

THE UNIVERSITY OF ALABAMA SCHOOL OF MEDICINE

DALE J. BENOS

MEDICAL STUDENT

Research Day

2013

Elizabeth Luke, Class of 2014

“The pursuit of knowledge is to see
beyond one's own reflection”

TUESDAY, OCTOBER 29, 2013
VOLKER HALL, 1ST FLOOR

10:00AM-12:30PM: ORAL PRESENTATIONS

12:30PM-1:00PM: POSTER SESSION & LUNCH

1:00PM-3:00PM: JUDGING OF POSTERS

JUDGES

Dr. Will Brooks <i>Dept. of Cell, Developmental and Integrative Biology</i>	Dr. Emmy Bell <i>Dept. of Medicine</i>
Dr. David Cleveland <i>Dept. of Surgery</i>	Dr. Laura Cotlin <i>Dept. of Cell, Developmental and Integrative Biology</i>
Dr. Judy Creighton <i>Dept. of Anesthesiology</i>	Dr. Christine Curcio <i>Dept. of Ophthalmology</i>
Dr. Gareth Dutton <i>Dept. of Medicine</i>	Dr. Devin Eckhoff <i>Dept. of Surgery</i>
Dr. Gregory Friedman <i>Dept. of Pediatrics</i>	Dr. Catherine Fuller <i>Dept. of Cell, Developmental and Integrative Biology</i>
Dr. James George <i>Dept. of Surgery</i>	Dr. Corinne E Griguer <i>Dept. of Neurosurgery</i>
Dr. Lynae Hanks <i>Dept. of Nutrition Sciences</i>	Dr. Fadi Hage <i>Dept. of Medicine</i>
Dr. Patricia L. Jackson <i>Dept. of Medicine</i>	Dr. Edgar Jaimes <i>Dept. of Medicine</i>
Dr. Tamas Jilling <i>Dept. of Pediatrics</i>	Dr. Charles Landen <i>Dept. of Obstetrics and Gynecology</i>
Dr. Silvio Litovsky <i>Dept. of Pathology</i>	Dr. Colin Martin <i>Dept. of Surgery</i>
Dr. Carmel McNicholas <i>Dept. of Cell, Developmental and Integrative Biology</i>	Dr. Spencer Melby <i>Dept. of Surgery</i>
Dr. Andrew Paterson <i>Dept. of Medicine</i>	Dr. Ji-Bin Peng <i>Dept. of Medicine</i>
Dr. William Placzek <i>Dept. of Biochemistry & Molecular Genetics</i>	Dr. Christopher Pruitt <i>Dept. of Pediatrics</i>
Dr. Robert Russell <i>Dept. of Surgery</i>	Dr. Patricia Sawyer <i>Dept. of Medicine</i>
Dr. Masako Shimamura <i>Dept. of Pediatrics</i>	Dr. Peter Smith <i>Dept. of Cell, Developmental and Integrative Biology</i>
Dr. Marsha Sturdevant <i>Dept. of Pediatrics</i>	Dr. Elizabeth Sztul <i>Dept. of Cell, Developmental and Integrative Biology</i>
Dr. Henry Wang <i>Dept. of Emergency Medicine</i>	Dr. John Waterbor <i>Dept. of Epidemiology</i>
Dr. Douglas Weigert <i>Dept. of Cell, Developmental and Integrative Biology</i>	Dr. Roger White <i>Dept. of Medicine</i>
Dr. John Woods <i>Dept. of Obstetrics and Gynecology</i>	Dr. Bradford Woodworth <i>Dept. of Surgery</i>
Dr. Yang Yang <i>Dept. of Pathology</i>	

Dale J. Benos Medical Student Research Day

Oral Presentations

Tuesday, October 29, 2013

Lecture Room E

Short Term Research

10:00 – 10:15 am

Chad Colon, MS2

“Characterization of Refractory vs. Resistant Hypertension Phenotypes”

Mentor: Dr. Suzanne Oparil

10:15 – 10:30 am

David Dorn, MS3

“Adjuvant Stereotactic Body Radiation Following Chemoembolization Improves Survival In Patients with Non-Resectable Hepatocellular Carcinoma over 3 Centimeters?”

Mentor: Dr. Derek DuBay

10:30 – 10:45 am

Neha Hingorani, MS2

“The Role of Sp17 in Genetic Instability in Breast Cancer”

Mentor: Dr. Theresa Strong

10:45 – 11:00 am

Helen Lin, MS2

“The Association Between Health Literacy and Medication Self-Management in Community-Dwelling Older Adults”

Mentors: Dr. Richard Allman and Dr. Patricia Sawyer

11:00 – 11:15 am

Elizabeth Luke, MS4

“Pediatric Resident Survey of Their Self-Perceived Competency and Knowledge Regarding Anaphylaxis and Epinephrine Auto-Injectors”

Mentor: Dr. Nancy Tofil

11:15 – 11:30 am

Claire Sands, MS3

“A novel Catalytic Oxidoreductant Improves Functional Outcomes in Spinal Cord Injured Rats”

Mentor: Dr. Candace Floyd

11:30 – 11:45 am

Nicholas Scanlon, MS2

“Allogenic Responses as an Explanation for Higher Risk of Transmission of HIV-1 in HLA-B Matched Individuals”

Mentor: Dr. Steffanie Sabbaj and Dr. Paul Goepfert

11:45 – 12:00 pm

Derek Wells, MS2

“HCV Awareness, Risk Assessment and Healthcare Utilization Among “Baby Boomers” Presenting to the UAB Emergency Department”

Mentor: Dr. James Galbraith

Dale J. Benos Medical Student Research Day

Oral Presentations

Tuesday, October 29, 2013

Lecture Room A

Long Term Research

10:00 - 10:15 am

Jennifer Hadley, MSTP (GS4)

"Graph Theoretic Analysis of Network Interactions in Schizophrenia"

Mentor: Dr. Adrienne Lahti

10:15 – 10:30 am

Jon Lockhart, MSTP (GS2)

"Allogenic Bone Marrow Transplantation Without Cytoablative Conditioning to Cure Cooley's Anemia"

Mentor: Dr. Thomas Ryan

10:30 – 10:45 am

Catherine Poholek, MSTP (GS4)

"Interleukin-21 Drives Intestinal Inflammation by Bridging the Adaptive and Innate Immune Compartments"

Mentor: Dr. Laurie E. Harrington

10:45 – 11:00 am

Stephanie Robert, MSTP (GS3)

"Brain Tumor Associated Excitotoxicity and Seizures as a Result of System xc- Expression"

Mentor: Dr. Harald Sontheimer

Intermediate Term Research

11:00 – 11:15 am

Charis Chambers, MS4

"Perinatal Outcomes in Obese Women with Preterm Rupture of Membranes"

Mentors: Dr. Joseph Biggio and Dr. Amelia Sutton

11:15 – 11:30 am

Jonathan Landham, MS4

"Penetrating Limb Injuries: A 5 year Retrospective Analysis from a Level 1 Trauma Facility"

Mentor: Dr. Duraid Younan

11:30 – 11:45 am

Shalini Vaid, MS4

"Determinants of Apolipoprotein B in Children with Type 1 Diabetes Mellitus"

Mentor: Dr. Ambika Ashraf

- A-1 Stephanie Brosius, MSTP (GS3)**
“Combinatorial Treatment of Malignant Peripheral Nerve Sheath Tumors with Tyrosine Kinase Inhibitors Hinders Tumor Survival and Proliferation”
Mentor: Dr. Steven Carroll
- A-2 Philip Cezayirli, MS4 (will not be presenting)**
“Post-treatment Peritumoral Cerebral Blood Flow (CBF) Can Better Predict Overall Survival in Newly Diagnosed Glioblastoma Multiforme Patients Compared to Tumoral/Peritumoral Cerebral Blood Volume (CBV)”
Mentor: Dr. Asim Bag
- A-3 Maryam Ehtsham, MS2**
“Role of Calcium as a Regulator of Glioma Pathophysiology”
Mentor: Dr. Harald Sontheimer
- A-4 Lauren Gibson, MS2**
“Analysis of the Effects of AT101 on the CXCL 12-CXCR4/CXCR7 axis on GBMs”
Mentor: Dr. Kevin Roth
- A-5 Avinash Honasoge, MSTP (GS4)**
“Autocrine Regulation of Glioma Cell Proliferation via pH-sensitive K⁺ Channels”
Mentor: Dr. Harald Sontheimer
- A-6 Margaret Marks, MS2**
“The Potential Role of JAK1 Inhibitor AZD3715 in Glioblastoma Therapy”
Mentor: Dr. Tika Benveniste
- A-7 Kelsey Patterson, MSTP (MS2)**
“Human Glioma Cells In Tumors of Varying Size Differentially Associate with Blood Vessels”
Mentor: Dr. Harald Sontheimer
- A-8 Nathan Reeve, MS2**
“CD13 is a Potential Novel Cancer Stem Cell Marker for Malignant Glioma”
Mentor: Dr. Corrine Griguer
- A-9 Lindsay Stoyka, MSTP (MS1)**
“Psalmotoxin-1 Inhibits Phosphorylation of ERK1/2 in Glioma Cells”
Mentor: Dr. Catherine Fuller
- A-10 Jennifer Yang, MS2**
“The Role of Reactive Astrocytes in Tumor-Associated Epilepsy”
Mentor: Dr. Harald Sontheimer

- B-1 Taylor Cruce, MS2**
"Pregnancy, Labor, Delivery, and Postpartum Outcomes of Women with and without Spinal Cord Injury: An Observational Study"
Mentor: Dr. Amie B. McLain
- B-2 Russell Fung, MS2**
"Predictors of Post-Operative Pain After Shoulder Arthroscopy"
Mentor: Dr. Nabil Elkassabany
- B-3 Jason Hall, MS3 (will not be presenting)**
"Systemic Administration of 5-HTP has Opposing Effects on Visceral and Somatic Nociceptive Processing"
Mentor: Dr. Meredith Robbins
- B-4 Jonathan Isbell, MS2**
"Road Map Past the Lateral Femoral Cutaneous Nerve During the Modified Anterior Hip Approach: A Cadaver Study"
Mentor: Dr. Herrick Siegel
- B-5 Melissa Jordan, MS2**
"Identifying Differences in Spinal Cord Injury-Related Neuropathic Pain: Virtual Illusion Treatment Outcomes as a Function of Subtype of Pain"
Mentor: Dr. Elizabeth Richardson
- B-6 Brad Langston, MS2**
"Contribution of Intraretinal Scatter to Single Photoreceptor Threshold Discrimination"
Mentor: Dr. Lawrence Sincich
- B-7 Allen Oak, MS2**
"Subretinal Duresnoid Deposit: Further Characterization by Lipid Histochemistry"
Mentor: Dr. Christine Curcio
- B-8 Nidal Omar, MS3**
"The Non-Surgical Nature of Patients with Subarachnoid or Intraparenchymal Hemorrhage Associated with Mild Traumatic Brain Injury"
Mentor: Dr. Mamerhi Okor
- B-9 Mark Pepin, MSTP (MS1)**
"Effect of Paralysis on the Sensitivity of Human Satellite Cell Differentiation"
Mentor: Dr. Marcas Bamman
- B-10 Cory Smith, MS2**
"Evaluation of a Novel Catalytic Oxidoreductant to Confer Tissue Protection on the Brain after Concussion"
Mentor: Dr. Candace Floyd

- C-1 Heather Allen, MSTP (GS4)**
“Role of C3 and C5 Complements Components in the AAV-SYN Model of PD”
Mentor: Dr. David Standaert
- C-2 Joshua Cohen, MSTP (GS1)**
“Maternal Style Differences Shape Emotional Behavior in Rats Genetically Prone to High-Anxiety”
Mentor: Dr. Sarah Clinton
- C-3 David Figge, MSTP (GS2)**
“Epigenetic Regulation of the Insulin-Like Growth Factor System in Memory Consolidation”
Mentor: Dr. J. David Sweatt
- C-4 Andrew Hardigan, MSTP (MS2)**
“Identification of Novel Transcripts Associated with Neuropsychiatric Disorders”
Mentor: Dr. Richard Meyers
- C-5 Mikael Guzman Karlsson, MSTP (GS3)**
“Transcriptional Regulation of Intrinsic Excitability and Memory Allocation”
Mentor: Dr. J. David Sweatt
- C-6 John Killian, MS2**
“Pubertal Development Deviates from Norm in Rett Syndrome”
Mentor: Dr. Alan Percy
- C-7 Jarrod Meadows, MSTP (GS3)**
“Epigenetic Regulation of Synaptic Scaling via DNA Methylation”
Mentors: Dr. J. David Sweatt & Dr. John Hablitz
- C-8 Chase Mitchell, MS3**
“Disease Subtype in Parkinson Disease is Associated with Specific Changes in the Cerebellum and Thalamus”
Mentor: Dr. Frank Skidmore
- C-9 Brian Warmus, MSTP (GS4)**
“Mutant Tau Causes NMDAR-mediated Insulostratal Dysfunction and Behavioral Abnormalities in a Mouse Model of Frontotemporal Dementia”
Mentor: Dr. Erik Roberson
- C-10 Dylan Whisenhunt, MS4**
“MER-determined STN Width as a Predictor of Postoperative UPDRS Improvement”
Mentor: Dr. Barton L. Guthrie

- D-1 Ashley Barnett, MS2**
"Insulin Resistance and Bone Strength"
Mentor: Dr. Crista Casazza
- D-2 Elizabeth Ma, MSTP (GS1)**
"Novel Small Molecule Agonists of the Orphan Nuclear Receptor NR4A3 Increase Glucose Transport and Uptake in Skeletal Muscle Cells and Adipocytes"
Mentor: Dr. Timothy Garvey
- D-3 John Obert, MS2**
"Understanding the Role of Nicotine in the Progression of Kidney Disease in Diabetics"
Mentor: Dr. Edgar Jaimes
- D-4 Shyam Patel, MS4**
"Correlation Between Hemoglobin A1C and Response to Bevacizumab Therapy in Diabetic Macular Edema"
Mentor: Dr. John Mason
- D-5 Scharlene Powell, MS2**
"Impact of Obesity on Gestational Diabetes Mellitus"
Mentor: Dr. Lori M. Harper
- D-6 Bobby Sistani, MS2**
"Effects of Nicotine Use on Expression of VEGF, ETS-1, and Nephrin in a Diabetes Model"
Mentor: Dr. Edgar Jaimes
- D-7 Andrew Smith, MS2**
"Pediatric Roux-en-Y Gastric Bypass: A Single Site Study of Long Term Outcomes in Adolescents and Teens"
Mentor: Dr. Carroll M. Hammond
- D-8 Jeffrey Tapley, MS2**
"Feasibility and Efficacy of Diabetic Retinopathy Screening in Children with Diabetes"
Mentor: Dr. Cynthia Owsley
- D-9 Vedran Oruc, MS4**
"Familial and Genetic Components of Early Onset Obesity"
Mentor: Dr. Molly Bray

- E-1 Chris Baker, MS2**
“*Dosimetric Predictors of Erectile Function after External Beam Radiotherapy for Prostate Cancer with Emphasis on Fractionation Scheme*”
Mentor: Dr. John Fiveash
- E-2 Kent Burton, MS4**
“*Negative Predictors of Positive Margins in Patients Undergoing Transoral Robotic Surgery for Head and Neck Cancer*”
Mentor: Dr. Eben Rosenthal
- E-3 Bobby Foster, MS3 (will not be presenting)**
“*Characterizing Fluorescent Imaging Properties of Antibodies Conjugated to IRDye800CW for Use in Cancer Imaging*”
Mentor: Dr. Eben Rosenthal
- E-4 LaKeshia Hyndman, MS2**
“*Weight Loss Barriers: Cancer Survivors versus Non-Cancer Controls*”
Mentor: Dr. Laura Rogers
- E-5 Lucy Johnson, MS2 & Madison Plash, MS2**
“*The Efficacy of Using Indocyanine Green for Sentinel Lymph Node Biopsy in Endometrial and Cervical Cancer*”
Mentor: Dr. Warner Huh
- E-6 Tasnia Matin, MS4**
“*The Charleston Comorbidity Index Predicts Survival in Women with Epithelial Ovarian Cancer Independent of Surgical Debulking Status*”
Mentor: Dr. Charles Leath and Dr. Britt Erickson
- E-7 Reshu Saini, MS2**
“*An Evaluation of Contrast Enhanced Ultrasound Imaging in Patients with Breast Cancer: A Feasibility Study*”
Mentor: Dr. Heidi Umphrey
- E-8 Jennifer Stanley, MS2**
“*Contextual Synthetic Lethality in Human Triple Negative Breast Cancer Cells Involving EGFR, BRCA1 and PARP1*”
Mentor: Dr. Eddy Yang
- E-9 Terence Zimmerman, MS4**
“*Expression of Poor Prognostic Biomarkers in Cutaneous Squamous Cell Carcinoma of the Parotid*”
Mentor: Dr. Eben Rosenthal
- E-10 Mike Zhang, MS2**
“*Investigating the Effectiveness of the Dynasplint Trismus System*”
Mentor: Dr Eben Rosenthal

