increased gene expression in H-IR endometrial cancer patients that recurred: MMP3, GZMB, INHBB, E2F1, CCNB3, PLA2G3, RAC3, CCNO, CDC25A, and TNF. There were 8 genes with more than 1.5-fold (range 1.54 – 3.60) decrease in gene expression in H-IR endometrial cancer patients that recurred: IL5RA, PTPN5, BAIAP3, MAP3K13, PLCB1, IL1R1, NOS3, and COL27A1.

Conclusion: A panel of 18 genes are significantly different in their level of RNA expression based on the Nanostring analysis between H-IR EMCA patients who recurred compared to patients that do not recur. Findings support a possible genetic signature that corresponds to the risk of recurrence in H-IR EMCA patients which could guide clinicians in identifying which patients warrant adjuvant treatment after surgery.

Project Length: Short
A-2

Title: Investigating the role of elective radiation of the seminal vesicles (SVs) in men with intermediate or high risk prostate cancer

Author(s): **Garrett T. Dunn**, Andrew M. McDonald, M.D., *Rojymon Jacob, M.D.*

Affiliations: Department of Radiation Oncology, University of Alabama in Birmingham School of Medicine, Birmingham, AL.

Introduction: Elective radiation to the proximal 1cm of the seminal vesicles is currently recommended for men with intermediate risk prostate cancer and the entire SVs with lower dose radiation in high risk prostate cancer enrolling in current RTOG protocols (see RTOG 0815 and 0924 CTV definitions). This recommendation is based on pathologic radical prostatectomy specimens by *Kestin et al.* (PMID: 12377319) who reported a risk of SV invasion exceeding 15% in men with only one high-risk feature, specified as intermediate risk, and an increased risk to 58% in men with all three high-risk factors. Despite the widespread adoption of elective SV coverage there is a paucity of clinically reported outcomes necessitating this approach.

Objectives: The primary objective of his study was to correlate biochemical control of prostate cancer with SV radiation dosimetry.

Methods: This was a retrospective chart review in which a set of patients were gathered who met the criteria of intermediate or high-risk prostate cancer. Data for last PSA check and positive recurrence of prostate cancer were extracted from the patient chart. The pre-treatment CT scans of the patients were used to contour the seminal vesicles using the Eclipse software. Radiation volume and dose to the seminal vesicles was then extracted and correlated to the PSA and recurrence data previously gathered to be compared to Kaplan-Meier biochemical failure rates.

Results: A total of 137 men were included in this analysis, 64 (47%) with intermediate risk disease and 73 (53%) with high risk. The Kaplan-Meier estimate of biochemical failure at 5 years was 5.4% for intermediate risk patients compared to 16% for high risk patients (p=0.148). When seminal vesicle dose-volume histograms were analyzed as a possible predictor of biochemical failure, patients whose V56 was less than 8cc had a 5-year failure rate of 13.4% compared to 0% for patients whose V56 was greater than 8cc (p=0.006).

Conclusion: These early results suggest that elective coverage of the SVs may be associated with improved disease control. Further work will investigate possible confounders such as use of androgen deprivation therapy.

Project Length: Short
A-3

Characterization of Estrogen Receptor Positive/Progesterone Receptor Negative Breast Cancer

Jacob P Britt, Tao Guo, MD, PhD, Tiansheng Shen, MD, PhD, Omar Hameed, MD, Gene P Siegal, MD, *Shi Wei, MD, PhD*

Department of Pathology, University of Alabama at Birmingham, Birmingham, AL

Introduction: Hormonal receptor status helps guide treatment for breast cancer (BC). While most of estrogen receptor-positive (ER+) BCs express progesterone receptor (PR), about 12-20% of BCs have an ER+/PR- immunophenotype.

Objectives: This study seeks to characterize the clinicopathologic features and prognostic outcomes of ER+/PR- BCs as compared to ER+/PR+ tumors.

Methods: BCs diagnosed from 1998 to 2013 at the authors' institution were analyzed. Clinicopathologic parameters, therapeutic modalities, and outcomes were recorded. Those with metastasis at diagnosis were excluded. Kaplan-Meier method and the log-rank test were used to analyze distant relapse-free survival (RFS).

Results: A total of 3107 ER+/PR+, and 637 ER+/PR- BCs met the inclusion criteria. The proportion of BCs with a HER2+ phenotype was significantly higher in the ER+/PR- tumors (24.3% vs 14.3%, $P<0.0001$). When compared to the ER+/PR-/HER2- BCs, the ER+/PR+/HER2- tumors were associated with a significantly prolonged RFS in all age groups. However, in the subset of patients receiving endocrine therapy, a significantly favorable RFS associated with ER+/PR+/HER2- BCs was seen in premenopausal women and in advanced BC (Stage IIB/III) when compared to ER+/PR-/HER2- tumors, while the ER+/PR+/HER2+ phenotype was associated with a significant survival advantage in postmenopausal patients, in all races, in Grade III tumors, and in early stage (I/IIA) tumors when compared to ER+/PR-/HER2+ BCs.

Conclusions: Currently, ER+ BCs are treated similarly, but these observations have suggested that the ER+/PR- tumors have different clinicopathologic features and prognostic outcomes from the ER+/PR+ BCs. The ER+/PR- phenotype suggests aberrant growth factor signaling that could contribute to resistance to endocrine therapy, thus may have a significant impact in the pursuit of precision medicine.

Project Length: Short
A-4

Fluorescent-labeled Cetuximab for Image-guided Soft Tissue Sarcoma Surgery

Andrew S. McGee[1], Andrew C. Prince[1], *Jason M. Warram[2]*, Ph.D., Nicole K. Behnke[2], M.D.; 1 The University of Alabama at Birmingham, School of Medicine, Birmingham, Al, USA; 2 The University of Alabama at Birmingham, Department of Surgery, Birmingham, Al, USA

Introduction: Soft tissue sarcomas (STS) are a heterogeneous group of solid malignancies whose treatment includes margin-negative resection. Fluorescence-guided surgical resection can help delineate intraoperative margins; preclinical studies demonstrate improved oncologic outcomes in other malignancies using cancer-specific imaging probes. This novel strategy may decrease unnecessary healthy tissue resection and improve oncologic outcomes by reducing margin-positive resections. Cetuximab, an FDA-approved, anti-EGFR, is shown to be safe and augment margin assessment in head and neck cancer. EGFR is similarly overexpressed in multiple subtypes of STS.

Objectives: To evaluate the tumor-targeting specificity of cetuximab, DC101 (anti-VEGF receptor 2), and two cathepsin-activated probes in STS.

Methods: Athymic nude mice with subcutaneous HT1080 fibrosarcoma tumors received one of five probes: IRDye800CW fluorescent probe conjugated to either: cetuximab, DC101, an IgG isotype control, or a cathepsin-activated probe (IntegriSense 750 and Prosense 750). Daily fluorescence imaging used open- and closed-field systems. Tumor-to-background ratios (TBR) were evaluated. Peak TBRs were determined for each probe from an initial trial experiment. On respective peak TBR days, assessment of probe sensitivity was evaluated with successive decremental tumor fragments in the wound bed to evaluate the smallest tumor mass accurately detectable.

Results: On day of peak TBR, the TBR of cetuximab-IRDye800CW (11.1, Day-9) was significantly greater than Integrisense750 (6.68, p=0.005, Day-9), IgG-IRDye800CW (4.44, p=0.00005, Day-9), Prosense750 (2.35, p=0.00009, Day-5), and DC101-IRDye800CW (1.87, p=0.00003, Day-7). Peak cetuximab-IRDye800CW TBR was also several folds higher that other agents *in vivo*. Additionally, cetuximab-IRDye800CW was able to accurately localize as small as a 1mg tumor fragment.

Conclusion: This study demonstrates superiority of cetuximab-IRDye800CW for disease-specific imaging in a subcutaneous animal model for STS. The novel strategy of coupling improved margin-negative surgical resection with established chemotherapy has considerable translation significance and is an avenue for exploration with other drugs used to treat STS.

Project Length: Short
A-5

Translation of Oncologic Imaging Agents for Fluorescence-Guided Surgical Resection: A Comparison of 5-Aminolevulinic Acid and IntegriSense750

Aditi H. Jani, BS[1], Denzel A. Cole, MD[2], Kiranya E. Tipirneni, MD[2], Yolanda E. Hartman, BS[2], *Jason M. Warram, PhD*[2]
[1]School of Medicine, University of Alabama at Birmingham, Birmingham, AL
[2]Department of Surgery – Division of Otolaryngology, University of Alabama at Birmingham, Birmingham, AL

Introduction: The invasive nature of glioblastoma multiforme (GBM) causes tumor visualization and subsequent resection to be difficult. Fluorescence-guided surgery in management of GBM is ideal in identification and removal of disease that may otherwise be undetected. 5-Aminolevulinic acid (5-ALA), an orally administered compound, is converted in tumor cells to a fluorescent molecule, protoporphyrin IX (PpIX) and serves as a "proof of principle" agent in GBM resection. However, it has limitations, including significant tissue autofluorescence and reduced tissue penetration compared to molecules in the near-infrared (NIR) range (>700nm). Comparatively, IntegriSense750 (PerkinElmer), a small, NIR-active molecule, largely eliminates tissue autofluorescence. Also, Integrisense750 avidly targets αvβ3 integrin, which is widely expressed in GBM cells, thus improving specificity in tumor identification.

Objectives: To characterize the activity of IntegriSense750 as a safe and specific agent in fluorescence-guided surgery for GBM, and to compare this to the current standard imaging agent, 5-ALA.

Methods: Orthotopic GBM tumor models were created in female nude athymic mice. Five mice were intravenously injected with 5-ALA, and five with IntegriSense750. These were sacrificed after 4 hours and 24 hours, respectively, and their brains extracted, fixed, and sectioned. The sections were imaged using NIR modalities and fluorescence microscopy, and stained using H&E. The images were analyzed to obtain fluorescence intensity, specificity, and tumor-to-background ratios.

Results: Preliminary qualitative data indicated appreciably increased specificity of tumor visualization using IntegriSense750 when compared to 5-ALA. Tumors identified with IntegriSense750 in NIR showed greater concordance with H&E staining and notably, sub-millimeter skip lesions in contralateral hemispheres were identified with NIR fluorescence. 5-ALA-based imaging was significantly less specific in comparison.

Conclusion: Although 5-ALA is the tested standard in fluorescence imaging of GBM, IntegriSense750 serves as a more specific, targeted probe which could be reliably translated to surgical resection of GBM in patients.

Project Length: Short
A-7

Andrew R. Schroeder, Colleen M. Britain, *Susan L. Bellis**
* Cell, Developmental and Integrative Biology, University of Alabama at Birmingham, Birmingham, Alabama

Abstract
Title: ST6Gal-I Serves as a Major Pro-Survival Molecule in Tumor Cells
Authors: Andrew R. Schroeder, Colleen M. Britain, *Susan L. Bellis**

Objectives: In this study we set out to evaluate how cancer cells expressing the glycosyltransferase ST6Gal-I are able to resist serum deprivation and maintain proliferative ability even in the absence of growth factors.
Methods: OV4 ovarian cancer cells with forced ST6Gal-I over expression (OE) and BxPC3 pancreatic cancer cells with shRNA knockdown (KD) of ST6Gal-I were serum starved for varying time points. Serum deprived cells were collected and analyzed via western blot for the expression of the pro-survival molecules p-Akt and p-p70S6K. These cells were also evaluated by qRT-PCR for the relative expression of cIAP2, an inhibitor of apoptosis, and IL6 and IL8, cytokines involved in inflammatory response and angiogenesis.
Results: Upon serum starvation, ST6Gal-I expressing cells, OV4 OE and BxPC3 EV, showed increased activation of Akt and p-70S6K and increased expression of cIAP2, IL6, and IL8 when compared with non-ST6Gal-I expressing counterparts.
Discussion: The activation of Akt and p70S6K by cells expressing ST6Gal-I indicates that the addition of sialic acids to surface glycoproteins by ST6Gal-I plays a critical role in cell survival. The activation of Akt and p70S6K upon serum starvation suggests that ST6Gal-I expression is enabling proliferation despite adverse conditions. The increased expression of cIAP2, IL6, and IL8 in ST6Gal-I expressing cells suggests that elevated surface sialylation not only allows cells to evade apoptosis, but also suggests that ST6Gal-I activity enables tumors to continue growing by prompting angiogenesis to supply energy and growth factors.
Conclusion: In this study, we demonstrated that cancer cells were able to survive growth factor deprivation in a ST6Gal-I-dependent manner. This novel finding could aid in the development of future treatments for both pancreatic and ovarian cancer.

Project Length: Short
A-8

Induction of Somatostatin Receptor Expression on Medullary Thyroid Tumors Using Histone Deacetylase Inhibitors

Andrew Janssen, Zhihuan Sun, Zviadi Aburjania, Clay Kerby, Renata Jaskula-Sztul and Herbert Chen

Introduction: Medullary Thyroid Cancers (MTC) are neuroendocrine tumors (NETs) that arise from C-cells of the thyroid gland. MTCs are frequently metastatic at the time of discovery and also secrete excessive hormones, often causing debilitating symptoms such as facial flushing and diarrhea. Somatostatin receptors (SSTRs) are a family of five receptors that are overexpressed in 85% of NETs. Somatostatin (SST) analogs have been used for treatment and imaging studies in NETs, but have not shown to be very practical in MTCs due to low SSTR expression. Herein, we describe the novel use of a class of drugs known as histone deacetylase inhibitors (HDACi) that have the unique ability to up regulate expression of SSTRs on MTCs. The use of HDACi will further advance SST analog therapies imaging studies in NETs.

Methods: Quantitative real time PCR (Q-PCR) was used to evaluate basal expression of SSTRs on two MTC cell lines. Time dependent induction of SSTRs were evaluated at 12, 24, and 48 hours. Furthermore, dose dependent induction for SSTRs were assessed at 48 hours with four separate HDACi-- FK228, SAHA, TDP-A and VPA-- using Q-PCR and Western Blot analysis.

Results: Basal expression for both cell lines showed an increased expression in one or more SSTRs. After Treatment with HDACi, both MZ and TT cells showed a dramatic increase in SSTRs at message and protein levels. More importantly, TT cells had no basal expression of SSTR4, but treatment showed to actually induce expression of SSTR4.

Conclusion: We demonstrated that HDACi increased message and protein levels of SSTRs in MTC cells in a time and dose dependent manner. We also showed that HDACi have the capability to induce expression of SSTRs even if there is no basal expression. This novel finding provides an avenue to improve SST analog therapies and imaging studies for MTCs.

Project Length: Short
A9

Computational Trials: Unraveling Motility Phenotypes, Progression Patterns, and Treatment Options for Glioblastoma Multiforme.

Authors: **Raman F**, Scribner E, Fathallah-Shaykh HM

INTRODUCTION: Glioblastoma multiforme is a malignant brain tumor with poor prognosis and high morbidity due to its invasiveness. Hypoxia-driven motility and concentration-driven motility are two mechanisms of glioblastoma multiforme invasion in the brain. The use of anti-angiogenic drugs has uncovered new progression patterns of glioblastoma multiforme associated with significant differences in overall survival.

OBJECTIVE: Here, we apply a mathematical model of glioblastoma multiforme growth and invasion in humans and design computational trials using agents that target angiogenesis, tumor replication rates, or motility.

METHODS/RESULTS: The findings link highly-dispersive, moderately-dispersive, and hypoxia-driven tumors to the patterns observed in glioblastoma multiforme treated by anti-angiogenesis, consisting of progression by Expanding FLAIR, Expanding FLAIR + Necrosis, and Expanding Necrosis, respectively. Furthermore, replication rate-reducing strategies (e.g. Tumor Treating Fields) appear to be effective in highly-dispersive and moderately-dispersive tumors but not in hypoxia-driven tumors. The latter may respond to motility-reducing agents. In a population computational trial, with all three phenotypes, a correlation was observed between the efficacy of the rate-reducing agent and the prolongation of overall survival times.

CONCLUSION: This research highlights the potential applications of computational trials and supports new hypotheses on glioblastoma multiforme phenotypes and treatment options.

Project Length: Short
A-10

Title: How levels and causes of distress in older cancer patients vary by race

Authors:

Jay V. Dasigi, School of Medicine, University of Alabama at Birmingham, Birmingham, AL

Maria Pisu Ph. D., Division of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL

Kelly Kenzik Ph. D., M.S., Division of Hematology & Oncology, University of Alabama at Birmingham, Birmingham, AL

Introduction: Research has shown racial disparities in psychological and emotional distress levels following diagnosis for cancer patients >65, but correlations between race and specific causes of distress have not been fully elucidated.

Objectives: To characterize how levels and causes of distress in older cancer patients vary by race.

Methods: Patients were participants in the Patient Care Connect Program, a lay navigation program for Medicare patients >65 treated at twelve cancer centers in five southern states. Participants submitted distress thermometers with associated problem lists while in the program: the thermometer was a modified from the Distress Thermometer developed by the National Comprehensive Cancer Network. Scores ranged from 0-10, where 0 indicated no distress and 10 extreme distress. Causes of distress were grouped into ten domains: physical, informational, emotional, practical, cognitive, family, spiritual, functional, mobility, and other. We included in the analysis black and white patients who filled out at least one distress assessment during the first quarter of enrollment. We report frequency of patients with high distress levels (score >3) and of patients who indicated causes of distress in each of ten distress domains. Differences by race were assessed using Chi-square test.

Results: The patient population consisted of 4233 white and 683 black patients. 46.1% were female. 44.3% were >75. 25.5% had zero and 36.5% had >3 comorbid conditions. 53.6% had high-risk cancers. 46% had common cancers. Black patients had higher distress levels than white patients (27.7% vs. 24.8%, p=0.10) and were more likely to report causes of distress in these domains: practical (21.2% vs, 11%, p<0.0001), cognitive (8.6% vs. 6.1%, p=0.01), and mobility (13.2% vs. 9.7%, p=0.005).

Conclusion: Differences in levels and causes of distress between white and black patients were noted in this study. Causes for these discrepancies warrant future studies, and effects of additional confounders, such as socioeconomic status, need to be analyzed.

Project Length: Short
A-11

Fluorescence imaging to localize head and neck squamous cell carcinoma for enhanced pathological assessment

Stephanie L Bevans,[1] *Jason M Warram,*[2] Esther de Boer,[2,3] Gooitzen M van Dam,[3] Lindsay S Moore,[2] Erika M Walsh,[2] Erik S Young,[4] William R Carroll,[2] Todd M Stevens,[4] Eben L Rosenthal[5]

[1]University of Alabama at Birmingham School of Medicine, [2]Department of Otolaryngology, University at Birmingham, [3]Department of Surgery, Nuclear Medicine and Molecular Imaging, and Intensive Care, University Medical Center Groningen, [4]Department of Pathology, Division of Anatomic Pathology, University of Alabama at Birmingham, [5]Department of Otolaryngology, Standford University

ABSTRACT

INTRODUCTION: Accurately identifying positive margins in real-time permits re-excision during surgical procedures. Intraoperative assessment of margins via gross examination and frozen section is a widely used tool to assist the surgeon in achieving complete resection. While this methodology permits diagnosis of freshly resected tissue, the process is fraught with misinterpretation and sampling errors. During fluorescence-guided surgery, an exogenous fluorescent agent specific for the target disease is imaged in order to navigate the surgical excision.
OBJECTIVES: As fluorescence-guided surgery quickly advances into the clinic, we hypothesize that the disease-specific fluorescence inherently contained within the resected tissues can be used to guide histopathological assessment.
METHODS: To evaluate the feasibility of fluorescence-guided pathology, we evaluated head and neck squamous cell carcinoma tumour specimens and margins resected from animals and patients after systemic injection of cetuximab-IRDye800CW.
RESULTS: In a preclinical model of luciferase-positive tumour resection using bioluminescence as the gold standard, fluorescence assessment determined by closed-field fluorescence imaging of fresh resected margins accurately predicted the presence of disease in 33/39 positive margins yielding an overall sensitivity of 85%, specificity of 95%, positive predictive value (PPV) of 94%, and a negative predictive value (NPV) of 87%, which was superior to both surgical assessment (54%, 61%, 57%, and 58%) and pathological assessment (49%, 95%, 91%, and 66%), respectively. When the power of the technique was evaluated using human-derived tumour tissues, as little as 0.5mg ($1mm^3$) of tumour tissue was identified (tumour-to-backgroundratio:5.2). When the sensitivity/specificity of fluorescence-guided pathology was determined using traditional histological assessment as the gold standard in human tissues obtained during fluorescence-guided surgery, the technique was highly accurate with a sensitivity of 91%, specificity of 85%, PPV of 81%, and NPV of 93% for 90 human-derived samples.
CONCLUSION: This approach can be used as a companion to the pathologist, eliminating confounding factors while impacting surgical intervention and patient management.

Project Length: Short
A-12

Hospital Readmissions in Gynecologic Oncology Patients – A Target for Quality Improvement

Carolina E. Temple, Haller J. Smith, M.D., *J. Michael Straughn, M.D.*

INTRODUCTION: Reported readmission rates among gynecologic oncology patients range from 5%-19%. An improved understanding of factors associated with readmissions in gynecologic oncology is needed to decrease readmission rates. Our primary objective is to identify factors associated with 30-day readmissions to the gynecologic oncology service at our institution as defined by University HealthSystem Consortium (UHC) criteria.

METHODS: A retrospective review was performed using the UHC database for gynecologic oncology readmissions at the University of Alabama at Birmingham from May 2015 to April 2016. Data abstracted included demographics, medical comorbidities, diagnosis, disease status, length of stay, and etiology for readmission. Planned admissions for chemotherapy, radiation, and surgery were excluded.

RESULTS: There were 151 readmissions in 105 patients. 35 readmissions were excluded: 7 due to planned surgery, 1 that left the hospital against medical advice and returned, and 27 that occurred in 8 terminally ill patients. There were 116 evaluable readmissions in 90 patients. 27 patients had 2 readmissions. The most common cancer diagnosis was ovarian (50%) followed by uterine (24%). 62% of patients had Stage III/IV cancer; 41% of patients had recurrent disease. 54% of patients had surgery during their primary admission; 88% of the patients had a laparotomy. The most common readmission diagnoses were surgical site infections (20%), small bowel obstruction or ileus (18%), and symptoms of progressive disease (15%). The mean time from discharge to readmission was 10 days (0-28). The mean readmission LOS was 5.3 days (0-35). The outcomes after readmission included: discharge to home (56%), home health care (24%), hospice (4%), nursing facility (6%), and death (10%).

CONCLUSION: The most common reason for readmission on the gynecologic oncology service is surgical site infection. These readmissions likely represent the best initial target for quality improvement. Earlier initiation of hospice will also decrease readmissions in terminally ill patients.

Project Length: Intermediate
A-13

Oncometabolite L-2HG : A potential regulator of the nucleus and mitochondria in renal cancer

Garrett Brinkley, Eun-Hee Shim, Hyeyoung Nam, Richard Kirkman, Sunil Sudarshan

Purpose: Oncometabolites are small molecules that are associated with tumorigenesis. Clear cell renal cell carcinoma (ccRCC) is the most common form of renal cancer. Loss of 14q is associated with more aggressive disease. L-2Hydroxyglutarate Dehydrogenase (L2HGDH) is located on chromosome 14q and is often lost in these patients. The loss of this metabolic enzyme leads to accumulation of L-2 Hydroxyglutarate (L-2HG). L-2HG is thought to be created by the "off target" activity of various enzymes including from Malate Dehydrogenase (MDH). There are two forms of this enzyme: MDH1 (cytoplasmic) and MDH2 (mitochondrial). It is unknown if MDH 1/2 produce L-2HG in the context of ccRCC. It has been proposed that L-2HG is an epigenetic regulator via inhibition of Ten Eleven Ten translocation (TET) enzymes which convert DNA 5-methylcytosine (5mC) to 5hmC. In addition, TET enzymes have previously been demonstrated in the mitochondria. Hence, L-2HG could exert its effects at the level of both the nucleus and mitochondria. This study examines the biochemistry and epigenetic implications of raised L-2HG in order to develop novel therapeutic targets.

Methods: This project utilized normal renal cell lines (RPTEC and HK2) and renal cancer cell lines (RXF-393, OSCR-2 and A498) as well as xenograft models. shRNA was used to create knockdown models. In addition, an L2HGDH knockout mouse was created using CRISPR/Cas9 technology.

Results: Knockout mouse models of L2HGDH demonstrate decreased expression of several mitochondrial genes in the kidney. MDH1 and MDH2 knockdown in RCC cell lines leads to reduced 2HG levels and attenuated cell growth.

Discussion/Conclusion: L-2HG generation in RCC cells is mediated by MDH. In addition, L-2HG's extra nuclear activity may play a role in regulating mitochondrial gene expression. Collectively, these studies provide new insight into the biochemistry and epigenetic impact of raised L-2GH in RCC.

Project Length: Long
A-14

Title:
Basal Interferon Stimulated Gene Expression Influences the Productive Infection of Oncolytic HSV in Malignant Peripheral Nerve Sheath Tumor Cells

Authors:
Joshua D. Jackson, Ph.D.[1], *James M. Markert, M.D.*[1,2,3], Li, Li, M.D.[1], Steven L. Carroll, M.D., Ph.D.[4], and *Kevin A. Cassady, M.D.*[2,5]
1 Department of Neurosurgery, 2 Department of Pediatric, 3 Department of Cell, Developmental and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL 35233, USA; 4 Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC, 29425, USA; 5 Nationwide Children's Hospital and The Ohio State University, OH 43205, USA

Introduction:
Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive cancers of the nerve sheath. Nearly half arise sporadically while the other half are associated with neurofibromatosis type 1 (NF1), however among all patients, median survival is a dismal 24 months following diagnosis. MPNSTs are typically refractory to traditional chemotherapy and radiotherapy, with surgical resection as the only demonstrable benefit to survival, therefore oncolytic HSV virotherapy has been suggested as an alternative.

Objective:
Our objective was to determine the extent to which MPNST cells resist the productive infection of oncolytic herpes simplex virus (oHSV) through activation of the JAK/STAT1 pathway and resultant upregulation of interferon stimulated genes (ISGs). ISGs encode diverse proteins that mediate intrinsic antiviral resistance in infected cells.

Methods:
Twenty-one human and mouse MPNST cells were used to explore the relationship between STAT1 activation and the productive infection of $\Delta\gamma_1$34.5 oHSVs.

Results:
STAT1 activation in response to oHSV infection was found to associate with diminished $\Delta\gamma_1$34.5 oHSVs replication and spread. Multi-day pre-treatment, but not co-treatment, with a JAK inhibitor significantly improved viral titer and spread. ISG expression was found to be elevated prior to infection and downregulated when treated with the inhibitor, suggesting that the JAK/STAT1 pathway is active prior to infection. Conversely, upregulation of ISG expression in normally permissive cells significantly decreased oHSV productivity. Finally, a link between NFκB pathway activation and ISG expression was established through the expression of inhibitor of kB (IκB) which decreased basal STAT1 transcription and ISG expression.

Conclusion:
While cancer-associated ISG expression has been previously reported to impart resistance to chemotherapy and radiotherapy, these data show that basal ISG expression also contributes to oncolytic HSV resistance.

Project Length: Short
B-1

RNAi-mediated knockdown of tRNA modification genes *UBA4, CTU1,* or *CTU2* enhance HEK-293 cell resistance to the cancer chemotherapeutic topotecan

Emily N. Hayward, Amanda Cunningham, MS, Tania Coric, PhD, Adam Burgunder, *Mary-Ann Bjornsti, PhD*; Department of Pharmacology & Toxicology, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: The enzyme DNA topoisomerase I catalyzes the relaxation of DNA supercoils during replication through the creation of a transient single-stranded DNA break, subsequently releasing the torsional energy in the DNA. Topotecan, a widely utilized camptothecin analog for the treatment of malignancies like lung and ovarian cancer, intercalates into the topoisomerase I-linked DNA nick and prevents re-ligation, leading to toxicity in actively dividing tumor cells. However, some patients are more responsive to topotecan than others.

OBJECTIVE: Previous work in the Bjornsti lab identified six candidate genes that altered cell sensitivity to camptothecin in *Saccharomyces cerevisiae*, each of which is involved in modification of tRNAs at the wobble position (*CTU1, CTU2, UBA4, URM1, ELP1,* and *ELP3*). This study sought to investigate the currently unknown role of these genes in human cell responses to topotecan.

METHODS: Human Embryonic Kidney 293 (HEK-293) cells were cultured in Dulbecco's Modified Eagle Medium plus 10% Fetal Bovine Serum. At 80-90 percent confluence, cells were transfected with several, individual siRNAs for the gene of interest in 96 well plates. After 24 hours, various doses of topotecan were administered for five days. Cell viability was assessed with AlamarBlue staining at 37°C and read hourly for three hours. Confirmation of gene knockdown was achieved by measuring mRNA levels before and after topotecan administration using RT-PCR.

RESULTS: We found that individual siRNA knockdown of *UBA4, CTU1,* and *CTU2* increased topotecan resistance in HEK-293 cells.

DISCUSSION: These results indicate that *UBA4, CTU1,* and *CTU2* alter cell susceptibility to topotecan and that patients with decreased expression of these genes may be less responsive to the chemotherapy. In the future, this information might be utilized to predict patient outcomes or potentially suggest novel therapeutic modalities such as co-administration of topotecan with agents that increase its effectiveness at the genetic level.

Project Length: Short
B-2

Neutrophil-to-Lymphocyte Ratio and White-Blood-Cell Counts as Predictors of Overall Survival in Head and Neck Cancer Patients Treated with Radiotherapy

Chris Veale, MS[1], Andrew McDonald, MD[2], *Hunter Boggs, MD*[2]
[1]University of Alabama at Birmingham School of Medicine, Birmingham, AL [2]Department of Radiation Oncology University of Alabama at Birmingham, Birmingham, AL

Introduction: Elevated peripheral neutrophil-to-lymphocyte ratio (NLR) >2 is an established negative prognostic factor in head and neck cancer. However, it is unclear whether elevated neutrophil levels or decreased lymphocyte levels are the primary driver of adverse outcomes.
Objectives: To determine if elevated WBC levels independently predict for inferior survival in head and neck cancer patients with NLR>2.
Methods: Previously untreated oropharyngeal head and neck cancer patients treated with definitive radiotherapy between January 2009 and June of 2016 were included in this retrospective analysis. NLR was calculated as the neutrophil count divided by the lymphocyte count on routine laboratory testing prior to radiotherapy. Overall survival was calculated from the time of first radiation fraction to time of death. Local control was calculated from first radiation fraction to recurrence date. Survival statistics were determined using Kaplan-Meier estimates.
Results: Eighty-six patients met the inclusion criteria and the median follow-up of surviving patients was 34.9 months. The mean pre-treatment WBC was 8.1 $x10^9$/L (SD=2.65 $x10^9$/L) and NLR was 3.4 (SD=2.4). The Kaplan-Meier estimate of overall survival at 3 years was 71.8% for patients with NLR>2 compared to 95% for patients with NLR≤2 (p=0.059); estimated local control at 3 years was 100% for patients with NLR>2 compared to 81.2% for patients with NLR≤2 (p=0.089). Within the subgroup of patients with NLR>2, WBC>7 $x10^9$/L was predictive of worse overall survival (HR=3.691, p=0.041) but not local control (HR=2.53, p=0.248).
Conclusion: In our study, elevated NLR in conjunction with elevated neutrophils was associated with inferior survival compared to elevated NLR and normal WBC counts. These results suggest that neutrophilia may be a potent predictor of adverse outcomes within the elevated NLR population.

Project Length: Short
B-3

IMMUNOMODULATION OF PD-1 IN A MURINE MODEL OF SYNGENEIC OVARIAN CANCER AND DOSE DENSE CHEMOTHERAPY

Jacelyn E. Peabody, Taylor Bono, Jeremie M. Lever, Cindy Tawfik, Ashwini Katre, Selene Meza-Perez PhD, Angelina Londono PhD, Haller Smith MD, Lyse Norian PhD, Rebecca C. Arend MD

Department of Obstetrics and Gynecology, University of Alabama at Birmingham, Birmingham, AL

Objective: Metabolic syndrome (MS) is associated with a poor prognosis in ovarian cancer (OC), but the mechanism causing increased morbidity is unclear. Overexpression of PD-L1, a T-cell suppressive co-signaling molecule, correlates with poor outcome in OC. Our hypothesis is that PDL-1 expression is one mechanism through which MS contributes to worse outcomes in OC patients through compromised anti-tumor immune responses. Immunotherapy targeting the PD-1/PD-L1 interaction promises a novel approach to ameliorate the immunosuppressive changes at the tumor site following chemotherapy, but the population in which this treatment is most effective is unknown. The objective of our study was to examine the association between BMI and PDL-1 expression in OC patients and investigate anti-tumor immune response to dose dense chemotherapy (DD) plus anti-PD-1 immunotherapy in a OC murine model with MS compared to normal wild-type mice without MS.
Methods: Paraffin embedded tumor samples from 29 patients were processed and stained via immunohistochemistry for PDL-1 expression. H-scores were obtained to quantify PDL-1 expression and compared between obese, overweight, and lean patients. Genetically obese (OB), leptin-knockout mice and wild-type (WT) mice were injected subcutaneously with ID8 syngeneic OC cells to create a novel model system that recapitulates comorbid OC and MS. Tumor size was measured twice weekly in OB and WT mice treated with combined DD (cisplatin and paclitaxel) and anti-PD-1 immunotherapy, DD alone, and no treatment (n=5 per strain, per group).
Results: Obese OC patients (BMI > 30) had lower H-scores than lean patients (BMI 18.5-24.9) and overweight patients (BMI 25-29.9). There was no significant difference between tumor measurements in OB and WT groups, but mice treated with the combination of anti-PD1 and DD chemotherapy had slower tumor growth than the DD chemotherapy group alone, irrespective of the mice strain.
Conclusion*:* Results were not consistent with our hypothesis, such that higher BMI did not correlate with higher PDL-1 expression and there was no difference in tumor growth in the OB compared to WT mice treated with immunotherapy and chemotherapy. Immunotherapy did significantly improved response to DD chemotherapy. Further studies are needed to better understand how MS relates to immune response in OC patients.