- F-1 John Doughton, MS4**
“*The Impact of ACGME 2011 Resident Work Hour Rules*”
Mentor: Dr. Nancy Tofil
- F-2 Sarah Foppe, MS4**
“*Development of Anatomically Realistic, Low-Cost Transvaginal Hysterectomy Surgical Model for Obstetrics and Gynecological Resident Training*”
Mentor: Dr. John Woods
- F-3 Danielle Franklin, MS4**
“*Procedural Skills Training for New Pediatric Interns*”
Mentor: Dr. Marjorie Lee White
- F-4 Charles Fryberger, MS2**
“*Pilot Study: Virtual Interactive Presence in Teaching a Manual Task*”
Mentor: Dr. Brent Ponce
- F-5 David George, MS4**
“*An Exploratory Study of Fatigue and Alertness Among Attending Physicians*”
Mentor: Dr. Marjorie Lee White
- F-6 Katie Leonard, MS4**
“*Perceptions of Simulations at a School Nurse Workshop*”
Mentor: Dr. Marjorie Lee White
- F-7 Lauren Lewis, MS4 (will not be presenting)**
“*3rd Year Resident Self-Reporting of Lumbar Puncture Success in Attempt to Quantify Baseline Success Rates*”
Mentor: Dr. Marjorie Lee White
- F-8 John Musgrove, MS4**
“*Utilizing Iterative Case Presentation to Demonstrate Concepts of Clinical Reasoning*”
Mentor: Dr. Carlos Estrada
- F-9 David Parks, MS4**
“*A Novel Teaching Mechanism in Nephrology of the Dangers of Hypocalcemia in Chronic Renal Failure*”
Mentor: Dr. Nancy Tofil
- F-10 Kristin Sawyer, MS4 (will not be presenting)**
“*Pilot Survey of Components of EMS Emergent Handoffs*”
Mentor: Dr. Marjorie Lee White
- F-11 Maya Vankineni, MS4**
“*The Use of Reflection in Measuring Professionalism in Medical Education*”
Mentor: Dr. Stanford Massie
- F-12 Mallory Youngstrom, MS2**
“*Systematic Review of the Literature for Patient Safety During Handoffs*”
Mentor: Dr. Lee Ann Reisenberg

- G-1 Davis Bradford, MS2**
“Clinical and Surgical Predictors of Fistula Outcomes”
Mentor: Dr. Michael Allon
- G-2 Steven Brown, MS4 (will not be presenting)**
“Establishment of a Multidisciplinary Concussion Program: Impact of Standardization on Patient Care and Resource Utilization”
Mentor: Dr. James Johnston
- G-3 Mary Bryant, MS3**
“Change in Psoas Muscle Mass Correlates with Survival Following Transarterial Chemoembolization”
Mentor: Dr. Derek DuBay
- G-4 Andrew Chou, MS2**
“Socioeconomic Factors and Early Hospital Readmission in Live Transplant Patients”
Mentor: Dr. Derek DuBay
- G-5 Frank Crisona, MS2**
“Evaluation of Kyphoplasty Outcomes”
Mentor: Dr. Melissa Chambers
- G-6 Luke Farmer, MS4**
“Beyond Pain: A Description of Symptom Burden Among Hospitalized Older Adults”
Mentor: Dr. Cynthia Brown
- G-7 Marc Fawal, MS2**
“Evaluating Risk Factor for Overuse Injuries in Baseball Athletes: A Prospective Study of UAB Baseball Team”
Mentor: Dr. Reed Estes
- G-8 Steven Mann, MS3**
“Therapeutic Apheresis Use at UAB: A Ten-year Analysis”
Mentor: Dr. Jill Adamski
- G-9 Paul Sauer, MS2**
“Intraoperative Predictors of Liver Transplant Outcomes”
Mentor: Dr. David Eckhoff
- G-10 Swaroop Vitta, MS2**
“Assessing Unmet Need for Medical Care and Safety Net Accessibility Among Birmingham’s Homeless and the Impact of Major Changes to the Safety Net”
Mentor: Dr. Stefan Kertesz
- G-11 George Waits, MS3**
“Evaluating Hospitalized Older Adults with the Acute Care Mobility Assessment”
Mentor: Dr. Cynthia Brown

- H-1 Victoria Bennett, MS3**
“Patient and Caregiver Disease Knowledge and Understanding in Huntington’s Disease”
Mentor: Dr. Victor Sung
- H-2 Benjamin Davis, MS2**
“Assessing the Readability of Online Shoulder and Elbow Related Patient Education Materials”
Mentor: Dr. Brent Ponce
- H-3 Megan Ehlinger, MS3**
“Survey of Heart Rhythm Specialists and Cardiologists’ Hopes to Gain New Information on Genetic Services Offered to Long QT Syndrome Patients”
Mentor: Dr. Nathaniel Robin
- H-4 Shubi Goyal, MS2**
“Caring for Children with Life-Threatening, Primary Neurological Conditions at the End-of-Life”
Mentor: Dr. Christina Ullrich
- H-5 Hannah Machemehl, MS2**
“Improving Patient Referral Partner Notification: Delivering a Sexual Health Centered Message”
Mentor: Dr. Nicholas Van Wagoner
- H-6 Neha Manikonda, MS2**
“Correlates of Condom Knowledge, Skills and Intent to Use Condoms in Incarcerated Adolescents”
Mentor: Dr. Marsha Sturdevant
- H-7 Ivey Partain, MS4** (Will not be presenting)
“The Associations Between Health Risk Behaviors, Executive Function Deficits, and ADHS Symptoms in University Students”
Mentor: Dr. Mark H. Thomas
- H-8 Shaan Patel, MS3**
“Evaluating the Readability of Online Patient Education Materials Related to Bone and Soft-Tissue Sarcomas”
Mentor: Dr. Brent Ponce
- H-9 Katherine Rainey, MS2**
“Parents’ attitudes toward pediatric genetic testing and incidental findings”
Mentor: Dr. Leon Dure
- H-10 Christen Roth, MS4**
“Use of High Fidelity Simulation to Explore Pediatric Critical Care and Emergency Physicians Communication Surrounding End-of-Life Care”
Mentor: Dr. Marjorie Lee White
- H-11 Zaki Yazdi, MS2**
“Reproductive Decisions after Genetic Evaluation”
Mentor: Dr. Nathaniel Robin

- I-1 Sergey Antipenko, MSTP (GS1)**
“Biological Variance Between Caucasians and African Americans and its Effect on Transplant Outcome”
Mentor: Dr. Jamye Locke
- I-2 Jessica Davis, MS2**
“The Role of Langerhans Cells in UV-induced Inflammation and Immunosuppression”
Mentor: Dr. Laura Timares
- I-3 Daniel DiToro, MSTP (GS2)**
“Insulin-like Growth Factors in Th17-mediated Autoimmunity”
Mentor: Dr. Casey Weaver
- I-4 Luke Ellenberg, MS2**
“The Role of AhR Signaling in the Pathogenesis of Necrotizing Enterocolitis”
Mentor: Dr. Colin Martin
- I-5 Meredith Hubbard, MS2**
“Differentiation Induced Pluripotent Stem Cells from Skin Cells of Immunodeficient Patients to T-lymphocytes”
Mentor: Dr. Tim Townes
- I-6 Andrew Jones, MS2**
“Influence of CsA Upon Antiviral Immune Responses in a Murine Model for Renal Transplantation”
Mentor: Dr. Masako Shimamura
- I-7 Jason LeGrand, MSTP (GS3)**
“Identification of Cytogenetically normal human CD34+CD38- Hematopoietic Stem/Progenitor Cells from inv(16)+ Leukemic Bone Marrow”
Mentor: Dr. Christopher Klug
- I-8 Vincent Laufer, MSTP (GS1)**
“Reclassification of Autoimmune Disease by Applying Machine Learning Algorithms to Genetic Variants used as Essentially Bayesian Priors”
Mentor: Dr. Jonas Almeida
- I-9 Carson Moseley, MSTP (GS3)**
“The Regulation of Interleukin 10 Transcription in Autoimmunity”
Mentor: Dr. Casey Weaver
- I-10 Ashley Shafferman, MS4**
“Changes in Body Mass Index in Children with Juvenile Idiopathic Arthritis Treated with Tumor Necrosis Factor Inhibitors”
Mentor: Dr. Timothy Beukelman

I-11 Jeff Singer, MSTP (GS2)

“The HAT-BAC Mouse Model: tuning Statistical Association in Biological Relevance for Inflammatory Bowel Disease”

Mentor: Dr. Casey Weaver

I-12 Sara Stone, MSTP (GS2)

“T-bet and IFNyR signaling regulate germinal center responses and long-lived plasma cell development in an influenza model”

Mentor: Dr. Frances Lund

- J-1 Chaitanya Allamneni, MS2**
"Risk Factors Associated with Epstein-Barr Virus Acquisition in Pediatric Renal Transplant Recipients"
Mentor: Dr. Masako Shimamura
- J-2 Emily Blosser, MSTP (GS5)**
"The Role of Commensal Microbes in Mucosal Defense of the Neonatal Gut"
Mentors: Dr. Casey Weaver and Dr. David Randolph
- J-3 Evida Dennis, MS2**
"The Impact of MCK-2 Mutation on Monocyte Recruitment and Viral Infiltration to the CNS in Murine Cytomegalovirus Congenital Infection"
Mentor: Dr. William Britt
- J-4 Nicholas Eustace, MSTP (MS2)**
"Ergothioneine Levels in Mycobacterium tuberculosis Infected Lung Tissue"
Mentor: Dr. Ardie Steyn
- J-5 John Evans, MS2**
"Pseudomonas aeruginosa Pneumonia in the ICU: Outcomes in ExoY+ Strains and Evaluated Risk of Development in TBICU"
Mentor: Dr. Jean-Francois Pittet
- J-6 Tim Kennell, MSTP (MS1)**
"A Novel Approach to Targeted Gene Therapy"
Mentor: Dr. Selvarangan Ponnazhagen
- J-7 Jeremie Lever, MSTP (MS1)**
"Mycobacterium tuberculosis Nanocompartments and Copper Toxicity Resistance"
Mentor: Dr. Michael Niederweis
- J-8 Mike Lopker, MSTP (GS5)**
"Cryptic Epitope in the 5' Leader of SIVmac239"
Mentor: Dr. George Shaw

- K-1 Amy Banks, MS2**
“Application of the CRISPR/Cas System to Knockout of Kinases Possibly Involved in Hemoglobin Switching”
Mentor: Dr. Tim Townes
- K-2 David Barrington, MS3, Frank Gleason, MS2, and Richard Tanner, MS2**
“Investigation of DFO as a Novel Treatment for Contaminated Open Fractures”
Mentor: Dr. Shawn Gilbert
- K-3 Ryan Berry, MSTP (GS1)**
“IGF-1R-Luciferase Constructs to Elucidate Crosstalk Between GH and IGF-1 Receptors”
Mentor: Dr. Stuart Frank
- K-4 Alex Dussaq, MSTP (MS2)**
“KAOS- An RDF Data Model for Kinomic Peptide Arrays”
Mentor: Dr. Jonas Almeida
- K-5 Muhan Hu, MSTP (MS1)**
“Characterization of G-Protein Estrogen Receptor Expression in Zebrafish Embryos”
Mentor: Dr. Daniel Gorelick
- K-6 Thy Huynh, MS4**
“Whole Exome Sequencing in Family with Unspecified Genodermatosis of Sclerodermod Features”
Mentor: Dr. Naveed Sami
- K-7 Morgan Locy, MSTP (MS2)**
“Heme Oxygenase 1 Deficiency Exacerbates Cisplatin Induced JNK Activation in Kidney Proximal Tubule Cells”
Mentor: Dr. Anupam Agarwal
- K-8 Melissa Mays, MS3**
“Probing for Novel Interactions of the Homology Downstream of Sec7 3 (HDS3) Domain in the ARF-GEF GBF-1”
Mentor: Dr. Elizabeth Sztul
- K-9 Michael Xu, MS2**
“Characterization of rBH3 Specificity to Anti-Apoptotic Bcl-2 Family Members”
Mentor: Dr. William Placzek

- L-1 Tyler Argent, MS2**
"Risk Factors for Prolonged Hospitalization after the Fontan Procedure"
Mentor: Dr. David Cleveland
- L-2 Sima Baalbaki, MS3**
"Benefit vs. Risk of Lumbar Punctures in Extremely Low Birth Weight Infants"
Mentor: Dr. Namasivayam Ambalavanan
- L-3 Chelsea Cernosek, MS3**
"Sickle Cell Trait and Wound Healing: Beware the Use of Epinephrine. A Report of Three Cases"
Mentor: Dr. Luis Vasconez
- L-4 Anna Graves, MSTP (GS1)**
"The Impact of the Intrauterine Environment of Offspring Metabolic Outcomes: A Systematic Review"
Mentor: Dr. Nir Menachemi
- L-5 Abhay Kulkami, MS4 (will not be presenting)**
"Unintentional Poisoning in the Pediatric Population"
Mentor: Dr. Chris Pruitt
- L-6 Brittney Lantrip, MS2**
"Epidemiology of Pediatric Inflammatory Bowel Disease - A Tertiary Pediatric Hospital Experience from 2000-2010"
Mentor: Dr. Kimberly Coveney
- L-7 Eleanor K. Mathews**
"Clinical Predictors of Perforated Appendicitis: the Utility of Immature Granulocyte Percentage"
Mentor: Robert Russell, MD
- L-8 Kristen McFalls, MS2**
"Neonatal Patient Safety"
Mentor: Dr. Namasivayam Ambalavanan
- L-9 Mallory Scogin, MS4 (will not be presenting)**
"Assessing Health-Related Quality of Life in Children with Spina Bifida"
Mentor: Dr. Jeffrey Blount
- I-10 MacKenzie Wilson**
"Temporal Relationship between Administration of Antenatal Indomethacin and Steroids and Intestinal Perforation in Premature Infants"
Mentor: Dr. Wally Carlo

M-1 Chidinma Anakwenze, MS2

"Evaluating a Theory-Based Health Educational Intervention to Improve Awareness of Breast and Cervical Cancer in Western Jamaica"

Mentor: Dr. Pauline Jolly

M-2 Divya Carrigan, MS2

"Healthy Food Choices at the Dollar General: Feasible Dietary Advice for Low Income, Rural Populations"

Mentor: Dr. Monika Safford

M-3 Shima Dowla, MS2

"Primary Care Provider, Peer Advisor, and Patient Reported Barriers to Improvement of Cardiovascular Health for Individuals Living in the Alabama Black Belt"

Mentor: Dr. Monika Safford

M-4 Stacy Ejem, MS2

"Smoking Cessation in Hospitalized Patients"

Mentor: Dr. Kathy Harrington

M-5 Sandhya Kumar, MS3

"Examining Perceived Barriers to Good Nutrition in Birmingham's Urban Homeless Women"

Mentor: Dr. Andrea Cherrington

M-6 Cory Luckie, MS2

"Waking Buses for Adults: A Pilot Program to Decrease Obesity"

Mentor: Dr. Adrienne Milner

M-7 Jamie Powell, MS3

"Using a DVD Intervention for Parents and Caregivers of Children Hospitalized fro Respiratory Illnesses to Improves Knowledge and Reduce Secondhand and Thirdhand Tobacco Smoke Exposure"

Mentor: Dr. Susan Walley

M-8 Jackson Reynolds, MS2

"The Utilization of Genetic Evaluation and Services by Family Medicine Physicians in Rural Alabama"

Mentor Dr. Nathaniel Robin

M-9 Andrew Wilson, MS2

"Trust in Physicians and Its Link to Intermediate Diabetic Outcomes"

Mentor: Dr. Andrea Cherrington

- N-1 Paul Boothe, MS2**
“The Evolution of Mitochondrial Fission-Fusion Genes and Their Role in Cancer”
Mentor: Dr. Malay Basu
- N-2 Alexander Bray, MSTP (GS2)**
“The Role of Mitochondrial Background in B16 Melanoma Growth”
Mentor: Dr. Scott Ballinger
- N-3 Mata Burke, MS4**
“GSI-1 Synergizes with LDE225 in Ovarian Cancer Cells by Inhibiting the Proteasome”
Mentor: Dr. Charles Landen
- N-4 Zachary Dobbin, MSTP (GS4)**
“An Ovarian Patient-Derived Xenograft Model to Identify the Chemoresistant Population”
Mentor: Dr. Charles Landen
- N-5 Hillary DelaRosa, MS4**
“Toll-Like Receptor-4 Deficiency Enhances Repair of Ultraviolet Radiation Induced Cutaneous DNA Damage by Nucleotide Excision Repair Mechanism”
Mentor: Dr. Nabiha Yusuf
- N-6 Akash Kapadia, MS4**
“Pyruvate Dehydrogenase Kinase-1 Inhibitors Potentiate the Anti-Tumor Activity of Sorafenib Against Renal Cell Carcinoma Cells via Activation of the Tricarboxylic Acid Cycle”
Mentor: Dr. Sunil Sudarshan
- N-7 Tyler McCaw, MSTP (MS1)**
“Sequestration of Oxidized Lipids, Immunomodulation, and Tumor Progression in Pdx 1 Cre; Kras G^{12D/+}; p53^{-/-} Mouse Model”
Mentor: Dr. Christopher Klug
- N-8 Julia Powelson, MS2**
“Role ST6Gal-1 Expression in Cell Survival in Ascites”
Mentor: Dr. Susan Bellis
- N-9 Ryne Ramaker, MSTP (MS2)**
“Applying Metabolomics to Pancreatic Cancer”
Mentor: Dr. Sara Cooper
- N-10 Patrick Rowan, MS2**
“Heparanase Induces EMT-Like Phenotype in Human Myeloma Cells”
Mentor: Dr. Yang Yang
- N-11 Iman Tamimi, MS2**
“Loss of p16/INK4a Gene Enhances UVB-Induced Inflammation-Mediated Cutaneous Tumor Development”
Mentor: Dr. Nabiha Yusuf
- N-12 Alice Weaver, MSTP (GS1)**
“DNA Repair Deficiency and Sensitivity to PARP Inhibition in HPV-Positive Head and Neck Cancer”
Mentor: Dr. Eddy Yang

- O-1 Carolyne Craig, MS2**
“*Early Vitamin D Supplementation for Prevention of Respiratory Morbidity in Extremely Preterm Infants*”
Mentor: Dr. Namasivayam Ambalavanan
- O-2 Courtney Culbreath, MS2**
“*Nasal Potential Difference in Influenza Infected Mice*”
Mentor: Dr. Sadis Matalon
- O-3 Joshua Gautney, MS2**
“*PGP Mediated Pulmonary Vascular Remodeling via Rho-kinase Activation*”
Mentor: Dr. J. Edwin Blalock
- O-4 Stephen Gragg, MSTP (MS1)**
“*Characterizing the Effects of CLU Expression on Matrix Synthesis by Lung Fibrosis*”
Mentor: Dr. Victor Thannickal
- O-5 Bradley Hicks, MS2**
“*Characterization of Primary Porcine Nasal Epithelium Model in Transepithelial Ion Transport and CFTR Function*”
Mentor: Dr. Bradford Woodworth
- O-6 Cate Li, MS2**
“*Transient Receptor Potential (TRP) Proteins: Novel targets of AMP-activated Kinase in Pulmonary Endothelial Barrier Function*”
Mentor: Dr. Judy Creighton
- O-7 Kavita Nadendla, MS2**
“*Changes in Circulating Levels of AMPK Correlate with Pulmonary Dysfunction in Hypertension*”
Mentor: Dr. Judy Creighton
- O-8 Neel Ranganath, MS3**
“*Porcine Nasal Epithelial Cultures for Studies of Cystic Fibrosis Sinusitis*”
Mentor: Dr. Bradford Woodworth
- O-9 Jay Watson, MS2**
“*Effect of a Novel Mucolytic on the Viscoelastic Properties of Cystic Fibrosis Mucus In Situ*”
Mentor: Dr. Steven Rowe
- O-10 William Webb, MSTP (MS2)**
“*Response of IPF Myofibroblasts to Mechanical Strain*”
Mentor: Dr. Joel Berry
- O-11 Shin Xu, MS2**
“*The effects of nebulized drugs on lung injury to chlorine gas in mice*”
Mentor: Dr. Timothy Ness

- P-1 Ron Baxter, MS3**
“Levels of Pro-Oxidant and Inflammatory Molecules in Postoperative Pericardial Fluid are Related to Atrial Fibrillation”
Mentor: Dr. Spencer Melby
- P-2 Kyle Bess, MS2**
“Postoperative Atrial Fibrillation Occurs in Two Distinct Phases After Cardiac Surgery”
Mentor: Dr. Spencer Melby
- P-3 Evan Harvey, MS2**
“Impact of Fluid Overload and Kidney Injury on Outcomes after the Arterial Switch Operation”
Mentor: Dr. Stephen Robert
- P-4 Travis Hull, MSTP (GS3)**
“Heme Oxygenase-1 Expression Prevents Doxorubicin-Induced Delayed Onset Heart Failure”
Mentors: Dr. James George and Dr. Anupam Agarwal
- P-5 Kayla Isbell, MS2**
“Levels of Pro-Oxidant and Inflammatory Molecules in Postoperative Pericardial Fluid are Related to Atrial Fibrillation”
Mentor: Dr. Spence Melby and Dr. James George
- P-6 Davis Lester, MS2**
“The Prognostic Value of Transient Ischemic Dilation of the Left Ventricle with Regadenoson Myocardial Perfusion”
Mentor: Dr. Fadi Hage
- P-7 John Merriman, MS2**
“Correlation Between Sublingual Small Vessel Density and Blood Lactate Levels in the Neonatal Cardiac Surgical Patient”
Mentor: Dr. David Cleveland
- P-8 Robert Ryan, MS2**
“Adverse Cardiac Events: The Risky Business of non-cardiac surgery for patients with a prior cardiac stent”
Mentor: Mary T. Hawn
- P-9 John Thomas, MS2**
“TXNIP Modulates miR-33a and SREBP-2 in Human Ventricular Cardiomyocytes”
Mentor: Dr. Anath Shalev
- P-10 Ashlee Vinyard, MS4**
“The Use of Moderate Dose of Recombinant Factor VIIa for Postoperative Hemorrhage is Not Associated with Thromboembolic Complications After Open Cardiac Surgery”
Mentor: Dr. Spence Melby
- P-11 Justin Webb, MS2**
“Cardiac Optogenetics: Optical Pacing of Heart Tissue”
Mentor: Dr. Lufang Zhou

Allamneni, Chaitanya (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	O'Brien Center Fellowship
Faculty Advisor:	Dr. Masako Shimamura, MD
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Grant Paulsen, MD
Title:	Risk Factors Associated with Epstein-Barr Virus Acquisition in Pediatric Renal Transplant Recipients

Epstein-Barr virus (EBV), a member of the herpesvirus family, is best known for its role in infectious mononucleosis. After infection, EBV remains latent lifelong within B-lymphocytes. Under cases of immunosuppression, such as following a solid-organ transplant (SOT), EBV-infected B-lymphocytes can proliferate uncontrollably, unchecked by T-lymphocytes. Such unchecked B-lymphocyte proliferation can lead to post-transplant lymphoproliferative disease (PTLD), which often manifests as a lymphoma. Persistent EBV viremia is a risk factor for PTLD development, yet other risk factors for and treatment of EBV/PTLD are inadequately understood. Treatment for viremic SOT recipients often begins with reduction of immunosuppression, which increases risk of SOT rejection. This project focused on elucidating risk factors for EBV viremia. Achieving this goal will allow treatment to be targeted towards high-risk patients. Pediatric SOT recipients are an inherently high-risk group for EBV/PTLD because many are EBV (-) and receiving EBV (+) organs, and on high levels of immunosuppression.

A retrospective cohort study was performed on 54 pediatric kidney allograft recipients transplanted at Children's of Alabama between 2010-2012. Demographics (age/sex/race), EBV load, Donor/Recipient serology, reason for transplant, HLA allele subtypes and mismatch with donor, biopsy results, antiviral prophylaxis and immunosuppressive regimen/dose were tracked and recorded in a database. The relationship of the above factors on EBV load is currently being statistically analyzed. The Pediatric SOT recipients at Children's are closely monitored, allowing data to be collected from ~25 clinic visits in the 2 years following transplant. The relationship of both transplant cause and HLA typing on EBV load is of particular interest, as it could indicate a genetic predisposition to EBV viremia. Subjects are currently being added to the database, with a goal of 100 subjects.

Allen, Heather Elizabeth (MSTP-GS4)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: David G. Standaert, MD, PhD

Abstract Approved By Advisor: Yes

Co-Authors: Ashley S. Harms, PhD, David G. Standaert, MD, PhD

Title: Role of C3 and C5 complement components in the AAV-SYN model of PD

Parkinson disease (PD) is a neurodegenerative disorder characterized by a loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and intraneuronal aggregates of alpha-synuclein (a-syn), resulting in tremor, rigidity, bradykinesia and postural instability. In human PD and animal models, there is evidence of chronic neuroinflammation; however, the mechanism by which these neuroinflammatory changes lead to neurotoxic effects are unclear. This study investigates a possible role for the complement system in a-syn based models of PD. Previously, we have shown that targeted overexpression of a-syn in the SNpc of mice driven by an adeno-associated virus (AAV) vector drives an inflammatory response and leads to a 30% reduction in the total number of dopaminergic neurons 6 months post-injection. We assessed C3 and C5 production via qPCR, ELISA and immunohistochemistry in this model. At 4 weeks post-injection of AAV-SYN, we observed induction of C3 mRNA, 4.8 fold over AAV-GFP ($p<0.05$); however the amount of total C3 protein in the substantia nigra was unchanged by ELISA. We observed little evidence for the presence of C5 in our mouse model; C5 mRNA and protein were undetectable at 4 weeks post injection of AAV-SYN. We also examined the effect of a-syn on complement expression in vitro. In primary microglia treated with aggregated a-syn, we observed that after 4 hours, C3 protein was significantly upregulated ($p<0.001$). These data suggest that a-syn can modulate expression of the C3 component of complement. It will be important to determine whether loss of C3 or C5 protect against microglial activation and dopaminergic cell loss in this model system.

Funded by Parkinson's Association of Alabama, NIH UAB Medical Scientist Training Program, NIH F31
NS076017-03

Anakwenze, Chidinma Pamela (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Dr. Pauline Jolly
Abstract Approved By Advisor:	Yes
Co-Authors:	Evelyn Interis, Dr. Maung Aung, Dr. Pauline Jolly
Title:	Evaluating a theory-based health educational intervention to improve awareness of breast and cervical cancer in Western Jamaica

While breast and cervical cancer mortality rates are declining in developed countries, incidence and mortality rates remain high in Jamaica due to low levels of screening. 90% of Jamaican women who eventually die from cervical cancer have never been screened. The low breast cancer survival rates in developing countries has been attributed to a lack of early detection programs as well as insufficient numbers of diagnosis and treatment facilities, which have led to the majority of cancers being diagnosed in late stages. Therefore, early detection to improve breast and cervical cancer outcome and survival is the cornerstone strategy for control of breast and cervical cancer. We hypothesized that a theory-based health education intervention would increase the awareness of breast and cervical cancer and intention to screen among women in Western Jamaica. 491 women attending hospitals or clinics completed an interviewer-administered pretest survey. The pretest covered attitudes, knowledge, risk factors, symptoms, perceptions and behaviors regarding breast and cervical cancer. Following the pretest, participants received a health education intervention related to breast and cervical cancer and an immediate post-test survey. The post-test assessed participants' knowledge of breast and cervical cancer screening tests, risk factors and intention to screen. There were statistically significant increases in the percentage of correct responses between the pre and post-test. Participants moved across the Stages of Change theoretical constructs indicating intention to screen. The sample was receptive to information about breast and cervical cancer and the use of a theory-based educational intervention positively influenced knowledge of breast and cervical cancer risk factors, symptoms, and types of screenings. Participants will be followed at three and six months to determine whether they have accessed breast or cervical cancer screening. This theory-based patient educational intervention can be replicated to promote awareness of breast and cervical cancer.

Antipenko, Sergey (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Jayme Locke
Abstract Approved By Advisor:	Yes
Co-Authors:	Jianguo Chen, Roslyn Mannon, Jayme Locke
Title:	Biological Variance Between Caucasians and African Americans and Its Effect on Transplant Outcome

African Americans are at a greater risk of end-stage renal disease than Caucasians and are less likely to receive optimal therapy when it develops. Those that do receive allografts have a graft half-life of about 40% of that of Caucasians. These differences in outcome are invariant of socioeconomic status.¹ It has been observed that African American recipients receiving kidneys donated after cardiac death (DCD) from African American donors have a reduced risk for graft loss and death compared to those receiving standard criteria (SCD) kidneys donated after brain death (DBD).²

Therefore, we hypothesized that there are differences in immunologic response to both brain death and cardiac death that is race specific. These differences in donor response are hypothesized to affect recipient graft outcome and survival.

To assess these differences between races, donors were divided into 4 groups: African American DBD, Caucasian DBD, African American DCD, and Caucasian DCD. For each group, both wedge kidney biopsies and blood samples were evaluated for mRNA expression. Additionally, toll-like receptors (TLRs) of peripheral blood monocytes (PBMCs) were stimulated and cytokine expression was measured.

Inflammatory gene expression in biopsies trended higher for African American DBDs than Caucasian DBDs. This trend appeared to be reversed in blood samples, with inflammatory gene expression trending higher in Caucasian DBDs. In all cases, gene expression tended to be higher than normal living patients. When evaluating cytokine release of stimulated PBMCs, however, levels trended lower in DBDs than in normal living patients.

In conclusion, donor organs undergo race-dependent changes in inflammatory gene expression and TLR response during death. These results demonstrate the need for continued examination of these differences in order to improve graft and patient survival in African Americans.

References

1. Gaston RS. The relationship between ethnicity and outcomes in solid organ transplantation. *The Journal of Pediatrics*. 2005
2. Locke JE. Donor ethnicity influences outcomes following deceased-donor kidney transplantation in black recipients. *Journal of the American Society of Nephrology*. 2008

Argent, Robert Tyler (MS2)

Project Length:	Short
Prior Research Experience:	No
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	David Cleveland, M.D.
Abstract Approved By Advisor:	Yes
Co-Authors:	Cleveland, D., Alten, J., Borasino, S., Kirklin, J., Dabal, R., Roberts, S., Hock, K., Smith, K., Smitherman, K., Phillips, P., Earman, B., Harvey, E., Mahdi, A., Merriman, J.
Title:	Risk Factors for Prolonged Hospitalization after the Fontan Procedure

Introduction

The Fontan procedure is a palliative surgical procedure used in children with single ventricle physiology in which systemic venous return is routed directly to the pulmonary arteries, bypassing the heart. Despite significant improvements in surgical mortality and long-term outcomes, perioperative morbidity continues to be high. Pleural effusions are common, and lead to prolonged hospitalization. We sought to identify risk factors for prolonged hospital length of stay (LOS) in this population.

Design

Single center retrospective chart review of all patients who underwent Fontan surgery from January 2008 to December 2012. Patients were identified using the Society of Thoracic Surgeons database. All variations of Fontan were included; Fontan revisions were excluded. Prolonged LOS was defined as ≥ 12 days.

Results

78 patients were identified; 3 excluded. Mean age was 5.6 ± 6 years, mean weight was 18.3 ± 11.1 kg, and 50% were male. 54.1% had non-fenestrated external conduit, 37.8% fenestrated external conduit, 4.1% Kawashima variant, and 4.1% direct atriopulmonary connection. Cardiopulmonary bypass time was 118.3 ± 45.8 minutes. There were no deaths. Median LOS was 9 days; 28% had prolonged LOS. Prolonged LOS was associated with positive net fluid balance (-41.6ml/kg vs. 394.4ml/kg , $p=0.001$), 5% albumin administration in the first 24 hours (9.4ml/kg vs. 48ml/kg , $p\leq 0.001$), total chest tube output (88.5ml/kg vs. 201.4ml/kg , $p=0.001$), inotrope score at 12 hours (3.3 vs. 6.7, $p=0.015$) and length of oxygen requirement (87.8 hours vs. 187 hours, $p\leq 0.001$). It was not associated with any other patient demographic, intraoperative, hemodynamic (including central venous pressure), respiratory, or ICU-related complication variables. Chest tube output was also significantly correlated with albumin boluses in first 24 hours $r=0.66$ ($p\leq 0.001$). Preoperative catheterization data was not associated with postoperative outcomes.

Conclusion

Perioperative fluid overload and albumin administration is associated with increased chest tube drainage and prolonged LOS after the Fontan procedure.