Project Length: Short
B-4

TITLE: Smoking Status and Postoperative Complications Following Cardiopulmonary Bypass: A Retrospective Study.

AUTHORS: **Joshua A. Blackwell**[1]; *Ahmed F. Zaky, MD, MPH, FCCM*[2]*; Ayesha S. Bryant, MD, MSPH*[2].
[1]UAB School of Medicine, Birmingham, AL. [2]Department of Anesthesiology and Perioperative Medicine, UAB School of Medicine, Birmingham, AL.

INTRODUCTION: It is well-established that tobacco smoking increases the risk of developing a variety of health issues such as lung cancer, diabetes, and cardiovascular disease. However, the effect of a patient's smoking status on surgical outcomes and postoperative complications is an active area of research.

OBJECTIVES: The objectives for this study were to determine whether patients with a history of smoking are at an increased risk of developing complications following cardiopulmonary bypass surgery (CPB), and to determine whether such risks are dose-dependent.

METHODS: This study was a retrospective chart review of patients who were admitted to UAB Hospital for operations requiring CPB. Patients were categorized by smoking status and subcategorized by smoking history. Smoking status categories included Never Smokers (NS), Former Smokers (FS), and Current Smokers (CS). Smoking history subcategories included Former Smokers who quit smoking greater than 15 years prior (FS>15YA), Former Smokers who quit smoking less than 15 years prior (FS<15YA), Current Smokers with a history of less than 25 pack-years (CS<25PY), and Current Smokers with a history of greater than 25 pack-years (CS>25PY). Variables analyzed included total postoperative length-of-stay, postoperative mortality, and postoperative complications, which were compared by organ system involved and total categorical complications.

RESULTS: Eighty-seven patients were included. Mean postoperative length-of-stay was statistically similar among groups (Range: 5.55-7.38 days). Mortality rate, while variable, was statistically similar among groups (Range: 0-0.143). Mean number of total complications was greatest in the FS>15YA group (2.00 vs. 1.35 among NS, p=0.01). Differences in incidence of wound infections (Range: 0-0.143), renal complications (Range: 0-0.353), and cardiovascular complications (Range: 0.143-0.588) were found not to be statistically significant among groups. Incidence of pulmonary complications was greatest in the CS<25PY group (RR: 1.586, 95% CI: 1.038-2.423, p=0.033). Incidence of pleural effusions was greatest in the CS<25PY group (RR: 1.866, 95% CI: 1.175-2.962, p=0.008), while the incidence of atelectasis among groups was statistically similar (Range: 0.143-0.364). Incidence of neurological complications was greatest in the FS>15YA group (RR: 19.000, 95% CI: 1.080-334.256, p=0.044).

CONCLUSION: The incidence of pleural effusions was greatest in current smokers with a history of less than 25 pack-years, and the incidence of neurological complications was greatest in former smokers who quit smoking greater than 15 years prior. While variable, mean postoperative length-of-stay; mortality rates; and the incidence of wound infections, renal complications, and cardiovascular complications were not found to be statistically greater among patients with a history of smoking. Further research is needed to expand upon the relationship between tobacco smoking and postoperative complications.

Project Length: Short
B-5

In Vivo Fluorescence Imaging of the Pelvic Ureter During Minimally Invasive Surgery for Endometrial and Cervical Cancer

John L. Johnson, *Kenneth Kim, MD, Warner K. Huh, MD*

Introduction: Over 600,000 hysterectomies are performed each year in the United States. Of these procedures, 70% are performed using minimally invasive approaches. The risk of ureteral injury associated with a minimally invasive approach, is as high as 2%. Previous reviews have shown that this is a significantly higher risk than open and vaginal approaches.

Objectives: The primary objective of this study was to test the viability and efficacy of in vivo fluorescence imaging of the pelvic ureter as a method of minimally invasive surgery in an animal model

Methods: This study was performed using minimally invasive surgical techniques on 12 female pigs. The pigs were separated into three groups of four. Each group was given a varying dose of fluorescent dye 30, 60, 90, and 120 mg/kg, respectively. The pelvic ureters of each pig were then inspected at the time of administration, (insert time points). The pigs were monitored for systemic and injection site adverse effects throughout the study.

Results: The fluorescent dye was used to successfully visualize the pelvic ureters at several time points with each dose. No systemic or injection site adverse-affects were observed on any of the twelve pigs during the course of the study.

Conclusion: Clear visualization of the ureter was achieved with each dose of the dye. The results suggest that this could be a viable visualization technique to lower the risk of ureteral injury during minimally invasive hysterectomy procedures. However, differences in pig and human anatomy could present an issue in a clinical trial.

Project Length: Short
B-6

Identification of PTBP1-induced aberrant splice isoforms and their impact on patient survival in glioblastoma

Dewey Brooke, Susan Nozell PhD, Markus Bredel MD PhD
[1]Department of Radiation Oncology, UAB Comprehensive Cancer Center, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, USA.

INTRODUCTION: Gliomas as well as glioblastoma (GBM) are amongst the deadliest of malignancies where most patients succumb within 18 months. In the current paradigm, aberrant splice isoforms contribute to the pathogenesis of gliomas and GBM by serving as oncogenic drivers in these tumors. Polypyrimidine tract–binding protein 1 (PTBP1), an RNA-binding protein that regulates alternative splicing (AS), is often aberrantly overexpressed in these tumors and promotes the invasive and rapid growth of glioma cell lines. However, a majority of the vast number of AS events regulated by PTBP1 that potentially contribute to GBM pathogenesis remain to be investigated.

OBJECTIVES: To discover additional targets of PTBP1 that alter patient survival outcome and contribute to glioma and GBM pathogenesis.

METHODS: A list of 173 PTBP1 AS-regulated genes were examined through genomic profiles and clinical profiles of three separate patient cohorts from The Cancer Genome Atlas Pilot Project (TCGA); 516 glioma tumor samples for identification of genes with coincident genetic alterations, correlated gene dosage and gene expression, and multiple functional interactions, 1084 samples from a merged LGG/GBM cohort and 291 samples from a GBM-only cohort to assess association between those genes and patient survival (PS) for glioma/GBM and GBM alone.

RESULTS: From the 173 candidates, differential expression of 38 genes strongly correlated with PTBP1 expression were associated with unfavorable or improved survival (global log-rank $P<0.05$) for glioma and GBM patients. From this set, 30 genes had copy number alterations with matched alterations in mRNA expression, and were significant predictors of PS for a combined glioma and GBM patient pool. Furthermore, 12 of these genes were specifically predictive for survival of patients with GBM.

CONCLUSION: PTBP1 dysregulation can affect PS through many distinct AS events, and could be central to the extensive cellular and molecular heterogeneity characteristic of GBM tumors.

Project Length: Short
B-7

The Effect of a Ketogenic Diet on Ovarian Cancer Angiogenesis

Taylor Bono[2], Caroline Cohen[1], Angelina I. Londoño[3], Barbara Gower[1], Rebecca C. Arend[4]
[1]Department of Nutrition Sciences, [2]School of Medicine, [3]Department of Radiation Oncology, [4]Department of Obstetrics and Gynecology, [5]Department of Health Behavior, University of Alabama at Birmingham, USA, [6]HudsonAlpha Institute for Biotechnology, Huntsville, AL USA

Purpose: The goal of our study is to use dietary macronutrient modification to disrupt cancer growth and metabolism. Cancer is closely linked to obesity in the US and the KD has been shown to reduce body fat due to enhanced use of fat as a fuel, and thereby may improve prognosis. This study is designed to test the hypothesis that a Ketogenic Diet will, reduce total and central body fat, reduce circulating insulin and glucose, reduce circulating markers of angiogenesis

Methods: Women diagnosed with recurrent ovarian cancer receiving care at UAB or Brookwood Hospital between January 2015 and March 2016, >19y of age with body mass index (BMI) between 18.5 and 45 kg/m2. Measurements of the following were taken at baseline and at 12 weeks:
CA-125, markers of angiogenesis, markers of inflammation, fasting concentrations of glucose, insulin, IGF-1, IGFBP-1, c-peptide, ketones, and lipids (total, TG, LDL, HDL).

Results: Fasting insulin decreased an average of 5.72 µIU/ml and fasting glucose decreased an average of 6.89 mg/dL in the KD group. Decreases in total fat and android fat for patients in the KD group reached statistical significance ($P<0.05$). Average decreases were 4.8kg and 0.5kg, respectively. Markers of angiogenesis (VEGF, b-FGF, and sFLT-1) tended to decrease ($0.05<P<0.10$).

Conclusion: A KD reduces total and android body fat, fasting glucose, fasting insulin, and markers of angiogenesis. These metabolically favorable changes may improve prognosis. Enrollment in the study is still continuing and the trial is on-going.

Project Length: Short
B-8

Single-Institution Examination of Patients with Primary CNS Lymphoma

Christian A. Mays[1]**,** Louis B. Nabors, M.D.[2]**,** *Paula S. Province Warren, M.D.*[2]
University of Alabama School of Medicine[1], Department of Neurology[2]

Abstract
INTRODUCTION: Primary central nervous system lymphoma (PCNSL) is an aggressive, rare form of extranodal non-Hodgkin's lymphoma that accounts for 3% of all primary brain tumors. Currently, first-line therapy for PCNSL is intravenous high-dose methotrexate (MTX) with additional first-line treatments under investigation.

OBJECTIVES: The primary objective was to examine demographics and survival proportions for non-acquired immunodeficiency syndrome PCNSL patients at the University of Alabama at Birmingham (UAB).

METHODS: This was a single-institution, IRB approved, retrospective study of PCNSL patients at UAB. The primary endpoints in data collection for this study included progression-free survival (PFS), overall survival (OS), and percent of patients with complete response to treatment within 6 months (%CR). Secondary endpoints included patient survival outcomes for 15 patients treated with MTX and rituximab (RTX) compared to 17 patients treated with MTX alone. Response to treatment was determined by neurologic evaluation and magnetic resonance imaging (MRI) studies.

RESULTS: The population included 32 patients (59% male, 41% female) with a median age of 62.5 years. Diagnoses of PCNSL was confirmed by brain biopsy in 30 patients (94%) and by cerebrospinal fluid analysis in 2 patients. After 6 months of therapy, 10 patients (31%) achieved complete response, 14 (44%) achieved a partial response, 4 (12.5%) did not respond to treatment, and 4 were excluded due to lack of MRI data. Median PFS and median OS for all 32 PCNSL patients was 34 and 53.5 months, respectively. 5-year survival for groups treated with MTX alone and RTX+MTX were 76.5% and 62.9%, respectively. This difference was statistically insignificant (p= 0.4103).

CONCLUSIONS: UAB patient demographics and epidemiology are consistent with other national studies. Increasing the number of patients in this study and following them for a longer period of time will be necessary in order to assess more accurately patient responses to RTX+MTX.

Project Length: Short
B-9

Aldehyde Dehydrogenase as a Stemness Marker in Ovarian Carcinoma

Robert D. Stibolt, M.S., Brian Spurlock, and *Kasturi Mitra, Ph.D*.
Department of Genetics, University of Alabama at Birmingham, Birmingham, AL.

Introduction: Epithelial Ovarian Cancer (EOC) is the fifth most common cause of cancer death in the US. It is estimated that over 22,000 women will be diagnosed this year in the US. Tumor relapse continues to be a barrier toward improving patient outcomes, and it has been demonstrated that Cancer Stem Cells (CSCs) contribute significantly in the relapse of chemoresistant EOC tumors. The isoenzyme Aldehyde Dehydrogenase (ALDH) has been shown to be involved in CSC maintenance, and is used as a functional marker for CSCs; ALDH-High cells have strong CSC properties including small size and a capability of giving rise to bulk tumor.

Objectives: Isolated CSCs from EOC patients can be proliferated in culture using a functional ALDH marker that is stable in activity and expression.

Model: 1) A2780 EOC cell line. 2) Human cells drawn from ascites samples of consenting EOC patients at UAB Medical Center.

Methods: ALDH-High Ovarian CSCs were isolated using fluorescence-activated cell sorting (FACS) after incubating the parental cell population with ALDEFLUOR reagent, and the ALDH-High cells were then grown in low attachment plates with stem-cell medium containing appropriate growth factors. Thereafter, ALDH activity was quantified using fluorescent microscopy.

Results: Isolated patient CSCs did not proliferate based on mitotic index being closed to zero, while isolated CSCs from the cell line proliferated over a period of 15 days. Among viable cells, ALDH levels began decreasing between 10-12 days post-sorting, eventually falling below 1% by day 15 . These levels then resurged to maximal levels before day 20.

Conclusion: ALDH levels were not stable in activity and expression; our data suggests a cyclic course that likely involves cell-signaling patterns, possibly following an unidentified stimulus. Future experiments will be necessary to fully appreciate the kinetics behind ovarian CSC growth *in-vitro*.

Project Length: Short
B-10

The role of osteocytes in multiple myeloma progression

Mary Fok[1], Timothy N. Trotter[1], and *Yang Yang*[1,2]

[1]Department of Pathology, University of Alabama at Birmingham, Birmingham, AL; [2]Comprehensive Cancer Center and the Center for Metabolic Bone Disease, University of Alabama at Birmingham, Birmingham, AL

Multiple myeloma (MM) is a malignancy of plasma cells that thrive in and spread throughout the bone marrow (BM). Many BM cell types have been extensively studied for a role in MM progression, however osteocytes remain poorly understood in MM and cancer in general. We have previously shown increased osteocyte apoptosis in MM patients compared to normal BM. In addition, animal models show enhanced osteocyte apoptosis from more aggressive tumors. Importantly, this is seen at a secondary site before MM cells are detected. Therefore, we wanted to determine how osteocyte apoptosis at distant bone sites, prior to MM metastasis, feeds back to MM cells to promote MM progression.

We developed a unique, syngenic model of MM in which apoptosis can be induced specifically in osteocytes. TUNEL staining confirmed both the extent of and specificity of osteocyte apoptosis. Because apoptotic osteocytes or surrounding, live osteocytes secrete soluble molecules that induce changes in the BM, we evaluated expression of soluble molecules via immunohistochemistry. The results revealed increased expression of Hypoxia inducible factor 1 alpha (HIF-1α), a principle molecular responder to hypoxia that promotes angiogenesis and accumulation of immune suppressor cells, in mice with osteocyte apoptosis compared to control. We also found increased expression of Receptor activator of nuclear factor kappa-B ligand (RANKL) in osteocytes and Vascular endothelial growth factor (VEGF) in total bone marrow in mice with apoptotic osteocytes compared to normal osteocytes. This suggests an increase in both osteoclast formation and angiogenesis following osteocyte apoptosis.

In conclusion, we have generated a syngenic MM model with specific osteocyte apoptosis. Multiple soluble molecules important for MM progression are increased in osteocytes or BM after osteocyte apoptosis. These results indicate osteocyte apoptosis may aid in generation of a pre-metastatic niche more hospitable to MM cells, ultimately resulting in enhanced MM progression.

Project Length: Short
B-11

Title: Inhibition of Prolyl-4-Hydroxylase, Alpha Polypeptide I Slows Growth of Non-Small Cell Lung Carcinoma

Authors: **Ryan McMonigle**[*#], Chakravarthi V.S.K. Balabhadrapatruni[*], Sooryanarayana Varambally[*]
Affiliations:
*Department of Pathology & Comprehensive Cancer Center, University of Alabama Birmingham Al
#Medical Science Training Program, University of Alabama, Birmingham Al

Introduction: Cancer is characterized by rapid and uncontrolled cellular growth, invasion and metastasis. Many chemotherapies block replication of deoxyribonucleic acids as a strategy to inhibit the growth of cancer cells. Unfortunately, the success of chemotherapy in non-small cell lung cancer (NSCLC) is limited, as demonstrated by the 17% 5-year survival rate for these patients.
Our integrative analysis identified overexpression of Prolyl-4-Hydroxylase, Alpha Polypeptide I (P4HA1) in lung adenocarcinoma. This enzyme specifically modifies extra cellular matrix protein collagen by hydroxylating proline residues.
Overexpression P4HA1 drives the 3 dimensional structural alterations in collagen thus potentially leading to invasion and metastasis of cancer cells.

Objective: To determine if the P4HA1 inhibitor pythiDC slows growth of NSCLC in vitro.

Methods: Utilizing an *in vitro* system of NSCLC cell line (H1437), we measured cell growth in the presence of the small molecule inhibitor of P4HA1, diethyl-pythiDC (pythiDC). Cell growth was measured indirectly using the Promega Cell Titer Glo Assay, which utilizes an adenosine triphosphate linked luminescence assay. Cell growth results were verified using a direct cell counting assay.

Results: Growth of H1437 NSCLC cells was significantly inhibited by 50 micro-molar pythiDC as compared to control cells at 72 hours of incubation.

Conclusion: Our data indicates that pythiDC may have potential therapeutic use in the treatment of NSCLC. Future studies will focus on investigating the effectiveness of pythiDC on a broader range of NSCLC and test the effects of *in vivo* NSCLC tumor growth.

Project Length: Short
B-12

Pre-processing Pipeline for MethylationEPIC Data.

Bethany Johnson[1], Megan Breitbach[2,3], *Devin Absher, PhD*[3]
[1]School of Medicine, University of Alabama at Birmingham, Birmingham, AL
[2] Department of Chemistry, University of Alabama in Huntsville, Huntsville, AL
[3]Absher Lab, HudsonAlpha Institute for Biotechnology, Huntsville, AL

INTRODUCTION: Many diseases alter normal DNA methylation patterns. A recent study confirmed the reliability of the Infinium MethylationEPIC microarray for DNA methylation studies.[2] MethylationEPIC data require pre-processing, including quality control and correction for batch-to-batch variation. Since MethylationEPIC microarrays use two different chemistries (Infinium I and II) to measure methylation, pre-processing also corrects for variation between chemistries[1]. Manual pre-processing is time-consuming.

OBJECTIVES: The purpose of this study is to develop a pipeline that accepts raw MethylationEPIC data, preprocesses those numbers, and produces analysis-ready data.

METHODS: The researchers first created an R script that pre-processed one specific data set. Next, they converted this script into multiple smaller scripts that function with any data set. Finally, the researchers created a Python script to read in data, execute each small R script, and return pre-processed data and pertinent graphs.

RESULTS: The researchers developed a pre-processing pipeline that executed without any errors. The quality control (QC) step produced graphs that highlight outlying samples. However, until the data undergoes further analysis, it remains unclear whether the QC step successfully limits data noisiness. Since the current data lack significant batch effects, more data are needed to clarify the efficacy of the pipeline's batch correction. Pipeline graphical output reveals that the chemistry correction functions properly, adjusting the Infinium II distribution to resemble the Infinium I distribution.

CONCLUSIONS: The researchers developed a pre-processing pipeline which successfully corrects for variation between Infinium chemistries. Due to data limitations, the success of pipeline quality control and batch correction remains unclear.

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Project Length: Short
B-13

Historical bone fractures and risk of multiple myeloma

Philip W. Dockery[1,2], MaryAnn E. VanValkenburg[1], Christina Boddiford Pillion[1], Luciano J. Costa[3,4] and Elizabeth E. Brown[1,4]

[1]Department of Pathology, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama; [2]School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama; [3]Division of Hematology and Medical Oncology, Department of Medicine, School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama; [4]UAB Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama;

Background. Multiple myeloma (MM) is the most common hematologic malignancy affecting blacks in the US. It is characterized by prolonged survival and accumulation of clonal plasma cells in the bone marrow microenvironment, presence of monoclonal protein in serum, urine or both, and end organ damage that includes skeletal destruction, defined by lytic bone lesions and severe diffuse osteoporosis. Historical bone fractures leading to altered risk of MM has not been evaluated in a population that includes both whites and blacks. Evidence of bone pathology several years prior to diagnosis may provide an opportunity for improved clinical monitoring, particularly among patients with the at-risk condition, monoclonal gammopathy of undetermined significance.

Methods. Using participants enrolled in the Molecular And Genetic Epidemiology (iMAGE) study of myeloma (259 MM cases; 461 age-, sex-, race-matched controls), we examined the risk of MM associated with historical bone fractures and differences by race. Historical bone fractures were defined as those occurring at least 2 years prior to MM diagnosis. Risk estimates were calculated using odds ratios and corresponding 95% confidence intervals from logistic regression adjusted for confounders.

Results. Overall, MM risk was significantly increased among cases who reported having broken a bone in the 10 years leading up to diagnosis (OR=1.54, CI 1.00-2.36; P=0.05). In addition, this effect was greater for blacks (OR=3.93, CI 1.59-9.75; P=0.003) than in whites (OR=1.16, CI 0.70-1.93; p=0.57).

Conclusion. The excess risk of MM observed in blacks relative to historical bone fractures may be attributed to differences in underlying bone physiology by race. Alternatively, the disparity could be attributed to factors related to access to healthcare, which could delay diagnosis.

Project Length: Long
B-14

Title: The Impact of MARCKS Phosphorylation on Glioblastoma Growth and Migration.

Authors: Nicholas J. Eustace, Patricia H. Hicks, Joshua C. Anderson, John S. Jarboe, Christopher D. Willey.

Background: Glioblastoma multiforme (GBM) is the most common and deadly form of glioma, with a median survival of 14 months. GBM remains a deadly disease due to its diffuse nature, high proliferative capacity and therapeutic resistance. Improving our understanding of these tumor promoting properties is vital to improving outcomes. MARCKS is a natively unstructured protein found in the brain that can potentially influence tumor growth, therapeutic resistance and migration through its ability to electrostatically sequester signaling phospholipids on the cytoplasmic membrane, bind calmodulin and the actin cytoskeleton. 88% of GBM's have mutations that generate tumor promoting phospholipids driving growth and survival pathways. MARCKS can potentially suppress multiple common mutations by electrostatically sequestering its phospholipid substrate; however, MARCKS is poorly understood in GBM.
Methods U87 with doxycycline inducible MARCKS mutants were generated to test MARCKS impact on tumor growth and migration. Growth was assessed in-vitro by colony formation assays and ATPlite. Migration was assessed by scratch assay.
Results Overexpression of MARCKS (WT+) and a non-phosphorylatable (NP) MARCKS mutant showed a decrease in colony number and size compared to a scrambled vector control line in the clonogenic assay, while the pseudo-phosphorylated (PP) MARCKS mutant had a marked increase in colony number and size compared to control. ATPlite data also shows a highly significant ($P<0.001$) decrease in cell viability with the WT+ and NP mutant but no impact with the PP mutant. The migration assay showed MARCKS overexpression and both phosphorylation mutants to have significantly decreased migration compared to control.
Conclusion In-vitro findings suggest knowing the MARCKS phosphorylation status is essential for understanding the growth effects of MARCKS overexpression. The WT+ and NP variant shows anti-proliferative effects whereas the PP variant was found to be pro-proliferative. Migration was inhibited by MARCKS overexpression, however, how MARCKS phosphorylation impacts this is still not clear.

Project Length: Short
C-1

The Effect of Presence of a State Trauma System on Intentional Firearm-Related Mortality Rate

Colin K. Cantrell, Russell L. Griffin, PhD, Thomas A. Swain, MPH, *Kimberly M*. *Hendershot, MD;* Department of Surgery, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: To decrease injury mortality, the ACS COT recommended states implement a state trauma system. Firearm mortality rate and presence of a state trauma system were examined.

OBJECTIVES: The objective was to determine if implementation of statewide trauma systems had the same negative effect on firearm-related injury mortalities as it did on overall injury mortalities.

METHODS: For this cross-sectional study, data on firearm-related intentional deaths (suicides and homicides excluding legal intervention) were collected by state for 2000-2014 from the CDC's Web-based Injury Statistics Query and Reporting System (WISQARS). For each state, presence of a state trauma system was determined by year as derived from state Public Health Department information. A General Estimating Equations negative binomial regression was used to estimate rate ratios (RRs) for the association between presence of a state trauma system and intentional mortality rate using the state's population as an offset.

RESULTS: The proportion of states with state trauma systems nearly doubled from 2000 to 2014. Overall, there was no association between presence of state trauma systems and intentional firearm-related mortality rate. The lack of association remained for both firearm homicides and suicides. The lack of association was observed across 5-year categories; there was noted difference in the associations by year for firearm homicide, with 23% decrease observed among states with a trauma system in 2005-2009 while a near-null effect was observed for 2010-2014. Near-null associations were observed across the board for firearm suicide rate.

CONCLUSION: The lack of effect of trauma system presence on firearm suicide rate is not unexpected given the high case fatality rate of these injuries. Though presence of a state trauma system is not associated with the mortality rate, it would be of interest to determine whether the case fatality rate of intentional injury varies by presence of a trauma system.

Project Length: Short
C-2

Pittsburgh Cardiac Arrest Category Severity Score is Useful Despite Poor External Validation

Dylan J. Nichols[1], Henry E Wang[2], Jarred J Thomas[2], James S Booth[2], Derek A Robinett[2], Adam Kessler[2,3], William Rushton[2], *Michael C. Kurz*[2]

[1]University of Alabama School of Medicine, Birmingham, Alabama.

[2]Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham, Alabama

[3]Department of Anesthesia, University of Alabama School of Medicine, Birmingham, Alabama

Abstract

BACKGROUND: The Pittsburgh Cardiac Arrest Category (PCAC) is a four level severity score that relies upon immediately available data and has been highly associated with survival following cardiac arrest. We sought to externally validate PCAC upon a cohort of cardiac arrest victims outside the deriving institution.

METHODS: We retrospectively assigned PCAC scores to both out-of-hospital (OHCA) and in-hospital cardiac arrest (IHCA) patients treated by the UAB Hypothermia Team between July, 1, 2009, and July, 1, 2016. Assignments were made retrospectively according to physical exam conducted within six hours of arrest. Patients without necessary data recorded in the medical record were excluded. Our primary outcome was survival to hospital discharge. Secondary outcomes were good functional outcome (discharged to home or acute rehab), Cerebral Performance Category (CPC), and modified Rankin Scale (mRS) at discharge.

RESULTS: Among 160 eligible subjects, mean age was 59 years (sdv. +/- 15y), male 66%, 79% OHCA, initial shockable rhythm 40%, and survival 31%. Survival to discharge based upon PCAC I = 50% (95% CI 0.29, 0.71), II = 42% (0.40, 0.44), III = 36% (0.34, 0.38) and IV = 13% (0.12, 0.15). Good functional outcome based upon PCAC I = 33% (95% CI 0.13, 0.54), II = 34% (0.33, 0.36), III = 24% (0.22, 0.26) and IV = 6% (0.05, 0.07) did not differ from CPC score or mRS at discharge.

CONCLUSION: While our application of PCAC is not congruent with previously reported rates of survival or good functional outcome, it still provides a stepwise assessment of prognosis in the immediate post-arrest period that has significant advantages over other systems. Future efforts will be directed at including the remaining 179 patients and multivariable regression analysis to further define the utility of PCAC for neuro-prognostication in the immediate post-arrest period.

Project Length: Short
C-3

Title: Performance of ECG morphologic criteria for differentiation of VT from SVT in sinus rhythm, in patients with a wide QRS at baseline

Authors: **Wagle AA**, Doppalapudi H

Introduction: Wide-complex tachycardia (WCT) often presents a diagnostic dilemma for physicians. Current criteria for differentiating VT from SVT have been derived from patients with a normal QRS morphology at baseline. The accuracy of these criteria in patients with known wide QRS at baseline is unknown. Therefore, assessing the accuracy of current criteria in correctly identifying a supraventricular origin of rhythm in patients who have wide QRS complexes is crucial in accurate diagnosis of the rhythm of such patients presenting with tachycardia.

Objectives: The aim of this project is to determine the validity of existing electrocardiographic morphological criteria in determining if the origin of the tachycardia is ventricular or supraventricular in patients with a wide QRS complex in sinus rhythm.

Methods: The ECGs of patients admitted to the CCU, HTICU, and CVICU were screened on a daily basis to identify those with a wide QRS (>120ms) in sinus rhythm and ECGs were performed on willing patients. Electrocardiograms were compiled and data sheets completed for each patient.

Results: 23 of the 35 patients (66%) were misidentified as having ventricular origin of rhythm. Of those patients, when lead placements for V1 and V2 were shifted higher on the precordium, the diagnosis changed from a ventricular to a supraventricular origin of rhythm in 4 of the 23 patients (17%). Similarly, when the lead placements for V5 and V6 were shifted lower on the precordium, the diagnosis changed from a ventricular to a supraventricular origin of rhythm in 4 of the 23 patients (17%) and from supraventricular to ventricular in 1 of the 12 patients (8%).

Conclusion: In this preliminary study, a significant proportion of patients with wide QRS complexes during sinus rhythm were misidentified as having a ventricular origin of rhythm. Changing precordial lead placement could increase diagnostic accuracy. However, a larger patient population needs to be investigated before any recommendations can be made.

Project Length: Short
C-4

Title: Sinus of Valsalva Aneurysm Repair: A Historical Analysis

Authors: **Zachary A. Mosher**; Woodrow F. Farrington, MD; David C. Mauchley, MD; Robert J. Dabal, MD; *David C. Cleveland, MD*

Affiliations: Department of Surgery, Division of Cardiothoracic Surgery, Section of Pediatric Cardiac Surgery; University of Alabama-Birmingham; Birmingham, AL

Introduction: Sinus of valsalva aneurysms (SOVA) are an uncommon cardiac condition with a poorly elucidated natural history and severe complications. With SOVAs, proper treatment is a necessity; however, little literature exists regarding the methods and outcomes of surgical repair.

Objectives: A retrospective study describing the experiences of a single, academic medical center in treating SOVAs.

Methods: A retrospective, IRB-approved, review of the UAB Cardiac Surgery Database accessed records of patients' with SOVAs from January 1967 to December 2014. Pertinent information regarding diagnoses, treatments and outcomes was attained. Lastly, the data was analyzed using SPSS 23.

Results: 64 patients were enrolled in this study. Of these, 19 were female, 45 were male, and the age at operation was 36.6±19.8 years. Twenty-six (41%) of the aneurysms were ruptured at presentation, with 16 (62%) rupturing into the right ventricle and 8 into the right atrium (31%). Thirty (47%) of the aneurysms originated in the right coronary sinus, while 19 (30%) and 5 (8%) originated in the non-coronary and left coronary sinuses, respectively. Aortic valve replacement was the most common approach to treatment, occurring in 25 (39%) patients. Excision and closure of the aneurysm with suture occurred in 17 (27%) patients, a synthetic patch was used to close the defect in 19 (30%) patients, and an aortic root replacement was used in 3 (5%) patients.

Cardiopulmonary bypass time was 92.7±56.6 minutes, and aortic cross-clamp time was 56.5±37.9 minutes. There was no correlation between the age at operation and bypass time (p=0.794).

Conclusion: SOVAs are an uncommon, highly morbid cardiac pathology. This study found a smaller percentage of right coronary sinus aneurysms compared to prior literature. Additionally, the male/female ratio of this cohort differed from prior literature. Further investigation into post-operative morbidity, 1 and 5-year mortality rates, and detailed patient demographic profiling is required.

Project Length: Long
C-5

Acute Behavioral Stress Induces a Pressor Response via ET_A Receptor Activation by Endothelial-Derived ET-1

Brandon M. Fox[1], Analia S. Loria[2], Kelly A. Hyndman[1], Robin Johns[3], Chunhua Jin[1], David M. Pollock[1], Masashi Yanagisawa[4], Jennifer S. Pollock[1]

[1]Cardio-Renal Physiology & Medicine, Division of Nephrology, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL 35233, [2]Department of Pharmacology, University of Kentucky, Lexington, KY, [3]College of Nursing, Augusta University, Augusta, GA 30912, [4]Department of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX; International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba, Tsukuba, Japan.