Baalbaki, Sima Hisham (MS3)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Namasivayam Ambalavanan
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Namasivayam Ambalavanan and Sima Baalbaki
Title:	Benefit vs. Risk of Lumbar Punctures in Extremely Low Birth Weight Infants

Introduction: Meningitis is diagnosed by evaluation of cerebrospinal fluid (CSF) obtained by lumbar puncture (LP). Extremely Low Birth Weight (ELBW) infants are sometimes evaluated by LP soon after birth if exposed to preterm prolonged rupture of membranes (PPROM) or chorioamnionitis, which are known risk factors for early onset neonatal sepsis. However, it is unknown if the increased venous pressure associated with infant positioning for LP increases the risk of severe intraventricular hemorrhage (IVH). We hypothesized that LPs on the first day of life (DOL) are associated with increased risk of severe IVH that may outweigh the benefits of confirming meningitis in ELBW infants.

Methods: Retrospective data analysis of electronic medical records of 343 ELBW infants born at the University of Alabama in Birmingham Hospital in 2010-12 was performed to quantitate the identification of meningitis and incidence of severe IVH in relation to other clinical variables. A p<0.05 was considered significant.

Results: Ninety-two of 343 neonates underwent a LP on DOL1. Infants receiving a LP were significantly heavier at birth and their first CBC had higher white blood cell counts, percentage of neutrophils, and platelet counts. Their mothers were more likely to be diagnosed with clinical chorioamnionitis and to have had longer PPROM. Only 1 CSF culture was positive, but the organism (coagulase negative staphylococcus) was considered a contaminant. Of those receiving a LP, 27.2% (25) developed severe IVH compared to 13.5% (34/251) of those who did not. Patients receiving a LP were 2.97 times more likely to develop severe IVH after adjustment for other clinical variables using logistic regression.

Conclusions: LP on DOL1 is associated with a higher risk of severe IVH in ELBW infants and a low yield of positive cultures. Clinical algorithms including LPs as part of the sepsis workup in preterm infants may need reevaluation if these findings are validated in larger or multicenter studies.

Baker, Christopher Barnett, Jr. (MS2)

Project Length:	Short
Prior Research Experience:	No
Source of Funding:	CaRES Program
Faculty Advisor:	John B. Fiveash, M.D.
Abstract Approved By Advisor:	Yes
Co-Authors:	Andrew M. McDonald, M.D.; Richard A. Popple, Ph. D.; John B. Fiveash, M.D.
Title:	Dosimetric predictors of erectile function after external beam radiotherapy for prostate cancer with emphasis on fractionation scheme

Background: Different radiation therapy treatment methods have arisen in time for patients with prostate cancer such as conventionally fractionated external beam radiation therapy (EBRT), hypofractionated EBRT, and brachytherapy. There has been recent research into how the different radiation delivery methods affect biochemical control, rectal toxicity and urinary toxicity. However, few publications have investigated the rates of sexual dysfunction among men who receive hypofractionated EBRT treatment of prostate cancer. This study compares patients receiving hypofractionated and conventionally fractionated EBRT, as well as the dose distributions across anatomic structures involved in erectile function.

Methods and Materials: This study analyzes patient outcomes following treatment, focusing primarily on the rates of sexual dysfunction and the overall sexual health of the patients. Based on previous studies, the penile bulb and the crura of the corpora cavernosa were chosen as structures of interest. Sexual function of the patients in this study was obtained from previous physician encounters in which a Sexual Health Inventory for Men (SHIM) survey was filled out by the patient. This information was then correlated to the radiation dose distribution across these two structures.

Results: The initial results of this study indicate that no difference exists in the rates of sexual dysfunction between the hypofractionated and conventionally fractionated group; however, we are continuing to investigate the effect of the dosimetry.

Conclusion: Using these findings, we predict that generating plans utilizing the penile bulb and crura as avoidance structures will improve sexual outcomes in men undergoing external beam irradiation for prostate cancer.

Banks, Amelia Elizabeth (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Tim Townes Abstract
Approved By Advisor:	Yes
Co-Authors:	Dewang Zhou, Erik Westin, Dr. Tim Townes
Title:	Application of the CRISPR/Cas system to knockout of kinases possibly involved in hemoglobin switching

Recently, a lentiviral short hairpin RNA (lenti/shRNA) screen in human bone marrow CD34+ cells revealed several mRNA knockdowns that resulted in upregulation of fetal hemoglobin after these cells were induced into hematopoietic differentiation. Many of the genes involved are kinases responsible for cellular signaling mechanisms that may result in hemoglobin switching. Two of these kinases, Kinase1 and Kinase 2, have been used as candidates for testing the efficacy of a newly discovered gene editing technique known as the CRISPR/Cas system. In order to explore the efficiency of this system in incorporating knockout vectors for Kinase 1 and Kinase 2, a DNA sequence coding for a single guide RNA was designed and ligated into a Cas9 endonuclease vector. This designed vector was electroporated into mouse embryonic fibroblasts as well as mouse embryonic stem cells. It was hypothesized that the single guide RNA would localize Cas9 to the DNA sequences of the Kinase 1 and Kinase 2 genes. A surveyor assay was performed in order to observe whether double strand breaks occurred. Surveyor gel electrophoresis revealed light bands at 400-500bp, which suggests that the Cas9 endonuclease created cuts and inserted/deleted nucleotides within the gene. Oligonucleotide correction vectors were designed with a stop codon as well as a frameshift mutation in order to produce a knockdown vector. The correction vectors were electroporated into mouse embryonic stem cells along with the designed CRISPR DNA in order to induce cellular repair mechanisms. Deep sequencing will be performed to analyze the efficiency of the CRISPR/Cas system in mutating the Kinase 1 and Kinase 2 genes. If the knockout of Kinase 1 and Kinase 2 genes produces a significant upregulation of fetal hemoglobin in mouse models, then it may be possible to begin the search for a drug that alleviates the symptoms of hemoglobinopathies such as sickle cell disease and beta-thalassemia.

Barnett, Ashley Shayne (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Krista Casazza, Ph.D., R.D.

Abstract Approved By Advisor: Yes

Co-Authors: Krista Casazza

Title: Insulin Resistance and Bone Strength

Background: While the increased risk of chronic diseases such as type 2 diabetes and cardiovascular disease with pediatric obesity have been widely studied, the detrimental effects of obesity on long-term bone health have recently emerged as significant concerns. While obese/overweight children are reported to higher bone mineral content (BMC) relative to their normal weight peers, the strength-structure development of skeletal system is altered in overweight/obese children, as seen by the greater risk of fracture. The mechanism behind these alterations has yet to be identified, but recent studies have suggested the presence of obesity-induced deviations in insulin dynamics occurring prior to and during puberty may be responsible for the altered qualitative aspects of the bone.

Purpose: To evaluate the correlation between insulin resistance and impairment in bone strength in overweight/obese girls.

Methods: A liquid meal test was performed to measure the insulin secretion of each participant. The obtained measurements were used to calculate the insulin AUC, which was used as an indicator of degree of insulin resistance. Dual-energy X-ray absorptiometry (DXA) was used to assess BMC and body fat mass. Bone strength was conducted with peripheral quantitative computer tomography (pQCT) scans that evaluated the trabecular and cortical properties of bone.

Results: We hypothesized that greater insulin AUC would be negatively associated with the bone strength even in the absence of decrement in BMC.

Conclusion: The results of this study could provide evidence that it is the obesity-induced changes in insulin dynamics that lead to decreased bone quality. This would explain the overall decreased bone strength that has been witnessed in overweight/obese children. If the results of the study are as we hypothesized, this study would also lead to further investigation into the exact role of insulin in the process and the mechanisms that occur within the bone.

Barrington, David Allen (MS3)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Shawn Gilbert, MD
Abstract Approved By Advisor:	Yes
Co-Authors:	Richie Tanner, Frank Gleason
Title:	Investigation of DFO as a novel treatment for contaminated open fractures

Desferrioxamine (DFO), a hypoxia inducible factor (HIF) pathway activator, is a pharmacologic agent that has been shown to increase bone vascularity and improve healing in acute fracture and distraction osteogenesis models (9,10). The goal of this research project is to determine the effectiveness of local application of DFO in the definitive management of open fractures with established infections. We hypothesize that improving local vascularity following severe extremity injury will improve the local tissue environment and help prevent the development of complications such as failure of bone and muscle healing.

Following the model developed in the first aim of this project, we created open fractures in the lower extremity of 60 adult male brown Norway rats. The wounds were contaminated with methicillin resistant *Staphylococcus aureus* and *acinetobacter baumannii* complex and temporarily fixed. Four days following the initial injury, wounds were irrigated and debrided, and definitively fixed with an intramedullary K-wire and composite scaffold. Either tobramycin or a combination tobramycin and DFO was applied to the scaffold. Following the surgery 40 rats were euthanized at 6 weeks post-op and 20 rats were euthanized at 12 weeks. The muscle and femur segments were harvested at the time of euthanasia and were examined for the following data: 1)muscle histology, 2) bone histology, 3) bacterial burden, and 4) CT angiography.

It is expected that local antibiotic delivery will decrease but not completely eradicate infection in this model. We anticipate that an improved local environment will be established by increasing vascularity through the addition of DFO and that the result will be further improvement in the clearance of infection, improved muscle and bone repair, or both. We predict to detect increased vascularity and perfusion, less muscle fibrosis, and increased bone healing by microCT with the combined treatment group.

Baxter, Ronald Dennis, Jr. (MS3)

Project Length:	Long
Prior Research Experience:	No
Source of Funding:	Other
Faculty Advisor:	Spencer Melby
Abstract Approved By Advisor:	Yes
Co-Authors:	Spencer J Melby, Kayla D Isbell, James F George
Title:	Levels of Pro-Oxidant and Inflammatory Molecules in Postoperative Pericardial Fluid are Related to Atrial Fibrillation

Purpose: Causes of postoperative atrial fibrillation (AF) have been linked to inflammation in the serum. However, few studies have evaluated pericardial fluid (PCF) for its contribution. We hypothesized that post-operative PCF is a separate, distinct entity from the serum and, in addition to being pro-inflammatory, is also pro-oxidant. Cardiac myocytes exposed to this environment are oxidatively damaged, resulting in AF.

Methods: Plasma and PCF from 18 adult patients were taken at the start of cardiac surgery (CABG and/or valve replacement) and then at 4, 12, 24, and 48 hours after surgery. Levels of cell-free methemoglobin (metHgb), cell phenotypes, and myocardial breakdown products and cytokines were measured at each time point by spectrophotometry, flow cytometry, and multiplex bead assays. Statistical analyses were performed using a student t-test.

Results: Post-surgery mean concentration of pro-inflammatory and myocardial damage markers were significantly increased in PCF vs serum: IL-6 (50460 vs. 7020 ng/mL, p<0.0001), IL-8 (11960 vs. 1550 ng/mL, p<0.0001), myeloperoxidase (7870 vs. 760 ng/mL, p<0.0001), troponin-I (148780 vs. 21760 ng/mL, p<0.0001), CK-MB (244110 vs. 96480 ng/mL, p<0.0001), and myoglobin (6530 vs. 660 ng/mL, p<0.001). At 12 hours post surgery an increase of mean concentration of MetHgb (11.1±7.7 to 83.7±10.4) and Myeloperoxidase (647 ± 286 to 13110 ± 4290) was seen in the PCF of AF patients vs. 9.3±1.6 to 44±6.7 and 494±149 to 7010±800, in patients who did not experience AF (p=.005 and p=0.12, respectively). This preceded the marker of elevated myocardial damage at 48 hours [troponin level 217600 ± 25300 in AF pts (n=4) vs 91000 ± 25400 in non-AF pts (n=8), p=0.01].

Conclusion: The presence of highly pro-oxidant and pro-inflammatory factors in the postoperative PCF was found to be predictive of atrial fibrillation. These markers of postoperative AF are distinct from markers found in the serum, and provide new insights into mechanisms of its onset and allow for new directed treatment modalities to be developed for cardiac surgery patients.

Bennett, Victoria Lisa (MS3)

Project Length:	Intermediate
Prior Research Experience:	No
Source of Funding:	Other
Faculty Advisor:	Victor Sung
Abstract Approved By Advisor:	Yes
Co-Authors:	Victoria Bennett
Title:	Patient and Caregiver Disease Knowledge and Understanding in Huntington's Disease

Huntington's Disease (HD) is a complex genetically inherited disease affecting many aspects of patient health, including motor, cognitive, and mood functions. It is slowly progressive, and requires a large support system consisting of health care professionals and family members. Given the complexity of the disease and the propensity for the disease process to affect a patient's cognitive processing capacity, it is possible that the patient has a poorer understanding of their own disease than their caregiver. The goal of this study was to assess basic caregiver and patient knowledge of the disease and to determine how patients and caregivers prefer to receive disease information. The study was conducted through an online survey distributed to patients and caregivers of the UAB HD Clinic as well as to patients and caregiver attendees at the National HD Convention in June 2013. Part 1 consisted of 11 True/ False basic knowledge questions and Part 2 assessed personal experience with HD education. Twenty-nine caregivers, seven patients, and one patient/caregiver completed the survey. Part 1 showed discrepancies between patient and caregiver knowledge with patients answering 57% correctly and caregivers answering 72% correctly, with a clear need for better education in both subsets. Part 2 further outlined the importance of several topics to understanding the disease and to explaining the disease to others. In addition, the data demonstrated a clear importance of understanding the disease to living with it. In conclusion, this data shows a need for better HD education and provides information on how to best present HD information to patients and caregivers in the future.

Berry, Ryan D. (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Stuart J. Frank
Abstract Approved By Advisor:	Yes
Co-Authors:	Ying Liu
Title:	IGF-1R - Luciferase constructs to elucidate crosstalk between GH and IGF-1 receptors

Growth hormone (GH) is an anterior pituitary hormone which acts through GH receptor (GHR), stimulating production of Insulin-like Growth Factor 1 (IGF-1) which binds IGF-1 receptor (IGF-1R) in many different cells of body to affect growth and metabolism. GHR is produced as a monomer and IGF-1R as a heterodimer which must form a dimer or heterotetramer respectively before signal transmission may occur. Previous studies have shown that the presence of IGF-1R serves to facilitate GHR signal transduction independent of the presence of its intracellular tyrosine kinase domain. It is not known whether IGF-1R interacts directly with GHR or if an intermediate molecule is involved. An assay has been developed to assess proximity and multimerization of hormone receptors. One of two luciferase domains (N-luc or C-luc) is added to the intracellular domain of each of the receptors in question such that no luciferase signal is produced unless the N-luc and C-luc domains are within sufficient proximity to interact. Here we discuss the production of IGF-1R constructs containing the N-luc or C-luc domains to be used elucidate details of the IGF-1R/GHR interaction.

Bess, Kyle Mitchell (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Spencer J Melby
Abstract Approved By Advisor:	Yes
Co-Authors:	Kayla D Isbell, Spencer J Melby, James F George
Title:	Postoperative Atrial Fibrillation Occurs in Two Distinct Phases After Cardiac Surgery

Purpose: New onset postoperative atrial fibrillation (POAF) is a common complication of cardiac surgery associated with increased morbidity, mortality, and cost of care. However, a time-related risk hazard after surgery has not been described. The objective of this study was to determine the continuous time-related risk (hazard) for new-onset POAF among patients who underwent cardiac surgery for coronary artery disease or valvular pathology.

Methods: Between Jan 2009 and Jan 2012, 1528 patients underwent CABG, valve surgery or both at a single institution. A total of 422 patients with no history of atrial fibrillation experienced POAF. The time to first onset of POAF was recorded and a multiphase hazard model was fitted to the data. Multivariate analysis of each phase was also conducted.

Results: Of the 422 who developed POAF, 66 (16%) experienced first-onset during the first 24 hours, 203 (48%) between 24-72 hours, and 153 (36%) at >72 hours. The parametric hazard for POAF is highest immediately after surgery and then decreases for 24 hours (1st phase). It then increases again to a peak at two days and decreases thereafter (2nd phase, see figure). The majority (408, 97%) of POAF occurred within seven days. Multivariate analysis of each phase showed risk factors for the 1st phase were older age ($p=.01$), longer ischemic time ($p=.01$), and mitral valve procedure ($p=.0002$). Risk factors for the 2nd phase were older age ($p<.0001$), white race ($p=.007$), increased weight ($p<.0001$), and longer ischemic time ($p=.05$).

Conclusion: In patients undergoing cardiac surgery for coronary disease and/or valve pathology, the POAF hazard was bimodal, suggesting that the two phases of risk are the result of distinct mechanisms that overlap in time. Further investigation into the mechanisms of POAF with respect to time (1st vs. 2nd phase) is warranted. Subsequent interventions could then be tailored for each phase.

Blosser, Emily Greenwood (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Casey T. Weaver, MD and David A. Randolph, MD, PhD

Abstract Approved By Advisor: Yes

Co-Authors: Emily Blosser, David Randolph, MD*, PhD, Casey Weaver, MD

Title: The role of commensal microbes in mucosal defense of the neonatal gut.

PURPOSE:

Late-onset bacterial sepsis (LOS) is a leading cause of morbidity and mortality among premature infants worldwide. Infections with Gram-negative bacteria, such as *Klebsiella pneumoniae*, occurring when bacteria translocate across premature gut epithelium into the bloodstream, can be particularly severe. Preterm infants often undergo intense antibiotic regimens to combat high risk of infection. Paradoxically, prolonged empiric antibiotic therapy is associated with increased risk of intestinal infection and death after adjustment for covariates. Commensal microbes in the mature gut are believed to confer protection from bacterial translocation by competing with pathogens for space and resources, and by inducing development of gut immune defenses. The purpose of this study was to determine whether maternal antibiotics increase risk of LOS in neonates by altering microbial colonization and to identify microbial founder families of gut flora. We have developed a model of neonatal LOS in which 5 day-old C57BJ/6 mouse pups are inoculated with bioluminescent, pathogenic *K. pneumonia*. As in humans, resistance to bacterial dissemination is age-dependent, with neonatal pups being highly susceptible and adults being resistant. Here, we show that administration of maternal antibiotics increased the risk of *Klebsiella* sepsis in neonates and was associated with an altered microbiome in pups. High throughput 16S ribosomal RNA sequencing of neonatal microbiomes identified three principle microbial founder bacterial genera — *Lactobacillus*, *Pasteurella*, and *Streptococcus* — the relative abundance of which was significantly altered depending on the presence and type of maternal antibiotics administered. Further studies will determine whether constituents of these genera are necessary or sufficient for protection from LOS. These findings provide novel insights into the natural colonization process and microbiome-dependent development of neonatal mucosal barrier defenses.

Boothe, Paul Donald (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Malay K Basu
Abstract Approved By Advisor:	Yes
Co-Authors:	Boothe PB ¹ , Basu MK ²
Title:	The Evolution of Mitochondrial Fission-Fusion Genes and their Role in Cancer.

The evolution of eukaryotic cells is punctuated by several rounds of endosymbioses. One such event gave rise to mitochondria, originally belonging to α -proteobacteria. The traditional role of mitochondria is generally believed to be the generation of ATPs. However, recent studies are finding new roles of this multifaceted organelle. One such role is the control of cell division by mitochondrial fission-fusion. It is now known that mitochondria undergo morphological changes, either fusing to form a mitochondrial network (fusion) or as separate organelles (fission). These dynamics act as checkpoint for cell cycle. Very little is known about the evolution of molecules that control mitochondrial fission-fusion and how they got involved with the host cell division cycle. The two goals of this project are: 1) to understand the evolution of mitochondrial fission-fusion genes and their involvement in host cell-division cycle. 2) to investigate the alteration of these genes in cancer genomes to understand their roles controlling cell division.

We investigated the evolution of mitochondrial fission-fusion genes by using known fission-fusion genes as probes in PSI-BLAST and following their evolution by creating phylogenetic trees. We could not find any distinct pattern of evolution of these genes. We conclude that the fission-fusion genes evolved not simultaneously, but in several stages in eukaryotic cells, and the role of mitochondrial dynamics in controlling cellular division is a recent phenomenon in evolution.

To understand the roles of fission-fusion proteins, we used all of the genes in a mitochondrial proteome database, Mitocarta (<http://www.broadinstitute.org/pubs/MitoCarta/>). We extracted the genetic alterations in these genes in The Cancer Genome Atlas (TCGA). We found significant alterations in these genes, particularly copy number variation, in several cancer genomes, more prominently in lung and ovarian cancers. Ongoing work is probing these alterations in greater details.

Bradford, Davis Nathaniel (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	O'Brien Center Fellowship

Faculty Advisor: Dr. Michael Allon

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Clinical and surgical predictors of fistula outcomes

The current practice in vascular access for hemodialysis favors the creation of arteriovenous fistulas (AVFs) over other access types. While mature fistulas offer clear advantages—specifically, an increased patency period and decreased infection, thrombosis, and costs—over grafts and catheterization, the potential for failure of fistula maturation remains as a factor that both nephrologists and vascular access surgeons must consider in their clinical decision-making. This study seeks to improve risk stratification of patients approaching fistula placement by 1) evaluating an established risk equation based on age, race, and the presence of peripheral vascular and coronary artery disease, 2) exploring other comorbidities and patient descriptors as risk factors, and 3) determining the significance of post-operative predictions of fistula success made by the vascular access surgeon. 188 patients with fistula placement in the past three years that had hard fistula outcomes (i.e., mature or immature) served as the study cohort. By combining clinical and surgical predictors of fistula success, a systematic approach will be suggested to guide nephrologists and surgeons as they explore vascular access options and follow the patient after fistula placement.

Bray, Alexander Wendell (MSTP)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Scott Ballinger, PhD
Abstract Approved By Advisor:	Yes
Co-Authors:	Alexander W. Bray, Kyle P. Feeley, David G. Westbrook, Douglas R. Hurst, Scott W. Ballinger
Title:	The Role of Mitochondrial Background in B16 Melanoma Growth

Melanoma incidence rates have been increasing for at least 30 years and it is estimated that an additional 76,250 individuals were diagnosed with the disease in 2012. While presence of metastasis remains the single most important factor in determining prognosis, tumor thickness and mitotic rate also possess a well demonstrated mathematical relationship with patient outcome.

Although several nuclear genes and polymorphisms have been implicated in melanoma progression, a resurgence of interest in the metabolic properties of cancer cells has also generated curiosity surrounding the contribution of mitochondrial genetics to carcinogenesis, and our lab has developed a novel technique to examine this phenomenon in the form of Mitochondrial – Nuclear eXchange (MNX) mice. These mice possess nuclear DNA from one inbred mouse strain coupled with mitochondrial DNA from another, and preliminary studies in our lab have demonstrated that certain pre-existent mitochondrial DNA polymorphisms may influence tumor latency and growth rate. Similarly, we hypothesized that B16F10 mouse melanoma cells injected into the flanks of syngeneic C57BL6 (C57) mice carrying CH3 mouse mitochondria ($C57_nCH3_{mt}$ MNX) would display alterations in tumor cell proliferation relative to B16F1 cells in wild type B6 controls ($C57_nC57_{mt}$). Our results indicate this to be true, as tumor growth as measured by bioluminescence imaging differed significantly between $C57_nC57_{mt}$ and $C57_nCH3_{mt}$ MNX mice. Based on these findings, mitochondrial haplotype may prove to be an important prognostic marker for individuals diagnosed with malignant melanoma.

Brosius, Stephanie Nicole (MSTP)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Steven Carroll
Abstract Approved By Advisor:	Yes
Co-Authors:	Steven Carroll
Title:	Combinatorial treatment of malignant peripheral nerve sheath tumors with tyrosine kinase inhibitors hinders tumor survival and proliferation

Malignant peripheral nerve sheath tumors (MPNSTs) are aggressive sarcomas arising from cells within the Schwann cell lineage. These tumors occur spontaneously in the general population and are the most common cause of death patients with the genetic tumor susceptibility disorder neurofibromatosis type-1. Surgery is the only viable treatment for these aggressive sarcomas. Currently, the 5 year survival rate is approximately 33%, mainly due to the paucity of effective chemotherapeutic regimens. Therefore, identifying and targeting key signaling cascades mediating tumor proliferation and survival is of utmost importance to improving patient prognosis. We have shown that erbB receptor tyrosine kinases (RTKs) promote MPNST proliferation and invasion and pan-erbB inhibitors like canertinib have potent cytostatic effects on MPNST cells. However one main barrier to developing chemotherapeutics has been tumor resistance and we hypothesize this is due to coactivation of multiple RTKs within the tumor, thereby requiring combinatorial therapy to overcome resistance. To assess global signaling in MPNSTs, we utilized antibody arrays which analyze the phosphorylation status of 45 different RTKs. Based on these results, we treated four human MPNST cell lines with a series of RTK inhibitors and analyzed the cellular survival and proliferation. We found that phosphorylation status of surveyed RTKs was not necessarily indicative of tumor response to targeted therapy, as treatment with inhibitors of platelet derived growth factor receptor, vascular endothelial growth factor receptor and hepatocyte growth factor receptor failed to inhibit tumor proliferation when used as monotherapies, despite consistent activation in all four cell lines. Importantly, treatment with canertinib or the Raf kinase inhibitor sorafenib individually proved to be cytostatic, while combinatorial treatment was cytotoxic. Considered collectively, these data suggest that combinatorial therapy will be required in MPNSTs to prevent the development of resistance and that dual treatment with canertinib and sorafenib may be effective against MPNSTs *in vivo*.

Brown, Steven Tyler (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	
Faculty Advisor:	James Johnston, M.D.

Abstract Approved By Advisor:	Yes
Co-Authors:	SA Wilkins, MI Falola, MJ Crowther, KA Gran, CN Shannon, JM Johnston
Title:	Establishment of a multidisciplinary concussion program: impact of standardization on patient care and resource utilization

Introduction: Recent legislation and media reporting has heightened awareness of concussion in youth sports. Previous work by our group defined significant variation of care in management of children with concussion. To address this issue, we established a multidisciplinary concussion program with an institution-wide management protocol, with an emphasis on community outreach and education via traditional media sources and the Internet. This study evaluates the impact of standardization on patient care and resource utilization.

Methods: This retrospective study included all patients younger than 18 years of age evaluated for sports-related concussion between the years 2007-2012. Emergency department (ED), sports medicine, and neurosurgery records were reviewed. Data included demographics, injury details, clinical course, SCAT2 scores, imaging, discharge instructions, and referral for specialty care. The cohort was then analyzed comparing those patients seen pre and post standardization of care.

Results: 589 patients, 270 pre (2007-2011) and 319 post (2011-2012) standardization were identified. Statistical significance ($p < .0001$) was seen between the pre and post groups in multiple variables: there were more girls, more first time concussions, fewer initial presentations to the ED, fewer imaging studies, more consistent administration of the SCAT2, and more consistent supervision of return to play after adoption of the protocol.

Conclusions: The combination of increased public awareness and statewide legislation has led to a 500% increase in the number of youth athletes presenting for concussion evaluation at our center. Establishment of a multidisciplinary clinic with a standardized management protocol has resulted in more consistent concussion care and decreased institutional resource utilization.

Bryant, Mary Katherine (MS3)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	
Faculty Advisor:	Dr. Derek DuBay
Abstract Approved By Advisor:	Yes
Co-Authors:	Mary K Bryant, Stephen H. Gray, David P Dorn, Jessica Zarzour, J Kevin Smith, David T Redden, Souheil Saddekni, Ahmed Kamel, Jared White, Devin E Eckhoff, and Derek A DuBay
Title:	Change in Psoas Muscle Mass Correlates with Survival Following Transarterial Chemoembolization.

Background:

Transarterial chemoembolization (TACE) is recommended as treatment for unresectable hepatocellular carcinoma (HCC). Recently, sarcopenia has been used as a marker of surgical risk based on cross-sectional imaging, however little has been done to describe sarcopenia following interventional procedures. We hypothesize that total psoas muscle area (TPA) will show dynamic changes post-TACE and correlate with survival.

Methods:

All “first” TACE interventions for HCC performed at a single institution from 2008–2013 were retrospectively reviewed. The study sample was limited to patients with CT scans within 120 days pre and post-TACE. TPA was calculated at the L4 level on CT imaging. Covariate adjusted outcomes were assessed using multivariable regression.

Results:

Overall there were 187 patients available for analysis; the mean age was 62.3

\pm 9.4 years of age, and the mean MELD score was 11.1 ± 3.6 . The mean TPA was -5.38 ± 8.86 (cm^2) for the patients. Median survival was 23.4 (95% CI 20.1, 32.0) months. Change in TPA was stratified into tertiles and survival distributions were examined using Kaplan Meier estimates and Log-Rank Survival Tests. Change in TPA was associated with survival ($p = .02$). Change in TPA remained significantly associated with survival after adjusting for HCC specific covariates using Cox Proportional Hazards. The increased risk of death in the greatest TPA change vs. least TPA change (HR 2.2 95% CI 1.22-3.80).

Conclusion: Total psoas area changes following TACE procedures in patients with HCC. Increasing sarcopenia significantly correlates with mortality.

Burke, Mata Rodopoulos (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Charles Landen

Abstract Approved By Advisor: Yes

Co-Authors: Adam Steg, Dae Hoon Jeong, Zachary C. Dobbin, Ashwini Katre, Charles N. Landen.

Title: GSI-1 synergizes with LDE225 in ovarian cancer cells by inhibiting the proteasome

Background: Previous research has suggested that targeting stem cell pathways, such as Notch and Hedgehog, may aid in overcoming the chemoresistant properties of cancer stem cells. However, attempts to combine Notch and Hedgehog inhibitors synergistically have had varying results, and the mechanism through which these inhibitors act is not fully understood.

Objective: To explore the potential synergy of combined Notch and Hedgehog targeting, and the mechanism through which this may occur.

Methods: SKOV3TRip2 (taxane-resistant) ovarian cancer cells were treated with Notch inhibitors (GSI-1 and

GSI-XXI), a Hedgehog inhibitor (LDE225), and a proteasome inhibitor (Bortezomib). The effects of these drugs were assessed by MTT assay, PI staining, PARP cleavage, qPCR, and a cell-based proteasome assay. Results: GSI-1 decreased cell viability alone and synergized with LDE225, while GSI-XXI had no effect. In addition, siRNA-mediated downregulation of Notch did not result in synergy with LDE225, suggesting a Notch-independent mechanism of synergy with GSI-1. To elucidate differences between GSI-1 and GSI-XXI, we examined effects of these drugs on the proteasome. GSI-1 inhibited the proteasome to the same extent as bortezomib, while GSI-XXI did not. Combination treatment with bortezomib and LDE225 also resulted in synergy. Monotherapy with both GSI-1 and bortezomib decreased transcription of the Hedgehog target genes Patched, Gli1, and Gli2. Combination therapy resulted in G2/M/S phase arrest (60% with combination therapy vs. 38% of control, $p<0.001$) and induced apoptosis.

Conclusion: The results of this study suggest that the Notch inhibitor GSI-1 acts synergistically with Hedgehog inhibition through a Notch-independent decrease in proteasome activity. Similar synergy was demonstrated with the proteasome inhibitor bortezomib. This synergistic combination appears to be working through S/G2/M phase arrest. Combined Hedgehog and proteasome inhibition offers a promising approach to targeting chemoresistant cells in ovarian malignancies.

Burkett, Wesley Croft, Jr. (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Mac Harmon

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Reed Dimmitt

Title: Gastroschisis in Alabama: Prevalence, Locality, and Demographics from 2003 to 2011

OBJECTIVE: To identify counties in Alabama with a higher prevalence of gastroschisis than what is expected based on demographics to support a clustering hypothesis, and to determine whether an increasing trend of gastroschisis is present statewide from 2003 to 2011.

METHODS: This study examined 210 cases of gastroschisis from 2003 to 2011 reported at three pediatric surgical centers across Alabama. Cases were compared with publicly available natality data sets to identify risk factors and county demographics. Only infants whose mothers resided in Alabama were used.

RESULTS: The prevalence of gastroschisis in Alabama increased from 2.527 in 2003 to 4.552 cases per 10,000 live births in 2011. 5 out of 67 counties were at an increased risk of gastroschisis. Bibb, Cherokee, Coffee, Elmore, and Escambia counties had a prevalence of 21.570, 13.699, 10.315, 11.150, and 11.452 cases per 10,000 live births, respectively. Young maternal age showed an increase in prevalence of gastroschisis as mothers less than 20 years old had a prevalence rate of 11.107 cases per 10,000 live births. Deliveries paid by Medicaid (4.697 cases per 10,000 live births), preterm births (15.405 cases per 10,000 live births for gestation weeks 32 to 36), and infants with small birth weights for their respected gestational age (14.130 cases per 10,000 live births for infants <10% of population) were at an increased risk of gastroschisis. Compared to non-Hispanic whites, non-Hispanic blacks were at a lower risk for gastroschisis (crude prevalence ratio of 0.490 with a 95% confidence interval of 0.338-0.711) while Hispanics had the same risk as non-Hispanic whites (crude prevalence ratio of 1.145 with a 95% confidence interval of 0.711-1.844). Sex of the newborn had no affect on the prevalence of gastroschisis.

CONCLUSION: The prevalence of gastroschisis in Alabama increased from 2003 to 2011. 5 counties appear to be at an increase risk for gastroschisis. Higher rates of gastroschisis were also seen in young mothers (especially those less than 20 years of age), preterm and low birth weight infants, and deliveries that were paid for by Medicaid. Non-Hispanic black mothers had less incidence of gastroschisis compared to non-Hispanic white and Hispanic mothers.