In both humans and animal models, acute behavioral stress induces increased circulating endothelin-1 (ET-1) levels. However, the functional consequences of elevated plasma ET-1, as well as the cellular source of the ET-1, are unknown. We hypothesized that acute behavioral stress induces an acute pressor response via activation of the ET_A receptor by endothelial-derived ET-1. We utilized vascular endothelial-specific ET-1 knockout (VEETKO) and flox control mice for all experiments. VEETKO mice demonstrated significantly reduced aortic and renal vascular preproET-1 mRNA compared with flox mice (1.0 ± 0.2 vs. 0.03 ± 0.01 A.U. and 1.0 ± 0.2 vs. 0.3 ± 0.1 A.U. respectively, $p<0.05$). Adult male mice were exposed to cage switch stress (CSS), an established model of acute behavioral stress. Plasma ET-1 was significantly elevated in control mice in response to CSS (0.92 ± 0.04 vs. 1.2 ± 0.08 pg/ml, $p<0.05$), whereas CSS did not elicit an increase in plasma ET-1 in VEETKO mice (0.52 ± 0.09 vs. 0.63 ± 0.08 pg/ml, $p>0.05$). Blood pressure, heart rate, and activity were measured by radiotelemetry in conscious freely moving mice. CSS induced an acute pressor response in both VEETKO and control mice, however, the pressor response was significantly blunted in VEETKO mice (MAP, $p<0.05$). In mice pretreated for 3 days with the ET_A antagonist, ABT-627, the pressor response to CSS was similar between genotypes (MAP, $p>0.05$). No difference in the CSS induced response was observed for pulse pressure, heart rate, or activity in either condition. Importantly, vascular reactivity of third-order mesenteric arteries to phenylephrine was similar between genotypes, suggesting that α_1-adrenergic sensitivity of resistance arteries does not explain the difference in blood pressure responses. These results indicate that the acute behavioral stress induced pressor response is mediated, in part, by ET_A receptor activation by endothelial-derived ET-1.

Project Length: Short
D-1

Title: Identification of Learning Gaps in the Treatment of Children with Autism Spectrum Disorder who Present with Acute Illnesses

Author: Kristine Ann P. Austriaco, *Dr. Michele Kong, M.D.*, Department of Pediatrics, Children's Hospital of Alabama, Birmingham, Alabama

Introduction: Autism spectrum disorder (ASD) is a developmental disorder that is characterized by deficits in communication, difficulties in social situations, and repetitive motions. Because of this characteristic triad commonly associated with ASD, it can make it difficult for health care professionals to assess or treat a child who presents to the clinic or emergency room with an acute illness.

Objectives: The primary aim of this study was to find learning gaps that were present between medical students, pediatric residents, and pediatric fellows through the use of an online survey.

Methods: A 23 question survey was utilized. Questions included frequency of interaction between participants and children with ASD, their perceived baseline knowledge of ASD and sensory regulation, and the format that they believe would be best to learn about children with ASD.

Results: Preliminary results showed that as the education level increased, the likelihood of encountering a child in a clinical setting increased and those with higher educational levels had some knowledge of ASD. However, even at the highest level of training, responses showed that pediatric fellows felt inadequately educated, and were unfamiliar with sensory dysregulation that may be present with ASD children. Students across all educational levels felt that they should have more training and education regarding ASD children, especially when they present with an acute illness.

Conclusion: The findings of this survey suggest that medical students across all training levels perceived a lack of knowledge regarding ASD and the associated issues with sensory regulation. Even at the highest level of pediatric training, fellows similarly reported a perceived lack of knowledge. All of the trainees reported the need for increased education and training in relation to communication during treatment of children with ASD in general, as well as when they present with an acute illness.

Project Length: Short
Poster D2

Caregiver Reception of High-fidelity Simulation – Enhanced Tracheostomy Discharge Education

Sloane PA(1), Hillman K(1), Zinkan JL(2), Youngblood AQ(2), Tofil NM(1)

1 - University of Alabama at Birmingham
2 - Children's of Alabama, Birmingham, AL

Introduction

Discharge education is a goal of family-centered patient care. Proper tracheal tube maintenance and emergency management improves outcomes and reduces emergent presentations and re-admissions. Simulation training has historically improved the skills and confidence of professional caregivers and students. Here we extend simulation training to families of children with a new tracheostomy.

Objectives

Our objective is to elicit how family caregivers benefit from simulation training with equipment and emergency scenarios in management of new tracheostomies.

Methods

Simulation training occurred after the traditional didactic and hands-on bedside training. Simulation-enhanced training consisted of a session with a high-fidelity simulator matched to age. Caregivers completed a 10-statement Likert-style survey and answer three open-ended questions eliciting levels of preparedness, confidence, knowledge and satisfaction with simulation training, as well as critical feedback, respectively. The 10 statements were analyzed and reported descriptively, and open responses were grouped thematically.

Results

Caregivers strongly agreed with 9 of 10 statements regarding preparedness, confidence and emergency management (n = 29). Though 13/29 (45%) would decline further simulation training, 13/29 (45%) would welcome it, and 3/29 (10%) were not sure. Twenty-eight of 29 (97%) would recommend simulation training to other parents before discharge. Responses to open-ended questions varied. First, describing what participants appreciated and learned, 8/29 (28%) noted simulation experience itself, 7/29 (24%) noted general tracheostomy care, and 14/29 (48%) noted emergency management. Second, 22/29 (76%) offered no topics for greater focus and improvement, and 7/29 (24%) suggested specific improvements. Third, general comments about training were 23/29 (79%) positive.

Conclusion

Overall, caregivers favorably reported greater preparedness, confidence and knowledge of emergency management. Open-ended feedback indicates that parents could express not only specific skills and benefits of simulation training, but also the majority appreciated the experience.

Project Length: Short
Poster D3

Abstract Title: Post Partum Bleeding Due to Choriocarcinoma: A Standardized Patient Case in an Ambulatory Care Setting

Shelton EA, White ML, Blanchard E, Woods JB

Introduction:
In academic centers, experiences for ambulatory medicine may be fewer than experiences within the hospital. For this simulated case, a standardized patient (SP) was used to portray a postpartum patient with abnormal uterine bleeding in an ambulatory setting.

Objectives:
The primary objective for this simulation was to expose nursing and medical students to a case in a non-acute ambulatory care setting. This case is a teaching activity and intended to be formative. The domains covered include communication, with the patient, interprofessionally, and with supervising physician; professionalism; history taking; physical exam skills; clinical reasoning; patient education; and outpatient management.

Methods:
This SP case is held in a clinic setting. Nursing students evaluated the patient first, and presented patient to medical students via SBAR. Medical students then evaluated the patient, and exited to present the patient to an expert attending. At this point, nursing and medical students formed differential diagnosis and requested appropriate laboratory and diagnostic tests. Medical students evaluated results and returned to room to deliver diagnosis to patient.

Results:
This case was piloted on fourth year medical students and third semester nursing students. These learners have participated in many simulations through out their training. This case received a score of 5/5 from each learner for each of the evaluation criteria including being a valuable experience for education and future clinical practice.

Conclusion:
This case permits the learners to experience the rhythm and pace of the outpatient setting where access to labs and or imaging can be limited or delayed. In clinic residents are expected to speak with attending before moving forward with labs/imaging/diagnosis. The time involved in removing learners from room to speak with attending is similar to time out of the room in actual clinic. In the future, more outpatient cases using SPs and phases should be created.

Project Length: Short
D-4

Reclaiming Operative Vaginal Deliveries as an Optimal Intrapartum Management Choice

LaChaundra L. Johnson, Julie B. Covarrubias, Ed.D., *John B. Woods, M.D.*
Department of Obstetrics and Gynecology, University Hospital, Birmingham, Alabama

INTRODUCTION: Although operative vaginal deliveries account for 3% of deliveries, it continues to be a safe, effective intrapartum choice of management, requiring adequate physician expertise and experience.

OBJECTIVES: The primary objective of this study is to enrich post-graduate medical education curriculum through creation of simulated clinical scenarios focused on operative vaginal deliveries. The scenarios aim to increase expertise and knowledge base of prerequisites, indications, and contraindications for operative vaginal deliveries.

METHODS: We developed a hybrid simulation of two clinical scenarios utilizing operative vaginal delivery instruments, the Simpson-Luikart forceps and Kiwi vacuum Extractor, to safely expedite delivery for fetal and maternal benefit. The first scenario, a young, first time mother becomes fatigued during the second stage of labor, meeting indications for operative vaginal delivery for maternal benefit. The second scenario involves a fetal heart tracing displaying fetal bradycardia meeting indications for operative vaginal delivery for fetal benefit. During the scenarios, participants will be expected to display effective communication skills with the standardized patient to obtain informed consent for the procedure and proper clinical assessment through knowledge of prerequisites for operative vaginal delivery. Then, participants will be expected to make use of the appropriate instrument to successfully perform delivery. Following completion of the simulation, participants will participate in a debriefing session to discuss performance and review fundamentals of operative vaginal deliveries.

RESULTS: Four OB/GYN resident physicians will be evaluated on communication skills, proper assessment of the clinical situation, recognition of indications and contraindications for operative vaginal deliveries, and successful performance of the procedure on the hemipelvis. Participants will partake in a survey evaluating effectiveness of the simulation on improvement of their mastery of operative vaginal deliveries.

CONCLUSION: Operative vaginal deliveries remain a safe, advantageous method of delivery in appropriate clinical situations, but also require sufficient skill and knowledge. Through development of these scenarios as a complementary component to our *Operative Vaginal Delivery Curriculum*, residents can practice and enhance skills and knowledge necessary to perform operative vaginal deliveries.

References

1. *Operative Vaginal Deliveries.* ACOG Practice Bulletin No 154. Nov 2015, pgs. 1-10.
2. *Brumfield CG: Operative Vaginal Delivery. Obstet Gynecol; Principles for Practice Textbook.* McGraw-Hill, pgs. 490-516, 2001.

Project Length: Short
D-5

Simulated Artificial Rupture of Membranes with Initiation of Internal Uterine and Fetal Monitoring

Georgia B. Gamble[1] and *John B. Woods, M.D.*[2]
[1]University of Alabama at Birmingham, School of Medicine, [2]University of Alabama at Birmingham, Department of Obstetrics and Gynecology. Contact: John Woods, M.D., Assistant Professor and Director of UAB Obstetrics and Gynecology Simulation (johnwoods@uabmc.edu)

Introduction: An increased incidence of cesarean deliveries (C/S) with no evident decrease in morbidity/mortality of mother or baby may indicate that C/S are over used (Caughey, 2014). The most common indications for C/S are labor dystocia and non-reassuring fetal heart tracings (FHTs), accounting for over one-half of C/S performed – a large number considering, with a 35.5% rate, Alabama has one of the highest nationally. We developed a model simulating cervical dilation, amniotic sac, and fetal presentation. We also designed scenarios illustrating the need for monitoring in patients experiencing these indications. We hope to create a mindset focused on optimizing safety, allowing participants to practice clinical judgement relevant to precise intrapartum monitoring, specifically intrauterine pressure catheter (IUPC) and fetal scalp electrode (FSE) placement.
Objective: We will reinforce a mindset of documenting labor and precise fetal status assessment, improving overall maternal and fetal safety.
Description/Methods: a) polyethylene foam "pool noodle" (cervix) – $1.50, one noodle. b) plastic wrap (amniotic membranes)- $3.00, 200ft roll. c) tennis ball (fetal head) - $2.00, pack of three. d) FSE, IUPC, amniotomy hook – UAB Labor and Delivery. Total cost of one model = $0.80. Construction time was 10 minutes.
Evaluation: Following simulations, we will assess the comprehension of the clinical judgement skills and the physical proficiency in documenting adequate labor and monitoring. Overall, we anticipate by emphasizing the importance of intrapartum monitoring, with the new ACOG and SMFM recommendations, there will be fewer C/S performed at UAB for these indications.
Discussion: To safely decrease the number of C/S, logical management steps for each indication for C/S should be established. We strive to instill the clinical judgement necessary to navigate the two most common indications. Furthermore, we hope to strengthen the procedural skills. We plan to integrate this into the acting intern rotation and orientation of OB/GYN PGY-1s.

American College of Obstetricians and Gynecologists (College); Society for Maternal-Fetal Medicine, Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol. 2014 Mar;210(3):179-93. doi: 10.1016/j.ajog.2014.01.026. PubMed PMID: 24565430.

Project Length: Short
E-1

Title
Diabetes and Life-Space Mobility Decline in Older Adults

Authors
David Hall
Richard Kennedy, MD, PHD[1]
Cynthia J. Brown, MD, MSPH[1,2]

Abstract
Introduction: The prevalence of type 2 diabetes in adults older than 65 in the United States is estimated to be about 26% representing the largest disease burden of any age group. Diabetes has been shown to have a profound effect on older adults in regards to functional status and disability, but no studies to-date have analyzed the effect of diabetes on life-space, a measurement of community mobility.

Objectives: The primary objective of this study was to assess the association of diabetes and diabetes-related complications and life-space in older adults.

Methods: This was a cross-sectional study that utilized participants from the UAB Study of Aging I, a longitudinal study of community-dwelling older adults over the age of 65 from five counties in Alabama. The primary associations examined included type 2 diabetes diagnosis, presence of diabetic comorbidity (e.g. coronary artery disease, chronic kidney disease, peripheral neuropathy, retinopathy), and life-space score. Life-space measures mobility using the frequency in which individuals visit zones ranging from their bedroom to places outside their town, with higher scores being indicative of greater community mobility. Regression analysis was used to adjust for demographics, cognition, depression, transportation difficulty, length of follow-up, and diabetes complications.

Results: Of the 588 participants in this study, 167 (28.4%) had a diagnosis of type 2 diabetes. Participants with a type 2 diabetes diagnosis had lower life-space scores ($P<.05$).
This association with life space decline remained significant after adjusting for age, race, gender, education, cognition, depression, transportation difficulty, year 4 life space, time since last life space assessment, and the presence of any diabetic complication ($P<.0001$).

Conclusion: Type 2 diabetes diagnosis is associated with mobility decline in older adults when measured with life space. This study underscores the importance of prevention and management of type 2 diabetes in the older adult, which may help preserve mobility in later life.

[1] Division of Gerontology, Geriatrics, and Palliative Care, University of Alabama at Birmingham, Birmingham, Alabama
[2] Birmingham/Atlanta VA Geriatric Research, Education, and Clinical Center, Birmingham Alabama

Project Length: Short
E-2

Assessing Community Members' Preferences of a Family-Based Diabetes Prevention Program in Rural Alabama

Alexandra B. Khodadadi, Susan J. Andreae MPH, *Andrea L. Cherrington* MD/MPH
Department of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: Developing strategies to engage all family members in a lifestyle management program may be a promising strategy to improve the health of families living in rural underserved communities in Alabama.

OBJECTIVES: The aim of this study was to better understand barriers and facilitators in engaging the entire family in a family-centered diabetes prevention program.

METHODS: Five focus groups were held in 2016 in a rural, southern Alabama community with community members who had diabetes or cared for a family member with diabetes. Of the 58 focus group participants, 50 were women, 41 were over the age of 50, 53 had graduated from college or high school, and 16 worked full or part time. Participants were asked to discuss their current beliefs about diabetes and obesity and ideas on how to involve all family members in lifestyle changes. Focus group findings were analyzed by two coders using open coding.

RESULTS: Findings suggest that barriers such as the limited availability of community level resources, existing misconceptions regarding the causes and risk factors of diabetes, family level barriers such as scheduling and multiple competing demands, and individual level barriers such as stress and chronic pain in some family members that could make implementation of a family centered program challenging. However, several themes emerged indicating family centered programs would be acceptable including: high levels of family cohesion, health information shared among family units and neighbors, and the expressed need for acquiring health knowledge and skills necessary for healthy lifestyles as a family unit.

CONCLUSIONS: With multiple generations living close by and a strong sense of family, a family based intervention would be relevant and feasible in this community. Findings from this study provide insight to creating a culturally relevant lifestyle intervention applicable to the whole family.

Project Length: Intermediate
E-3

Using radiolabeled estradiol to quantify uptake in zebrafish embryos and larvae

J. Paige Souder, *Zachary Tibbs, Daniel Gorelick*

The zebrafish model system is of great utility in assessing the molecular and cellular effects of exposure to toxic chemicals during embryonic development. To study the effects of environmental endocrine disruptors, embryos and larvae are commonly exposed to supraphysiologic doses of estrogens, but their bioavailability in zebrafish is largely unknown. One hypothesis is that supraphysiologic doses of estrogens in the water are required to achieve physiologic levels *in vivo*, however this has not been directly tested. To test this hypothesis, we are developing an assay using radiolabeled estradiol to quantify percent uptake from treatment water in developing zebrafish. We are exposing embryos and larvae for different time periods to various concentrations of estradiol with a defined percentage of tritiated estradiol. Following exposure, we then measure the radioactivity of embryo media before and after treatment, and measure the radioactivity of whole embryos after treatment. Results will allow us to determine environmentally relevant exposure concentrations that lead to physiologic concentrations *in vivo*, and will provide a foundation for determining the uptake of other compounds in zebrafish for drug discovery, toxicology, and developmental studies. Furthermore, this method provides an avenue to screen for drugs and/or genes that modulate the absorption of exogenous compounds by developing zebrafish.

Project Length: Long
E-4

Differential responsiveness and sensitivity of major metabolic tissues to growth hormone.

Ryan Berry1, Martin E. Young4, Stuart J. Frank1,2,3 , 1Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL; 2Department of Cell, Developmental, and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL; 3Endocrinology Section, Medical Service, Birmingham VA Medical Center, Birmingham, AL; 4Division of Cardiovascular Disease, Department of Medicine, University of Alabama at Birmingham, Birmingham, AL.

INTRODUCTION: While knowledge of growth hormone (GH) and its somatogenic properties reaches back for decades, it has yet to be explicitly described whether major metabolic tissues in mouse have different responses and sensitivities to a pulse of GH.

OBJECTIVES: The objective of this study was to understand the relative responsiveness and sensitivities of major metabolic organs, in mice, to a pulse of GH.

METHODS: Male C57B6J mice, 15 weeks old, were housed in standard conditions under a 12hr:12hr light:dark cycle with ad libitum access to a standard chow diet. At week 16.5 (+/-3d), food and bedding were removed from the cages and wire bottoms were inserted at Zeitgeber Time (ZT) 0 (lights on). Six hours later, mice were injected via the inferior vena cava with either Saline or hGH (2, 4, 8, 12.5, 20, 50, 80, 120, 200 ng/$g_{(bw)}$). After circulating 5 minutes, the needle was withdrawn and the heart, liver, kidney, epididymal fat, and gastrocnemius were resected and flash frozen in liquid nitrogen. The tissue was analyzed via western blot.

RESULTS: Responsiveness and sensitivity were assessed by pSTAT5/STAT5 ratio. The liver displayed the greatest response (100%) followed by gastrocnemius (61%), heart (30%), white adipose tissue (21%), and whole kidney (8%). The relative responses of heart, white adipose tissue and kidney, but not liver, gastrocnemius, and heart were explained by total abundance of STAT5. Sensitivity analysis showed Liver and kidney to be statistically the same and more sensitive than, WAT, heart and gastrocnemius. These differences were not explained by growth hormone receptor (GHR) protein abundance.

CONCLUSIONS: This study has shown that different major metabolic tissues in mouse are distributed over a wide range of relative responsiveness and sensitivity and the differences between tissues are loosely associated with the relative abundances of GHR and STAT5.

Project Length: Long E-5

TrkA Activity is Reduced in Streptozotocin Induced Diabetes Rat Brain

Katie R. Vines, M.S., *Geetha Thangiah, Ph.D, and Ramesh B. Jeganathan, Ph.D.*
Department of Nutrition, Dietetics and Hotel Management, Auburn University, Auburn, AL

INTRODUCTION: Abnormal blood glucose homeostasis and subsequent hyperglycemia, due to insufficient insulin production, is characteristic of type 1 diabetes mellitus. Neuronal cells are classified as insulin insensitive, therefore insulin is incapable of increasing glucose uptake in neurons. Tropomyosin receptor kinase A (TrkA) is a transmembrane receptor for nerve growth factor (NGF), which is responsible for regulating neuronal survival and differentiation. We have previously shown in our lab that NGF or insulin elicits TrkA to complex with insulin receptor (IR) and insulin receptor substrate -1 (IRS-1), and phosphorylation of these proteins requires a functional TrkA kinase in PC12 cells. It was also shown that a functional TrkA kinase is necessary for Akt activation in PC12 cells.
OBJECTIVE: The primary objective of this study was to assess if the activity of TrkA in the higher model of type I diabetic rat brains was similar to its activity seen in the PC12 cell line.
METHODS: Eight week old Wistar rats were induced with T1DM and confirmed hyperglycemic with urine glucose test. Control rats were administered a vehicle injection of only citrate buffer. Whole brain homogenates were Western Blotted for analysis of IR, IRS-1, and Akt in terms of interaction and phosphorylation.
RESULTS: TrkA exhibited **a** decrease in phosphorylation and increase in nitrosylation, as compared to control rat brain samples. The interaction of TrkA with IR and IRS-1 as well as the tyrosine phosphorylation of these signaling proteins is decreased in STZ rat brain samples. Lastly, STZ rat brain samples had decreased phosphorylation of Akt, as compared to control rat brain samples. **CONCLUSION:** A functional TrkA is necessary for proper functioning of the insulin signaling proteins IR, IRS-1, and Akt in neuronal cells, and disruption of its functioning can be seen in neuronal cells of the type 1 diabetic rat model.

Project Length: Long
E-6

GADD45B is a novel candidate regulator of Epigenetic Reprogramming in Human Diabetic Heart Failure

Mark E. Pepin[1,2,3], David K. Crossman[4], Steven M. Pogwizd[1,5] and *Adam R. Wende*[1]*

[1]Department of Pathology, Division of Molecular and Cellular Pathology, [2]Department of Biomedical Engineering, [3]Medical Scientist Training Program, [4]Department of Genetics, Heflin Center for Genomic Science, [5]Department of Medicine
University of Alabama at Birmingham, Birmingham, AL 35294, USA

Purpose: Diabetes mellitus, independent of coronary artery disease or hypertension, is associated with up to a 4-fold increase in risk of developing heart failure (HF). While ischemic etiologies of heart failure can be managed with diuretic and inotropic therapies, diabetic HF is particularly resistant to these first-line agents. Thus, the development of targeted therapies may provide a means of addressing an underlying cardiac pathogenesis that is distinct to diabetic HF. Previous work has identified a connection between alterations in DNA methylation and the transcriptional profile in ischemic heart failure. However, the concerted regulation of cardiac DNA methylation remains unknown, as does its impact on the heart in the context of diabetes mellitus. **Results**: The current study has exposed a distinct signature of promoter-associated DNA demethylation in human diabetic HF that corresponds with inversely altered transcriptional activity. Furthermore, this study has identified Growth Arrest and DNA Damage inducible 45 beta (GADD45B) as a putative epigenetic regulator of the observed DNA methylation profile. Previous studies have presented an intimate role of GADD45B as a stress sensor that activates cellular apoptosis, a well-established finding in HF. However, relatively little is known about GADD45B in the heart, as significant previous work has focused on its regulation of neuronal DNA demethylation in the context of new memory formation. GADD45B is also known to respond to many intracellular signals in order to regulate DNA methylation status, thereby orchestrating gene expression changes in response to environmental and/or metabolic stresses. **Conclusions**: Therefore, this study supports the hypothesis that epigenetic reprogramming in the diabetic heart predisposes patients for cardiac dysfunction. Determining whether GADD45B is a mediator of cardiac function may define a novel mechanism through which the heart could be epigenetically reprogramed to reverse the cardiac dysfunction in diabetic heart failure.

Project Length: Short
F-1
Replication and Confirmation of Novel Loci Identified in Systemic Lupus Erythematosus in a Genome-Wide Association Study of an Amerindian Ancestry Population

Milza C Opper[1], *Marta E. Alarcón-Riquelme, MD, PhD*[2], *Jeffrey C. Edberg, PhD*[3], *Maria Teruel*[2]
1. University of Alabama at Birmingham School of Medicine, Birmingham, Alabama **2.** Center for Genomics and Oncological Research: Pfizer/University of Granada/Andalusian Government, Granada, Granada, Spain **3.** Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama

Introduction: A genome-wide association study (GWAS) has revealed 23 novel loci associated with systemic lupus erythematosus (SLE) in a population of individuals enriched of Amerindian ancestry. However, these loci have not been replicated or confirmed.
Objectives: The primary objective of this study is replication and confirmation of 23 novel loci discovered in a GWAS of patients with SLE enriched of Amerindian ancestry.
Methods: Genotyping of 700 new SLE cases and 1000 controls was performed using HumanCorev24 custom arrays from Illumina that include the fine mapping of the 23 previously identified loci. Samples and single nucleotide polymorphisms (SNPs) with a call rate of <95% will be excluded. Principal component analysis will be performed on all remaining SNPs to recognize patterns, visualize variations, and avoid stratification bias. Imputation will be done. Odds ratios and 95% confidence intervals will be calculated.
These data will be compared to the original GWAS data of the project with the aim to replicate statistically suggestive loci. This will show whether the loci can be confirmed as associated with SLE. Fine mapping will be performed to identify potential new loci, and eQTL analysis and GENOVAR analysis to determine possible causality of the SNPs. Stepwise logistic regression will be done to determine independent effects within single loci and identify the variants contributing to risk for SLE.
Results: Genotyping has been performed and analysis is in progress; results are pending.
Conclusion: If confirmed and replicated, these 23 novel loci will provide insight into SNPs specific to SLE in patients enriched of Amerindian ancestry, which is important as the clinical manifestations differ among ethnic groups. Additionally, it will drive further discovery of the cellular mechanics that underlie SLE and allow therapeutic efforts to be driven by the genetic basis of the disease.

Project Length: Short
F-2

TITLE: Initial Whole Genome Analysis of SFARI Phase I

AUTHORS: Matthew B. Neu, Ben Weaver, David Gray, Michelle Thompson, Susan Hiatt, Jana Whittle, Kevin Bowling, James Lawlor, *Gregory Cooper PhD*

INTRODUCTION: Nearly 1 in 68 children are diagnosed with an Autism Spectrum Disorder, and boys are affected more than girls at a 4.5:1 ratio. While there have been nearly 65 genes associated with the development of Autism, this represents a small fraction of an estimated 400-1,000 genes involved in Autism susceptibility. Previous literature suggests that de novo events contribute significantly to Autism risk, however a large exome sequencing effort of the Simons Simplex Collection reveals hundreds of cases in which no likely gene-disrupting de novo event or copy number variation is present. As part of the Simons Foundation Autism Research Initiative (SFARI) Phase 1 study, over 500 of these families have received whole genome sequencing (WGS) in an effort to discern further genetic causes of Autism.

OBJECTIVE: We hypothesize that analysis of whole genome sequences of the SFARI Phase 1 cohort will reveal intronic variation causative for Autism. Initial summary statistics of this cohort will yield features consistent with similar cohorts.

METHODS: Summary statistics such as number and type of variants present in probands are gathering using R and python scripts. Combined Annotation Dependent Depletion (CADD) scores are evaluated in consideration of population allele frequency. We use computational methods to logically group intronic variants associated with known Autism gene and sexually dimorphic pathways via copy number analysis, algorithmic pathogenicity modeling, and presence in topologically associated domains. Manual analysis of variants will allow us to combine SFARI data with whole genome data gathered from CSER, a separate in-house project to identify variants associated with pediatric development disease.

RESULTS: Initial summary statistics are consistent with similar cohorts.

CONCLUSION: The SFARI Phase I whole genome sequence cohort will be a useful dataset for determining further genetic mechanisms of Autism development.

Project Length: Intermediate
F-3

Title: Recognition of Neurofibromatosis Type 1 with Facial Dysmorphology Novel Analysis

Author: Carly A. Cignetti. *Anna C. E. Hurst, M.D., M.S.,* Department of Genetics, University of Alabama at Birmingham, Birmingham, Alabama.

Introduction: A wide variety of dysmorphic facial features have been reported in people with the genetic condition Neurofibromatosis type 1 (NF1), but a characteristic facial gestalt has not been described. NF1 has not previously been studied with facial analysis software.
Objectives: The primary objective of this study is to determine whether NF1 can be recognized by a distinct facial pattern, and to assess for *NF1* genotype-facial phenotype relationships.
Methods: Up to three full-face photographs (frontal, left-lateral, and right-lateral views) of 100 people with clinical and/or molecular diagnoses of NF1 will be captured and submitted to FDNA® to be analyzed by Facial Dysmorphology Novel Analysis (FDNA) software, a technology that generates topographical data from two-dimensional images. FDNA's research experts will fully analyze the data, assessing for patterns within the NF1 cohort, associations between *NF1* genotype (self-reported deletion or other mutation) and facial phenotype, and relationships to other genetic conditions previously characterized by FDNA.
Results: This research will either identify or fail to identify a distinct facial gestalt associated with NF1, *NF1* genotype-facial phenotype correlations, and similarities between the facial phenotype of NF1 and that of other genetic conditions previously characterized by FDNA.
Conclusion: In the case that a distinct facial pattern associated with NF1 is identified, the results would be added to the FDNA database, and the NF1 facial gestalt would be screened for with every FDNA search. This would support an early diagnosis of NF1, and the clinical utility of the non-invasive and cost-effective FDNA technology as a screening tool for this condition. Benefits include saving time and money that might be spent exploring other causes of symptoms, and knowing to screen for and manage potentially life-threatening complications associated with NF1.

Project Length: Intermediate
F-4

Title: Hypomethylation of ADORA1, SBNO2, and WIZ is associated with risk of multiple myeloma, smoldering myeloma, and monoclonal gammopathy of undetermined significance.

Authors: Stephen D. Gragg[1], Devin Absher[2], Degui Zhi[3], *Elizabeth E. Brown*[4].

Affiliations: 1. Medical Scientist Training Program, University of Alabama at Birmingham, Birmingham, AL. 2. HudsonAlpha Institute for Biotechnology, Huntsville, AL. 3. School of Biomedical Informatics, University of Texas Health Science Center at Houston, Houston, TX. 4. Department of Pathology, School of Medicine, University of Alabama at Birmingham, Birmingham, AL.

Introduction: Multiple myeloma (MM) is the second most common hematological malignancy, presenting as a neoplastic proliferation of plasma cells within the bone marrow. As a complex disease, MM is caused by a combination of genetic and environmental factors. Thus, epigenetic factors, such as DNA methylation, represent one mechanism which may influence the development and maintenance of MM as well as its asymptomatic precursor conditions including monoclonal gammopathy of undetermined significance (MGUS) and smoldering myeloma (SMM).

Objectives: The objective of this study was to identify differentially methylated positions in the genome of patients with MM, SMM, and MGUS.

Methods: We assessed genome-wide DNA methylation in total leukocytes from peripheral blood obtained from patients with multiple myeloma (n=56), smoldering myeloma (n=31), and monocolonal gammopathy of undetermined significance (n=60) and controls (n=79) enrolled in the Molecular and Genetic Epidemiology (iMAGE) study of myeloma. We quantified DNA methylation using the Illumina 450K array and we detected differences in methylated positons using a general linear model framework adjusted for confounders.

Results: In MM cases, we identified 7 hypo-methylated positions compared to controls including CA6 (P=4.30e-08), ADORA1 (P=9.86e-08), PLEKH4B (P= 7.71e-08), SBNO2 (P= 4.65e-10), and WIZ (P= 1.45e-08), as well as two intergenic loci (P = 2.94e-09 and P=4.05e-08), with genome-wide significance. Each of these loci (with the exception of CA6 and PLEKHG4B), were significantly different in SMM and MGUS patients compared to controls (P<0.05), but without genome-wide significance.

Conclusions: Our findings suggest that differences in DNA methylation may contribute to altered risk of MM and may play a role in its development as a consequence of inherited environmental exposure

Project Length: Long
F-5

HCV Genie V 2.0: A Web Platform for the Versant Hepatitis C Virus (HCV) Genotype Line Probe Assay

Authors: Alex Dussaq[1,3], Abha Soni, D.O.[1]; Seung L Park M.D.[2], *Christopher Willey M.D. Ph.D[3]*, Shuko Harada, M.D.[1]
[1]Pathology; University of Alabama at Birmingham; Birmingham, AL
[2]CMIO; Community Health Systems; Franklin, TN
[3]Radiation Oncology; University of Alabama at Birmingham; Birmingham, AL

Introduction: Hepatitis C virus (HCV) genotyping at our institution is performed using the Versant Hepatitis C virus genotype 2.0 Line Probe Assay (LiPA). The last steps of this procedure are a manual, time-consuming, error prone process that involves the identification of bands and matching to a physical reference table. A resident had developed an HCV genotype interpretation platform that identifies the strain of HCV based on the banding. However, identifying bands on the strip was done manually. This study serves as a follow-up with an MD/PhD student porting this system to an open web environment and adding an analytical step utilizing a scanned LiPA image to generate the genotyping results.

Methods: We (a) ported the original, clinically validated, HCV genotype interpretation program, from an SQL database to JSON object, (b) created image analysis algorithms that convert LiPA images into band and genotype calls, and (c) built a user interface to utilize these tools. Client side JavaScript allows the analysis to be performed without any data leaving the investigator's computer and download results as a printable report.

Results: The original HCV Genie was written, deployed, clinically validated, and proven to be identical to human expert interpretation (n = 200). It decreased the time needed to interpret results by 53% for residents. Since the most time-consuming part is to identify each band on the strip, HCV-Genie 2 allows us to further minimize analysis time and eliminate errors, thereby, increasing the quality of patient care. Available at: HCVgenie.com.

Conclusion: This iteration of HCV Genie focused on developing lane and band detection algorithms, and creating a publically available tool that eliminates data privacy concerns. Future iterations of this program will focus on allowing users to store and aggregate results in a database of their choosing, allowing for advanced data analytics of HCV genotypes.