Burton, Kent Lane (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Eben Rosenthal
Abstract Approved By Advisor:	Yes
Co-Authors:	Kent Burton, Alexandra Kejner, Eben L. Rosenthal, Kirk Withrow, J. Scott Magnuson, William Carroll
Title:	Negative Predictors of Positive Margins in Patients Undergoing Transoral Robotic Surgery for Head and Neck Cancer

BACKGROUND: The DaVinci robot is a useful tool for exposure and resection of tumors located in the head and neck. One of the major disadvantages is the absence of tactile feedback, which limits the surgeon's ability to recognize margin status.

OBJECTIVES: Determine if the site, subsite or surgeon are negative predictors of positive margins in patients undergoing transoral robotic surgery (TORS) for head and neck cancer.

METHODS: Retrospective chart review from 2007 through 2011 for patients undergoing TORS for head and neck cancer. Intraoperative margin status, number of margins and final margin status were collected. Close margins were defined as <5 millimeters from the cut edge, negative margins were defined as >5 millimeters. The percentage of positive, close, initial and final margins based on site, subsite and surgeon were documented and evaluated.

RESULTS: 131 patients were included. Surgeon A performed 44 cases, Surgeon B performed 87. Surgeon A had 20 (45%) positive initial margins, 7 (16%) close initial margins, 3 (7%) close final margins, and 4 (9%) positive final margins. Surgeon B had 42 (48%) positive initial margins, 23 (26%) close initial margins, 21 (24%) close final margins, and 12 (14%) positive final margins. Surgeons differed in the number of close final margins ($p=0.02$). Based on site, the supraglottis had a higher percentage (58%) of positive initial margins compared to the oropharynx (43%), but a lower percentage (4%) of positive final margins compared to the oropharynx (15%). Divided into subsites, the supraglottic larynx had the highest percentage (69%) of positive initial margins, but only 8% positive final margins. The tonsil had the highest percentage of positive final margins (18%), but the lowest rate of positive initial margins (39%).

CONCLUSIONS: The rate of close margins with TORS varied between surgeons. The supraglottis, specifically the supraglottic larynx, were more likely to yield positive initial margins with TORS.

Carrigan, Divya Alapati (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Diabetes Research and Training Center Fellowship
Faculty Advisor:	Dr. Monika Safford

Abstract Approved By Advisor: Yes

Co-Authors: Monika Safford, MD

Title: Healthy Food Choices at the Dollar General: Feasible Dietary Advice for Low Income, Rural Populations

Diet plays an important role in preventing and treating chronic diseases and obesity. However, many rural populations lack access to supermarkets selling the fresh produce essential for a healthy diet. As a result, many rural residents purchase a substantial proportion of their groceries local stores such as the Dollar General. Practical advice on how to make healthy food choices at the Dollar General is currently unavailable. It is possible to create a culturally adapted, educational video on how to make healthy food choices here. The rural Alabama Black Belt is characterized by steep poverty, among the worst health outcomes in the US, and scarce resources. We used the infrastructure of a community-based research program in partnership with Black Belt communities to collaboratively develop an educational video. We used data from focus groups and previous research projects to inform the intervention design. In the future, we will show the video to 50 area residents and quantify how useful they find the video and whether it will change their food choices when shopping at the Dollar General. If found to be acceptable, the video will be integrated into a community-based intervention in order to test the hypothesis that the intervention will lead to weight loss and healthier eating patterns. The video contains 3 messages: 1) eat fewer second helpings; 2) use the “plate method” 3) eat fewer fried foods and drink fewer sugar sweetened beverages. The video demonstrated a community member in the Dollar General making choices for snacks and meals and how these items can be integrated into healthy snacks and meals. Using just a few key messages about healthy eating specifically targeted at major challenges to healthy eating in the rural Alabama Black Belt, and using a visual approach to information is intended to improve comprehension and uptake of information.

Cernosek, Chelsea Ashton (MS3)**Project Length:** Intermediate**Prior Research Experience:** Yes**Source of Funding:****Faculty Advisor:** Luis Vasconez**Abstract Approved By Advisor:** Yes**Co-Authors:**

Title: Sickle Cell Trait and Wound Healing; Beware the Use of Epinephrine. A Report of Three Cases.

Background: Breast reduction is a very common procedure, which is performed on young patients of all ethnicities for relief of symptoms. We would like to call attention to the possibility that epinephrine may have deleterious effect on wound healing in patients with sickle cell trait. We also present a discussion of the possible mechanism of action occurring in the adhesion events of the erythrocytes leading to partial anoxia in sickle cell trait patients.

Methods: Three patients, all with a diagnosis of sickle cell trait, underwent reduction mammoplasty. In two of the patients, the procedures were performed with the use of xylocaine with epinephrine for its vasoconstricting effects. In the third patient xylocaine with epinephrine was not used.

Results: In the two sickle cell trait patients receiving xylocaine with epinephrine, skin necrosis and sloughing occurred, as well as necrosis of the underlying breast tissue. In the patient not receiving xylocaine with epinephrine, no complications ensued.

Conclusions: We would like to present a warning concerning the use of epinephrine in patients with sickle cell trait. Although screening for sickle cell trait before aesthetic surgery is uncommon, it would be worthwhile to screen for sickle cell trait if warranted by the patient's history.

Cezayirli, Phillip Cem (MS4)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Asim Bag
Abstract Approved By Advisor:	Yes
Co-Authors:	L B Nabors, MD; J J Davenport, MD; J R Hackney, MD; A K Bag, MD
Title:	Post-treatment peritumoral cerebral blood flow (CBF) can better predict overall survival in newly diagnosed glioblastoma multiforme patients compared to tumoral/peritumoral cerebral blood volume (CBV).

Purpose: Glioblastoma multiforme (GBM) is the most common primary adult brain tumor, which is frequently fatal. With current standard treatment (resection followed by chemoradiation [CR]), the overall survival (OS) is only 14.6 months. There is no universally accepted biomarker that can reliably predict OS. Relative cerebral blood volume (rCBV), a parameter derived from perfusion MRI (pMRI), has been used in the past to predict OS in GBM patients. Relative cerebral blood flow (rCBF), another parameter derived from pMRI, has never been investigated for prediction of overall survival in GBM patients. We hypothesized that rCBF can also predict overall survival in newly diagnosed GBM patients. **Materials and Methods:** We retrospectively reviewed all newly diagnosed GBM patients who presented in our institution between Jan 2011 and Dec 2011. We included all the patients who were treated with standard therapy (as above) and had MRI (including pMRI) before initiation as well as after completion of CR. We evaluated maximum peritumoral and tumoral rCBV and rCBF on pre-therapy as well as posttherapy MRI for prediction of OS. We also evaluated several other clinical, pathological and imaging parameters in predicting OS. We performed univariate and multivariate regression analysis using SAS software. 17 patients had posttherapy MRI and 12 patients had pre and posttherapy MRI.

Results: On univariate analysis, variables significantly ($p < 0.05$) associated with OS included pretreatment tumoral rCBV (Hazard ratio [HR] = 1.05, $p = 0.05$), posttherapy peritumoral rCBF (HR = 1.96, $p = 0.05$), posttherapy tumoral rCBF (HR = 1.35, $p = 0.05$) and posttherapy tumoral rCBV (HR = 1.1, $p = 0.01$). There was no statistically significant association between OS and other parameters examined. Multivariate regression analysis failed to clarify relationship of the predictor variables with OS. **Conclusion:** Our study demonstrates posttherapy peritumoral and tumoral rCBF are strong predictors of overall survival, in addition to tumoral rCBV; however, these results should be validated in a prospective study.

Chambers, Charis Nailah (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Dr. Joseph Biggio and Dr. Amelia Sutton
Abstract Approved By Advisor:	Yes
Co-Authors:	Amelia L. Sutton, Victoria Jauk, Hannah C. Machemehl, Charis N. Chambers, Joseph R. Biggio, and Alan T. Tita
Title:	Perinatal outcomes in obese women with preterm premature rupture of membranes

Obesity is associated with a multitude of adverse maternal and neonatal outcomes. Preterm premature rupture of membranes (PPROM) is the leading identifiable cause of prematurity. PPROM remote from term is managed with prophylactic broad-spectrum antibiotics to prolong latency. We hypothesized that obese women with PPROM have shorter latency periods and higher rates of perinatal complications due to their increased volume of distribution and likely altered tissue levels of antibiotics.

We performed a retrospective cohort study of singleton pregnancies diagnosed with PPROM before 33 weeks from 2007-2012. The patients received antibiotics for group B streptococcus prophylaxis and at least one dose of azithromycin for latency. Management also included inpatient management, daily fetal monitoring, steroid administration if less than 32 weeks, and delivery by 34 weeks or 32-33 with fetal lung maturity. Neonatal and maternal outcomes were compared between women with a body mass index (BMI) < 30 and those with a BMI ≥ 30 .

The gestational age at ROM and delivery as well as the median latency were comparable between non-obese and obese women (Table). There were no differences between the two groups in the frequency of the composite neonatal outcome. The infants of non-obese and obese women had similar individual neonatal outcomes, with the exception of BPD, which was 70% less frequent in the obese cohort. There was no difference in the prevalence of maternal infection or chorioamnionitis between the two groups.

Despite an estimated larger volume of distribution for latency antibiotics, obesity was not associated with a reduction in the latency period or an increase in adverse perinatal outcomes in pregnancies complicated with PPROM.

Chou, Andrew Daoan (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Derek DuBay
Abstract Approved By Advisor:	Yes
Co-Authors:	Paul Sauer, David Redden, Devin Eckhoff, Derek DuBay
Title:	Socioeconomic Factors and Early Hospital Readmission in Liver Transplant Patients

Background: Patients who undergo liver transplant operations often require follow-up hospital readmissions subsequent to the transplant procedure, resulting in higher costs and increased resource utilization. The goal of this study will be to examine various predictors for early hospital readmission following liver transplant procedures. Some studies have analyzed various medical factors (such as discharge creatinine) that may predict the likelihood of early hospital readmission following liver transplantation. In contrast, this study will measure the association of several prospectively collected socioeconomic factors (level of education, household income, caregiver support, etc.) with early hospital readmission rates and incidence of missed clinic appointments.

Hypothesis: We hypothesize that patients with lower socioeconomic status will have a higher incidence of early hospital readmission and missed clinic appointments.

Methods: A retrospective chart analysis of liver transplant patients at the University of Alabama at Birmingham ranging from July 2008 to January 2013 was performed. Multiple socioeconomic variables were extracted, including functional status, household income, marital status, marital length, ability to read/write, last employment, education, primary/secondary insurance, prescription coverage, household size, primary/secondary caregiver relationship, primary/secondary caregiver age, tobacco use within one year, history of alcohol abuse, alcohol consumption within one year, and illegal drug use within one year. Clinical factors were also extracted to allow the statistical analysis to account for severity of disease. The statistical analysis is currently still underway.

Results: The results are not available pending the completion of the statistical analysis.

Conclusions: No conclusions can be drawn until analysis has been completed.

Cohen, Joshua L. (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Dr. Sarah Clinton
Abstract Approved By Advisor:	Yes
Co-Authors:	Glover ME, Pugh P, Simmons RK, Akil H, Clinton SM
Title:	Maternal Style Differences Shape Emotional Behavior In Rats Genetically Prone To High-Anxiety

We utilized two strains of selectively-bred Sprague-Dawley rats that respond differentially to mild anxiety-producing novel environments. Our Bred High Responder (bHR) rats exhibit exaggerated aggression, novelty-induced locomotor activity, impulsivity, and drug-seeking tendencies – behavioral features commonly present in human “externalizing” disorders, such as drug addiction and attention deficit hyperactivity disorder. The Bred Low Responder (bLR) rats are prone to excessive depressive- and anxiety-like behaviors, which is reminiscent of human “internalizing” disorders such as major depression. One hypothesis for the behavioral differences observed in bHR/bLR rats comes from previous studies noting a discrepancy in maternal care, most notably during the second week postpartum. In the current study, we implemented a cross-foster paradigm to study the effects of maternal care on bLR pups; we hypothesized that cross-fostering bLRs to bHR mothers may improve their anxiety and depressive phenotype. Thus, at birth bLR litters were assigned to one of three maternal care conditions; litters were reared by their biological bLR mothers, a bLR foster mother, or cross-fostered to a bHR foster mother. Adult offspring were subjected to tests of anxiety, depression, and a Social Interaction Test. Interestingly, we found that maternal care condition did influence bLRs’ behavior. Specifically we found that bLR pups fostered to bHR dams demonstrated a reduction in anxiety-like behaviors through multiple behavioral assessments. Microarray analysis to determine the underlying neurobiological changes that occur in the early weeks of life resulting in the reduced anxiety observed in the cross-fostered bLR pups has shown significant changes in gene expression in the amygdala and hippocampus. Further work is underway to confirm these results with qPCR and to identify critical pathways in these regions that cause the observed phenotypes.

Colon, Chad Michael (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Department of Medicine Fellowship
Faculty Advisor:	Suzanne Oparil
Abstract Approved By Advisor:	Yes
Co-Authors:	Eric Judd, Muhammad Balouch, Suzanne Oparil, David Calhoun
Title:	Characterization of Refractory vs. Resistant Hypertension Phenotypes

Purpose: Refractory hypertension is a recently proposed phenotype of antihypertensive treatment failure. A prior retrospective analysis revealed higher resting heart rates in refractory patients, suggesting heightened sympathetic tone as an important characteristic of the phenotype. The current study was done to further characterize refractory hypertension and identify potential mechanisms of antihypertensive treatment failure.

Methods: Adults referred to the UAB Hypertension Clinic since January 2008 for resistant hypertension, defined as uncontrolled blood pressure (BP) (<140/90 mm Hg) were analyzed. Refractory hypertension was defined as failure to control BP on ≥ 5 different classes of antihypertensive agents. Patients whose BP was controlled while taking ≥ 3 medication classes were defined as controlled resistant and served as the comparator group. Demographics, comorbidities, risk factors, and biochemical data were analyzed.

Results: Refractory (n=86) and Controlled Resistant (n=202) patients were similar demographically without statistically significant differences in age, sex, race, self-reported years of hypertension, or body mass index. Chronic kidney disease (CKD), diabetes mellitus, and coronary artery disease (CAD) were more prevalent in the refractory group (30.2 vs. 17.3 %, p = 0.014; 39.5 vs. 27.2 %, p = 0.039; and 24.4 vs. 14.4 %, p = 0.039), respectively. There were no significant differences in serum sodium, potassium, aldosterone-to-renin ratio, 24-hour urinary aldosterone or sodium. However, renal function was worse in the refractory group compared to controls (serum creatinine 1.47 ± 1.35 vs. 1.10 ± 0.41 mg/dL, p = 0.0005, respectively).

Conclusions: Patients with refractory hypertension are more likely to have CKD, diabetes and previous CAD, consistent with a higher overall cardiovascular risk profile compared to patients with controlled resistant hypertension. Aldosterone status was not different in the 2 groups, indicating that refractory hypertension is not attributable to greater aldosterone excess. These findings implicate CKD and diabetes as important causes of antihypertensive treatment failure.

Craig, Carolyne Marie (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Namasivayam Ambalavanan, MD
Abstract Approved By Advisor:	Yes
Co-Authors:	Tara McNair
Title:	Early Vitamin D Supplementation for Prevention of Respiratory Morbidity in Extremely Preterm Infants

Purpose: To determine if vitamin D supplementation to extremely preterm infants reduces respiratory complications, reduces infection, and prevents bronchopulmonary dysplasia.

Background: Lung immaturity is a major cause of morbidity and mortality in extremely preterm infants. Vitamin D may play an important role in lung maturation and lung immune responses. Preterm infants have much lower vitamin D concentrations than term infants. Vitamin D is essential for lung and immune development, but the optimal supplemental dose for preterm infants is unknown.

Methods: Extremely preterm infants born at 28 gestational weeks or less were randomized to receive a placebo, high dose: 800 IU/day or low dose: 200 IU/day oral vitamin D; each infant received the dose for 28 days. This project was an interim analysis of the first 25 patients enrolled in this study (planned total enrollment=100). An enzyme immunoassay (ELISA) for 25(OH) vitamin D was done on blood samples from: cord blood (day 1), postnatal day 14, and postnatal day 28.

Results: Vitamin D concentrations were compared to the number of days requiring respiratory support, defined as the need for supplemental oxygen or positive pressure ventilation to maintain oxygen saturation levels between 88-95%. The average vitamin D concentrations were 13.57ng/ml in cord blood, 29.5ng/ml in day 14 blood, and 34.14ng/ml in day 28 blood (normal range 30-50ng/ml). The rank correlation coefficient for the length of stay in the hospital was R=-0.33 and p=0 for cord blood, R=-0.15 and p=0 for day 14, and R=-0.08 and p=0 for day 28.