Project Length: Long
F-6

RBRSA: A Ranked-Based Method for Two-Class RNA-seq Differential Expression Analysis

Ryne C. Ramaker[a,b], *Sara J. Cooper, PhD*[a], and *Richard M. Myers, PhD*[a]

[a]HudsonAlpha Institute for Biotechnology, Huntsville, AL, USA
[b]Department of Genetics, University of Alabama at Birmingham, Birmingham, AL, USA

Introduction: Decreasing costs of RNA-sequencing (RNA-seq) have made data readily available for basic science and clinical applications. The discretized nature and non-normal distribution of RNA-seq data make normalization and differential expression analysis challenging. Several parametric methods that assume an underlying count distribution have been developed for the analysis of RNA-seq data, however these methods can be inaccurate when transcripts violate the assumed distribution. Non-parametric approaches can bypasses data distribution assumptions, but few methods are currently available for RNA-seq data and existing methods can be inaccurate on small sample sizes ($n<50$) and perform inefficiently on large sample sizes ($n>1000$).

Objective: The objective of this study was to develop a non-parametric method for RNA-seq analysis in an open-source statistical programming language that was robust to sample size and capable of accurately identifying differential expression at a range of sequencing depths.

Methods: We developed an efficient rank-based method for RNA-seq differential expression analysis that relies on the conserved hierarchy of transcript expression levels across biological replicates to identify robust expression anomalies and penalize low-confidence transcripts. Performance of our method was compared to two parametric methods (DESeq2 and EdgeR) and three non-parametric methods (SAMseq, LFCseq, and NOIseq) using two RNA-seq data simulators (SIMseq and Polyester) as well as actual cancer and psychiatric disorder datasets.

Results: Our method is able to identify differentially expressed transcripts with a higher sensitivity ($p<0.0001$), specificity ($p<0.0001$), and precision ($p<0.0001$) than all three non-parametric methods for both RNA-seq data simulation methods at small sample sizes ($n<50$). It also outperforms the two parametric methods assessed at several of the sample sizes and sequencing depths examined. Finally, our method scales more efficiently than currently available tools with larger sample sizes ($n>1000$).

Conclusion: We developed a method for differential expression analysis that shows improved accuracy and efficiency on a variety of RNA-seq datasets.

Project Length: Long
F-7

Title – Enabling Precision Medicine in Rheumatoid Arthritis through Prioritization of Genetic Variants

Authors - Vincent A. Laufer, BA[1,2], Hemant K. Tiwari PhD[1], Richard J. Reynolds PhD[1], Maria I. Danila MD[1], Devin Absher PhD[3], Carl D. Langefeld PhD[4], Ted R. Mikuls PhD[5], Peter K. Gregersen MD[6], Robert P. Kimberly, MD[1], Donna K. Arnett, PhD[7], and *S. Louis Bridges Jr. MD, PhD[1]*

[1]University of Alabama at Birmingham, [2]University of Alabama at Birmingham Medical Scientist Training Program, [3]Hudson Alpha Institute for Biotechnology, [4]Wake Forest School of Medicine, [5]Veteran Affairs Nebraska Western Iowa Health Care System and University of Nebraska Medical Center, [6]Feinstein Institute Medical Research and North Shore-Long Island Jewish Health System, [7]University of Kentucky, College of Public Health

Introduction – There are over 100 genetic risk loci for Rheumatoid Arthritis (RA). However, each of these risk loci contains dozens of genetic variants, some of which presumably cause RA, and others of which are merely associated due to linkage with the causal variants. Therefore, identifying which of these genetic variants are causal and which only associated is a major contemporary obstacle in RA functional genomics.

Objectives – The objective of this study is address this obstacle by producing a ranked list of candidate causal variants in each RA risk locus in order to guide functional studies into the genetic basis of RA.

Methods – We have association summary statistics (Z-scores) from GWAS of over >100,000 RA patients and controls of 4 global ancestries (Asians, Caucasians, African Americans, and South Africans). We integrated this with SNP linkage information calculated using 1000 genomes data or calculated from our data and with functional annotation from sources such as ENCODE and ROADMAP using an algorithm called PAINTOR2. We then applied this algorithm to over 80 RA risk loci in order to prioritize genetic variants by their Project Length: ior probability of being causal in RA.

Results - Our approach identified several genetic variants with a very high Project Length: ior probability of being causal variants. Many of these lie in key RA risk loci, such as *CD28/CTLA4*, *AFF3*, *TNFAIP3*, *TAGAP*, *NFKBIE*, and *CCR6*.

Conclusions – This study utilizes a large, ethnically diverse population of RA patients and controls to prioritize candidate causal variation in many RA risk loci. We present these as a service to RA researchers, in order to increase cost efficacy of validation studies designed to establish the functional role of associated risk variants. Overall, this study uses a cutting edge approach to address a major contemporary issue in the genetics of RA, and by extension, complex disease.

Project Length: Long
F-8

Title:
Mutations in EBF3 disturb transcriptional profiles and underlie a novel syndrome of intellectual disability, ataxia and facial dysmorphism

Authors:
Andrew A. Hardigan[1,2], Frederike Leonie Harms[2], Katta Mohan Girisha[3], Kevin M. Bowling[1], Susan M. Hiatt[1], Kerstin Kutsche[2], Richard M. Myers[1], Gregory M. Cooper[1]

[1]HudsonAlpha Institute for Biotechnology, Huntsville, AL USA
[2]Department of Genetics, University of Alabama at Birmingham, AL USA
[3]Institute of Human Genetics, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[4]Department of Medical Genetics, Kasturba Medical College, Manipal University, Manipal, India

Introduction: Developmental delay and intellectual disability (DD/ID) is characterized by limitations in cognitive and adaptive behavior and represents a heterogeneous group of syndromic and non-syndromic disorders. Identifying and evaluating the phenotypic contribution of variants and genes of unknown significance (VUS/GUS) to DD/ID etiology represents a major unmet clinical and scientific need.

Objectives: We identified ten individuals with intellectual disability, speech delay, ataxia and facial dysmorphism carrying a deleterious variant in the EBF3 gene detected by whole-exome sequencing (WES), and performed functional assays to identify potential mechanisms by which the VUS may disrupt EBF3 function.

Methods: Targeted enrichment and massively parallel sequencing were performed on genomic DNA extracted from circulating leukocytes. Sequence processing and variant identification was performed following the Genome Analysis Toolkit's (GATK) best practice recommendations. Further functional experiments to evaluate the identified EBF3 VUS included structural modeling, *in situ* subcellular fractionation, transactivation reporter assays, and RNA- and Chromatin immunoprecipitation (ChIP) – sequencing.

Results: Structural assessment of the five amino acid substitutions predicts that they disrupt the ability of EBF3 to bind DNA. Transient expression of EBF3 mutant proteins in HEK 293T cells revealed mislocalization of all but one mutant in the cytoplasm in addition to nuclear localization. By transactivation assays, all EBF3 mutants showed significantly reduced or no ability to activate transcription of the CDKN1A reporter gene, which corresponds well with loose association of EBF3 mutants with chromatin as demonstrated by in situ subcellular fractionation experiments. Finally, RNA-seq and ChIP-seq experiments demonstrate that EBF3 acts as a transcriptional regulator and EBF3 mutant protein had reduced binding and gene regulatory activity.

Conclusion: These findings demonstrate that EBF3-mediated dysregulation of gene expression has profound effects on neuronal development in humans and that deleterious variants in EBF3 underlie a novel intellectual disability and developmental delay syndrome.

Project Length: Short
G-1

Title: Psychological Stress During Pregnancy Alters Immune Function in Maternal and Neonatal Mice

Authors: Sara E. Deas, BS[1], Miguel Melendez-Ferro, PhD[1], Venkat Yeramilli, PhD[2], Courtney Culbreath, MD[3], Robin G. Lorenz, MD, PhD[4], *Colin A. Martin, MD[1,5]*

Affiliations:
1. Department of Surgery, University of Alabama at Birmingham, Birmingham, AL
2. Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL
3. Department of Surgery, Inova Fairfax Hospital, Falls Church, VA
4. Department of Pathology, University of Alabama at Birmingham, Birmingham, AL
5. Department of Surgery, Children's of Alabama, Birmingham, AL

Introduction*:* During pregnancy, stress can negatively affect both mother and child. The impact of maternal psychological stress on neonatal immunity is presently unknown. Early immune development in neonates is largely dependent upon transfer of antibodies from the mother. Immunoglobulin A (IgA) is a protective antibody that protects the host from pathogenic bacterial invasion.
Objectives: To determine the effect of maternal psychological stress on immune function and passive immunity in neonates.
Methods*: 8 week old* C57BL/6 littermates underwent timed breeding. The females of three mating pairs were subjected to daily psychological stress by using a well-established restraint model during days 7-14 of the gestational period. The control group experienced no stress. Maternal vaginal colonization was sampled 1 day prior to delivery via vaginal lavage; samples were then cultured on Schaedler agar in aerobic conditions for 24 hours at 37°C. Enzyme-linked immunosorbent assay (ELISA) was used to measure fecal IgA levels in in 2 week old pups.
Results*:* Two-week old mice from the stressed group had significantly less fecal IgA compared with the control group; stress group mean = 51658.51 ng/mL, standard error = 11982.92; control group mean = 200320.22 ng/mL, standard error = 57674.83 (P value = 0.0033). Microbial culture of vaginal microbiome from the mother revealed 98 colony forming units (CFUs) for the stressed group, and 187 CFUs for the control group.
Conclusions*:* Maternal gestational stress results in significantly less fecal IgA in offspring compared to controls. Additionally, stressed dams had lower vaginal bacterial colonization compared to controls which could explain this finding. Future experiments will further elucidate this mechanism by analyzing serum IgA levels in pups, and stress hormones in dams and pups.

Project Length: Long
G-2

Immunity to influenza requires T-bet expression in B cells.

Sara Stone[1,2*], André Ballesteros-Tato[3], *Frances Lund*[2]
[1]UAB Medical scientist training program
[2]UAB Department of Microbiology
[3]UAB Department of Clinical Immunology and Rheumatology
*Corresponding author

Germinal center B (GCB) cells can differentiate into either memory B cells (Bmem) or terminally differentiated effector cells – referred to as long-lived antibody-secreting cells (LL-ASCs). The transcription factor Bcl6 promotes GCB cell survival and Bmem development while simultaneously inhibiting LL-ASC differentiation by repressing the transcription factor Blimp1, which normally induces LL-ASC development. To date, it is not clear how these opposing transcription factors are regulated in GCB cells. In T lymphocytes, the transcription factor T-bet modulates the balance between Blimp1 and Bcl6 and controls whether the T cell will become a memory cell or an effector cell. We previously showed that T-bet regulates ASC development from naive B cell precursors activated *in vitro* with T helper 1 cells. Therefore, we tested the hypothesis that B cell T-bet expression is also necessary for the development of LL-ASCs from GCB cell precursors. Interestingly, we found that influenza infection induced T-bet expression in a subset of GCB cells, Bmem cells, and ASCs. In chimeric mice in which 50% of cells are T-bet deficient (*Tbx21*$^{-/-}$), GCB cells were preferentially derived from *Tbx21*$^{-/-}$, rather than WT B cells and *Tbx21*$^{-/-}$ GCB cells expressed lower mRNA levels of *Prdm1* (Blimp1) than WT GCB cells. Additionally, we found reduced numbers of flu-specific LL-ASCs and lower anti-flu titers in chimeric animals with *Tbx21*$^{-/-}$ B cells compared to control chimeras with WT B cells. Although most Bmem cells express T-bet, we observed no impairment in Bmem formation when all B cells were *Tbx21*$^{-/-}$. However, induced deletion of T-bet from Bmem cells nearly ablated the secondary ASC response to a challenge influenza infection. These results support a role for T-bet in determining fate of GCB cells following influenza infection and moreover show that T-bet serves as a transcriptional regulator of both primary and secondary ASC responses in mice.

Project Length: Long
G-3

The insulin-like growth factor system is a critical regulator of the balance of Th17 and Treg CD4s in autoimmunity

Daniel DiToro[1], Jens Bruning[2], PhD, *Casey Weaver, MD*[1].

1. Department of Pathology, University of Alabama at Birmingham, Birmingham, AL.
2. Institute for Genetics, University of Koln, Koln, DE.

Appropriate regulation of the balance of Th17 and Treg CD4s is essential in maintaining tolerance to host and microbial antigens and in mounting effective responses to pathogens. However, the factors that modulate this balance remain incompletely understood. Here we show that Th17 and Treg CD4s express multiple components of the insulin-like growth factor (Igf) system. Signaling through Igf1R reciprocally regulates Th17 and Treg differentiation, biasing cell fate outcomes and amplifying the magnitude of the pro-inflammatory response. This effect is mediated by at least three mechanisms. First, Igfs suppress the induction of Foxp3 and augment expression of IL-17a following activation. Second, they selectively suppress apoptosis in IL-17a+ cells. Third, they alter the transcriptional and translational state of IL-17a+ cells, imparting a pathogenic expression signature.

Project Length: Long
G-4

What Does the Anti-SLA Antibody See?

Joseph M Ladowski, Luz Reyes, Zheng-Yu Wang, Greg Martens, Matt Tector, Joseph Tector

Abstract:

Purpose: Xenotransplantation, using genetically modified pig organs, could provide a new supply of organs to decrease the waiting list. The creation of a triple-xenoantigen knockout (TKO) pig eliminated antibody binding in nearly 75% of patients. The 25% of sera samples that bind the TKO cell contain antibodies against the swine major histocompatibility complex (MHC). Given that the carbohydrate barrier is removed, the field will focus on the antibodies that bind the swine MHC.
Methods: A swine MHC class II positive cell line was created by transfection with the human class II transactivator (CIITA) and an antibody binding assay was performed. The individuals deemed "extraordinary binders" were analyzed for their previous anti-human MHC binding patterns to determine if a propensity for binding –DQ or –DR was present. The known cross-reactive groups (CREGs) in human MHC were compared by NCBI BLAST and then modeled in the NCBI C3nD software.
Results: Successful generation of a class II positive cell was established and a human antibody binding assay was performed. Twelve individuals who bound the swine class II positive cells with 100% greater MFI compared to class II negative cells were considered "extraordinary" binders and were found to have a high likelihood of anti-HLA-DQ antibodies in their sera. Human MHC-DQ sequences were compared to swine MHC-DQ and the location of known anti-human CREGs were mapped. The structural biology of the eight CREGs found in both human and swine MHC-DQ was mapped in NCBI C3nd.
Conclusion: Of the eight known CREGs, only one mapped to a single amino acid. This CREG would be the easiest to manipulate and disrupt antibody binding in downstream experiments. Assays are currently being developed to determine the antigenicity of this amino acid, but the relative isolation represents a potential target for genetic manipulation.

Project Length: Short
G-5

Title: The differential transcriptional landscape between genders during immune response

Emma C. Dean, Danielle A. Chisolm, *Amy S. Weinmann, Ph.D.*
Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL

Introduction
Understanding the role that gender plays in autoimmunity is paramount to understanding both the underlying etiology of autoimmune diseases, as well as the optimal disease management. There are clear gender tendencies in autoimmune diseases; for example, only 1 in 9 patients diagnosed with systemic lupus erythematosus is male. Past studies have considered the role of hormones on modulating immune response, the phenomenon of X chromosome inactivation escape, as well as the influence of gender on the robustness of immune response. It has been well established that women exhibit a more robust response, but previous studies have done little to examine the influence of gender on immune response to various stimuli.

Objectives
We are interested in understanding what changes occur in gene regulatory networks between genders under immune-stimulatory contexts. We hypothesize that gender influences the transcriptional programs in place during both immune development and response and that these influences are context dependent.

Methods
Primary $CD4^+$ T cells were isolated from the spleens and peripheral lymph nodes of 2 male and 2 female C57BL/6 mice; the cells were polarized in type 1 conditions and maintained in either high or low IL-2. qRT-PCR analyses were performed to examine whether candidate genes identified from a previous RNA-seq analysis were differentially expressed between male and female Th1 cells.

Results
Candidate genes were analyzed by qRT-PCR. The data indicated that many genes were similarly expressed between male and female Th1 cells, however, there might be modest differences in the expression of select genes. Further experiments need to be performed to confirm the expression differences before then undertaking studies to elucidate the specific role the modulators might be playing in inducing immune responses between the sexes.

Conclusion
Understanding the differential transcriptional landscape between males and females during pro-inflammatory responses is critical in both further understanding autoimmune disease etiologies, as well as determining optimal disease management for both men and women with autoimmune disease. Through this work, we hope to identify specific, key immune modulators that could be used in targeted therapies.

Project Length: Short
G-6

Altered Oxidative Stress Response in Cells with Telomere Dysfunction.

Madeline M. Dills[1], Erik R. Westin, PhD[1], Larisa Pereboeva, MD PhD[2], *Frederick D. Goldman, MD*[1]

1. Department of Pediatrics, Division of Hematology Oncology, Children's Hospital of Alabama, Birmingham, Alabama, United States of America
2. Department of Medicine, Division of Hematology Oncology, University of Alabama at Birmingham, Birmingham, Alabama, United States of America

INTRODUCTION: Dyskeratosis congenita (DC) is an inherited, multisystem aging disorder with a predisposition to bone marrow failure and cancer. Mutations are found in a number of telomerase and telomere-related genes leading to a mobilized DNA damage response (DDR) and heightened reactive oxygen species (ROS). Preliminary evidence has indicated that DC cells suppress antioxidant expression of *NFE2L2* and *NFE2L3* genes and downstream gene targets (*HO1*, *TXN*, *NQO1*). Our hypothesis states that telomere shortening promotes entry into senescence by suppressing the cell's ability to mount an effective antioxidant response to oxidative stress.

OBJECTIVES: Assess protein levels of NFE2L2 protein and associated antioxidant genes in primary DC and 'rescued' cells (*TERT* overexpression, p53 shRNA).

METHODS: Cells (lymphocytes, skin fibroblasts) were acquired from DC patients and controls following IRB approved protocols. Each patient carries a mutation in one of the following genes: *TINF2, DKC1, TERT.* 'Rescue' of skin fibroblasts was performed with either viral *TERT* expression or p53 shRNA (Open Biosystems). Standard western blotting techniques were executed as previously published using SDS electrophoresis, nitrocellulose membrane transfers and stained with corresponding antibodies (NFE2L2, NFE2L3, HO1, and GAPDH) plus respective secondary antibodies.

RESULTS: Steady-state levels of NFE2L2 and NFE2L3 proteins appeared to be increased in DC fibroblasts compared to controls. Surprisingly, expression of *TERT* in *TINF2* or *DKC1* fibroblasts decreased NFE2L2, NFE2L3 and HO1 in most experiments (TERT mutated cells appeared unchanged). However, HO1 appeared suppressed in DC lymphocytes. Interestingly, upon introduction of p53 shRNA into DC fibroblasts, we found no evidence of changes in antioxidant proteins levels.

CONCLUSIONS: For most experiments, antioxidant protein levels appeared to be elevated in DC cells compared to control cells. Further, experimental telomere elongation dramatically decreased antioxidant protein levels in DC cells (but not upon p53 shRNA expression). These results contradict our original hypothesis and will undergo further validation.

Project Length: Short
H-1

Title: Killing of *Serratia marcescens* Biofilms with Chloramphenicol

Authors: Christopher A. Ray; Anukul T. Shenoy; *Carlos J Orihuela, PhD*; Norberto González-Juarbe, PhD (Department of Microbiology, University of Alabama at Birmingham, Birmingham AL)

Introduction: *Serratia marcescens* is Gram-negative bacterium shown to be resistant to multiple antibiotics that can cause catheter-associated blood stream infections (CABSI). Bacterial colonization of catheters occurs mainly by biofilm formation. High-dose antibiotic locks can be used to clear colonized catheters, but have not been tested against *S. marcescens* biofilms.

Objectives: We aim to explore the susceptibility of *S. marcescens* biofilms *in vitro* against high doses of antibiotics and non-antibiotic agents for use in catheter salvage.

Methods: A clinical isolate of *S. marcescens* was exposed to varying concentrations of antibiotics and non-antibiotic compounds to determine its *in vitro* susceptibility to these agents (ceftriaxone, gentamicin, kanamycin, chloramphenicol, ursolic acid, and polysorbate-80). These compounds were then added at varying concentrations (10, 100, and 1000 times the minimum inhibitory concentration were used for the antibiotics) to *S. marcescens* biofilms pregrown in 6-well plates. The plates were then incubated with the compounds, and the biofilm mass was quantified using crystal violet staining and compared to the biofilm mass in untreated control wells.

Results: *S. marcescens* demonstrated susceptibility to ceftriaxone, kanamycin, gentamicin, and chloramphenicol in its planktonic form; however, only chloramphenicol consistently reduced both biofilm biomass and viability. Polysorbate-80 and ursolic acid had minimal effect on both planktonic and biofilm grown of *S. marcescens*.

Conclusion: Our study offers confirmation that supratherapeutic doses of chloramphenicol can be used against *S. marcescens* biofilms, and potentially to treat *S. marcescens* infected catheters. Furthermore, we are the first to demonstrate the potential use of chloramphenicol in the salvage of infected catheters by any organism (which avoids the toxicities that have limited its use); confirmation of its effectiveness *in vivo* could offer a new indication for an old antibiotic.

Project Length: Short
H-2

Experimental Trial of FDA-Approved Therapeutics in a Mouse Model of Acute Infection with *Mycobacterium tuberculosis*

Hayden Pacl, BA[1,2], Shannon Russel, PhD [2], Chivonne Moodley, MSc [2], *Adrie JC Steyn, PhD [2,3]*
[1]Medical Scientist Training Program, University of Alabama at Birmingham, Birmingham, AL
[2]Kwazulu-Natal Research Institute for Tuberculosis and HIV, Durban, KZN, South Africa
[3]Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL

Introduction: *Mycobacterium tuberculosis* (MTB) poses a significant threat to public health around the world. However, only one new drug has been approved for MTB infection in over 40 years. This underscores the dire need for novel therapeutics in the treatment of tuberculosis—a disease that is rapidly developing widespread drug resistance.
Objectives: The primary objective of this study was to determine if host-directed therapeutics approved by the FDA—5-azacytidine (AZA), rapamycin (RAP), and metformin (MET)—will reduce MTB proliferation *in vivo*.
Methods: Using a mouse model of acute MTB infection, 80 BALB/C mice were inoculated with approximately 10,000 aerosolized MTB bacilli. Infected mice were divided into four groups of 20 animals treated with either AZA (2mg/kg/day, 5days/week, Intraperitoneal), RAP (.5mg/kg/day, 5days/week, Intraperitoneal), MET (500mg/kg/day, 5days/week, oral gavage), or untreated (control). Five mice from each treatment group were sacrificed at 6, 14, 21 and 24 days. Lungs were removed and analyzed for the number of colony forming units (CFUs) present. Lung tissue was homogenized, diluted logarithmically, and plated on 7H10 medium.
Results: Analysis of the initial infection in three control mice on day 3 revealed that mice were infected with approximately 9600 ± 2750 CFUs. Comparison of CFUs present in the lungs of different treatment groups at the final time point showed that the only significant increase in CFUs was within the lungs of the MET treated group compared to the untreated controls ($F = 10.83$; $P > .05$), contrary to published data.
Conclusion: This study suggests that the courses of AZA, RAP, and MET treatment are not appropriate monotherapies for acute MTB infection in the mouse model for TB. Preliminary analyses from splenocytes, however, suggest differing systemic immune responses by treatment group. As such, further research will investigate potential synergistic effects between host-directed therapies and approved anti-tuberculosis drugs.

Project Length: Intermediate
H-3

TITLE
A Case for Point-of-Care Testing for Chlamydia and Gonorrhea in the Emergency Department Setting

Kristin M. Olson, MPH[1,2], James W. Galbraith, MD[3], Grace N. Cain[4], William M. Geisler, MD MPH[2,5]
UAB: Department of Biostatistics[1]; Medical Scientist Training Program[2]; Department of Emergency Medicine[3]; School of Medicine[4]; Division of Infectious Diseases, Department of Medicine[5]

ABSTRACT
Background: Previous studies suggest emergency departments (EDs) may be an ideal setting for chlamydia and gonorrhea screening. However, limited data exists on frequency of adequate treatment for chlamydia and gonorrhea in the ED at the time of testing and the ability of ED staff to contact and reach patients to ensure treatment.
Objectives: The primary objective of this study was to describe the frequency of adequate empirical treatment of chlamydia and/or gonorrhea at the time of visit in the ED. The secondary objective was to describe the frequency of treatment initiated by callback of those who did not receive adequate empirical treatment.
Methods: We conducted a retrospective analysis of clinical and STI callback data collected at the University of Alabama at Birmingham Hospital ED of patients with a positive chlamydia and/or gonorrhea test, diagnosed by nucleic acid amplification testing, from January 2013 to April 2014.
Results: 114 women and 40 men were included: 95 (62%) with chlamydia, 42 (27%) with gonorrhea, and 17 (11%) with co-infection. Rates of adequate treatment at time of visit were 83% for chlamydia alone, 48% for gonorrhea alone, and 53% for co-infection. Of those not empirically treated (n=46), 74% were successfully notified. Average time to successful notification was 4.2 days (95% CI 3.3-5.1), requiring an average of 1.9 callback attempts (95% CI 1.6-2.2). Age, race, and insurance type did not affect rates of adequate treatment or successful notification.
Conclusions: A significant proportion of chlamydia and gonorrhea is not adequately treated in the ED setting at the time of visit. Callback by ED staff may be an effective method of notifying patients of their diagnosis; however, one in four could not be contacted and may not have been treated. Our results suggest ED settings may benefit from point-of-care tests to facilitate screening and prompt treatment.

Project Length: Long
H-4

Cytomegalovirus Blocks Mucosal TGF-β-induced Inflammation Anergy by Up-regulating Macrophage MyD88-dependent NF-κB Signal Transduction and Smad7 Expression

Evida A. Dennis[*], Lesley E. Smythies, PhD[*], Lois C. Musgrove[*], Mao Li, MD[#], Masako Shimamura, MD[¶], *William J. Britt, MD[#] and Phillip D. Smith, MD*[*§]

[*]Departments of Medicine (Gastroenterology), [#]Pediatrics (Infectious Diseases). University of Alabama at Birmingham, Birmingham, Alabama 35294; [¶]Nationwide Children's Hospital (Infectious Diseases), Columbus, Ohio 43205; and the [§]VA Medical Center, Birmingham, Alabama 35233

Introduction: Cytomegalovirus (CMV) is a herpesvirus that induces severe inflammatory disease in immunocompromised persons. The gastrointestinal mucosa is one of the most common sites of CMV disease and mucosal macrophages are involved in mediating the inflammatory response. However, under homeostatic conditions, monocytes that recruit to the intestinal mucosa differentiate into resident macrophages that are strictly non-inflammatory (inflammation anergic) through stromal TGF-β-mediated inactivation of NF-κB.

Objectives: The objective of this study was to elucidate the mechanism by which CMV promotes macrophage-mediated mucosal inflammation despite the local abundance of stromal TGF-β.

Methods: We used primary macrophages isolated from human intestinal mucosa and blood monocytes, the exclusive source of intestinal macrophages, exposed to stromal TGF-β, which induces cells with the phenotype and function of non-inflammatory intestinal macrophages, to determine whether CMV reverses or prevents the induction of inflammation anergy.

Results: CMV infected, but did not replicate in or induce TNF-α, IL-6, or IL-1β release by, primary intestinal macrophages. However, pre-infection of monocytes with CMV (1) caused macrophage-mediated inflammatory responses (TNF-α, IL-6, IL-1β production) despite the presence of down-regulatory stromal TGF-β; (2) up-regulated MyD88 expression in the presence of stromal products, thereby enhancing responsiveness to TLR4/5 stimulation, which was confirmed in MyD88 siRNA knock-down studies; (3) blocked stromal inactivation of NF-κB; and (4) up-regulated expression of Smad7, the antagonist of TGF-β signaling, which blocked inducible phosphorylation of Smad2, thereby enhancing the resistance of CMV-infected monocytes to stromal TGF-β immunosuppression.

Conclusions: These findings suggest that blood monocytes infected with CMV prior to their recruitment to the intestinal mucosa are resistant to stroma-driven induction of inflammation anergy leading to heightened pro-inflammatory cytokine release in response to TLR ligation. Thus, CMV-infected mucosal macrophages are primed to induce or exacerbate mucosal inflammatory disease in response to bacteria or bacterial products.

Project Length: Long
H-5

Virologic characteristics associated with transmission of CMV via breast milk

Noora Siddiqui, *Suresh Boppana, MD*, Sunil Pati, PhD.

Pediatric Infectious Disease, UAB, Birmingham, AL.

Introduction: Cytomegalovirus (CMV) is a leading non-genetic cause of hearing loss and developmental disabilities. About half of the infants exposed to CMV in breast milk (BM) will become infected during the first 6 months. The overall goal of the project is to exploit this *in vivo* model acquisition to define virologic and immunologic correlates of CMV transmission.

Objectives: The objective was to examine virologic characteristics associated with BM transmission of CMV.

Methods: CMV seropositive mothers and their babies were enrolled in a prospective study to monitor for CMV acquisition during the first 6 months of life. Using real-time PCR, CMV shedding in BM samples from 28 mothers whose infants acquired CMV (transmitters) and 20 mothers with uninfected infants was determined. CMV load and duration of shedding were compared between transmitters and non-transmitters. Genotyping of CMV envelope glycoproteins, gB, gH, and gN in BM and infant saliva was performed.

Results: All study women had CMV in BM at least once during the study. More transmitters (46%) had CMV in BM at the 1st visit compared with 20% of non-transmitters. Most transmitters (82%) had CMV in BM at ≥3 visits compared with only 15% of non-transmitters (p=<.0001). Transmitters also shed CMV in BM for significantly longer periods (60.7 ± 43.0 days) than non-transmitters (10.4 ± 17.3 days). The mean peak BM CMV load was significantly higher for transmitters ($2.3x10^4$ copies/mL) than non-transmitters ($1.4x10^3$ copies/mL). Two or more genotypes were observed in majority of BM and infant saliva without significant statistical difference.

Conclusions: Significant differences in CMV shedding and viral load in BM were observed in transmitters and non-transmitters. Transmitting women shed longer with higher viral loads compared to non-transmitters. The occurrence of transmission of multiple virus strains via breast milk was documented. The study is ongoing to examine immunologic correlates of transmission.

Project Length: Long
H-6

Jeffrey Singer

Disturbed Succession of the Microbiome in Neonates Allows Opportunists to Bloom

Primary succession of microbial species that populate the mammalian intestinal tract is critically important to host health. During infancy, especially in premature infants, the microbiome is vulnerable to blooms of opportunistic pathogens. These microbes may also translocate from the intestines into the bloodstream, causing Late Onset Sepsis (LOS). Clinical investigations have suggested a role for the microbiome in the pathogenesis of LOS, but the exact mechanisms remain unclear.

Using a novel murine model of LOS with culture-based and 16s rRNA sequencing techniques, we show that early microbiome "health" is essential to buffer intestinal blooms and prevent blood-borne infection. We find gnotobiotic rearing or broad-spectrum antibiotic exposure increases opportunistic outgrowth and rates of sepsis. Susceptibility correlates with decreased richness in the intestinal microbiome and increased translocation. Interestingly, only gram-negative and not gram-positive-specific antibiotics negatively alter the susceptibility to blooms from either gram-negative or gram-positive organisms.

Taken together, these data suggest that the pioneering members of the microbiome offer an important buffering capacity to prevent overgrowth and blood-borne infections by potentially invasive organisms. Perturbing colonization dynamics of the microbiome through the use of broad-spectrum gram-negative antibiotics may dramatically reduce this capacity and lend an already vulnerable host further susceptible to opportunistic infections.

Project Length: Short
I-1

Title: Ocular and Vestibulo-Ocular Biomarkers for Concussion in Collegiate Student Athletes

Authors: **Graham D. Cochrane**[1], *Jennifer Braswell-Christy, PT, PhD*[2], Claudio Busettini, PhD[3], Anwar Almutairi, PT[2], Katherine K. Weise, OD[3]

1. Medical Scientist Training Program, University of Alabama at Birmingham, Birmingham AL
2. Department of Physical Therapy, University of Alabama at Birmingham, Birmingham AL
3. Department of Vision Sciences, University of Alabama at Birmingham, Birmingham AL
4. Department of Optometry, University of Alabama at Birmingham, Birmingham AL

Introduction: Sports-related mild traumatic brain injuries, also known as concussions, are now known to be incredibly common and yet are difficult to diagnose. Concussion diagnoses are primarily based on subjective symptom scores. Two of the most common symptoms of concussion are dizziness and blurred vision, suggesting there may be a visual and/or vestibular component to concussion. **Objectives:** Determine whether or not measurable, consistent changes in vestibulo-ocular function occur following concussion. **Methods:** Using a rotary chair equipped with an infrared eye tracking system, and in partnership with UAB athletics, we will complete baseline ocular and vestibulo-ocular testing on an extensive eye tracking battery on student athletes. Any athlete diagnosed with a concussion will return to complete a post-injury battery within 48 hours of injury to see any changes in eye or vestibular function related to concussion injury. Our battery includes horizontal/vertical saccades, anti-saccades, predictive saccades, visual and auditory reaction times, subjective visual horizontal/vertical (SVH and SVV), and vestibulo-ocular function tests. **Results:** 30 athletes (age 19.8±1.7, 11 female, 19 male) from the football and women's soccer teams have been recruited for baseline testing. Preliminary data shows an anti-saccade error rate of 60±20%, visual and auditory reaction latency of 278±76ms and 285±44ms, respectively, an SVH mean error of 0.81±1.7 and SVV mean error of 0.54±1.68 degrees. A significant difference in predictive saccades between genders was found with women performing significantly better ($p = 0.01$) by predicting 10 out of 12 pattern movements vs 5 of 12 for males. **Conclusions:** While our primary goal is investigating post-injury outcomes, our preliminary baseline data and feedback from athletes indicates that our methods of data collection are producing expected results and that the battery is not too cumbersome mentally on the athletes.

Project Length: Short
I-2

TITLE
UTILITY OF LABORATORY TESTING IN PEDIATRIC DEMYELINATING DISORDERS

AUTHORS
Claire E.C. Cordes, MS2; University of Alabama School of Medicine; Birmingham, Alabama
Pallavi Ghosh, M.D., MPH; Department of Pediatric Emergency Medicine; Children's Hospital of Alabama; Birmingham, Alabama
Jayne M. Ness, M.D., Ph.D; Department of Pediatric Neurology; Children's Hospital of Alabama; Birmingham, Alabama

INTRODUCTION
Pediatric demyelinating diseases can often pose a diagnostic challenge to clinicians; thus, it is important for health care providers to be aware of how laboratory testing can facilitate the correct diagnosis of demyelinating disease versus its mimicking diseases (including infectious, rheumatologic, neoplastic, and vascular syndromes).

OBJECTIVES:
The primary objective of this study is to determine the utility of laboratory evaluation in differentiating demyelinating vs. non- demyelinating disease.

METHODS:
This retrospective study is analyzing laboratory values in >470 pediatric patients with suspected demyelinating diseases that have been prospectively followed through the UAB Center for Pediatric Onset Demyelinating Disease (CPODD) at Children's of Alabama.
Extensive chart review and data collected included the following: CSF: cell count, glucose, protein, bacterial cultures, and multiple sclerosis panel (oligoclonal bands, IgG Index) Serum: Inflammatory markers: *erythrocyte sedimentation rate (ESR);* Autoantibodies associated with autoimmune disease: *anti nuclear antibody(ANA), rheumatoid factor (RF), Smith RNP Antibody, antineutrophil cytoplasmic antibody (ANCA), Sjogren antibodies SSA/SSB*; *anti-phospholipid and anticardiolipin antibodies*; Sarcoid disease: *Angiotension Converting Enzyme (ACE);* Endocrine function: thyroid function tests *(T4, TSH-thyroid stimulating hormone)*; Vitamin D3; Aquaporin 4 antibody for suspected NMO.
Normal vs. abnormal lab results were compared in patients with demyelinating vs. non demyelinating disease with regard to lab values with highest yield; difference in timing (acute vs. convalescent) and possible predictors to identify non-demyelinating mimics over time. Results were classified as acute if obtained within 30 days of initial symptom onset, and convalescent if drawn >30 days later.

RESULTS
Preliminary results suggest that ESR, ANA, and anti-phospholipid antibodies provide the highest yield in screening pediatric demyelinating patients for autoimmune disorders.

CONCLUSIONS
This study will identify laboratory tests that aid in distinguishing demyelinating disease from non-demyelinating mimics. Ultimately, this study will aid clinicians in reducing the amount of laboratory tests done, and thus provide a cost-effective, evidence-based evaluation.

Project Length: Short
I-3

Title: Age-Related Macular Degeneration and Visualizing Cholesterol within Photoreceptors

Authors: **Benjamin Echols**; *Christine A. Curcio, Ph.D.*, Department of Ophthalmology, UAB, Birmingham, AL; Jeffrey D. Messinger, DC, Dept. of Ophthalmology, UAB, Birmingham, AL.

Introduction: Age-related macular degeneration (AMD) is the leading cause of untreatable blindness of the elderly in the developed world. AMD results when the macula, the central portion of the retina deteriorates. Two lesions associated with AMD are drusen and sub-retinal drusenoid deposits. One factor common to both is the presence of cholesterol, yet differences in the type of cholesterol have been shown. This variation has been hypothesized to be the result of the variation of membrane cholesterol content in rods and cones, the two types of photoreceptors in the retina. No study previously has attempted to demonstrate this variation visually.

Objectives: The primary objective is to establish protocols for tissue handling, staining, and photomicrography to visualize cholesterol forms via histochemistry.

Methods: The methods included sectioning wild type mouse retinas at a thickness of 0.5 µm using a cryostat. Upon sectioning, fluorescent histochemical staining was preformed using a variety of stains. These stains included, DAPI (4',6-diamidino-2-phenylindole), propidium iodide, phalloidin, and filipin. Each of these stains are specific for different histological features within the retina. Once the staining protocols were established and followed, the stained sections were imaged using fluorescent microscopy and the images analyzed.

Results: The fluorescent stains proved that they will bind to their intended cellular structures and this allows for the proper identification of photoreceptor nuclei, cell membranes, and the cholesterol within those membranes.

Conclusion: Though the use of fluorescent histochemistry, cholesterol could be properly visualized in in the outer segments of both rods and cones. However, further methodological development is necessary to allow for the differentiation of rods and cones, if such exists.

Project Length: Short
I-4

The role of lipid accumulation in the pathogenesis of acute spinal cord injury

Hamelmal Kassahun, Betty Pat, Candace Floyd

Abstract
INTRODUCTION: The pathophysiology of spinal cord injury (SCI) can be divided into two phases, primary mechanical injury that directly disrupts axons, blood vessels and cell membranes and a secondary injury phase involving free radical production and apoptosis. Several studies have shown that free radical-induced lipid peroxidation (LP) plays a significant role in post-traumatic spinal cord degeneration and development of neuropathic pain.

OBJECTIVES: The primary objective of this study was to determine changes in lipid and fatty acid accumulation following acute cervical SCI.

METHODS: Adult male rats were used to evaluate the effect of hemi-contusion injury on acute histological changes in lipid accumulation. Animals were divided into two groups: (1) uninjured laminectomy (LAM) control (N=3); (2) hemi-contusion SCI at cervical level 5 (N=3). At 48 hours post-SCI, animals were euthanized and perfused. Cervical spinal cord segments were extracted and prepared for histological analysis. Tissue sections were stained using Oil Red O (ORO) in order to quantify neutral lipid accumulation.

RESULTS: Area and Integrated Density (product of area and mean pixel intensity of ORO staining) were analyzed for rostral (C4), epicenter (C5) and caudal (C6) sections from LAM and SCI animals. Rostral and caudal sections did not show a significant difference between the two groups for both parameters (area, $p=0.4107$ (rostral); $P=0.6270$ (caudal) and IntDen, $P=0.1910$ (rostral); $P=0.5785$ (caudal)). There was significantly less ORO staining at the epicenter of SCI animals, area ($p<0.05$) and IntDen ($P<0.05$).

CONCLUSION: No significant neutral lipid accumulation was seen in SCI animals at this acute time point. However, there was a significant reduction in ORO staining intensity at the epicenter in SCI animals which can be explained by the loss of myelin rich white-matter after 48 hours.

Project Length: Intermediate
I-5

Experience Dependent Epigenomic Reorganization in the Hippocampus

Corey G. Duke*, Andrew J. Kennedy+, J. David Sweatt++, *Jeremy J. Day**
*Department of Neurobiology and Evelyn F. McKnight Brain Institute, University of Alabama at Birmingham, Birmingham, AL,
+Department of Neuroscience, Bates College, Lewiston, ME
++Department of Pharmacology, Vanderbilt University, Nashville, TN

Introduction: The formation and maintenance of new memories requires transcription and translation of genetic material, and epigenetic mechanisms such as DNA methylation and demethylation serve as powerful regulators of this gene expression that is crucial to these processes. Moreover, aberrant DNA methylation has been identified in neurological and psychiatric disease states associated with impaired cognition, such as Alzheimer's disease, autism-spectrum disorders, schizophrenia, and drug addiction. Despite the clear necessity for epigenetic and transcriptional changes in memory formation, the precise nature of these phenomena has not been comprehensively explored.
Objective: Our objective was to illuminate this area by harnessing whole-genome sequencing tools to systematically characterize memory-related changes in gene expression and DNA methylation status following memory acquisition.
Methods: Using a hippocampus-dependent memory task (contextual threat learning), we report widespread and coordinated DNA methylation changes in the hippocampus (CA1) of Sprague-Dawley rats that are specific to threat learning and target genes involved in synaptic transmission and neuronal communication.
Results: We observed thousands of significant gene expression and epigenomic changes that are experience dependent, and these modifications were evident as early as one hour following the learning experience, becoming more marked and pronounced after twenty-four hours. Gene ontology term analysis showed that significantly hypomethylated genes were enriched for functional categories related to synaptic transmission. Additionally, we integrated these datasets with previously characterized epigenetic and transcriptional changes in brain disease states to provide a comprehensive resource to aid in the identification of memory-relevant therapeutic targets.
Conclusion: Our results shed new light on the gene expression and methylation changes involved in memory formation suggesting that this process is dynamic and experience dependent, in addition to providing a roadmap for future work to identify therapeutic targets.

Project Length: Intermediate
I-6
Assessment of Neuronal Activity in Reward-Associated Behavioral Circuits

Morgan E. Zipperly[12], John J. O'Malley[2], Andrew C. Brane[2], Kaela J Kelly[2], & *Jeremy J. Day, PhD*[2]

[1]Medical Scientist Training Program, University of Alabama at Birmingham, Birmingham, AL
[2]Department of Neurobiology, University of Alabama at Birmingham, Birmingham, AL

Purpose: Addiction is an increasingly prevalent problem in the United States, associated with progressively higher rates of morbidity and mortality. Exposure to drugs of abuse leads to reorganization of neural circuits and alteration of synapses, which outlive the direct effects of the drug and may contribute to addiction. The nucleus accumbens (NAc) has a significant role in motivation, pleasure, and reward, and has been identified as a key area in the development and maintenance of addiction. The present study aims to determine how neuronal activity in the NAc is altered in response to cocaine. Our central hypothesis is that administration of cocaine will increase neuron firing in the NAc, and that optogenetic photoactivation of different circuits involving the NAc will affect reward-seeking behavior and drug-evoked neuroplasticity.

Methods: In order to assess how neuronal activity in the NAc are altered as a result of drug exposure, cell firing was recorded in vivo from electrode microarrays bilaterally implanted in the NAc of naive male Sprague Dawley rats that have been exposed to either cocaine (10mg/kg) or saline. In an additional group of animals, channelrhodopsin (ChR2) was infused into target brain regions and optogenetic guides were surgically implanted over the NAc to determine if photostimulation of neurons and circuits in this area will affect reward-motivated behavior.

Results: As predicted, acute cocaine exposure increased activity of a subpopulation of neurons in the NAc, independent of environment or context. In addition, preliminary data show that protein expression and photostimulation of ChR2 in the NAc core seem to increase reward-seeking behavior.

Conclusions: By elucidating how cocaine exposure alters the activity of specific cell populations and specific neuronal circuitry involving the NAc, we may identify important mechanisms underlying the etiology of addiction and relapse, as well as propose novel targets for preventive and therapeutic interventions.

Project Length: Intermediate
I-7

Brandon J. Pope*, Etty T. Benveniste,Ph.D^, Hongwei Qin,Ph.D^, Erik Roberson,M.D.,Ph.D+;*UAB MSTP Program, Birmingham, Alabama, ^Cellular, Developmental, and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL, +Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama

Progranulin Deficiency and EAE: The Impact of Infiltrating Immune Cells and Resident Microglia

Purpose: Progranulin is a secreted protein that plays an important role in neurite outgrowth and proper lysosomal function in neurons. Mutations found within the bases that code for progranulin (GRN), have been shown to lead to lower levels of progranulin protein in vivo. A number of GRN mutations have been causally connected to certain subtypes of frontotemporal dementia and adult variant neuronal ceroid lipofuscinosis. Mouse models that lack progranulin have abnormal inflammation and immune cell activation within the central nervous system and the periphery. In our mouse model of global progranulin deficiency, mice develop specific abnormalities in fear conditioning, accelerated lipofuscin deposits within their brains, and exaggerated microgliosis with age.

We seek to investigate the role of JAK/STAT signaling in microglia and infiltrating immune cells in the context of experimental autoimmune encephalitis during progranulin deficiency.

Methods/ Results: On a C57BL6/J mouse background, we induced the deletion of the gene for progranulin, in one and both sets of chromosomes. We will induce experimental autoimmune encephalitis (EAE), by adoptive transfer and active immunization with MOG_{35-55}. From there, we will examine the surface and intracellular markers of immune activation in infiltrating macrophages and resident microglia within the CNS. From data gathered within the field, we predict there will be an increase in the amount of infiltrating macrophages and a proinflammatory shift in the phenotype of resident microglia that is exacerbated by the progranulin deficiency with age.

Conclusions: These experiments will shed light on the role that progranulin protein plays in driving inflammation and activation of inflammatory cells in the context of EAE within the central nervous system in a mouse model of progranulin deficiency.

Project Length: Long
I-8

Dynamic DNA Methylation Regulates Levodopa-Induced Dyskinesia

Authors: **David Figge[1]**, Karen L. Jaunarajs[1], David G. Standaert[1]

[1] Center for Neurodegeneration and Experimental Therapeutics, Department of Neurology, The University of Alabama at Birmingham, Birmingham, AL, USA

Levodopa-induced dyskinesia (LID) is a persistent behavioral sensitization that develops after repeated levodopa (L-DOPA) exposure in Parkinson disease (PD) patients. LID is a consequence of sustained changes in the transcriptional behavior of striatal neurons following dopaminergic stimulation. In neurons, transcriptional regulation through dynamic DNA methylation has been shown pivotal to many long-term behavioral modifications; however, its role in LID has not yet been explored. Using a rodent model, we show LID development leads to the aberrant expression of DNA demethylating enzymes and locus-specific changes to DNA methylation at the promoter regions of genes aberrantly transcribed following L-DOPA treatment. Looking for dynamic DNA methylation in LID genome-wide, we used reduced representation bisulfite sequencing and found an extensive reorganization of the striatal methylome. LID development led to significant demethylation at many important regulatory areas of aberrantly transcribed genes. We used pharmacologic treatments that alter DNA methylation bi-directionally and found them able to modulate dyskinetic behaviors. Together, these findings demonstrate that L-DOPA induces widespread changes to striatal DNA methylation, and that these modifications are required for the development and maintenance of LID.

Project Length: Long
I-9

Title: Memory retrieval triggers H3K4me3 in association with increased DNA hydroxymethylation activity at memory-permissive genes.

Authors: **William M. Webb**, Richard G. Sanchez, Gabriella Perez, Anderson A. Butler, Rebecca M. Hauser, Megan C. Rich, Aiden L. O'Bierne, Daniel L. Ross, Timothy J. Jarome, and *Farah D. Lubin*

Affiliations: University of Alabama at Birmingham

Introduction: Epigenetic mechanisms such as DNA methylation and post-translational histone modification have emerged as critical regulators of gene transcription changes during the memory formation (or consolidation) process; however, little is known about the role of these mechanisms during memory retrieval and reconsolidation.

Objective: To determine whether specific epigenetic mechanisms function together to regulate expression of memory-permissive genes during retrieval. Specifically, we tested a dynamic association between DNA hydroxymethylation (5-hmC) and H3 lysine 4-trimethylation (H3K4me3) in the hippocampus following retrieval of a recent or remote memory.

Methods: Using chromatin immunoprecipitation (ChIP), hydroxymethylated DNA immunoprecipitation, and mass spectrometry, we interrogated genes with a known role in reconsolidation and tested for correlations between epigenetic markers following context fear conditioning in rats.

Results: We found significant increases in global H3K4me3 and DNA 5-hmc levels in area CA1 region of the dorsal hippocampus following memory retrieval. ChIP analysis revealed that H3K4me3 and DNA 5-hmc levels were increased at CpG-rich regions of the *Npas4*, but not *c-fos*, gene. Surprisingly, retrieval of a 30-day old remote memory increased H3K4me3 and DNA 5-hmc levels at a CpG-rich region of *c-fos*—but not *Npas4*—in the anterior cingulate cortex, suggesting that while these two epigenetic mechanisms occur together following the retrieval of new and old memories, their gene targets differ. Furthermore, we found that *in vivo* siRNA-mediated knockdown of the H3K4me3 methyltransferase *Mll1* in the hippocampus abolished retrieval-induced increases in *Npas4* DNA 5-hmc levels, suggesting that H3K4me3 recruits DNA 5-hmc to regulate active transcription of the *Npas4* gene. Consistent with this, a loss of *Mll1* prevented increases in *Npas4* gene expression during memory reconsolidation.

Conclusion: These findings suggest an important molecular link between H3K4me3 and 5-hmC in the epigenetic control of gene transcription during the reconsolidation process.

Project Length: Long
I-10

Identification of region-specific miRNA-mRNA networks in the dorsal raphe and amygdala of high-responder/low-responder rats.

Joshua L. Cohen, B.S.[1], Anooshah E. Ata, B.S.[2], Nateka L. Jackson, B.S.[3], Elizabeth J. Rahn, Ph.D.[3], Ryne C. Ramaker, B.S.[1,4], Sara Cooper, Ph.D.[4], Ilan A. Kerman, M.D./Ph.D.[5], and *Sarah M. Clinton, Ph.D.*[5]

Introduction*:* Chronic stress triggers a variety of physical and mental health problems, and how individuals cope with stress influences risk for emotional disorders. To investigate molecular mechanisms underlying distinct stress coping styles, we utilized rats that were selectively-bred for differences in emotionality and stress reactivity. High Responder (HR) rats vigorously explore new environments compared to rats bred for low novelty response (Low Responders, LRs). In addition to differential stress responses, HR/LR rats recapitulate a phenomenon observed in humans, that proactive vs. reactive coping styles predict vulnerability to different stressors.

Objectives: Identify brain regions the determine if differences in transcriptomics within those brain regions may contribute to the HR/LR stress phenotype

Methods*:* Immunohistochemistry to measure the number of c-Fos (a marker of neuronal activation) and Tph (a marker of serotonin neurons) in the dorsal raphe and amygdala of shock-exposed HR/LR rats. Sequencing of mRNA and miRNA from dorsal raphe and amygdala of HR/LR rats.

Results*:* Shock exposure elicited greater activation of HR rats' caudal dorsal raphe serotonergic cells compared to LRs, but lead to more pronounced activation throughout LRs' amygdala compared to HRs. RNA-sequencing revealed 271 mRNA transcripts and 33 microRNA species that were differentially expressed in HR/LR raphe and amygdala. We identified microRNA-mRNA networks that differed in either the HR/LR dorsal raphe or amygdala. In the dorsal raphe, a predicted network linked three microRNAs down-regulated in LRs (miR-206-3p, miR-3559-5p, and miR-378a-3p) to repression of microglia and immune response-related genes (*Cd74*, *Cyth4*, *Nckap1l*, and *Rac2*) that were up-regulated in LR dorsal raphe. In the amygdala, another network linked miR-124-5p, miR-146a-5p, miR-3068-3p, miR-380-5p, miR-539-3p, and miR-7a-1-3p with repression of chromatin remodeling-related genes (*Cenpk*, *Cenpq*, *Itgb3bp*, and *Mis18a*).

Conclusion*:* Overall this work highlights potential drivers of gene-networks and downstream molecular pathways within the raphe and amygdala that contribute to individual differences in stress coping styles and stress vulnerabilities.

Project Length: Long
I-11

Effect of O-linked ß-N-acetyl-glucosamine post-traumatic brain injury

R M. Lockhart, MS[1], K. Wang[2], E. Taylor, PhD[2], K. Bradley[1], J. Chatham, PhD[3] L. McMahon, PhD[2], *C L. Floyd, PhD[1]*

[1]Department of Physical Medicine and Rehabilitation, [2]Department of Cell, Developmental and Integrative Biology, [3]Department of Pathology

The University of Alabama at Birmingham

Birmingham, AL

INTRODUCTION: Traumatic brain injury (TBI) is a leading cause of death and disability worldwide. Of all types of injury, TBI is among the most likely to result in permanent disability and is a significant risk factor in the development of neurodegenerative disease. There are currently no FDA-approved therapeutic agents for the treatment of TBI. It has been recently discovered that modification of proteins by the O-linked attachment of ß-N-acetyl-glucosamine (O-GlcNAc) reduces cellular damage after injury.

METHODS: In this study, the potential neuroprotective effects of a new drug, *thiamet-G,* which increases the amount of O-GlcNAc modifications on proteins in the brain, will be tested. TBI will be induced using a clinically-relevant translational rat model. Animals will be administered *thiamet-G* beginning at 30 min post-TBI at 10 mg/kg. The rodents will be humanely euthanized 12 and 24 hours post-TBI and brains extracted for biochemical and histological markers of O-GlcNAc signaling and cell death. Brains will also be extracted and evaluated using electrophysiological techniques to measure the electrical function of the brain that is related to learning and memory processes.

RESULTS: We observed a significant reduction in neuronal cell death in the *thiamet-G* treated group as compared to vehicle in the ipsilateral cortex and hippocampus ($p < 0.05$). Long term potentiation (LTP) on the ipsilateral side of injury was induced in the animals treated with *thiamet-G* but not in the injured vehicle group.

CONCLUSION: To our knowledge, this is the first demonstration that increasing protein O-GlcNAc levels can significantly reduce neuronal injury and this beneficial effect can be induced post-TBI. Therefore, the treatment of post-TBI protein augmentation of O-GlcNAc is a novel therapeutic approach for increasing cell survival and reducing TBI-induced pathology.

Project Length: Long
I-12

Title: Reduction in Tau as a Therapeutic Intervention for Nonmotor Manifestations of Parkinson's Disease

Authors: **Lindsay E Stoyka**+, *David G Standaert*+, MD, PhD, and Laura A Volpicelli-Daley*+, PhD*

Affiliations: *Center for Neurodegeneration and Experimental Therapeutics, University of Alabama at Birmingham, Birmingham, AL; +Department of Neuroscience, University of Alabama at Birmingham, AL

Introduction: Motor dysfunction in Parkinson's disease is a hallmark of the disease. Cognitive dysfunction and other nonmotor deficits, however, contribute to a greatly decreased quality of life for patients. Specifically, Parkinson's Disease Dementia (PDD) affects up to 80% of PD patients. Therapeutics are available to ameliorate motor symptoms, but current treatment for nonmotor symptoms of PD is limited and does not prevent disease progression. The protein tau is a microtubule associated protein that stabilizes the cytoskeleton, and abnormalities in tau characterize AD. Reducing tau prevents cognitive abnormalities in animal models of AD. Although genetic variation in tau consistently produces a strong signal in genome wide association studies (GWAS) evaluating risk factors for sporadic for PD, the link between tau and PD is unknown.

Objectives: Our objective is to determine if tau reduction is an effective therapeutic intervention for preventing or ameliorating nonmotor manifestations of PD, specifically dementia and mood disorders. We will determine if absence of tau reduces formation of aggregates of alpha-synuclein in the brain, a hallmark of PD. We will also determine if reducing tau prevents cognitive dysfunction in mice with alpha-synuclein aggregates.

Methods: Aged (>12 months old) tau -/- and tau +/+ mice were injected unilaterally into the somatosensory cortex with preformed fibrils of alpha-synuclein to induce Lewy body-like pathology. Four months post-injection, mice underwent behavioral testing to determine cognitive deficits, including open field test, novel object location, elevated zero maze, forced swim test, Morris water maze, and cued fear conditioning. At the conclusion of behavioral testing, mice underwent perfusion for immunohistochemistry. Coronal brain sections were stained for phosphorylated alpha-synuclein with a Nissl counterstain. Unbiased stereological counts of phosphorylated alpha-synuclein aggregates were completed in the amygdala, cortex, and striatum.

Results: At the time of abstract publication, data analysis was still underway and therefore results will be forthcoming.

Project Length: Long
I-13

MeCP2 Deficiency Results in Robust Rett-like Behavioral and Motor Deficits in Male and Female Rats

Kelsey C. Patterson*, Virginia E. Hawkins+, PhD, Kara M. Arps*, Daniel K. Mulkey+, PhD*, Michelle L. Olsen*, PhD*

*Department of Cell, Developmental, and Integrative Biology, University of Alabama at Birmingham, Birmingham, AL
+ Department of Physiology and Neurobiology, University of Connecticut, Storrs, CT

Introduction: Rett Syndrome (RTT) is an x-linked neurodevelopmental disorder affecting approximately 1/10,000 girls annually. Since the identification of MECP2 as the causative gene in the majority RTT cases, transgenic mouse models have played a critical role in our understanding of this disease. The use of additional mammalian RTT models offers the promise of further elucidating critical early mechanisms of disease as well as providing new avenues for translational studies.

Objectives: Here, we aim to address the utility of a novel zinc-finger nuclease model of RTT by tracking changes in growth as well as motor and behavioral deficits of male and female rats throughout development.

Methods: General locomotor activity was evaluated by open field, and motor capabilities were assessed by the RotorRod^{TM} and Catwalk^{TM} tests. Breathing parameters were measured by whole body unrestrained plethysmography. To confirm absence of MeCP2 protein, western blot was performed using cortical and brainstem tissue obtained from symptomatic MeCP2 deficient rats and wildtype controls.

Results: Male rats lacking MeCP2 ($Mecp2^{ZFN/y}$) were noticeably symptomatic as early as postnatal day 21, with most dying by postnatal day 55, while females lacking one copy of Mecp2 ($Mecp2^{ZFN/+}$) displayed a more protracted disease course. Brain weights of $Mecp2^{ZFN/y}$ and $Mecp2^{ZFN/+}$ rats were significantly reduced by postnatal day 14 and 21, respectively. Early motor and breathing abnormalities were apparent in $Mecp2^{ZFN/y}$ rats, whereas $Mecp2^{ZFN/+}$ rats displayed functional irregularities later in development.

Conclusions: The novel rat model in question recapitulates many hallmark features observed in existing RTT mouse models as well as human RTT patients. The large size of this species will provide profound advantages in the identification of early disease mechanisms and the development of appropriately timed therapeutics. The current study establishes a foundational basis for the continued utilization of this rat model in future RTT research.

Project Length: Short
J-1

TWEAK as a Marker for Muscle Inflammation Susceptibility in Total Hip and Total Knee Arthroplasty Patients

David Osula, *Irina Donahue*,PhD, and *Marcas Bamman*, PhD

Introduction: Elective total joint arthroplasty is the last resort for end-stage osteoarthritis (OA) and, in most cases, total hip or knee arthroplasty (THA or TKA) significantly improves pain, mobility, and quality of life. However, a large number of THA/TKA patients have significant difficulty recovering from THA/TKA, with continued pain, mobility impairment, and muscle atrophy. Impaired post-surgery recovery is believed to be due to impaired muscle regeneration caused by hyperactive, local pro-inflammatory signaling in the muscle, called **Muscle Inflammation Susceptibility (or MUIS)**. It is postulated that this inflammatory susceptibility is largely due to local upregulation of cytokine signaling pathways, i.e. TNF-alpha, IL-6, and a major protein of interest called **TWEAK (TNF-like weak inducer of apoptosis),** along with the expression of their respective receptors.

Objectives: Comparative studies of muscle tissue surrounding the diseased joint (i.e. surgical leg) vs muscle from the contralateral (control) leg of human subjects were conducted in order to make an $MuIS^{(+)}$ or $MuIS^{(-)}$ distinction for each patient.

Methods: Surgical vs. contralateral muscle samples were compared for myofiber size, type distribution, and cytokine receptor gene expression. Additionally, the myogenic potential of muscle-specific stem cells isolated and cultured from surgical vs. contralateral legs was assessed.

Results: Myofiber cross sectional area was indeed lower in surgical vs. contralateral muscle, indicating muscle atrophy of the affected (surgical) leg. Results of muscle tissue cytokine receptor gene expression and the myogenic behavior of primary muscle stem cells are currently being finalized and will also be presented.

Conclusion: Ultimately, these and future data will help determine, through the exercise rehabilitation component of the parent clinical trial, whether a resistance training regimen that is more robust than standard physical therapy improves outcomes for $MuIS^{(+)}$ patients.

Project Length: Short
J-2

Title/Authors:
Unbiased, comparative proteomic and genomic analysis of differentially regulated canonical pathways associated with hyperoxia-induced lung injury in newborn mice.

Joseph W. Granade. Tamas Jilling, Pankaj Jain, *Namasivayam Ambalavanan.* Division of Neonatology, Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, USA.

Introduction:
Bronchopulmonary dysplasia (BPD) is a chronic pulmonary disease that occurs in preterm infants that receive supplemental oxygen and mechanical ventilation as part of their respiratory management. The pathophysiological mechanisms of BPD have not been fully established.

Objectives:
We used an established murine model for BPD utilizing chronic hyperoxia exposure to explore differences in gene and protein expression profiles of hyperoxia-exposed mice and healthy controls. We performed unbiased transcriptome and proteomic analysis in order to identify potentially novel biomarkers and pathogenic mechanisms.

Methods:
Newborn C57BL/6 mice were exposed to 85% O2 (hyperoxia) or air (normoxia – 21% O2) from postnatal day 3 to 14 days. Whole lung homogenates were analyzed by gene expression profiling (microarray) and proteomic profiling by MALDI-TOF MS/MS. Ingenuity Pathway Analysis (IPA) software was used to perform analysis of significant expression differences for both the transcriptomic and proteomic datasets.

Results:
Our expression profiles revealed 602 differentially expressed genes (DEGs) of statistical significance ($P<0.05$) and 214 proteins with a greater than two-fold increase in protein expression in hyperoxia-exposed mice. IPA identified agranulocyte and granulocyte adhesion and diapedesis, hepatic fibrosis, oncostatin M signaling, IL-10 signaling, and inhibition of matrix metalloproteases as the most significantly DEG-enriched pathways. Though inflammatory pathways, such as acute phase response signaling and complement activation, were found to be dysregulated in our protein analysis, significant up-regulation of anti-inflammatory pathways was also evident. These pathways included FXR/RXR activation, LXR/RXR activation, and NRF2-mediated oxidative stress response. IPA's comparison analysis tool also highlighted a downregulation in the LXR/RXR activation pathway in the context of mRNA expression, but an upregulation in the protein expression of the pathway.

Conclusion:
Our findings indicate that various canonical pathways undergo both gene and protein dysregulation in hyperoxia-exposed mice. Further investigation of these altered pathways may be useful in establishing new potential treatment paradigms for attenuating the respiratory consequences of BPD.

Project Length: Short
J-3

Measurement and validation of step-length asymmetry using a novel clinical gait measurement tool
Jarvis J. Johnson; Avantika Naidu, PT; *David Brown, PT, PhD*

INTRODUCTION: Stroke is the leading cause of long term neurological disability in the US. Of the estimated 7 million current stroke survivors, greater than 50%, experience difficulty in community ambulating due to hemiparesis. Asymmetric, slow and inefficient gait patterns due to hemiparesis limit functional independence and negatively impact quality of life. In order to better design and implement rehabilitation measures, clinical gait analysis of all biomechanical parameters is necessary. Present biomechanical gait analysis to measure asymmetry requires sophisticated motion capture system (e.g. Qualysis). However, such analysis are time consuming, requiring extensive background training for use, and virtually impractical in the clinical setting. A new clinical gait analysis tool i.e. the Optogait, which is easy-to-operate, portable, and affordable may be viewed as a potential replacement.

OBJECTIVES: To examine the reliability and validity of the Optogait in measuring step-length asymmetry (SLA) in both non-impaired and individuals post-stroke, compared to the Qualysis system.

METHODS: A novel robotic device-split-belt treadmill interface was used to provide a safe walking environment and enable application of differential resistive forces. Participants targeted walking at their comfortable walking speed against differential force condition trials that induced step-length asymmetry. Spatiotemporal parameters using both systems was collected throughout all trials of the experiment.

RESULTS: Preliminary results of 5 individuals (3 non-impaired and 2 impaired) suggest that although biomechanical kinematic data can be collected by the Optogait, it is not accurate. The non-impaired trials lasted for 20 minutes with greater resistance on the left leg. From an observational standpoint, most individuals compensated for the resistance by taking shorter steps with the left leg and longer steps with the other leg. Additionally, the Optogaits data appears to confirm the observational results; however, in order to determine validity Qualysis data is needed for comparison. Note that post-stroke trials were modified based on the individual's capability.

CONCLUSION: Although, the Optogait is theoretically idea for clinical use, our results suggest that its measurements may not be valid. If used in a clinical setting, results have to be compared with established motion-capture systems like Qualysis to be deemed reliable and valid.

Project Length: Short
J-4

Intraluminal Thrombus Incidence in Clinically Significant Abdominal Aortic Aneurysm Patients is Markedly Higher Than the Currently Expected Rate

Zachary L. Whaley*, *Benjamin J. Pearce MD***

INTDROUCTION: Intraluminal thrombus (ILT) in abdominal aortic aneurysms (AAA) affects the rate of endoleak following endovascular repair of AAA (EVAR). Endoleak is a risk factor for postoperative sac expansion, which can lead to late failure of EVAR. Due to older and conflicting reports, the rate of ILT incidence and its specific effects on outcomes warrant further study.

OBJECTIVES: Establish a database describing the morphology and incidence of ILT and correlate it with postoperative outcomes of AAA repair.

METHODS: Perioperative data including patient history, CT imaging, surgical reports, and follow up exams from 271 patients who underwent EVAR at John Radcliffe Hospital (Oxford, UK) between 2009 and 2016 were used to create a database detailing the preoperative abdominal aortic morphology and postoperative outcomes of each patient. Criteria were set for the evaluation of ILT presence and quadrant location at the CT section containing the maximum aortic circumference. For this part of the study, the database was used to derive trends of the gathered data using simple statistics.