Conclusions: Nearly all extremely premature infants were found to be very deficient in vitamin D at birth. However, no correlation was found between serum vitamin D concentrations and respiratory morbidity. This preliminary analysis was limited due to small sample size; additional biochemical analyses will be performed after enrollment of an additional 50 infants.

Crisona, Frank Joseph, III (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Melissa Chambers

Abstract Approved By Advisor: Yes

Co-Authors: Kicielinski KP, Pritchard PR, Ruiz HE, Chambers MR

Title: Evaluation of Kyphoplasty Outcomes

Vertebral body compression fractures are a painful condition with many causes. The most common cause is minor trauma in osteoporotic patients. Treatment options include medical or surgical management. The medical regimen typically includes bed rest, narcotic analgesics, and bracing. Surgical management may include instrumented fusion, vertebroplasty, or kyphoplasty. Outcomes have been poor with instrumentation in osteoporotic bone. Vertebroplasty is a high-pressure percutaneous fluoroscopically guided injection of bone cement used to stabilize the fracture. Kyphoplasty is an advanced procedure, also performed percutaneously and with fluoroscopic guidance, using a balloon (bone tamp) in the cancellous bone of the collapsed vertebra to restore vertebral height and create a void so that bone cement can be placed under low-pressure, thereby reducing the risk of cement leakage and making it a much safer procedure.

The main aim of my research this summer was to assist in determining the degree of pain relief, the safety and the cost utility of kyphoplasty for the treatment of vertebral body compression fractures. During the ten-year period between 2003 and present, Drs. Chambers, Pritchard and Ruiz, all neurosurgeons, collectively treated 456 patients with kyphoplasty. Patients were interviewed before surgery and asked to complete surveys following surgery. Over 200 patients responded and were included in the study. The median follow-up period was 630 days.

I reviewed paper and electronic medical records and created a proto-database. The redacted database contained patient information including age, gender, height, weight, body-mass index, and the number, levels and causes of fractures in each patient. I then recorded data from patient surveys including pain, disability and quality of life before and after surgery. Pain was measured using the Visual Analog Scale (VAS). Degree of disability was determined by responses to the Roland Morris Disability Scale questionnaire. Using the European 5-dimension Quality of Life questionnaire responses, I calculated and recorded scores for each patient and these scores were used to determine quality-adjusted life years (QALY's) and cost utility analysis. I also recorded pre and post-operative narcotic use as a measure of pain relief.

From this database, we demonstrated that pain and disability were significantly lessened after kyphoplasty and quality of life was significantly improved. The response to surgery was rapid and results were sustained. These results have been included in our manuscript in preparation for publication enTitled "Long-term safety, efficacy and value of Kyphoplasty."

Cruce, Brittany Taylor (MS2)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Physical Medicine and Rehabilitation Fellowship

Faculty Advisor: Dr. Amie B. McLain

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Mindy Aisen, Dr. Christina Morgan, Dr.Claire Kalpakjian, Dr. Graves, Dr. Lisa Wenzel

Title: Pregnancy, Labor, Delivery, and Postpartum Outcomes of Women with and without Spinal Cord Injury: An Observational Study

Hypothesis: Women with spinal cord injury (SCI) require extra evaluation of their risk during pregnancy, labor, delivery and postpartum care due to the impact of medical, physical, and psychosocial conditions unique to this population as compared to their able-bodied counterparts.

Rationale for proposed research, innovation, and impact of research: The National Spinal Cord Injury Statistical Center at the University of Alabama at Birmingham¹ reports that 21.7% of all new spinal cord injuries occur among women. Currently there is an urgent need to better understand the medical management of women with SCI. The neurological changes that a woman undergoes during pregnancy can have a direct effect on her obstetrical outcomes. Additionally, the female reproductive neuro-endocrine system does have an effect on the acute and long-term neural responses to traumatic central nervous system injury. Evaluating the correlation between the female reproductive system and the adaptations that occur as a result of the neural injury can lead to a better understanding of the outcomes and thus improve medical management of women who are pregnant with spinal cord injury.

This study will provide knowledge to this SCI/disability-pregnancy model that will improve care and lessen the complications for women with SCI who become pregnant. Women with SCI will be identified and then matched by able body pregnant women and standard prenatal and postpartum assessments, labs, and testing will be obtained. All outcomes and complications will be recorded for both sets of women. The women with SCI will undergo further assessments related to their SCI-related conditions and additional tests will be conducted when necessary.

Results and Anticipated Outcomes: After having tested and revised the data collection forms, the first pair of matched women has been admitted to the study at the collaborating center in Louisville.

It is expected that specific risks, complications and outcomes will be identified for women with SCI that are greater than those for able-bodied women. From this, the collaborating centers plan to develop recommendations for future care of women with SCI who become pregnant. The outcomes observed from the study will lead to future research dedicated to establishing interventions aimed at preventing complications in women with SCI.

Culbreath, Courtney Leigh (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Foundation for Anesthesia Education and Research
Faculty Advisor:	Dr. Sadis Matalon
Abstract Approved By Advisor:	Yes
Co-Authors:	James Londino, Courtney Culbreath
Title:	Nasal Potential Difference in Influenza Infected Mice

Background: Influenza is an acute respiratory illness that occurs worldwide in annual outbreaks and epidemics. While the majority of infected individuals develop a self-limited acute respiratory illness, some individuals, especially those in high-risk groups, develop severe lower respiratory tract complications including pneumonia, alveolar flooding, and acute respiratory distress syndrome (ARDS). In the lung, ENaC and CFTR are the primary ion channels controlling sodium and chloride transport, respectively. Influenza infection has been shown to decrease ENaC activity due to virus binding and decrease alveolar fluid clearance due to enhanced CFTR secretion and decreased ENaC absorption. In this experiment, Nasal Potential Difference (NPD) was used to determine ENaC and CFTR channel contributions in control mice and in mice intranasally infected with Influenza A virus.

Methods: The nasal transepithelial potential difference was measured in C57/BL6 mice. At time point 0, the mice were anesthetized with isoflurane and intranasally infused with 90 μ l saline or PR8 Influenza A virus for control and experimental mice, respectively. After 1, 8, and 24 hours, the mice were given an intraperitoneal anesthesia injection (150mg/mL ketamine, 50 mg/mL xylazine) and a nasal catheter was inserted. Various agonists and antagonists were perfused at a speed of 200 μ L/hour to determine ENaC and CFTR channel contributions to NPD. Bronchoalveolar lavage (BAL) was performed before sacrificing the animals by way of bilateral thoracotomy.

Results: No significant difference was found for ENaC or CFTR NPD at 1, 8, or 24 hours post-infection. BAL protein was significantly increased in the virus infused mice after 8 and 24 hours. Interestingly, BAL cell counts were only increased after 24 hours post infection.

Conclusions: Unlike prior experiments, our work did not find that Influenza infection has significant influence on ENaC or CFTR ion channels.

Davis, Benjamin Joseph (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Brent Ponce
Abstract Approved By Advisor:	Yes
Co-Authors:	Evan D. Sheppard
Title:	Assessing the readability of online shoulder and elbow related patient education materials

Background: As patient understanding of disease and treatment improves, so too do patient outcomes. In addition to information provided directly by physicians, patients are increasingly seeking information by searching for medical educational materials on their own. The accessibility of these educational materials has grown through increased availability of the internet and easy dissemination of these materials online. The National Institutes of Health (NIH) recommends that patient educational material (PEM) is written at a 6th to 7th grade reading level. Evaluation of the reading level of PEM related to shoulder and elbow conditions have not been performed. We hypothesize that shoulder and elbow PEM is written at a reading level higher than recommended.

Materials and Methods: The study identified online shoulder and elbow PEMs made available by the American Academy of Orthopaedic Surgery (AAOS) and several academic orthopaedic departments. The original PEMs were evaluated for reading level with ten validated readability metrics designed to determine readability.

Results: PEMs from the AAOS and all of the surveyed academic programs had mean readability scores that did not meet the recommended 6th-7th grade reading level. The mean readability for all entities was 10.4 (tenth grade) with individual mean readability scores ranging from 8 to 13.5.

Conclusion: All shoulder and elbow patient education materials surveyed did not meet the NIH recommend reading level.

Davis, Jessika Marie Pinto (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Dr. Laura Timares
Abstract Approved By Advisor:	Yes
Co-Authors:	Tahseen H Nasti, Yuko Tsuruta
Title:	The Role of Langerhans Cells in UV-induced Inflammation and Immunosuppression

The role of Langerhans cells (LCs) in immunosuppression and tumorigenesis is controversial. To clarify LCs role in regulating UVB suppression and inflammation, we tested skin responses to UVB exposure in transgenic mice that selectively ablate epidermal LCs (LC-KO). After a single UVB dose (180mJ/cm²), we observed that ear swelling responses were significantly increased in LC-KO mice during the first 5 days, compared to WT mice ($400 \pm 75.1 \mu\text{m}$ vs $286.67 \pm 46.4 \mu\text{m}$, Day 5, $p<0.05$). Thereafter there was a significant decrease in inflammatory responses in LC-KO with a persistent inflammation in WT mice (157.2 ± 104 vs 316.1 ± 69.9 , Day 8, $p<0.05$), indicating LCs can regulate inflammation. By using standard protocols we tested LC's role in UVB-induced antigen-specific suppression and observed that contact hypersensitivity (CHS) responses were reduced by only 12% in LC-KO mice as compared to 65% in WT mice ($p< 0.001$), indicating that LCs are important for mediating hapten-specific UVB immune-suppression. qPCR analysis, 12 hours following UVB irradiation, revealed that anti-inflammatory cytokine IL-10 levels were 3 fold lower in the epidermis and 40 fold lower in the dermis of LC-KO as compared to WT skin, indicating that LCs are the main IL-10 producers following UVB. Phenotypic analysis by flow cytometry of skin draining lymph node cells of these mice indicated 50% fewer CD4+ FoxP3+ regulatory T-cells expressing IL-10 and 2-fold more APCs producing IL-12 were present in LC-KO compared to WT UVB-exposed mice. To determine whether LC-derived IL-10 was critical, we applied UVB suppression protocols to transgenic mice that lack the IL-10 gene in LCs (LC^{IL-10KO}) and to WT (LC^{WT}) mice. CHS responses in UV-treated LC^{IL-10KO} mice were only partially suppressed (33% for LC^{IL-10KO} vs 89% for LC^{WT}). Our studies support an important role for LCs in generating UVB-induced immune suppression, which depends, in part, on LC-derived IL-10.

DelaRosa, Hillary Jean (MS4)

Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Nabiha Yusuf

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Toll-Like Receptor-4 deficiency enhances repair of ultraviolet radiation induced cutaneous DNA damage by nucleotide excision repair mechanism

UVB induced DNA damage is not only of importance in UVB induced immune suppression in but also plays a critical role in development of skin cancer. The purpose of this study was to determine whether repair of UVB-induced DNA repair responses is regulated by Toll-like receptor-4 (TLR4). TLR4 gene knockout ($TLR4^{-/-}$) and TLR4 competent ($TLR4^{+/+}$) mice were subjected to a local UVB induced DNA damage regimen consisting of 90 mJ/cm^2 UVB radiation. $TLR4^{+/+}$ mice exhibited significant DNA damage in the form of CPD, whereas $TLR4^{-/-}$ mice developed significantly fewer CPD in their skin and bone marrow dendritic cells (BMDC). The expression of DNA repair gene *XPA* (Xeroderma pigmentosum complementation group A) was significantly less in skin and BMDC from $TLR4^{+/+}$ mice than $TLR4^{-/-}$ mice after UVB exposure. When cytokine levels were compared in these two strains after UVB exposure, BMDC from UV-irradiated $TLR4^{-/-}$ mice produced significantly more IL-12 and IL-23 cytokines ($p<0.05$) than BMDC from $TLR4^{+/+}$ mice. Addition of anti-IL-12 and anti-IL-23 antibodies to BMDC from $TLR4^{-/-}$ mice (prior to UVB exposure) inhibited the repair of CPD. This was followed by a concomitant decrease in *XPA* expression. Furthermore, addition of a TLR4 agonist to $TLR4^{+/+}$ BMDC cultures caused decrease in *XPA* expression and inhibited the repair of CPD. Thus, strategies to inhibit TLR4 may allow us to develop immunopreventive and immunotherapeutic approaches for management of UVB induced cutaneous DNA damage and skin cancer.

Dennis, Evida Adiko (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	William Britt
Abstract Approved By Advisor:	Yes
Co-Authors:	Marie Seleme
Title:	The Impact of MCK-2 Mutation on Monocyte Recruitment and Viral Infiltration to the CNS in Murine Cytomegalovirus Congenital Infection

Cytomegalovirus (CMV) is the most common cause of human congenital infection, and is often correlated with abnormal central nervous system (CNS) development and permanent deficits. It is thought that exaggerated host inflammation may be responsible for CNS damage in the developing brain; however, the mechanisms of disease associated with congenital CMV infection have not been definitively defined. We investigated the ability of a murine cytomegalovirus (MCMV) mutant strain lacking a secreted, pro-inflammatory chemokine-like-protein (MCK-2) to facilitate viral entry and inflammatory cell recruitment into the brain. MCK-2 has been previously shown to increase recruitment of leukocytes to some peripheral infection sites and to facilitate viral dissemination. We hypothesize that lack of MCK-2 will attenuate viral infiltration and inflammation in the developing brain. To characterize the role of MCK-2 in MCMV congenital CNS infection, we used a MCK-2 mutant strain and Wild-Type (WT) viral strain in a neonatal mouse model in which newborn mice are peripherally infected with MCMV, and develop pathogenic CNS sequela. We measured MCK-2 and WT viral titers in blood, liver, and brains of infected animals. We characterized mononuclear cell populations expressing pan-leukocyte marker CD45, myeloid markers CD11b and Gr1, differential expression of the monocyte marker Ly6C, and CCR2 – an inflammatory cell receptor that directs recruitment into inflamed tissues by binding to its ligand CCL2 –, in the brains, blood, livers, and spleens of infected animals. Results show that MCK-2 mutation impairs viral infiltration into the blood and brain, plays a role in the activation of CD11b⁺CD45^{low} quiescent microglia populations, impairs recruitment of CD11b⁺CD45^{high}, Ly6C^{high}/Gr1^{inter}, and CCR2⁺ inflammatory monocytes into the brain, and impairs recruitment of CC45⁺/CD11b⁺/CCR2⁺ inflammatory monocytes into the spleen and liver. We conclude that MCK-2 plays an important role in viral entry and inflammatory cell recruitment/ activation in the developing brain during congenital MCMV infection.

DiToro, Daniel Francis (MSTP)**Project Length:** Intermediate**Prior Research Experience:** Yes**Source of Funding:** NIH Medical Scientist Training Program**Faculty Advisor:** Casey Weaver**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** Insulin-like Growth Factors In Th17-mediated Autoimmunity

We have discovered a lineage-specific role for Insulin-like growth factors (Igfs), also known as Somatomedins A and C, in CD4 T cell differentiation and function. Specifically, we have found that Igfs promote differentiation of Th17 cells while repressing differentiation of Treg cells. In contrast to other CD4 T cell lineages (eg, Th1 and Th2), we have found that Th17 and Treg cells express both the signaling receptor, Igf1R, and the cytokine binding protein, Igfbp4, at significantly higher levels than naïve CD4 T cells. Through binding of Igf1R, Igfs induce activation of the PI3k/Akt/mTOR signaling pathway, promoting Th17 differentiation while simultaneously restraining Treg cell differentiation. Thus, Igfs substantially alter the Treg–Th17 developmental balance in favor of pro-inflammatory Th17 responses. Moreover, Igfs alter the development of Th17 cells to promote a more ‘pathogenic’ Th17 phenotype characterized by expression of increased pro-inflammatory genes, while suppressing expression of anti-inflammatory genes, including the *Il10* gene.

In our studies, deletion of Igf1R on CD4 T cells markedly enhanced Treg differentiation and prevented the up-regulation of pathogenic markers in response to Igfs both *in-vitro* and *in-vivo*. Furthermore, mice lacking Igf1R on CD4 T cells were resistant to experimental autoimmune encephalomyelitis (EAE; a model for multiple sclerosis), demonstrating reduced weight loss, reduced peak clinical scores, earlier and more rapid remission, and lower final clinical scores.

Our findings suggest novel targets for modulating the Treg–Th17 balance as a means to intervene in a number of immune-mediated diseases driven by dysregulated Th17 cell responses. In view of the ability of insulin-like growth factors to drive a pathogenic, pro-inflammatory Th17 response at the expense of a suppressive, anti-inflammatory Treg response, disruption of the Igf/Igf1R/PI3k/Akt/mTOR pathway in CD4 T cells may offer a novel means to ameliorate Th17-mediated diseases.