RESULTS: Of the 271 patients included in the database, 265 (98%) demonstrated intraluminal thrombus on preoperative CT imaging. At the maximum diameter of AAA, 107 (39%) were circumferential, 172 (63%) had ILT in each quadrant, 80 (30%) had ILT in 3 of 4 quadrants, and 7 (3%) had ILT in either 1 or 2 quadrants.

CONCLUSIONS: ILT rates are remarkably higher than the standard accepted rate of ILT in AAA, which is 75%. Because of the roles ILT plays in endoleak, and potentially postoperative sac expansion, further study could yield valuable information about preoperative morphology acting as an indicator of postoperative outcomes.

*-UAB School of Medicine, Birmingham, AL, in conjunction with The Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK

**-Department of Vascular and Endovascular Surgery, UAB, Birmingham, AL

Project Length: Short
J-5

Rehabilitation Referral for Patients with Irreversible Vision Impairment in a Publicly Funded County Clinic.

Michael A. Coker, *Cynthia Owsley Ph.D.*
Department of Ophthalmology, University of Alabama at Birmingham, Birmingham, AL

PURPOSE: A significant public health challenge for the U.S. is the large number of Americans with eye conditions that have caused irreversible vision impairment. African Americans, particularly those who are uninsured, have higher rates of irreversible vision impairment compared to other segments of the populations There is little to nothing known about their knowledge, attitudes, and beliefs about the availability, purpose, and benefits of visual rehabilitation services and their perceived barriers to rehabilitation care. The ophthalmology clinic at Cooper Green Mercy Health Services provides an excellent opportunity to address these questions.

OBJECTIVE: For patients with irreversible vision impairment, to examine their knowledge, attitudes, and beliefs about visual rehabilitation services including their purpose, benefits, and availability, and their perceived barriers to rehabilitation services and enablers to rehabilitation services.

METHODS: Written informed consent is obtained from all participants. The medical record from the most recent comprehensive eye examination provides information on visual acuity, visual field, demographics, etiology of vision impairment, whether vision impairment is stable or progressive, age of onset of eye condition causing impairment, age of onset for vision impairment, refractive error, current correction, referrals to visual rehabilitation services, and any follow-up referral reports on rehabilitation care. The participant will also be asked about previous use of visual rehabilitation services, the reasons for not going if referred to rehabilitation services, and experiences with rehabilitation services if they did in fact go (e.g., satisfaction, beliefs as to whether they helped).

RESULTS: The study is ongoing. 79 participants have been enrolled in the study to date. Thus far 80% of participants acknowledge that they have a vision impairment. 94% stated that they have never heard of “low vision rehabilitation services”.

CONCLUSIONS: Enrollment of participants will continue through the end of November 2016, at which time data will be analyzed.

Project Length: Short
J-6

Determination of Optimal Seeding Conditions of Fibroblasts in a Peptide Amphiphile Gel

Asher M. Krell, Chae Yun Bae PhD, Grant C. Alexander, *Ho-Wook Jun PhD*
Affiliation: Department of Biomedical Engineering

Introduction: The advent of minimally invasive cardiovascular stent placement has let to reduced mortality following acute myocardial infarction. Research in stent design and coating has been focused on reducing rates of restenosis and promoting endothelialization. However, there is a significant need for a blood vessel mimic allowing for rapid testing of new coatings in vitro. Our approach to developing this model includes layering conditioned sheets of aortic smooth muscle cells (AoSMCs) and human aortic fibroblasts (HF) in a tubular construct.
Objectives: The primary objective of this study was to characterize the growth and structural organization of HFs in a sheet-like nanomatrix gel under a range of seeding conditions.
Methods: HFs were encapsulated in a thin nanomatrix gel sheet, which is less than 100 μm in height. Encapsulation was done over a range of cell densities and for several different gel concentrations. Cross-linking reagent ($CaCl_2$, 100 mM), delivered as a mist from a humidifier, was applied onto the mixture to form a nanomatrix gel sheet. Tissue-like sheets were transferred to wells containing growth media and conditioned for variable amounts of time. Encapsulated cells inside the nanomatrix gel sheet were analyzed by Live/Dead and immunofluorescent staining.
Results: Images of live/dead staining for all HF conditions confirmed that cells were viable and growing inside nanomatrix gel sheets. Qualitative analysis of actin-stained images indicate that a seeding density of 9*10^5 cells/gel and a 1% gel concentration are ideal to promote cell expansion and physiological cell morphology. Confocal images of actin-stained constructs were taken following two weeks of cell growth and indicate cell division and development of cell-cell interactions.
Conclusions: We have developed optimal conditions for producing nanomatrix gel sheets containing viable HFs that can be used for producing in vitro blood vessels. Future studies include optimizing seeding technique for AoSMCs and development of a three layered vessel structure.

Acknowledgements: This program was supported in part by a grant to the University of Alabama at Birmingham from the Howard Hughes Medical Institute by the Med into Grad Initiative and NIH 1R01HL125391.

Project Length: Short
J-7

TITLE: Extubation to noninvasive ventilation versus supplemental oxygen after cardiopulmonary bypass in a pediatric cardiac intensive care unit

AUTHORS: R Wilson King, BS, Robert Richter, MD, Yuvraj Kalra, MD, Robert King, BS, Asaf Ganz, BS, *Santiago Borasino*, *MD, MPH*, Jeffrey Alten, MD

INTRODUCTION: Extubation failure occurs too often in the Children's of Alabama (COA) cardiac intensive care unit (CICU) after infants less than 200 days of age have undergone surgery using cardiopulmonary bypass (CPB). The decision to extubate to NIV or to supplemental oxygen needs to be examined in order to decrease extubation failure rate and other comorbidities associated with these patients.

OBJECTIVE: Evaluate whether these infants with increased risk for extubation failure have better outcomes if extubated to NIV versus extubation to supplemental oxygen in the CICU.

METHODS: 358 infants less than 200 days post congenital heart surgery requiring CPB were retrospectively analyzed by chart review. Relevant data elements were collected and analyzed for significant findings.

RESULTS: 28.5 percent of the patients were extubated to NIV, while the remaining 71.5% were extubated to supplemental oxygen. The NIV cohort had higher rates of extubation failure ($p = 0.009$) with an associated increase in hospital length of stay ($p < 0.001$), but were also found to be younger, smaller, and higher STAT category ($p < 0.01$). A neonatal subgroup analysis found that 54% of the neonates were extubated to NIV while the remaining 46% were extubated to supplemental oxygen. The NIV cohort had longer intubation times ($p < 0.001$) without significant difference in STAT category. No significant different in extubation failure rate was seen in this subgroup of patients.

CONCLUSIONS: The infants in the NIV cohort had an increased rate of extubation failure, but also were younger and had surgeries with a higher STAT category. The neonatal subgroup did not show a decreased extubation failure rate, but further analysis using multivariate and propensity score will be done to provide a more in depth assessment of the data. These findings will be the foundation for a future prospective trail.

Project Length: Short
J-8

Optimization of Laboratory Utilization Practices at UAB Hospital

Jeffrey Z Shen[1], Sherry Polhill[2], MBA, MT(ASCP)**,** Paula Evans[2], MT(ASCP)**,** David P Galloway[3], MD, Benjamin Hill[4], MD, Robert Johnson[2], RRT, MS, Lisa Rice-Jennings[2], MT(ASCP) *Robin G Lorenz[1] MD PhD*
[1]Department of Pathology, University of Alabama at Birmingham, Birmingham, AL
[2]University Hospital, University of Alabama at Birmingham, Birmingham, AL
[3]Department of Medicine-Gastroenterology, Children's of Alabama, Birmingham, AL.
[4]Department of Pathology, Children's of Alabama, Birmingham, AL.

Introduction

A national initiative called Choosing Wisely was founded in 2012 with the purpose of increasing awareness of unnecessary lab tests and encouraging progress to minimize them. As part of the national campaign, UAB Hospital has chosen to focus on two highly ordered tests – CBC and CBC with Diff.

Objectives

The primary objectives of this study was to investigate the effects of a quality improvement intervention on lab ordering practices of the Trauma Burn IC unit.

Methods

An investigation on lab ordering practices showed that at UAB Hospital, CBC with diff is ordered much more than CBC while the reverse is true in most hospitals. The UAB TBICU unit has the highest number of CBC and CBC w/diff orders, many of which were repeated on the same patient within less than 12 hrs. A tool was developed to guide ordering practices and implemented by the TBICU over a 2 week period in March 2016.

Results:

By comparison with 2 week periods in January and May 2016 (before and after the intervention) it was found that there was a statistically significant reduction in the amount of CBC with Diff ordered. There was also a significant change in the CBC with diff to CBC ratio as compared to other units such as NICU and SICU, which are the next top lab ordering units (these units have not undergone any intervention). The amount of lab tests repeated within 9-16hrs was also significantly reduced. All effects were retained at least until two months after the intervention.

Conclusions:

A quality improvement intervention optimized lab ordering practices of CBC with diff and CBC. These effects were retained for at least two months after the intervention. Future studies include seeing whether the same intervention can impact other units similarly and whether other tests can be optimized.

Project Length: Short
J-9

Title: Self-Compassion Scores in Post-Stroke Patients

Author Information: **Daniel P. McNeill**, MD Candidate University of Alabama at Birmingham School of Medicine, Class of 2019; *Dr. Victor W. Mark, M.D., Department of Physical Medicine and Rehabilitation, University of Alabama at Birmingham, Birmingham, Alabama; Dr. James H. Rimmer, Ph.D., Director of Lakeshore Foundation/University of Alabama at Birmingham Research Collaborative, Lakeshore Foundation and University of Alabama, Birmingham, Alabama*

Purpose: Self-compassion is a social characteristic involving how people view themselves during times of difficulty, including the areas of self-kindness, common-humanity, and mindfulness. While self-compassion has been studied clinically in the realm of mental illness, its possible role in patients with a new injury/disability, such as stroke, has not been examined.

Methods: Stroke patients were recruited from acute rehabilitation and outpatient rehabilitation with enrollment in an adapted fitness program at a local exercise facility. Inclusion criteria included >23/30 on the Mini-Mental State Exam. Overall self-compassion scores (SCS) and self-reported Functional Independence Measure scores (FIM) were collected on each participant (N=53). Participants were categorized into three groups: acute stroke rehabilitation patients performing 3 hrs/day of inpatient rehabilitation, 6 days/week (n=18); stroke patients actively participating in an adapted fitness program (n=12); and non-stroke participants who were members of the adapted fitness center and performed 150+ minutes/week of moderate to vigorous exercise (n=23). Linear correlation and significance tests were performed for SCS and FIM scores between groups. Similar correlations were performed between SCS and demographic information.

Results: Average SCS across all groups was 3.69 (maximum score=5.0). There was no significant relationship between SCS and FIM for any group. Stroke and non-stroke participants tended to differ on SCS scores ($p=0.06$; stroke=3.6, non-stroke=3.88). Self-compassion scores were strongly correlated with educational level ($p=0.009$, $r=0.4$).

Conclusion: Self-compassion scores were positively correlated with years of education and tended to be higher for non-stroke participants. The importance of self-compassion in post-stroke rehabilitation warrants further study given the significant literature base demonstrating its benefits in patients with post-traumatic stress disorder. Future work in rehabilitation settings regarding self-compassion should be performed longitudinally with a larger sample size to determine if self-compassion scores affect retention of gains during rehabilitation. Further study should also determine whether self-compassion is independent of years of education.

Project Length: Short
J-10

Evaluation of neurodevelopmental disabilities in children with complex congenital heart defects.
Ashley B. Steffens, *Myriam Peralta-Carcelen M.D.*
Department of Pediatrics, Division of Development and Behavior, University of Alabama School of Medicine, Birmingham, AL.

INTRODUCTION: Pediatric patients with complex congenital heart defects (CHD) that required surgical correction during infancy have an increased risk of adverse neurodevelopmental outcomes.

OBJECTIVES: The primary objective of this study was to explore and compare the developmental scores of a cohort of pediatric CHD patients and their associated surgical mortality risk measured by the STS-EACTS Congenital Heart Surgery Mortality Categories.

METHODS: This was a single center retrospective chart review of pediatric patients with complex CHD. In this study, children with CHD underwent developmental screening assessments at 2 and 3 years of age from 2009-2014. The primary outcome measures were the cognitive and language scores of the Bayley Scales of Infant Development (BSID), third edition and the Differential Ability Scales-II (DAS-II). The developmental scores were compared by gestational age, STS-EACTS mortality category, and associated genetic disorders.

RESULTS: One hundred and twenty-two patients were included. The mean birth weight was 2904 g (SD 650). The mean gestational age was 37.7 weeks (range, 27.4 to 41). Seventy percent of the patient population was insured under Medicaid; the remaining thirty percent had private insurance. Twenty-two patients had known genetic syndromes: trisomy 21 (9), velo-cardio-facial syndrome (8), Turner syndrome (3), other deletions/duplications (2). The BSID cognitive mean composite score was 87 (SD 19). The BSID language mean composite score was 86 (SD 19). The mean composite score for DAS verbal, nonverbal, and general conceptual ability were 92, 90, and 91, respectively (SD 15). No statistically significant difference was found between STS-EACTS mortality categories with regards to developmental scores. Patients with associated genetic syndromes had lower mean scores compared to patients without/with an unknown syndrome.

CONCLUSION: In this cohort of children, there was no statistically significant difference in developmental scores between STS-EACTS mortality categories; however, there was lower mean scores among patients with associated genetic syndromes.

Project Length: Short
J-11

THE ROLE OF NITRIC OXIDE IN CHRONIC RHINOSINUSITIS

Gobind Gill. Do-Yeon Cho, MD, Daniel Lim, PhD, Calvin Mackey. Department of Otolaryngology Head & Neck Surgery, University of Alabama School of Medicine, Birmingham, Alabama.

INTRODUCTION:
Chronic rhinosinusitis (CRS), chronic inflammation and infection of the nasal sinuses, is an increasingly common cause for patient visits to the doctor in the US, accounting for 13 million physician visits annually and responsible for an estimated total cost of $6 billion per year. CRS refractory to medical or surgical intervention may involve a particularly resistant form of infection known as a bacterial biofilm. Bacterial biofilms are a major contributing factor to medically recalcitrant CRS.

OBJECTIVE:
Nitric oxide (NO) is a pluripotent gaseous messenger with potent vasodilating and antimicrobial activity. It was shown that healthy paranasal sinus epithelium expresses an inducible NO synthase that continuously generates large amounts of NO. The role of NO in the sinuses is likely to enhance local host defense mechanisms by inhibition of pathogen growth and stimulation of mucociliary activity. We would like to determine the efficacy of Ciprofloxacin and NO on inhibition of *P. aeuroginosa* growth.

METHODS:
P. aeuroginosa broth culture was treated with the CF-NO-nanomatrix. For this experiment, NO-nanomatrix and CF-NO-nanomatrix groups were prepared by self-assembly of PA-YKNO with and without CF (0.1 μg/ml) into nanofibers through a water evaporation method. The concentration of incorporated CF (0.1 μg/ml) was only 1/10 of MIC (minimum inhibitory concentration) for *P. aeuroginosa*. The OD600 was measured from all samples including a control group without CF or NO-matrix.

RESULTS:
The control group, NO-nanomatrix without CF, NO-nanomatrix with CF, and CF-only had the following OD600 values, respectively: 0.76, 0.34, 0.16, 0.22.

CONCLUSIONS:
The NO-nanomatrix group without CF showed significant inhibition of *P. aeuroginosa* growth compared to the control group without any treatment after 2 hour-cultivation. In addition, the CF-NO-nanomatrix group showed the highest inhibition of *P. aeuroginosa* growth among all groups, which demonstrated a synergistic effect of CF and NO on *P. aeuroginosa* growth inhibition.

Project Length: Short
J-12

Title: Pathways toward Stopped-Flow Analysis of RNA Polymerase I Translocation

Authors: Hunter B. Dean*, Zachariah M. Ingram†, David A Schneider PhD‡, *Aaron L. Lucius PhD*†

*School of Medicine, University of Alabama at Birmingham, Birmingham, AL

†Department of Chemistry, University of Alabama at Birmingham, Birmingham, AL

‡Department of Biochemistry and Molecular Genetics, University of Alabama at Birmingham, Birmingham, AL

Introduction: In eukaryotic cells separate subtypes of nuclear RNA are synthesized by three different multi-subunit RNA polymerases. Of these, RNA Polymerase I (Pol I), which produces ribosomal RNA, contributes more than 60% of total transcription during cell growth. In contrast, RNA polymerase II, which synthesizes the more diverse mRNA, is the most studied of the three. However, despite high sequence and structural homology, studies have suggested that polymerases I and II differ in kinetic activity, which may be evidence of subtle mechanistic differences between the two enzymes.

Objectives: While attempts have been made to generate kinetic models of Pol I single nucleotide incorporation, these methods have proven inefficient at generating multinucleotide translocation models. At the same time, attempts to generate fluorescently-labeled Pol I for use in fluorescence resonance energy transfer assays have resulted in disassembled or inactive protein. This study aims to utilize proximity induced fluorescence enhancement to more efficiently generate a minimal kinetic model of Pol I translocation.

Methods: To develop this model, we utilized stopped-flow fluorometry to examine Pol Is approach toward a stationary fluorophore on a DNA template. Time courses generated from this assay were then fit to a translocation model and compared to prior studies of Pol I translocation.

Results: While the fluorescence curve is consistent in shape with our predicted translocation model, calculated rate constants were nearly an order of magnitude higher than previously reported. At the same time, our fluorophore system was shown to be less efficacious than predicted, with maximum signal changes as low as 1%.

Conclusion: If correct, our results suggest that other mechanisms may be involved in expediting multinucleotide incorporation; however, further study is still necessary to confirm the accuracy of our model as well as the nature of the differences between our calculated rate constants and those previously reported.

Project Length: Intermediate
J-13

Title: Surveying Physicians on the Advice Given to Women Regarding Exercise During Pregnancy

Authors: Lucas D. McGee, BS
Sara J. Gould, MD, MPH Department of Emergency Medicine/Division of Orthopaedics, UAB, Birmingham, AL
Lorie M. Harper, MD Department of Obstetrics & Gynecology, UAB, Birmingham, AL
Amelia M. Sutton, MD Department of Obstetrics & Gynecology, UAB, Birmingham, AL

Introduction:
The incidence of obesity during pregnancy is increasing, and exercise is a fundamental means of combating this epidemic. However, many women are abstaining from exercise during pregnancy.
Objectives:
The aims of this study were 1. To determine if physicians are routinely discussing exercise with pregnant patients, 2. To determine how physician advice relates to the most recent ACOG guidelines, and 3. To identify what barriers may be preventing physicians from discussing exercise with pregnant patients.
Methods:
Questionnaires were distributed at a regional meeting for Alabama and Mississippi ACOG members. Physicians were also recruited to complete the questionnaire via telephone calls, follow-up office visits, and hospital grand rounds.
Results:
Physicians reported that they do not routinely counsel women on exercise during pregnancy, with only 23.5% reporting that they do so regularly (>75% of the time). Of those who discuss exercise during pregnancy with their patients, 88.2% (n=60) were familiar with and able to correctly identify current ACOG Committee Opinions regarding exercise during pregnancy. With reference to the comfort level felt in advising pregnant patients about exercise, approximately 68% (n=46) of the physicians who completed the survey responded that they felt either comfortable or very comfortable in providing advice on exercise during pregnancy.
Conclusions:
Despite reporting a high comfort level in providing advice about exercise during pregnancy, a large percentage of physicians report that they do not discuss the issue of exercise with most of their pregnant patients. However, when exercise is discussed, the majority of physicians are prescribing exercise that is in accordance with the most recent ACOG guidelines. Therefore, further studies should be completed to determine what specific barriers are keeping physicians from discussing exercise with pregnant patients.

Project Length: Intermediate
J-14

Interventions to decrease youth injury risk: a literature review.

Benjamin K. Walters. Connor Read. *Reed Estes, MD*. Sports Medicine, UAB, Birmingham, AL.

Introduction: In 2014, 60 million youth ages 6-18 participated in some form of generalized athletics. 3.5 million children are injured annually participating in organized sport or recreational activities. While sound physical education can decrease the burden of youth sports injuries, the median annual physical education budget of $764 per school may not allow enough flexibility to apply evidenced-based guidelines.

Objectives: The primary objective of this review was to identify evidenced-based interventions that can decrease the incidence of youth sports injury.

Methods: The topics were selected after a careful review of the 2016 National Strength and Conditioning Association Position Statement on Long-Term Athletic Development. Articles used to summarize the topics were located by using and cross-referencing sources from this statement, as well as by using PubMed.

Results: Youth resistance training has been shown to decrease not only the risk of injury, but also of the development of diabetes and metabolic syndrome. Adequate recovery time also decreases injury risk, and resources such as the RESTQ-Sport are available to help coaches detect stress-recovery imbalances, which can be detected two months before an athlete becomes overreached. Through early detection of overtraining, a significant proportion of overuse injuries can be prevented. Early specialization causes fewer muscle groups to be worked and increased repetition, theoretically increasing the risk of injury and early sport dropout. Prior to puberty, increased neuronal activation and adaptation can be achieved through focusing on agility, balance and coordination, thus taking advantage of increased synaptoplasticity. In these early years, neuronal stimulation is more important than muscle hypertrophy, which plays a greater role in athletic development after puberty.

Conclusion: A substantial proportion of youth injuries are preventable. Coaches and physical educators who correctly understand and apply the principles outlined in this review can help youth under their supervision engage in healthy training for sport.

Project Length: Intermediate
Poster J15
Nicole Lau and **W. Blake Holloway**

Faculty Advisor – Lauren Walter, MD
September 15, 2016

Elucidation of Symptom Trends to Enhancing Diagnostic Efficacy in Patients with suspected Concussion:
An Elucidation of Symptom Trends seen in the Emergency Department

INTRO: In the U.S., it has been estimated that traumatic brain injury (TBI) accounts for 1.367 million emergency department (ED) visits annually annually. Researchers have noted that incidences of mild TBI (mTBI) may often be untreated and therefore unreportedunder-reported and under-treated in EDs due to the lack of concrete identifiable and quantifiable symptom trends in concussed patients. Consequently, it is critical to utilize a condensed toolkit similar to the Sport Concussion Assessment Tool -2 (SCAT-2) that helps to rapidly and accurately identify mTBI patients in acute care settings.

OBJECTIVE: The goal of this study was to use an abbreviated and modified SCAT-2 toolkit to identify and categorize symptom trends in mTBI patients who present to the ED.

METHODS: We recruited a sample of patients who presented to the University Hospital ED and met study criteria. to optimize the tool for future usage in the ED. 28 controls and _x_ participants were enrolled, all of which withoutdid not have acute changes in radiologic processimaging. 22 general symptoms and 2 physical signs were evaluated, and each symptom was evaluated on a scale of 0 (not present) to 6 (most severe). The two physical signs (loss of consciousness and loss of balance/unsteadiness) were evaluated based on presence or absence.

RESULTS: Of the 22 symptoms, 7 demonstrated a higher average severity among enrolled participants. These 7 symptoms were further subdivided based on the relative number of patients into 3 groups: high, moderate, and low incidence. The physical signs showed a higher prevalence among participants, however loss of balance/unsteadiness was present in over 60% of participants.

CONCLUSION: The modified SCAT toolkit survey effectively helped to identify and categorize specific physical symptom patterns in concussed patients in acute care settings. This succinct method for quantifying mTBI on a standardized scale has potential for being further incorporated into concussion diagnostic protocols for emergency departments nationwide.

Project Length: Long
J-16

Title: TGFβ and Prostaglandin Synthesis in *C. elegans*: Linking Environmental Cues to Sperm Motility Function

Authors: **Muhan Hu***, *Michael Miller***,* PhD. *Medical Scientists Training Program, **Department of Cell, Development, and Integrative Biology. University of Alabama at Birmingham. Birmingham, AL.

Introduction: Sexual reproduction is critical for maintaining population diversity and species survival. Environmental exposures are thought to influence animal fertility, but the underlying mechanisms are not well understood. Fertilization depends on sperm guidance mechanisms for locating maturing oocytes within the oviduct. The signaling pathways that mediate sperm guidance have been well studied in marine species, but less is known in internally fertilizing animals, such as *C. elegans*. We have shown that *C. elegans* oocytes synthesize specific classes of F-series prostaglandins (PGFs) that guide migrating sperm toward them.

Objective: The PGFs are synthesized via an unknown and possibly evolutionarily conserved metabolic pathway. The DAF-7 TGFβ homologue acts in ASI sensory neurons, downstream of ascaroside pheromones, to modulate oocyte PGF synthesis, linking environmental perception to sperm performance. Loss of the DAF-1 type I TGFβ receptor causes sperm guidance defects and decreased PGF synthesis. Our project aims to delineate the downstream mechanisms of DAF-7 TGFβ in prostaglandin synthesis and sperm guidance.

Methods: To identify the TGFβ targets, we conducted RNA sequencing analyses of wild type, *daf-1* mutant, and *daf-1;daf-3* mutant hermaphrodites. RNAi screens are being used to test whether the TGFβ target (direct or indirect) genes play roles in PGF metabolism. Genome-editing strategies are ongoing to investigate how TGFβ signals are transduced to the germ line. Mass spectrometry approaches are being developed to help identify biochemical steps mediated by TGFβ.

Results/Conclusion: We show that the PGF synthesis phenotype can be suppressed by *daf-3* co-SMAD loss. DAF-3 activity is required in part within the germ line, suggesting DAF-3 transcriptional targets in oocyte precursors modulate PGF metabolism. These efforts are providing insight into the molecular mechanisms of fertilization and the link between environmental factors and sperm function.

Project Length: Short
K-1

Timeliness of Therapies for Septic Shock in the Pediatric Emergency Department

Catherine E. Lumb

Christopher Pruitt, M.D., Department of Pediatrics, Division of Pediatric Emergency Medicine, University of Alabama at Birmingham

INTRODUCTION: Sepsis is a significant cause of morbidity and mortality for pediatric patients. Evidence-based, consensus guidelines dictate that rapid therapies are crucial to successful treatment – namely, isotonic fluids within 20 minutes of recognition, antibiotics within 60 minutes, and a third isotonic bolus (when needed) also by 60 minutes.

OBJECTIVES: The primary objective of our study was to examine whether patients identified by a standardized sepsis triage scoring tool received timely therapies. The secondary objective was to examine whether patients with delayed therapies had longer hospital stays than those who received timely treatment.

METHODS: This was a cross-sectional review of patients that visited a single, academic pediatric ED (May 2014 - May 2016). Time until intravenous fluids or antibiotics were calculated from time of arrival in the ED. Patients who received their treatments in an appropriate amount of time were then compared to patients who received delayed treatments by comparing their length of hospital stay.

RESULTS: During the study period, of the 194 patients that had a positive triage score for sepsis, 149 were treated for sepsis, and thus included for analysis. 66 patients (44%) did not receive a timely first fluid bolus; 43 of the 56 patients (77%) who needed a third bolus did not receive it in time. 26 patients (17%) did not receive antibiotics within an hour of arrival. While 30 of 95 patients with untimely therapies had a length of hospital stay greater than 4 days, this was not significantly different from those patients with more timely therapies in the ED.

CONCLUSION: A considerable number of ED patients with presumed sepsis do not receive therapies within recommended timeframes. In contrast to guidelines, antibiotics may be overemphasized as compared to fluid resuscitation. In our sample, delayed therapies were not associated with prolonged hospital stays.

Project Length: Short
K-2

TITLE: Aspirin Use and Long-Term Rates of Sepsis: A Population-Based Cohort Study

AUTHORS: Joann Hsu, BS (1), John P. Donnelly, MSPH (2, 3, 4)**,** Ninad S. Chaudhary, MBBS, MPH (2,4), Justin X. Moore, MPH (2,4)**,** Monika M. Safford, MD (5)**,** *Henry E. Wang*, MD, MS (2)

(1) School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama
(2) Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham, Alabama
(3) Division of Preventive Medicine, Department of Medicine, University of Alabama School of Medicine, Birmingham, Alabama
(4) Department of Epidemiology, University of Alabama at Birmingham, Birmingham, Alabama
(5) Department of Medicine, Weill Cornell Medical College, New York, NY

INTRODUCTION: Sepsis is the syndrome of infection complicated by systemic inflammation. Aspirin, an anti-inflammatory agent, may play a role in attenuating the inflammatory response during infection.

OBJECTIVE: The primary object of this study was to evaluate the association between regular aspirin use and long-term rates of sepsis.

METHODS: We analyzed data from 30,239 adult participants in the REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort. The primary exposure was regular aspirin use, reported by participants upon study enrollment The primary outcome was first sepsis event, defined as hospitalization for a serious infection with two or more systemic inflammatory response syndrome criteria. We fit Cox proportional hazards models assessing the relationship between aspirin use and rates of sepsis, adjusted for subject demographics, health behaviors, chronic medical conditions, medication adherence, and biomarkers.

RESULTS: Among REGARDS participants with complete data, 13,047 (43%) reported aspirin use. Aspirin use was associated with increased sepsis rates (HR 1.35; 95% CI: 1.22-1.49) but this relationship was attributable to confounders (adjusted HR 0.99; 95% CI: 0.88-1.12). The absence of association between aspirin and sepsis persisted in stratified and propensity-matched analyses.

CONCLUSIONS: In the REGARDS cohort, regular aspirin use is not associated with long-term rates of sepsis.

Project Length: Short
K-3

Matthew C. Hess, BS, *_Eugene W. Brabston, MD_; School of Medicine, University of Alabama School of Medicine, Birmingham, AL; *Department of Surgery: Division of Orthopaedic Surgery, University of Alabama School of Medicine, Birmingham, AL.

Injury Rates and Characteristics in the American Ultimate Disc League

Introduction:
Ultimate frisbee, or the sport of ultimate, is a fast-paced, team sport played around the world and commonly likened to a cross between American football and soccer. Despite ultimate's popularity, only a handful of studies on injuries in ultimate exist. The American Ultimate Disc League (AUDL) is the largest professional ultimate league and has never before been studied.

Objectives:
We aim to determine injury rates and characterize injuries in the AUDL.

Methods:
We surveyed 8 teams in the AUDL throughout the 2016 season. For each team, a trained study contact filled out a weekly, anonymous survey concerning games, practices, injuries, and associated variables. Injury incidence rates were calculated as injuries per athlete-exposure (AE) where one AE equals one player participating in one practice or one game.

Results:
The initial injury rate (IR) for the AUDL was 27.04 per 1000 AEs, and the injury rate ratio (IRR) for games versus practices was 6.46 (95%CI 3.55, 11.74). The most common injured body locations were the knee (IR 4.64), ankle (IR 4.12), and lower leg (IR 3.35). The most common injury determinations were strained muscle/tendon (IR 9.27), sprained ligament (IR 5.41), and abrasion/laceration (IR 3.35). The most common injury mechanisms were running (IR 7.21), jumping collision (IR 4.12), and layout collision (3.61). Non-chronic injuries occurred more frequently than chronic injuries (IRR 4, 95%CI 2.48, 6.44). Players were approximately twice as likely to be injured on artificial turf fields versus natural grass fields (IRR 2.05, 95%CI 1.31, 3.23).

Conclusion:
We reported the first ever AUDL injury incidence. In order to better characterize injuries in the AUDL, further injury data should be collected with more teams over future seasons. These baseline epidemiologic data may be used to guide changes in league play and direct future studies to test interventions that help prevent injuries.

Project Length: Short
K-4

Development of a Septic Shock Algorithm in the Pediatric ICU

Benjamin Palmer, *Leslie Hayes, M.D.,* Steven Nye, M.D., Nicki Sims, M.D.

Introduction: Sepsis is a leading cause of death [1], and early goal-directed therapy administered within the first hours of sepsis improves patient outcomes [2]. A review of the Children's of Alabama (COA) pediatric intensive care unit (PICU) data identified an opportunity to standardize care for patients with septic shock.

Objectives: We aimed to evaluate current sepsis management in the PICU and to identify variation in care compared with best practice. Our purpose is to standardize treatment and improve outcomes through implementation of an early, goal-directed septic shock algorithm.

Methods: We performed a retrospective chart review of all patients (n=104) admitted to COA PICU with septic shock between January 2014 and September 2015. Sepsis management goals were evaluated for the first six hours of care, including administration of fluids, time to first antibiotics, and placement of a central venous line (CVL) to measure central venous pressure (CVP) and obtain mixed venous oxygen saturation (SVO2). Other data parameters collected were vital signs, the need for inotropic or vasopressor support, vasoactive-inotrope score, urine output, and laboratory values of hemoglobin and lactate. Other significant interventions, such as endotracheal intubation and need for extracorporeal membrane oxygenation were recorded.

Results: Analysis of data revealed wide variation in management, particularly in the monitoring of CVP and SVO2. We developed an evidence-based Septic Shock Algorithm for the first six hours of care in the PICU.

Conclusions and Future Directions: Variation in treatment was prevalent in our patient population. Developing an algorithm for sepsis management will decrease variation and improve care for septic shock patients at COA PICU. We will pilot the algorithm in the PICU beginning September 19th, evaluate its efficacy, and make appropriate changes through the plan-do-study-act (PDSA) cycles.

References:

1. Busund R, Koukline V, Utrobin U, Nedashkovsky E. Plasmapheresis in severe sepsis and septic shock: a prospective, randomized, controlled trial. Intensive Care Med 2002; 28: 1434-1439.
2. Rivers E, et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. The New England Journal of Medicine 2001; 345: No. 19.

Project Length: Short
K-5

Characterization of Young Children Presenting to the Emergency Department for Mental Health Complaints

Keri A. Mallicoat*, Justin Schwartz*, MD, Jesse T. Martinez+, MD, Susan Bennett-Smith*, LCSW, PIP, *Kathy W. Monroe*, MD*; *Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL; +Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: Emergency departments across North America are seeing an increased incidence of pediatric mental health complaints. Previous research has focused on adolescent mental health, with little characterization of patients less than 10 years of age.

OBJECTIVES: The primary objective of this study was to characterize children less than 10 years of age who presented to a pediatric emergency department for mental health complaints.

METHODS: One researcher reviewed medical records of children less than 10 years old who presented to Children's of Alabama emergency department between January 2016 and April 2016 with a mental-health-related chief complaint. We then categorized patients based on demographic information, characteristics of the emergency department visit, and past medical and social history. Descriptive analyses were run using SAS® version 9.4.

RESULTS: 120 patients ages 10 years and under were seen between January and April 2016. This age group makes up 20% of all children seen in the ED for mental-health-related complaints. In this group of patients, 71% were male (n=85) and ages ranged from 3-10 years with a mean age of 7.7. Patients were 59% Caucasian (n=70), 40% African-American (n=48), and 1% other ethnicity (n=1). Patient's insurance coverage was 75% Medicaid (n=89), 18% private insurance (n=22), and 7% uninsured (n=8). 46% of patients were admitted (n=55). Univariate analyses showed increased odds of admission for children with 3 or more prior psychiatric diagnoses (OR = 3.97, $p < .01$), a family history of psychiatric illness (OR = 3.16, $p < .01$), and a history of Department of Human Resources (DHR) involvement (OR = 2.69, $p < .01$).

CONCLUSIONS: The pediatric emergency department sees a significant amount of children under age 10 for mental-health-related complaints. Nearly half of these children were admitted for psychiatric care. Several factors were found to predict admission, which reflect psychosocial influences.

Project Length: Short
K-6

Characterization of Pediatric Patients Identified by Septic Shock Pathway

Madeline I Bender, *Christopher Pruitt, MD*[2], Timothy A Edgil[1], Catherine E Lumb[1]
[1]University of Alabama School of Medicine, Birmingham, AL
[2]UAB Pediatric Emergency Department, Birmingham, AL

ABSTRACT

INTRODUCTION:
Pediatric sepsis and septic shock are responsible for over 720,000 hospitalizations annually in the United States. The CDC recently released a report emphasizing the importance of early recognition of sepsis in reducing mortality for both adult and pediatric patients. To aid in recognition of pediatric sepsis, many hospitals including the UAB Pediatric Emergency Room have implemented a sepsis identification pathway and treatment protocol that the emergency physician can elect to initiate or stop for each patient.

OBJECTIVES:
The purpose of this study was to examine the characteristics of patients that were identified by the pediatric sepsis pathway.

METHODS:
We reviewed charts of patients from several months who scored a 3 or greater on the sepsis identification tool and received treatment consistent with sepsis. We then identified the patients that were diagnosed with sepsis based on ICD-10 criteria and separated these patients into a group that received order sets and a group that stopped the treatment protocol. We compared the lab values, triage observations, and demographics of these patients.

RESULTS:
Thirty-eight patients were identified as “true positives” who received the order set and were diagnosed with sepsis, and twelve patients were considered “false negatives” who were chosen not to receive the order set, but were diagnosed with sepsis. The true positives were found to have higher average glucose levels (P=0.024), and higher triage temperatures (P=0.008) than the false negatives. In addition, the true positive group exhibited higher C reactive protein levels (P=0.19) and lactate levels (P=0.13).

CONCLUSION:
The differences between the true positives and false negatives identified in this study can be used to help refine identification tools for pediatric sepsis. The data that was collected has also been submitted to the Pediatric Septic Shock Collaborative which can be used for larger studies.

Project Length: Short
K-7

MSEP Experience in Granada, Nicaragua

Authors: Spenser Hayward*, Chisom Ifediba*, **MS, Shenila B. Lallani*,** *Nadia Richardson, PhD, Majd Zayzafoon, MD, PhD, MBA*
All authors contributed equally to this work
Affiliation: International Medical Education, University of Alabama at Birmingham, Birmingham, AL

Introduction: In June of 2016, 3 medical students from the University of Alabama School of Medicine traveled to Granada, Nicaragua through the Medical Student Enrichment Program (MSEP).

Objectives: The objectives of this MSEP program included: gaining cultural awareness, improving language skills, gaining research experience, acquiring better understanding of foreign and domestic health care systems, and exploring the social determinants of health in Nicaragua.

Methods: While in Granada, the students volunteered at Clinica Alabama-Granada for 4 weeks. At the clinic, the students assisted with patient check-in, triage, physical examination, and dispensing medication in the pharmacy. The students also shadowed the physicians at the clinic, the nearby Ministry of Health, and the La Providencia nursing home. Additionally, they conducted surveys to better understand the lifestyle of the patients presenting to the clinic and how those with diabetes mellitus managed their illness.

Results: By learning about the daily struggles of the patients at the clinic, the students better appreciate poverty as a social determinant of health. The variance between the Nicaraguan and American health system, including the costs and availability of care, gave the students an opportunity to think critically about American medical care. Speaking Spanish regularly, both with patients and outside of the clinic allowed the students to improve their language skills. By exploring the prevalence of diabetes and obesity in the Nicaraguan population, students gained experience in planning and designing a research study. Working in the triage daily allowed students to not only improve their interpersonal and rapport-building skills, but also to gain proficiency in many areas of the physical exam.

Conclusion: This experience helped the students broaden their cultural competency and gain an understanding of major health concerns in third world countries.

Project Length: Intermediate
K-8

The Almighty, Overridden Clinical Decision Support Alert

Timothy I. Kennell Jr., BS[1,2] and *James J. Cimino, MD*[2]

[1]NIH Medical Scientist Training Program, University of Alabama at Birmingham School of Medicine, Birmingham, AL

[2]Informatics Institute and Department of Medicine, University of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: Clinicians are bombarded daily with an unmanageable number of alerts. This problem results in alert fatigue, the desensitization of clinicians to individual alerts due to constant exposure, leading to high alert override rates. Several previous studies have shown alert override rates for many hospitals fall between 49 – 96%, varying based on the specific alert. The alert fatigue problem both decreases patient care and potentially endangers some patients.

OBJECTIVES: This study describes the number of alerts presented to UAB hospital clinicians by the Cerner electronic health record and the resulting override rates.

METHODS: This study retrospectively examined the de-identified, total number of alerts, their override status, and override reasons in the UAB Cerner EHR. We first calculated the number of alerts having override rates greater than the minimum 49% override rate found in the literature. Then, we calculated the alerts per day for each alert and the override rate of each alert. Finally, we examined each alert by override reason and then calculated the frequency that each alerts reason was used.

RESULTS: Overall, the data indicated that 25 out of the 108 alerts examined had an override rate greater than 49%. Several of these alerts were triggered multiple times per day, with one extreme alert being triggered over 167 times per day with an override rate of approximately 92%. The most common reasons for many of the alert overrides indicated some other form of necessary treatment such as the example “Essential therapy…”.

CONCLUSION: Override rates in the UAB Cerner EHR follow the typical patterns seen in the literature with many of the most prominent alerts being drug-related. Future directions will include using EHR data to predict the appropriateness of an alert before triggering.

Project Length: Long
K-9

Missed Opportunities for Repeat HIV Testing and Early ART Initiation during Pregnancy in Southwestern Kenya

Anna Joy Rogers[†], MA, Eluid Akama[§], BS, Elly Weke[‡], MS, Justin Blackburn[†], PhD, George Owino[‡], Elizabeth A. Bukusi[‡], MBBS, Zachary Kwena[‡], PhD, Craig R. Cohen[±], MD, MPH, and *Janet M. Turan*[†], PhD, MPH

[†] Department of Health Care Organization and Policy, University of Alabama at Birmingham School of Public Health, Birmingham, Alabama, USA
[§] Department of Epidemiology, University of Washington School of Public Health, Seattle, Washington, USA
[‡] Centre for Microbiology Research, Kenya Medical Research Institute, Nairobi, Kenya
[±] Department of Obstetrics, Gynecology & Reproductive Sciences, University of California at San Francisco, San Francisco, California, USA

Introduction: It is estimated that a third of all mother-to-child transmission (MTCT) of HIV occurs among women with incident infection during pregnancy, making HIV retesting during the late antenatal period a crucial time to identify and treat women for HIV infection. International recommendations for pregnant women in generalized epidemic settings suggest that repeat HIV testing be offered three months after an initial negative HIV test early in pregnancy.

Objective: To identify gaps in repeat HIV testing and early antiretroviral therapy (ART) initiation.

Methods: Longitudinal analyses were conducted among 2164 women attending antenatal care (ANC) at a rural district hospital in southwestern Kenya. Data were abstracted from registers for all women who attended ANC from the years 2011 to 2014.

Results: The majority of women (1954/2164, 90.2%) presented for their first ANC visit early enough (<28 weeks gestation) to later be eligible for a repeat HIV test, but several missed opportunities were noted for retesting including: (a) 310 (15.8%) women never returned to ANC and thus went to delivery with an unknown HIV status; (b) of the 495 women who returned to ANC when eligible, only 132 (36.6%) were retested and (c) in the same eligible group, 126 (25.5%) were not retested even though eligible at two or more visits. On retest, two women tested HIV-positive, suggesting a seroconversion rate of 1.5% from early to late pregnancy. A small proportion of women (210/2164, 9.8%) presented for their first ANC visit too late to later be eligible for retesting; among them 8 (3.8%) tested HIV-positive, constituting a missed opportunity for early ART intervention.

Conclusion: We identified multiple missed opportunities for repeat HIV testing and early ART initiation among pregnant women in a high HIV prevalence area of southwestern Kenya. Intervening on MTCT in this region and in similar sub-Saharan Africa will likely require addressing these missed opportunities.

Project Length: Short
L-1

Exosomes from activated human neutrophils produce COPD-like disease in mice.

Tarek Abdalla, Kristopher R. Genschmer, Derek W. Russell, Xin Xu, Liliana Viera, Carmel M McNicholas-Bevensee, Wilson King, Patricia Jackson, J. Michael Wells, Amit Gaggar, *J. Edwin Blalock*

Department of Medicine, Division of Pulmonary, Allergy, and Critical Care, University of Alabama at Birmingham

Introduction: COPD is a chronic inflammatory lung disease characterized by long term neutrophil (PMN) infiltration. This long term PMN influx seems to be prominently driven by the collagen-derived matrokine, PGP, in a feed forward inflammatory pathway by which PGP causes PMN influx and the resulting PMNs generate more PGP. Furthermore, chronic PGP administration into mouse airways causes a COPD-like phenotype including emphysema and right ventricular hypertrophy (RVH). Neutrophils, upon activation by various molecules, including PGP, can release small nanoparticles called exosomes. We have previously determined that such exosomes are proteolytic and among others contain the COPD associated protease, neutrophil elastase.

Objective: The primary objective was to determine if PMN derived proteolytic exosomes are key mediators of COPD.

Methods: Mice were treated intratracheally with 50 uL of PBS, unstimulated PMN exosomes (DMSO) or stimulated PMN exosomes (fMLP) following an exosome purification procedure. PMN derived exosomes were also pretreated with a general neutrophil elastase inhibitor. In both cases, Mean Linear Intercept (Lm) and right ventricular hypertrophy measurements were recorded.

Results: We observed that equivalent numbers of exosomes purified from COPD patients' bronchoalveolar lavage fluids (BALF), but not from healthy non-smoking control subjects' BALF, conferred a COPD-like phenotype when administered into the airways of mice. It was determined that exosomes from COPD patients' BALF were predominantly of PMN origin (CD66b+) while those from healthy control BALF were predominantly of airway epithelial origin (MUC4+). We found that CD66b+/CD63+ exosomes from activated, but not quiescent, PMNs caused alveolar enlargement and RVH when administered into the airways of mice. The disease causing ability of such exosomes was negated by prior treatment with NE inhibitors.

Conclusion: We conclude that activated PMN derived proteolytic exosomes are likely novel and key mediators of tissue destruction in COPD that is downstream of PGP.

Project Length: Short
L-2

The Effect of Maternal Smoking on CFTR Function of the Neonate

Lydia L. McCormick[1], Niroop Kaza, PhD [1,2], Li Ping Tang[1,2], Lawrence Rasmussen[2], Patricia Jackson, PhD, Stephen Byzek[2], S. Vamsee Raju, PhD[1,2], *Steven Rowe MD, MSPH* [1,2].

[1]Department of Medicine, [2]The Gregory Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham, Birmingham, Alabama, USA.

The cystic fibrosis transmembrane conductance regulator (CFTR) is crucial for proper airway, pancreatic, and reproductive tract function by regulating epithelial chloride and bicarbonate secretion. Cystic fibrosis (CF) is a consequence of defective CFTR function and results in impaired airway mucociliary clearance, chronic bronchitis, bacterial infections, and other manifestations. Even without genetic CFTR mutations, CFTR dysfunction is apparent in smoking-related illnesses like chronic obstructive pulmonary disease (COPD) by a process termed "acquired CFTR dysfunction." This dysfunction has been linked to toxic metabolites from cigarette smoke, namely acrolein, which causes ciliotoxicity, oxidative stress, transcription factor activation, and cell death. Work from our lab suggests that acrolein causes CFTR dysfunction in cigarette smokers.

Passive smoke exposure by infants causes respiratory dysfunction and increased infection risk that can persist into childhood. Whether maternal smoking adversely affects neonatal CFTR has not been explored. We hypothesized that cigarette toxins in smoking mothers cause neonatal CFTR dysfunction by trans-placental exposure.

Pregnant rats (n=8) were exposed to cigarette smoke for 10 days before fertilization and throughout their 21-23 day gestation (four hours/day, five days/week) using a whole body exposure chamber and smoking apparatus (SCIREQ, *InExpose* model, Toronto, Canada). Air-exposed control rats (n=4) were placed in identical chambers for the same duration. CFTR activity was measured in Day-0 and Day-3 old neonates in excised trachea using short circuit current analysis to evaluate epithelial ion transport. Results demonstrated a 44.5% reduction in CFTR dysfunction in the Day-0, smoke-exposed neonates (n=7) compared to controls (n=21). This attenuation in CFTR dissipated by Day-3. Separate measurements of *in vivo* CFTR activity by nasal potential difference (Day-10-12 neonates) further supported this finding. The role of acrolein in neonatal CFTR dysfunction will be evaluated by mass spectroscopy in Day 0-3 blood (in progress). These results support that maternal smoking is detrimental to neonatal CFTR function.

Project Length: Short
L-3

Title: Potential role for IL-7 immune complex therapy for the treatment of invasive fungal infection

Authors: Garrett A. Nix; *Chad Steele, PhD.; Joseph J. Mackel;* Division of Pulmonary, Allergy & Critical Care Medicine; The University of Alabama at Birmingham; Birmingham, Alabama.

INTRODUCTION: Invasive pulmonary aspergillosis (IPA) is an opportunistic infection commonly caused by the ubiquitous mold *Aspergillus fumigatus*. IPA reported mortality rates range from 50-80%, with the primary risk factor being neutropenia. Using genetically deficient mice and in vivo neutralization models, our lab has previously demonstrated a critical role for the cytokine IL-22 in innate lung clearance of *A. fumigatus*. More recently, our lab has discovered the cellular sources of IL-22 in the lung after AF exposure, all of which express the receptor for the common γ-chain cytokine IL-7, which is required for their development and homeostasis.
OBJECTIVES: We hypothesized that administration of an IL-7/anti-IL7 immune complex would induce proliferation of IL-22 producing cells in the lung, increasing the level of IL-22 and subsequently reducing fungal burden.
METHODS: Using a model of transient neutropenia induced by antibody-mediated depletion, we compared the efficacy of administering IL-7 alone vs. IL-7 immune complexes (IL-7 + anti-IL-7 Mab) on lung fugal burden.
RESULTS: The administration of IL-7 immune complexes to neutropenic mice during IPA lowered lung fungal burden by more than 50% ($1.01 \times 10^7 \pm 2.94 \times 10^6$, n = 10 vs. $4.04 \times 10^6 \pm 9.55 \times 10^5$, n = 10; P = 0.064). However, IL-22 levels surprisingly trended lower in the IL-7 immune complex group, suggesting that the protection observed with IL-7 immune complex administration is possibly via a different mechanism. Future studies will examine additional responses induced by IL-7 immune complex administration as well as the efficacy of other common γ-chain cytokine immune complexes.
CONCLUSION: Overall, our results suggest that optimal dosing and timing of common γ-chain cytokine immune complexes may be beneficial for the treatment of invasive fungal infections.

Project Length: Short
Poster L4

The Effects of Oxygen Exposure in Combination with Retinoic Acid on the Oxidant/Antioxidant Balance in Human Bronchial Epithelial Cells

Bria N. Williams, Stephanie B. Wall, Ph.D., Nelida C. Olave Concha, PhD., Namasivayam Ambalavanan, MD., *Trent E. Tipple, MD*.,

INTRODUCTION: Although vitamin A has been shown to reduce chronic lung disease in preterm infants requiring supplemental oxygen, the mechanistic actions of retinoids have not been well elucidated.

OBJECTIVES: The primary objective of this study was to determine the effects of retinoic acid (the active metabolite of vitamin A) on the oxidant/antioxidant balance in Human Bronchial Epithelial (HBE) Cells in settings of normoxia and hyperoxia.

METHODS: HBE cells were cultured and divided into (4) 6 well plates. After adherence, the cells were subjected to low serum media for a period of 24 hours for synchronization of cell cycle. Cells were then treated with retinoic acid (RA) dissolved in DMSO (1ug/ml) or DMSO alone (control). Following a 1 hour pre-exposure period, cells were exposed to normoxia (21% O_2) or hyperoxia (85% O_2) for either 4 hours or 24 hours. After collection, the following enzymatic activity assays were performed: 1) glutathione (24 hours); and thioredoxin reductase-1 (TrxR1, 4 hours). Additional analyses included western blotting for TrxR1. Data (n=3/group) were analyzed by 2-way ANOVA with Tukey's post-hoc and significance was accepted at $p<0.05$.

RESULTS: Cellular oxidized GSH was decreased by 20-30% ($p=0.0131$) while total glutathione was slightly, albeit significantly increased by 6% ($p=0.0487$) in RA-treated cells under room air or hyperoxia conditions. Data revealed no effects of RA or hyperoxic exposure on TrxR1 activity or protein levels at 4 hr; however, we detected an independent effect of hyperoxic exposure on TrxR1 protein expression in both control and RA-treated cells ($p=0.0109$). Fold Change analysis compared to treated hyperoxia control indicated a slight but significant decrease in TrxR1 expression with RA treatment ($p<0.05$).

CONCLUSION: RA treatment increases total glutathione and decreases oxidized glutathione through unknown mechanisms in both normoxia and hyperoxia. This work suggests that the therapeutic effects of retinoids involve regulation of the glutathione system.

Project Length: Short
L-5

Role of Pulmonary Microbiome Induced Inflammation in Bronchopulmonary Dysplasia

Alexandra Simpson[1], Gabriel Rezonzew[2], Xin Xu[3], Patricia Jackson[3], Edwin Blalock[3], Namasivayam Ambalavanan[2], Amit Gaggar[3], Charitharth Vivek Lal[2]
[1]Medical Student, University of Alabama School of Medicine, Birmingham, AL
Department of Pediatrics[2] and Medicine[3], University of Alabama at Birmingham, AL

Background:
Bronchopulmonary dysplasia (BPD) is a chronic lung condition of prematurity that is marked by alveolar hypoplasia and inflammation. Utilizing recent microbiome analyses, we have discovered that the airways of infants with BPD are marked by an increased abundance of *Proteobacteria*.
Hypothesis:
We hypothesized that increased abundance of *Proteobacteria* leads to increased inflammation, and hence contributes to the pathogenesis of BPD.
Methods:

a. *In vitro:* Human Bronchial Epithelial cells (NHBE), with and without collagen, were exposed to *Proteobacteria* (E.Coli) in both normoxic and hyperoxic conditions. Cell supernatents were taken at T0 and T12. The cell aspirates were analyzed using mass spectrometry (MS) for inflammatory matrikine Ac-PGP (a potent neutrophil chemotactic tripeptide).
b. *In vivo:* Using the established hyperoxia model of BPD, mice were exposed to hyperoxic conditions (85% O_2) or normoxic conditions (21% O_2) from PN 3-14. Both hyperoxic and normoxic mice were administered escalating doses of either Proteobacterial products (LPS) or control (PBS). Mice were harvested, serum and lung tissue were collected at PN 14. Lungs were also inflation fixed for histology and morphometry. Ac-PGP was measured in serum by MS.

Results:
In vitro: NHBE cells exposed to hyperoxic conditions showed more Ac-PGP expression than normoxic cells. Proteobacteria inoculation, in both normoxic and hyperoxic conditions significantly increased the Ac-PGP expression compared to controls ($p<0.001$).
In vivo: As expected hyperoxia mice had decreased alveolarization compared to normoxia mice (Radial Alveolar Counts, $p<0.05$), but the alveolarization in both normoxia and hyperoxia mice were worsened with the administration of LPS (Radial Alveolar Counts, $p<0.05$). Both normoxia and hyperoxia mice exposed to LPS had significantly increased expression of Ac-PGP in serum compared to controls ($p<0.05$).
Conclusion:
Proteobacteria exposure stimulates Ac-PGP release *in vivo* and *in vitro* in both normoxia and hyperoxia conditions. This *Proteobacteria* induced matrikine production may explain the mechanisms of inflammation in BPD.

Project Length: Short
L-6

Electrophysiological characterization of sweat gland cultures for the study of cystic fibrosis

Chandler S. Stisher[1], Dnika Joseph, MPH[1], Steve M. Rowe, MD, MSPH[2,3,4], *Carmel M McNicholas, PhD*[1,4]
[1]Department of Cell, Developmental, and Integrative Biology, Univ. of Alabama at Birmingham, Birmingham, AL
[2]Department of Pediatric Pulmonology, University of Alabama at Birmingham, Birmingham, AL
[3]Department of Pulmonary, Allergy, and Critical Care Medicine, University of Alabama at Birmingham, Birmingham, AL
[4]The Gregory Fleming James Cystic Fibrosis Research Center, Univ. of Alabama at Birmingham, Birmingham, AL

INTRODUCTION: Many cystic fibrosis (CF)-causing mutations are rare, and they are not currently within the scope of the FDA-approved target population. Because of this, the only means to test available modulators of CF that may benefit these sub-populations of patients are the costly 'n-of-one' trials. Recent focus has shifted to ex-vivo approaches, of which our chosen model is the culture of human sweat glands. Using a personalized medicine approach, ultimately, ex-vivo testing could be utilized to determine the efficacy of various CFTR modulators in patient samples.

OBJECTIVES: Our main objective is to optimize culture conditions of human sweat glands for functional characterization using patch clamp methodologies.

METHODS: Human sweat glands were isolated from remnant surgical specimens and punch biopsy samples. Following enzymatic digestion, microdissected sweat glands were laid down on a bed of irradiated 3T3 fibroblasts. Outgrowths were passaged and plated onto pre-coated coverslips or tissue culture treated flasks. The whole-cell perforated patch clamp technique was employed to characterize endogenous currents in P1-P3 cells.

RESULTS: We have optimized culture conditions that favor propagation and expansion of human sweat gland cells. Consistent with a variety of cell types in sweat glands duct and coil, a variety of electrophysiological profiles emerged demonstrating cells with varying levels of amiloride-sensitive, forskolin-activated, and CFTR(inh)172-sensitive currents. These data suggest low expression of CFTR in only a subset of cells under our current growth conditions.

CONCLUSION: Of the various coating protocols and conditions that were tested, initiation of culture was optimal with an irradiated 3T3 fibroblast feeder layer. For patch clamp experiments, collagen I -coated coverslips provided cells with optimal morphology. A mixed population of cells with functional variability was observed in sweat gland cultures. Studies are underway to identify specific cell populations using immunocytochemical techniques and media modifications to enhance CFTR expression.

Project Length: Long
Poster L7

Dityrosine Cross-linking of Fibronectin is Increased in Plasma of Human Subjects with Interstitial Lung Disease

Morgan L. Locy[1], Sunad Rangarajan[1], Ashish Kurundkar[1], Karen Bernard[1], Naomi Logsdon[1], Joao A.M. de Andrade[1], Subramaniam Pennathur[2,3], and *Victor J. Thannickal*[1]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Alabama at Birmingham, Birmingham, AL 35294, and Divisions of [2]Nephrology, Department of Internal Medicine, [3]Computational Medicine and Biology, University of Michigan, Ann Arbor, MI 48109

OBJECTIVE: Interstitial lung disease (ILD) is a variably progressive lung disorder resulting in impaired gas-exchange and respiratory failure with significant morbidity. Oxidative stress has been shown to play a role in the pathobiology of ILD, and we have previously shown that the oxidant-mediated tyrosine modification, *o,o*'-dityrosine, is increased within proteins in circulating plasma of ILD patients. This study sought to elucidate a protein target of *o,o*'-dityrosine cross-linking in plasma. Therefore, we tested the hypothesis that fibronectin (FN), a tyrosine-rich extracellular matrix protein shown to play a role in the fibrotic response of ILD, is modified by *o,o*'-dityrosine cross-linking and is increased in plasma of ILD patients.

METHODS: Fibronectin was immunoprecipitated from age- and sex-matched healthy control (n=20) and ILD patient (n=16) plasma and *o,o*'-dityrosine levels were quantified by tandem mass-spectrometry (MS/MS). The study was approved by the University of Alabama at Birmingham and the University of Michigan Institutional Review Board. Data were analyzed by unpaired t test with Welch's correction (mean ± SEM, $p<0.05$).

RESULTS: Fibronectin *o,o*'-dityrosine cross-linking was observed in plasma of human subjects. Furthermore, fibronectin-associated *o,o*'-dityrosine levels were significantly increased by 10.95 fold (14.34 ± 5.01 vs. 1.20 ± 0.16) in ILD patients when compared to healthy controls. The o,o'-dityrosine

Project Length: Short
M-4

Title: Key Determinants for Achieving Enteral Autonomy in Pediatric Intestinal Failure

Macie A. Enman[1], BS, UAB School of Medicine, Birmingham, AL
Linda T. Wilkinson[2] MSN, CRNP Division of Pediatric Gastroenterology, Hepatology, & Nutrition, UAB, Birmingham, AL
Michelle C. Shroyer[3], MPH, Division of Pediatric Gastroenterology, Hepatology, & Nutrition, UAB, Birmingham, AL
Katie B. Williamson[4], MS, RD, Department of Clinical Nutrition, Children's of Alabama, Birmingham, AL
Tracy F. Jackson[5], PharmD, Department of Clinical Pharmacy, Children's of Alabama, Birmingham, AL
Inmaculada Aban[6], PhD, Department of Biostatistics, UAB, Birmingham, AL
Reed A. Dimmitt[7], MD, Division of Pediatric Gastroenterology, Hepatology, & Nutrition, UAB, Birmingham, AL
Colin A. Martin[8], MD, Division of Pediatric Surgery, UAB, Birmingham, AL
David P. Galloway[9], MD, Division of Pediatric Gastroenterology, Hepatology, & Nutrition, UAB, Birmingham, AL

Abstract
Introduction: Enteral autonomy is a central goal of pediatric patients with intestinal failure and has been found to be strongly associated with various determinants in a previous large, multi-center cohort study. However, it remains to be seen if these determinants are applicable to other centers that manage pediatric intestinal failure.
Objectives: We sought to evaluate the relationship between determinants of intestinal failure (IF) and achieving enteral autonomy from parenteral nutrition (PN) in a large single-center cohort of children.
Methods: This is a retrospective chart review of pediatric subjects enrolled in a database for the Center for Advanced Intestinal Rehabilitation at Children's of Alabama from 1989 to 2016. IF was defined as dependence on PN for > 60 days. Subjects were included if they were followed since birth or infancy for a minimum of three months and sufficient documentation of study variables were available. Gestational age, diagnosis, anatomy (percent small and large bowel remaining, presence of ileocecal valve (ICV)), county of residence (rural/urban), and days of PN use were recorded. Kaplan-Meier curves and parametric survival regression models were used to investigate the relationship between the demographic and clinical variables with the length of PN use.
Results: Initially, 290 subjects were available to review. After inclusion/exclusion were applied, 158 subjects remained. Individually, the variables of gestational age, diagnosis (necrotizing enterocolitis), small bowel length (>10%), colon length (> 50%) and presence of an ICV were significant positive predictors for reaching enteral autonomy. Collectively, only diagnosis, small bowel length and colon length were positive predictors for emancipation from PN.
Conclusions: Enteral autonomy is a key outcome among children with IF. In our cohort, we found that diagnosis, remaining small bowel and colon length are positive predictors for reaching this important milestone while county type and presence of an ICV are less impactful.

Project Length: Short
M-1

Ho-1 Regulates Lymphatic Endothelial Cell Proliferation Following Hypoxia-Induced Inflammation

Patrick A. Molina[1], Sarah A. Bowhay[2], Laurence M. Black[2], James F. George, PhD[2], Abolfazl Zarjou, MD/PhD[2], *Anupam Agarwal, MD*[2], [1]Medical Scientist Training Program and [2]Department of Medicine, Division of Nephrology, University of Alabama at Birmingham School of Medicine, Birmingham, AL

Abstract

Purpose: Individuals with acute kidney injury (AKI), which includes up to 15% of admitted hospital patients, display an array of complications, including dysregulated fluid balance, and aberrant inflammation. The lymphatic system, which has a role in immune system transportation, has a role in AKI, but its function is not well understood. We explored whether lymphangiogenesis is altered in human-derived lymphatic endothelial cells (hLECs) following hypoxic media treatment, and whether heme oxygenase-1 (HO-1), a nephro-protective enzyme, has a central role in lymphangiogenesis. If yes, HO-1 might offer an additional pathway to ameliorate AKI.

METHODS: Human-derived lymphatic endothelial cells (hLECs) and HO-$1^{-/-}$ and HO-$1^{+/+}$ mice were used for all experiments, and the UAB IUCUC approved all protocols. Macrophages (MΦ) were cultured from HO-$1^{+/+}$ and HO-$1^{-/-}$ mice, following lower extremity bone marrow collection. MΦ's were then exposed to normoxic or hypoxic conditions for 24 hours. Following treatment, media was collected. hLECs were plated on matrigel-coated wells and then treated with normoxic, hypoxic or standard 24h MΦ-derived media. LEC expansion was visually analyzed using microscopy. To examine HO-1, hLECs were treated with known HO-1 inducers or inhibitors and western analysis was utilized to quantify changes in vascular endothelial growth factors (VEGFs), HO-1, and ferritin.

RESULTS: Visual analysis of hLECs treated with HO-$1^{-/-}$ MΦ-derived media following hypoxia demonstrated reduced proliferation when compared against hLECs treated with HO$^{+/+}$ MΦ-derived media. HO-1 stimulation demonstrated a marked increase in vascular endothelial growth factors VEGF-R3 and VEGF-C. An increase in HO-1 was verified through western blot analysis.

DISCUSSION: The reduced proliferation of hLECs treated with hypoxic HO-$1^{-/-}$ MΦ-derived lends to HO-1 being a central factor for lymphangiogenesis following ischemia. Furthermore, HO-1 inducers, such as hemin and hypoxia, show an increase in VEGFs and protective markers, such as ferritin. This novel demonstration supports HO-1 as having a central role in LEC development following insult.

Project Length: Short
M-2

Department of Nephrology, University of Alabama at Birmingham, Birmingham, AL

DIFFERENT CULTURE CONDITIONS ALTER GROWTH AND VIABILITY OF MESENCHYMAL STEM CELLS

Brendon R. Herring [1], *Lisa M. Curtis, PhD*, Chunlan Fan

Abstract

INTRODUCTION: Mesenchymal Stem Cells **(**MSCs) have been shown to exhibit a protective effect in many tissues. Specifically, their renoprotective effect in Acute Kidney Injury (AKI) shows promise in various treatment modalities. MSCs are difficult to study because they must be cultured from whole bone marrow for several passages to select for MSCs. Slow growth rates and high sensitivity to environmental stressors seen in MSCs, particularly those from aging individuals, necessitate careful consideration of culture conditions to make subsequent studies possible.

OBJECTIVES: The purpose of this study was to evaluate a novel method for improving the survivability and viability of MSCs in cell culture using a partial exchange of media versus a complete change in media.

METHODS: Whole bone marrow was obtained from 5- or 12-month old male and female C57BL/6 mice and established in culture. At each culture change, partial exchange of media was done by removing 2/3rds of the media and adding back the same volume of fresh media to the cells at each media change. Complete change of the media was done by removing the entire volume of media and replacing it fully with fresh media. Images were taken of the cell cultures at alternating three and four day intervals based on media changes and MSCs were counted using ImageJ.

RESULTS: Using partial change for MSC culture, we observed the growth and maintenance of MSC-like morphology over time was improved compared to MSC culture that was changed according to traditional full media change. MSC culture that underwent partial media change grew MSCs at a rate exceeding 18% faster than the culture that underwent whole media change. The culture undergoing partial media change was also able to sustain an average of 192% more MSCs than the culture undergoing whole media change. Lastly, cells undergoing partial media change were shown to resist senescence or failure to thrive for longer periods of time than cells undergoing whole media change. These differences were particularly striking for MSCs from aged individuals.

CONCLUSION: This work contributes a methodology by which MSC cultures can be improved for the purpose of various analyses to better understand their protective effects. Future studies will look at the specific levels of various key growth factors to determine how the concentrations differ between these two media changing techniques and will determine the effect of these different regimen on maintenance of stem cell multipotentiality.

Project Length: Short

Poster M3

Short Term Effects of Hepatitis C Virus Clearance Using Direct Acting Antivirals on Markers of Glomerular Damage in Kidney Transplant Patients

Goetsch MR[1], *Franco R*[2], Tamhane A[2], Varshney M[2], Kapil A[2], Overton ET[2], Towns GC[3]

1. School of Medicine, University of Alabama at Birmingham, Birmingham, AL.
2. Department of Medicine, Division of Infectious Diseases, University of Alabama School of Medicine, Birmingham, AL.
3. Department of Medicine, Division of Nephrology, University of Alabama School of Medicine, Birmingham, AL.

Introduction: Hepatitis C Virus (HCV) is a leading cause of liver disease morbidity and mortality worldwide, and an independent risk factor for chronic kidney disease progression, end stage renal disease, and poorer kidney graft survival. The role of HCV clearance in long-term kidney graft survival is unknown.

Objectives: In this study, we examined the short-term impact of direct acting antivirals (DAAs) on markers of glomerular damage in kidney allografts.

Methods: We conducted a retrospective study of kidney transplant patients with chronic HCV infection seen at the UAB 1917 Viral Hepatitis Clinic between January 2013 and July 2016. Of the 28 patients identified, 21 had received DAA treatment. Two patients who had achieved HCV cure were excluded due to 1) antibody-mediated rejection related to low levels of immunosuppression post HCV treatment; and 2) self-limited, unexplained proteinuria post HCV treatment. Glomerular damage was assessed using serial protein/creatinine (P/C) ratios measured pre- and post- treatment. We also described treatment efficacy using sustained virologic response at 12 weeks post HCV treatment (SVR12).

Results: Post-treatment P/C ratios (median=0.127, Q1=0.090, Q3=0.220) were significantly lower (p=0.01) than the pre-treatment ratios (median=0.168, Q1=0.118, Q3=0.385). P/C ratios decreased in 14 out of 19 patients (74%) with an absolute median change of -0.072 (median observed percent change=-40%). Seventeen out of 19 patients (89%) achieved SVR12, with two patients pending. Sixteen of the patients were treated with fixed-dose ledipasvir/sofosbuvir. Two patients were treated with sofosbuvir/simeprevir, and one with sofosbuvir/ribavirin.

Conclusions: In this preliminary study, there was a significant trend of decrease in P/C ratios associated with HCV clearance. These results suggest a promising role for DAAs and viral clearance in improving short-term kidney graft survival. In the future, larger cohort studies will be needed to assess the long-term benefits of DAAs in this special population of HCV-infected patients.

Project Length: Short
N-1

Slipped Capital Femoral Epiphysis Trends In Treatment: Analysis Of 11,002 Patients From 1997 To 2012

Ilya M. Gutman, *Shawn R. Gilbert*, MD

Division of Orthopaedic Surgery, University of Alabama at Birmingham, Birmingham, AL

Abstract

Introduction: Slipped capital femoral epiphysis (SCFE) is an adolescent hip condition with significant long term sequelae and evolving treatment options, including an emphasis on open reduction to restore anatomy.

Objectives: The purpose of this study was to evaluate trends in treatment using a prospectively collected pediatric nationally representative database.

Methods: Patients undergoing treatment for idiopathic SCFE were selected by querying the Healthcare Cost and Utilization Project's (HCUP) Kids' Inpatient Database (KID) for the years 1997, 2000, 2003, 2006, 2009, and 2012. The selected patients were separated based on operative approach and these cohorts were analyzed based on temporal and categorical differences in operative approach, patient demographics and clinical characteristics, comorbidities, and complications. Univariate and multivariate analyses were used when appropriate and Mantel-Haenszel test for trend was used in temporal analysis.

Results: Overall inpatient SCFE procedures have decreased 27.5% ($P < 0.001$). Closed procedures have decreased 28.5% ($P < 0.001$), while open procedures have decreased 44.8% ($P < 0.001$). Bilateral closed procedures have increased 7.2% ($P < 0.001$) and mixed open and closed procedures increased nearly 7 fold since 2006 ($P < 0.001$). The ratio of open to closed procedures decreased in Ages 9 to 12 and increased in ages 13 to 16 ($P < 0.001$). Depression is strongly associated with having an open procedure and increases the likelihood 3.160 times ($P = 0.003$). Obesity is not a significant predictor for having either an open or closed procedure.

Conclusions: While the rate of inpatient treatment of SCFE is declining, there is an increase in rates of bilateral procedures and open procedures in older patients.

Project Length: Short
Poster N2

Methicillin-resistant vs. methicillin-susceptible *Staphylococcus aureus* pediatric osteomyeltis: a retrospective analysis of the Kid's Inpatient Database (KID)

William T. Davis[1], *Shawn R. Gilbert, MD*[2]

[1]School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA

[2] aDepartment of Surgery, Division of Orthopedics bDepartment of Surgery cSchool of Medicine, University of Alabama at Birmingham, Birmingham, Alabama, USA.

PURPOSE: The incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) pediatric osteomyelitis has risen over the past two decades and has been associated with a more severe clinical course than methicillin-susceptible *Staph. aureus* (MSSA) infections. National databases have been underutilized to describe these trends. We sought to describe demographic factors predicting MRSA vs. MSSA osteomyelitis and to compare outcomes between MRSA and MSSA infections.

METHODS: We queried the 2009 and 2012 Healthcare Cost and Utilization Project (HCUP) Kid's Inpatient Database (KID) for discharge records with diagnosis codes for both osteomyelitis and *Staph. aureus*. We explored patient demographics predicting MRSA and evaluated MRSA vs. MSSA as predictors of multiple surgeries, length of stay, and total charges.

RESULTS: A total of 4214 discharge records were included. Of those, 2602 (61.7%) had MSSA and 1612 (38.3%) had MRSA infections. The odds of patients at Southern and Midwestern hospitals having MRSA were 1.83 [1.49-2.26] and 1.29 [1.02-1.63] times those of patients at Northeastern hospitals. Medicaid patients' odds of MRSA were 1.83 [1.57-2.13] times higher than those with private insurance. Black patients had 1.40 [1.16-1.70] times higher odds of MRSA compared to White patients. A total of 1388 (32.9%) patients had surgery. The odds of MRSA patients undergoing multiple surgeries were 1.85 [1.45-2.36] times those of MSSA patients. Patients with MRSA had 17.6% longer lengths of stay than those with MSSA ($p<.001$) and 7.1% higher total charges ($p=.002$) after controlling for length of stay.

CONCLUSION: Review of the KID database confirms that MRSA is now a prominent pediatric osteomyelitis pathogen and is especially common in the South, among Black patients, and among patients with Medicaid. The greater odds of multiple surgeries, longer length of stay, and higher costs associated with MRSA infections support the notion that MRSA infections result in more severe clinical courses than MSSA infections.

Project Length: Short
N-3

Title: Modifiable factors that impact long-term Quality of Life and development of chronic pain after pulmonary resection (an interim analysis)

Authors: **Alexia J. Powers**, Roland Short, MD, Benjamin Wei, MD, *Ayesha Bryant, MSPH, MD*

Introduction: Quality of life (QOL) may be severely compromised by the development of chronic post-operative pain.

Objective: The primary objective of this study was to determine if modifiable patient factors are associated with development of chronic pain and poor long-term QOL after lung surgery.

Methods: QOL was determined on a consecutive series of patients who underwent surgical resection for treatment of early stage lung cancer or benign pulmonary tumor using the Short Form-12 (SF-12) survey. Both the physical (PCS) and mental component scores (MCS) of the SF-12 survey were evaluated. Pain was assessed using a Visual Analog Scale (0 [no pain] – 10 [worst pain]), the Faces Pain Scale, and a modified McGill Pain Questionnaire.

Results: Between 2010- 2015, 803 patients underwent pulmonary resection. The median follow-up time was 2.9 years (range 0.5 to 6.7 years) from 205 responders to date. The median PCS was 36.8, the median MCS was 54.6, and the median VAS pain score was 1.3. Patients who had a pre-operative history of opioid use reported a greater pain score (VAS) compared to those that were opioid naive (1.2 vs. 2.9, respectively) at a median of 2.9 years postoperatively. Additionally, irrespective of a history of opioid use, patients who underwent surgery with a minimally invasive approach reported a significantly higher PCS compared to those who underwent thoracotomy (38.2 vs. 31.1, respectively, p=0.004) and a significantly lower pain score (VAS 1.0 vs 2.5, p=0.04) almost 3 years after surgery.

Conclusion: Patients who were opioid naive pre-operatively and underwent a minimally invasive surgical approach (robotic) reported higher physical QOL scores and lower pain scores at a median of 3 years after surgery. These findings indicate that cessation of opioid use pre-operatively and/or use of a robotic approach may reduce the risk of developing chronic pain post-operatively and improve long-term QOL.

Project Length: Short
N-4

The value of post-operative chest radiography immediately following Project Length: ior spinal instrumentation and fusion in adolescent idiopathic scoliosis cases

Robert A. Esposito. *Michael J. Conklin, MD. Shawn R. Gilbert, MD.*
Department of Surgery, Division of Orthopaedics, University of Alabama at Birmingham School of Medicine, Birmingham, AL

Introduction: Pneumothorax (PTX) is a known complication of Project Length: ior spinal instrumentation and fusion (PSIF) surgery in patients with adolescent idiopathic scoliosis (AIS). Some institutions utilize routine post-operative chest radiographs to rule out pulmonary complications. However, reports of post-operative pulmonary complications, such as PTX, appear to be low.

Objective: We have evaluated the usefulness of routine post-operative chest radiographs to detect immediate pulmonary complications following PSIF surgeries in AIS cases.

Methods: A query of Kids' Input Database (KID) and an institutional case review were performed. Frequencies of post-operative pulmonary complications, represented by the presence of PTX, and rates of surgical intervention and supplemental oxygen were recorded. Patient demographics and comorbidities were also noted for future statistical analysis.

Results: KID datasets revealed a PTX frequency of 0.33% (30/9,036) following PSIF for AIS patients with intervention required in 13.33% (4/30) of PTX positive patients. Retrospective analysis of institutional cases produced a PTX frequency of 3.28% (8/244) and an additional 4.10% (10/244) for cases that could not be excluded for PTX. No surgical intervention was required for any PTX positive institutional cases, although one required supplemental oxygen.

Conclusion: The rate of pneumothorax following PSIF is extremely low. Few identified cases require surgical or non-surgical intervention. Routine postoperative chest radiography following PSIF for AIS may not be necessary.

Project Length: Short
N-5

A comparison of post-operative MI rates based on the universal 2012 and NSQIP definitions

[1]**Kevin S. Shrestha**, [2]Allison A. Gullick MSPH, [2]Tyler S. Wahl MD, [2]Robert H. Hollis, [2]Joshua Richman MD, PhD, [2]James K. Kirklin MD, *[2]Melanie S. Morris MD, M*

[1]University of Alabama School of Medicine, University of Alabama at Birmingham
[2]Department of Surgery, University of Alabama at Birmingham

Introduction: The National Surgical Quality Improvement Program (NSQIP) provides benchmarking quality standards designed to improve quality of care and surgical outcomes. We explore NSQIP's current definition of myocardial infarctions (MI) and compare to an updated definition, the 2012 Universal Definition.

Methods: All NSQIP-assessed post-operative cardiac events in 2013-2015 from a single institution were examined as part of a quality improvement project. The study included all patients who met the NSQIP definition for postoperative MI. The 2012 definition was applied to this group with patient- and procedure-specific characteristics compared by MI definition (NSQIP vs. 2012) using Chi-Square tests.

Results: Eighty-one patients were identified. Only 27 (33.3%) of patients meeting the NSQIP definition also met the 2012 definition. Overall, the average patient was a 68.1 (SD 12.2) year old white (69.1%) male (54.3%) with a BMI of 28.2 (SD 7.8). There were no significant differences between definition groups regarding patient demographics or perioperative complications. Only 22.2% of the NSQIP-defined group had a troponin level 5-times the ULN meeting the 2012-defined group ($p<0.0001$). Patients classified using the 2012 definition had significantly more ischemic EKG changes (ST-elevation: 25.9% vs 3.7%, respectively, $p=0.01$; Q wave: 22.2% vs. 0%, respectively, $p= 0.001$). NSQIP-defined MI occurrences were more likely to be NSTEMI type II events (85.2% vs. 51.9%, $p = 0.003$). Patients with MI meeting 2012 definition were more likely to have ischemic symptoms (70.4% vs 37%, $p=0.005$) and abnormal imaging changes (33.3% vs 13%, $p=0.03$).

Conclusion: One-third of patients with a NSQIP-defined MI met the 2012 definition. Compared to NSQIP's MI definition, the 2012 definition captures patients with more ischemic symptoms, ischemic EKG changes, abnormal changes on imaging, and higher troponin levels with fewer NSTEMI Type II events. The NSQIP definition may over-estimate true coronary events. Consideration to update NSQIP's MI definition may be warranted.

Project Length: Short
N-6

A Formula for Planning and Predicting Post-Operative Mammoplasty Results

Mary Smithson; Mina S. Mousa; Carly Bramel; *Sherry S. Collawn, MD, PhD*

Department of Surgery, Division of Plastic Surgery, University of Alabama at Birmingham, Birmingham, Alabama

Introduction: Reduction mammoplasty is a safe and effective solution to increasing quality of life through alleviating pain and improving aesthetics. This study developed a way to combine a surgeon's view of breast measurement (volume) with a patient's view of breast measurement (distance between certain points on the breast) to provide patients with a better understanding of expected outcomes following reduction surgery.

Objectives: This study aims to determine the impact volume removed has on length of typical breast measurements in order to increase patients' understanding of expected outcomes.

Methods: A retrospective chart review was performed on all medial superior pedicle reduction mammoplasties performed by a single surgeon at a university medical center from 2008 to 2016. Measurements of interest for this study were nipple to sternal notch (N-S), nipple to inframammary fold (N-I), nipple to midline (N-M), and breast diameter (BD). The average bilateral change per measurement was calculated for each patient in centimeters and averaged. Grams removed per breast were also averaged. Each measurement of average change was divided by the gram average and multiplied by 100 to obtain centimeter change per 100 grams. Individual patient measurements per type of measurement were averaged to achieve a final improvement reported in centimeters per 100g tissue removed per breast.

Results: The average change in the N-S distance was calculated to be a decrease of 1.5 ± 0.8 cm/100 g of breast tissue removed; for N-I the overall decrease was 0.7 ± 0.5 cm/100 g and for N-M the decrease was 0.1 ± 0.3 cm/100 g. The average change in BD was calculated to be 0.0 ± 0.4 cm/100 g.

Conclusion: Results from this study can be used to increase patients' understanding of expected outcomes for breast reduction surgery.

Project Length: Short
N-7

Rohan Prabhu
Dr. Riesenberg

Title: **Total Intravenous Anesthesia (TIVA) compared to Inhalation Anesthesia: Which One Is Better for the Brain? A systematic review**

Abstract

Background: Reduced cognitive function and post-operative delirium (POD) are frequently observed symptoms after major surgeries involving the use of anesthesia, especially among geriatric populations. The term general anesthesia includes two major prototypes of anesthetic agents: inhalational and intravenous anesthetics.

Methods: We conducted a systematic review of the English-language literature published between 1990 and July 2016, using PubMed, CINAHL, Embase, PsychINFO, and Scopus comparing inhalational anesthesia (IA) vs. total intravenous anesthesia (TIVA). We started with a research protocol outlining the details and included operational definitions. Included studies had to compare the two anesthetic techniques; have a control or comparison group; include patients who were ≥60 years old; and use the Mini-Mental State Exam (MMSE) as an outcome measure. Teams of trained reviewers selected articles. Disagreements were discussed by the team until consensus was reached.

Results: Initial results from article review identified 8 relevant articles. Five studies showed non-significant results; all five had small samples sizes (43-200). Three studies showed statistically significant differences in MMSE scores post-operatively that favored TIVA. The largest study (2,000 subjects) demonstrated the greatest difference, as measured by p value. Overall, for the 8 studies, the baseline inhalation anesthesia MMSE scores ranged from 26.3 to 28.6 (IA) compared to 26.5 to 27.7 (TIVA) Post-operative MMSE scores operative ranged from 25.0 to 27.8 (IA) compared to 25.0 to 29.0 (TIVA).

Conclusion: Most studies examining this area found no difference between IA and TIVA. However, the largest study reported TIVA to be significantly superior to IA. Based on these initial results, IA may lead to decreased cognitive function amongst geriatric populations. Additional studies with larger sample sizes need to be conducted in order to draw a definitive conclusion.

Project Length: Short
N-8

How applicable are MOMS Trial results? A comparison of a single-institution cohort to the results from the randomized trial.

Nicholas M. B. Laskay, BS[*1], Anastasia A. Arynchyna, MPH[*1], Samuel G. McClugage III, MD[1], Betsy Hopson[1], Chevis Shannon, MPH, MBA, DrPH[2], Benjamin Ditty, MD[1], John C Wellons III, MD, MSPH[2], Jeffery P. Blount, MD[1], Brandon G. Rocque, MD, MS[1]

Object: The Management of Myelomeningocele Study (MOMS) compared prenatal versus postnatal repair of myelomeningocele. We evaluated a cohort of mothers over the same time period to determine if they would have been eligible for MOMS. In addition, we examine the hydrocephalus outcomes in our series compared to both the original and revised MOMS primary composite outcome (PCO).

Methods: A chart review identified all myelomeningocele patients born at the authors' institution (COA) between 2003-2009. We applied MOMS eligibility criteria to determine eligible mothers, and then compared sociodemographic variables between eligible, ineligible, and MOMS patients. We applied the original MOMS PCO and the proposed revised PCO to our cohort and compared to MOMS groups.

Results: Of 78 patients, 55 (70.5%) would have been eligible for the MOMS trial. Maternal age, race, and marital status were significantly different MOMS patients. Shunting rates were higher in our cohort (84.6%) versus both prenatal (44.0%) and postnatal (83.7%) MOMS infants. Fewer children met the original PCO than the postnatal group (84.6% vs. 97.8%, p=0.002), and there was no difference between our cohort and the prenatal group (84.6% vs. 72.5%, p=0.058). Applying the revised criteria, we find the opposite result: a significant difference between COA and MOMS prenatal (84.6% vs. 49.5%, p<0.001) but no difference between the COA group and MOMS postnatal (84.6% vs. 87.0%, p=0.662).

Conclusion: Mothers at COA differ from the mothers enrolled in the MOMS trial in age, race, and marital status. Baseline fetal characteristics of the COA cohort are similar to those of the MOMS postnatal group. Review of our series shows that treatment of hydrocephalus tracks almost identically with original MOMS shunt criteria. Revision of the criteria led to greater concordance between meeting the criteria and receiving a shunt in the MOMS patients, but dramatically changes the results of the comparison with our series.

Project Length: Short
N-9

Title: A Retrospective Case Series of Carbon Fiber Plate Fixation of Ankle Fractures

Authors: **Caleb Jones** BS[1], Kenneth Smith MD[2], Zach Pinter BS[1], Ryan Hadden BS[1], *Ashish Shah MD[2]*.

Affiliations: [1]University of Alabama School of Medicine; [2]University of Alabama at Birmingham Department of Surgery, Division of Orthopedic Surgery

Introduction:
Ankle fractures represent 9% of all orthopaedic fractures. When fibula fractures require surgical fixation, implant options include 1/3rd tubular plates, locking plates, interfragmentary lag screws, and intramedullary nails. These implants are typically made from stainless steel or titanium alloys. Carbon fiber implants have been used for a number of years, most frequently in the humerus, femur, and the spine. The advantageous properties of carbon fiber implants include a similar modulus of elasticity to bone, which decreases stress shielding; biocompatibility, which leads to a minimal histologic cellular response; increased fatigue strength; and radiolucency on radiography that allows for better visualization of fractures during healing. Our hypothesis is that carbon fiber plates provide similar clinical outcomes for ankle fracture fixation as titanium and steel implants.

Methods:
This is a retrospective chart review of 30 patients who underwent fibular open reduction internal fixation (ORIF) with carbon fiber plates from May 2014 to January 2016. All fibulas were fixated using a direct lateral approach to the fibula and the CarboFix distal fibula plate. One senior foot and ankle surgeon performed all surgeries. The main outcomes assessed were postoperative fusion rate and complication rate.

Results:
In our series, the non-union or failure rate was 4.2%. With a mean follow up time of 5.5 months, the complication rate was 13.3%. These results demonstrate that the fusion rate for a carbon fiber plates (95.8%) are comparable to the mean rate seen in fibular fracture repair with intramedullary nails (88.9-98.9%). Additionally, the complication rate for carbon fiber plates (13.3%) is superior to reported complication rates for standard metal plates used in fibula fractures (30%).

Conclusion:
The carbon fiber plate is a viable alternative to ankle fracture ORIF. Carbon fiber plates, when used in fibula fracture fixation, demonstrate comparable union and complication rates to traditional metal constructs. The many theoretical advantages of carbon fiber plates make them an attractive implant choice for ORIF of the fibula.

Project Length: Short
N-10

Title: Retrospective Case Series of Tibiotalocalcaneal Arthrodesis (TTCA) Using a Carbon Fiber Intramedullary Nail

Authors: **Caleb Jones** BS[1]**,** Kenneth Smith MD[2], Ryan Hadden BS[1], *Ashish Shah MD[2]*.

Affiliations: [1]University of Alabama School of Medicine; [2]University of Alabama at Birmingham Department of Surgery, Division of Orthopedic Surgery

Introduction:
Tibiotalocalcaneal (TTC) arthrodesis is a salvage option reserved for severe ankle and hindfoot deformities, arthritis of the ankle and subtalar joints, avascular necrosis of the talus, failed total ankle arthroplasty, and Charcot arthropathy. Implants have long been made from various metals, the most common being stainless steel or titanium alloys. Carbon fiber implants have been available for years and have been used in many applications. The advantages of carbon fiber implants include its radiolucency on plain radiographs, increased fatigue strength, similar modulus of elasticity as bone to decrease stress shielding and its biocompatibility.

Methods:
This is a retrospective chart review of 28 patients who underwent a TTC arthrodesis using the carbon fiber intramedullary nail. 5 patients were excluded because of loss to follow-up or having inadequate follow-up time to assess for fusion. Another 10 patients were excluded from analysis since their procedure was a revision of prior failed ankle or subtalar fusion. One senior foot and ankle surgeon performed all surgeries. The main outcomes assessed were postoperative fusion rate and complication rate. All radiographs were read by a senior radiologist and orthopedic surgeon to assess for consolidation and proper alignment.

Results:
The fusion rate in our series was 61.5% with a mean follow up time of 7.4 months. The mean time to union was 15.3 weeks, which aligns well with the fusion time observed with metal constructs. The overall complication rate was 61.5%, however, the vast majority were minor complications with only 23.1% of patients requiring repeat surgical intervention. Our fusion rate is lower than in prior published reports using metal implants. Our results suffer from small sample size error which could explain the relatively high nonunion rate.

Conclusion:
This case series has demonstrated comparable short-term success rates of carbon fiber implants to that of metal constructs for use in TTC arthrodesis. Outcomes using carbon fiber implants have been described in other applications but no studies have demonstrated outcomes in the context of TTC arthrodesis.

Project Length: Short
N-11

Evaluation of acute kidney injury in neonates less than thirty days old undergoing cardiac surgery requiring post-cardiopulmonary bypass.

Ashlyn M Alongi, B.A. *Jeffrey Alten, M.D*. Medical Director, Cardiovascular Intensive Care Unit, Department of Pediatric Cardiology, Children's of Alabama, Birmingham, Alabama.

Introduction: Acute kidney injury (AKI) is associated with increased morbidity and mortality; however, there is not a singular, substantiated framework to diagnose and classify neonates with AKI due to their immature nephrons, tendency for complex cardiac surgeries with longer bypass time, and exaggerated postoperative inflammatory response. Present studies use differing criterion, with inconsistent risk factors and specific outcomes. KDIGO is gaining acceptance to classify AKI in pediatric populations.

Objectives: This study aims to modify the KDIGO AKI classification in a neonatal postoperative cardiac surgery population at Children's and UAB Hospital, by diagnosing AKI within hours of CPB with data such as urine output and serum creatinine. Another objective is to investigate specific risk factors that predispose neonates to AKI after cardiac surgery, crucial for accurate risk stratification and prediction models for AKI to prevent common adverse sequelae, such as fluid overload and metabolic disturbances.

Methods: 249 patients younger than thirty days in the last ten years who underwent a cardiac operation at Children's of Alabama or UAB Hospital requiring cardiopulmonary bypass were included in the study. Demographic information, anesthesia and surgery information, as well as lab results, detailed fluid balance, and other post-operative outcomes were collected.

Results: Further investigation is necessary to quantify and prognosticate AKI in this patient population. Looking at this center's unpublished data: 74 neonates undergoing CPB since 2012, the incidence of AKI ranged from 41% to 67%, depending on the definitions of AKI, with multiple patients changing diagnostic cohort as AKI definition changed. Preliminary findings show that 13 patients required postoperative hemodialysis.

Conclusions: Our hypothesis that diagnosing AKI by modified KDIGO criteria is predictive of increased hospital length of stay, duration of mechanical ventilation, and mortality when controlled for complexity of surgery and other preoperative markers of illness severity is still currently under investigation.

Project Length: Intermediate
N-12

Patient-declared Sternoclavicular Joint Pain: The Shoulder's Waddell's Sign?

Adam T. Archie, BS, *Brent A. Ponce, MD*, Shawna Watson, BS, Mariano Menendez, MD, Eugene W. Brabston III, MD, Gerald McGwin, Phd
Department of Orthopaedic Surgery, The University of Alabama Birmingham, Birmingham, Alabama, USA

Introduction:
Beyond organic causes of pain, a patient's report of pain can be magnified by nonorganic sources (depression, anxiety, catastrophic thinking, etc). Previous studies have linked psychogenic pain to poor post-surgical outcomes in multiple surgical specialties; however, it has never been studied in shoulder surgery.
Objectives:
The primary objective of this study was to develop a physical exam technique to confirm or reject a nonorganic basis for pain.
Methods:
Consenting patients seeing one of two sports/shoulder fellowship trained surgeons at an academic practice were screened for study enrollment. Patients who met the inclusion criteria were given a set of five surveys to complete, which assessed physical disability, self-efficacy and psychological health. The physician then completed a comprehensive standardized physical examination with the examining physician being blinded to the patient's survey responses. Palpation of the SCJ was done with the examiner's thumbs and accompanied by the question, "Does this hurt?". Patients were then sorted into two groups based on their confirmation or denial of pain upon SCJ palpation. Responses to the 5 surveys were then compared between the two groups.
Results:
111 patients were enrolled. The mean patient age was 57.6 and 59.1% of the sample was female. Of the "positive" SCJ palpation patients, 14 were female, 7 were male with a mean age of 54.37. Patients with confirmed pain on SCJ palpation had significantly different survey scores when compared to patients who denied pain upon SCJ palpation. PCS survey (p-value = 0.002), PSEQ survey (p-value = 0.017), QuickDASH survey (p-value = 0.01), SPADI survey (p-value = 0.001), and PHQ-2 (p-value = 0.003).
Conclusion:
Patient confirmed pain upon SCJ palpation suggests the presence of nonorganic factors contributing to pain magnification and a possible underlying psychological diagnoses.

Project Length: Intermediate
N-13

Title: Thoracic Outlet Syndrome Decompression in Adolescents

Authors: Heather L. Minton, BS**,** Bradley L. Young, BS, Shawna L. Watson, BA, Erin F. Ranson, MD, Richard D. Meyer, *Brent A. Ponce, MD* -- Division of Orthopaedic Surgery, The University of Alabama at Birmingham

Introduction: Neurogenic thoracic outlet syndrome (NTOS) is a relatively uncommon but life-altering condition most often affecting young individuals. NTOS is characterized by compression of the brachial plexus and presents with pain, numbness, and paresthesia of the arm and hand, which is reproducible with overhead movements. Accompanying symptoms may include weakness of the arm and hand, headaches, and psychological distress due to limited use of the arm. Patients often see multiple healthcare providers, attempt physical therapy that exacerbates their condition, and receive injections or medications with minimal relief prior to seeking surgical treatment. Due to its limited prevalence, surgical treatment for NTOS has not been adequately studied.

Objectives: The purpose of this study is to characterize surgical outcomes following neurogenic thoracic outlet syndrome decompression in adolescents and identify relationships between perioperative factors and surgical outcomes.

Methods: A retrospective review of adolescent patients age 7-18, surgically treated at our institution between 2000 and 2015, was conducted. Perioperative factors were compared among patients. Functional outcomes were assessed using the quick Disabilities of Arm, Shoulder, and Hand (quick-DASH) survey, Cervical-Brachial Symptom Questionnaire (CBSQ), and a 10-point visual analog scale (VAS) for pain. Additionally, patients described their upper extremity function before and after surgery.

Results: Surgical decompression of NTOS in adolescent patients showed favorable outcomes. Overuse, especially in sports, was a common mechanism of injury. Congenital anomalies, such as presence of cervical ribs, enlarged cervical transverse processes, or coracocostal ligaments, were present in numerous patients. Surgical treatment most commonly involved neurolysis of the brachial plexus and excision of a cervical rib, transverse process, and/or scalenes. Repeat surgeries and post-operative complications were rare. Adolescent patients experienced relief of pain, numbness, and paresthesia after surgical decompression, with most patients returning to pre-operative activities, including sports.

Conclusion: Surgical decompression for NTOS has positive outcomes for adolescent patients.

Project Length: Long
N-14

Dennis Winn

Abstract Title: Telemedicine with mobile devices using merged-reality for early postoperative care: A feasibility study

Authors and Affiliations: Dennis K Winn, Shawna L Watson, Eugene W Brabston, Shin Xu, Dustin K Baker, Brent A Ponce, and Barton L Guthrie

Abstract Body: Abstract Telemedicine encounters requiring procedural guidance, such as surgical wound care, medical equipment management, etc. may benefit from more interactive ability. Recent development of “merged reality” capability for mobile devices may provide such enhanced interaction. In an effort to understand the potential for real-time augmented-, or merged-, reality for interactive postoperative wound care, we piloted a study to assess patient and physician satisfaction with the use of such technology on standard mobile devices. Two orthopaedists and one neurosurgeon enrolled 30 surgical patients for study. Each downloaded an application which enables real-time merged-reality interaction across iPhone or iPad (Help Lightning, Inc., Birmingham, AL). A virtual remote interactive encounter between surgeon and patient occurred shortly after postoperative discharge. The virtual interaction consisted of a typical follow-up consultation with surgical site inspection and wound care instructions as appropriate. Patient and physician experience was assessed via follow-up surveys. Patients (90%) and physicians (83%) were satisfied with the interaction and felt the encounter was reassuring and reflective of what was seen in subsequent physical follow-ups. Problems included difficulty with software download and registration, missed calls due to scheduling conflicts, and slow connection speeds leading to poor audiovisual quality. Neither group felt that quality of care was threatened. This pilot data supports the potential for mobile device-based interactive merged-reality use in early postoperative care. Larger studies are warranted to determine necessary policy and safety issues of remote presence for surgical patient care.

Project Length: Long
N-15

Which hepatocellular carcinoma staging system has the highest predictive value?

Shelby L. Bergstresser, Dr. Derek DuBay MD.

Introduction: Hepatocellular carcinoma (HCC) is the sixth most common cancer and third most common cause of cancer related deaths in the world. HCC incidence is trending upward and has become the fastest rising cause of cancer related death. 7 staging systems have been validated to varying degrees to reflect prognosis and therapeutic decision making in the management of HCC. Currently, there is no consensus on which staging system has the best predictive value in determining patient outcomes.

Objectives: Determine the predictive value of Okuda, TNM, CLIP, BCLC, CUPI, JIS, and GRETCH staging systems for HCC treatment modalities including surgical resection, transplantation, transarterial chemoembolization, radioembolization, ablation, and best supportive care using a large single-center database of HCC patients.

Methods: Using UAB's PowerChart system, retrospective chart analysis was performed on patients undergoing HCC treatment at UAB Hospital from January 2007 to December 2014. Variables collected include: liver disease etiology, performance status, pre-intervention lab data, post-intervention lab data, and tumor markers. Lab values were used to calculate MELD score and Child Pugh class, while data regarding patient performance status was collected from progress notes.

Results: Statistical analysis will be performed to calculate median and overall survival curves for patients diagnosed with HCC at the time of diagnosis and treatment. Each of the 7 staging systems will be analyzed accordingly to determine the relative predictive value for early, intermediate, and advanced HCC as it pertains to prognosis, treatment, and survival.

Conclusion: Concluding remarks will be dependent upon successful statistical analysis of the large UAB database following completion of the current stage of the project.