Dobbin, Zachary Christopher (MSTP)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Dr. Charles Landen
Abstract Approved By Advisor:	Yes
Co-Authors:	Ashwini K. Katre, Monjri M. Shah, Britt K. Erickson, Huaping Chen, Ronald D. Alvarez, Michael M. Conner, Dongquan Chen, and Charles N. Landen
Title:	An Ovarian Patient-DerivedXenograft Model to Identify the Chemoresistant Population

Introduction: A cornerstone of preclinical ovarian cancer research over the last 30 years has been the use of cell lines both *in vitro* and *in vivo*. This resource has underperformed in its ability to identify effective novel therapeutics and evaluate the heterogeneity of an ovarian neoplasm. Developing a patient-derived xenograft (PDX) allows for a comprehensive study of the heterogeneous tumor and potentially identification of cellular populations responsible for chemoresistance. We have developed an ovarian PDX model to demonstrate many important similarities and differences between these and primary patient tumors, and explore its utility in personalizing therapy with PARP inhibitors.

Methods: Tumors removed from patient's surgery were implanted into SCID mice. Tumors were analyzed for heterogeneity in the tumor initiating cell (TIC) populations, stromal content, and proliferation. PDX response to chemotherapy was compared to the patient's response. PDX lines were characterized for defects in homologous recombination (HR) repair, correlating HR status with response to PARP inhibition.

Results: PDX tumors maintain patient's histology, but the stromal component is replaced by murine cells. The xenografts retain primary tumor heterogeneity, at least in expression of TICs. Treatment with chemotherapy significantly increases TIC populations, suggesting a role in chemotherapy resistance. The treated PDX tumors decrease in proliferation, indicating dormancy is induced. PDX tumors correlate to the patient's clinical response. PDX tumors from patients with a partial response respond more slowly than those from patients achieving a complete response (Δ in tumor volume -5.11% vs -63.73%, $p=0.029$). Finally, patient tumors predicted to respond to PARP inhibition show regression of tumor or stable disease with single-agent PARP inhibitor.

Conclusions: The ovarian-PDX model recapitulates patient heterogeneity and mirrors response to chemotherapy. This model may prove superior in predicting response to therapy in patients, and allows a better model to study tumor biology that is impacted by tumor heterogeneity.

Dorn, David Paul, Jr. (MS3)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Derek DuBay

Co-Authors:

Rojymon Jacob, MD; Kimberly Keene, MD; Falynn Turley, MS; David Redden, PhD; Mary Kate Bryant, BS; Laura Dover, BS; Jared White, MD; Stephen Gray, MSPH, MD; Devin Eckhoff, MD; Derek DuBay, MD

Title:

Adjuvant Stereotactic Body Radiation Following Chemoembolization Improves Survival in Patients with non-Resection Hepatocellular Carcinoma over 3 centimeters

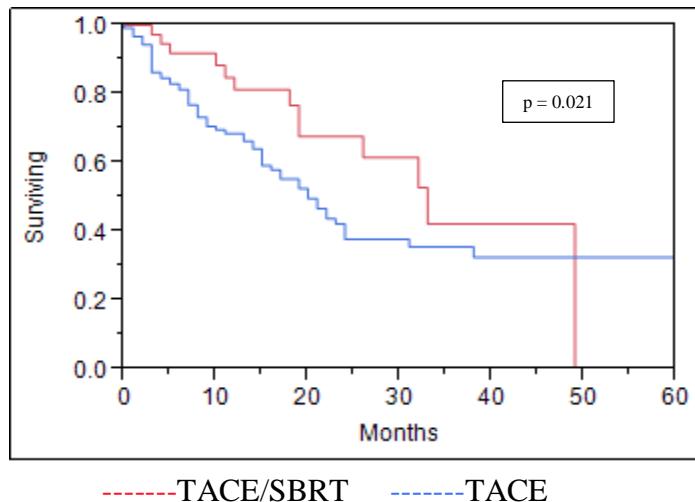
Background: The optimal locoregional treatment for non-resectable hepatocellular carcinoma (HCC) >3cm is unclear. Chemoembolization (TACE) is the most common initial intervention performed, but rarely completely eradicates the HCC. The purpose of this study is to measure survival in patients treated with adjuvant stereotactic body radiation (SBRT) following TACE.

Methods: Patients with HCC >3cm treated with TACE alone (n=124) were compared with those treated with TACE/SBRT (n=37). Standard survival analysis was performed.

Results: There were no significant differences between the 2 groups with regard to age, gender, race, or liver disease etiology. The MELD scores were not different between groups (TACE: 11.2 ± 4.2 vs. TACE/SBRT: 10.2 ± 3.6 , p=0.21) nor were measures of sarcopenia (TACE: 10.6 ± 3.4 vs. TACE/SBRT: 11.2 ± 3.8 , p=0.25). The mean number of tumors (TACE: 2.1 ± 1.6 vs. TACE/SBRT: 1.8 ± 1.1 , p=0.57), largest tumor size (TACE: $5.8\text{cm} \pm 3.0$ vs. TACE/SBRT: $6.1\text{cm} \pm 2.4$, p=0.09), and total tumor diameter (TACE: $7.7\text{cm} \pm 4.9$ vs. TACE/SBRT: 7.8 ± 3.3 , p=0.21) were not significantly different between groups.

Overall survival was significantly increased in the TACE/SBRT group compared to the TACE only group (33 vs. 20 months, p=0.02, Figure). There was no significant survival advantage to TACE/SBRT in unifocal HCC (49 vs. 31 months; HR 1.46; 95% CI 0.65-3.91, p=0.2) whereas a significant survival advantage was observed in patients with multifocal HCC (26 vs. 15 months; HR 2.52; 95% CI 1.16-6.31, p=0.02).

Conclusions: Adjuvant SBRT following TACE improves survival in patients with HCC greater than 3cm.



Doughton, John Michael (MS4)

Project Length:	Long
Prior Research Experience:	No
Source of Funding:	Other
Faculty Advisor:	Dr. Nancy Tofil
Abstract Approved By Advisor:	Yes
Co-Authors:	Marjorie Lee White, Dawn Taylor Peterson, Amber Youngblood, Lynn Zinkan
Title:	The Impact of ACGME 2011 Resident Work Hour Rules

Background/Objective: On July 1, 2011, the new resident work hour restrictions from the Accreditation Council for Graduate Medical Education (ACGME), aimed at improving patient safety and reducing fatigue-related errors, took effect. These restrictions were instituted at the recommendation of a 16-member ACGME Task Force. Work hours were reduced, with first year residents no longer allowed to work more than 16 hours in a row. Many specialties had to adjust work schedules and adopt a series of day and night shifts as opposed to the traditional call every 3 to 4 nights. As a result, residents in their second year began to work extended shifts for the first time. It is unclear how these shifts affect resident level of alertness. Using the Psychomotor Vigilance Test (PVT) a validated alertness tool, we planned to investigate differences in post-call alertness in our healthcare workers who had experienced the new hour restrictions in their intern year versus those who had not. Our hypothesis was that those residents without previous call hour restrictions would not have adapted strategies, such as effective napping, to help them better maintain alertness throughout their call shift and thus would be less vigilant post-call.

Setting and Participants: A total of 46 UAB pediatric residents participated in the study. The participants were in their 2nd year of residency (PGY2) and on their PICU rotation at the time of PVT completion. The study included both residents who were interns prior to the 2011 ACGME hour restrictions, labeled "Intern Call Group," and residents who were interns after the restrictions were in place, labeled "Intern No Call Group." One Emergency Medicine resident also participated. PVT testing took place in the Children's of Alabama Pediatric Simulation Center.

Description / Methods: Participating in the research study was voluntary. Participation consisted of completing a demographic form and a three-minute alertness test designed to measure changes in psychomotor speed, lapses in attention, and impulsivity induced by fatigue. The demographic form asked residents to quantify recent overnight calls, post-call months, hours in a row of call, and napping hours. A laptop was used to administer the PVT. The participant would click a box on the screen to begin the test and would then click each time they saw a flash or box appear on the screen. Response times to valid clicks, response times of false start clicks, and start and stop times of each test were automatically recorded on a data sheet in the PVT software. All residents took the PVT after completion of a 30-hour call shift in the PICU during their PGY2 year, with the exception of one PGY3 PICU resident and one Emergency Medicine resident. PVT testing of these different groups spanned 2 years. Reaction times from the Intern Call Group were compared to those from the Intern No Call Group. PVT data was analyzed by T-test using SPSS Statistics.

Evaluation / Results: Forty-six residents participated in this study. Residents in the Intern Call Group had an average PVT reaction time of 300.3 ± 81.3 ms. Residents in the Intern No Call Group had an average PVT reaction time of 297.6 ± 21.9 ms ($p=0.871$). The Intern Call Group did have an average age of 30 years, as compared to an average of 28.3 years for the Intern No Call Group. There was no statistically significant difference in the amount of napping time between the two groups.

Discussion/Reflection: Contrary to our hypothesis, there was no significant difference noted in average PVT reaction time between the two groups. Interestingly, the Intern No Call Group actually proved to have a slightly better reaction time. Other factors outside of previous call experience, such as age, could affect reaction time. It is important to note that there was no baseline PVT reaction time with which we could compare the post-call test. The possibility still exists that while the Intern No Call Group had a faster baseline reaction time, their

reaction time was more affected than the Intern Call Group after the 30-hour call. Further testing is necessary and beneficial to evaluate the effect of reduced intern year call.

Dowla, Shima Afroze (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Diabetes Research and Training Center Fellowship
Faculty Advisor:	Monika Safford
Abstract Approved By Advisor:	Yes
Co-Authors:	Monika Safford
Title:	Primary Care Provider, Peer Advisor, and Patient Reported Barriers to Improvement of Cardiovascular Health for Individuals Living in the Alabama Black Belt

Despite advances in prevention, management, and treatment, cardiovascular disease (CVD) remains the leading cause of death in the United States, with Alabama among the states having the most alarming statistics. To help combat this disease, the American Heart Association created several recommendations for cardiovascular health improvement, known as “Life’s Simple 7”, involving keeping blood pressure, cholesterol, blood sugar, and weight in normal ranges, as well as lifestyle modifications including eating a healthy diet, exercising and not smoking. People who reside in Alabama’s rural Black Belt region are especially prone to poor health outcomes, including poor measures on Life’s Simple 7. Our semi-qualitative research studied the barriers to achieving Life’s Simple 7 in the Alabama Black Belt from the perspective of 3 stakeholder groups (primary care providers, peer advisors, and patients) using the nominal group technique (NGT). The NGT is a form of information gathering used for focused problem identification, in which a facilitator solicits ideas from participants that are later added to and ranked. Results portrayed a high degree of agreement between nominal groups of each stakeholder. Peer advisors focused on barriers that they could specifically help patients with, whereas patients tended to focus on their own personal barriers. Physicians portrayed a more holistic understanding of barriers, citing both structural and personal barriers, but tended to rate all important barriers as being difficult to overcome, potentially suggesting burn-out and a degree of hopelessness in improving cardiovascular health in their patients. In contrast, the much lower scores, reflecting their perspective that barriers can be more easily overcome, in the peer advisor and patient groups suggest their receptiveness to overcoming barriers. Engaging stakeholders to provide perceptions prior to intervention development revealed important information that will be integrated into an intervention in the targeted communities intended to improve Life’s Simple 7.

Dussaq, Alex Maurice (MSTP)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Jonas Almeida
Abstract Approved By Advisor:	Yes
Co-Authors:	Joshua Anderson, Christopher Willey
Title:	KAOS - An RDF Data Model for Kinomic Peptide Arrays.

Motivation: A number of fast profiling methods have emerged in the functional proteomic domain as counterparts to the more widely available genomic approaches for profiling cancer cell signaling. The attraction of these new proteomic techniques is, unlike genomic information, the changes frequently correlate directly to phenotypic modifications, and alterations occur at levels that are targetable with therapeutic agents. With the creation of high throughput methods for measuring kinase activity, kinomics is quickly gaining notoriety; additionally several unique features including the ability to measure kinase activity enzymatically, and directly measure drug mediated activity against kinase activity directly make kinomics an object of particular validity in the subtyping of tumors and potential to directly guide therapeutic decision making. As with other molecular profiling techniques, the development of quantitative methods and software applications to properly analyze these data requires the formal identification of a data model for describing and processing Kinomics results.

Results: The recent emergence of Web 3.0 technologies based on the Semantic Web Resource Description Framework (RDF) enables formal data modeling with further reaching integrative abilities. Accordingly, KAOS was formalized using RDF Schema. The KAOS schema provides a framework for description and processing of kinomic peptide array data. The modularity of RDF was found to be instrumental in developing a software applications that use social computing infrastructure, such as Google's Fusion Tables, as the data management backend. These ideas were validated by developing a data management and processing application entirely contained, and delivered, within the social framework of web computing. These results raise entirely novel possibilities for the BigData future of acquisition, management and analysis of biomolecular profiles in Systems Biomedicine.

Availability and implementation: Computational tools used to create this document are available at <http://adussaq.github.com/KinomicsQC> with source code available at <https://github.com/adussaq/kinomicDataQC>.

Ehlinger, Megan Colleen (MS3)

Project Length:	Long
Prior Research Experience:	No
Source of Funding:	Other
Faculty Advisor:	Nathaniel Robin

Abstract Approved By Advisor: Yes

Co-Authors: Nathaniel Robin

Title: Survey of Heart Rhythm Specialists and Cardiologists' Hopes to Gain New Information on Genetic Services Offered to Long QT Syndrome Patients

Long QT syndrome (LQTS) is an inherited cardiac channelopathy that predisposes individuals to syncope, seizures, torsades de pointes, and sudden cardiac death. This condition may be treated either medically or with an implanted cardioverter-defibrillator, but diagnosis is essential for proper management¹. There are over six loci currently identified with mutations leading to LQTS, and there is evidence that there is a strong correlation between genotype and phenotype². Although genetic testing has been available for years, its cost-effectiveness among different populations, including definitive and inconclusive index cases and potentially affected family members, has been debated and genetic testing is not routinely performed in clinical settings¹. Although gene specific stratification of LQTS has been shown to be of use in clinical management of LQTS², guidelines for testing individuals have not been established and little is known about the genetic services currently offered by heart rhythm specialists treating LQTS patients. The goal of this study was to learn more about genetic services offered to definitive and inconclusive LQTS patients and potentially affected family members, which we achieved by distributing a survey among cardiologists and electrophysiologists in southeastern United States with 29 responses. The responses revealed that the 58% of respondents had limited to no training in genetics. Results also revealed that there are many different approaches to using genetic testing for both LQTS patients and their family members, and that the largest perceived barrier to genetic testing is the cost of the test. Utilizing these results can help standardize the use of genetic testing for LQTS in the future.

References:

- 1 Phillips KA, Ackerman MJ, Sakowski J, Berul CI. Cost-effectiveness analysis of genetic testing for familial long QT syndrome in symptomatic index cases. *Heart Rhythm*. 2005;2(12):1294-300.
- 2 Priori SG, Napolitano C, Vicentini A. Inherited arrhythmia syndromes: applying the molecular biology and genetic to the clinical management. *J Interv Card Electrophysiol*. 2003;9(2):93-101.

¹ Phillips KA, Ackerman MJ, Sakowski J, Berul CI. Cost-effectiveness analysis of genetic testing for familial long QT syndrome in symptomatic index cases. *Heart Rhythm*. 2005;2(12):1294-300.

² Priori SG, Napolitano C, Vicentini A. Inherited arrhythmia syndromes: applying the molecular biology and genetic to the clinical management. *J Interv Card Electrophysiol*. 2003;9(2):93-101.

Ehtsham, Maryam (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Harald Sontheimer
Abstract Approved By Advisor:	Yes
Co-Authors:	Avinash Honasoge
Title:	Role of Calcium as a Regulator of Glioma Pathophysiology

Gliomas are highly malignant primary brain tumors that are difficult to treat, resulting in poor patient prognosis. Diffuse invasion through surrounding brain tissue and rapid proliferation contribute to their striking malignancy. Glioma invasiveness is facilitated by Ca^{2+} influx, activating Ca-activated channels and leading to volume condensation (Cuddapah 2011), thus allowing glioma cells to navigate through tight brain space. These prior studies were conducted using endogenous ligands with potentially Ca^{2+} -independent effects. To test a more specific role for Ca^{2+} , we first inserted plasmids containing MrgA1 and gCAMP3 receptors into D54 human glioma cells. MrgA1 is only activated by an exogenous ligand, RF amide neuropeptide (FMRF), through a G_q -coupled pathway – this selectively results in Ca^{2+} release from internal stores; its plasmid also contained a TdTomato vector that fluoresces red. gCAMP3 is a Ca^{2+} sensor that is tied to green fluorescent protein (GFP) and thus fluoresces green. Together, we could theoretically cause Ca^{2+} release in these glioma cells and detect that release without needing to load a Ca^{2+} indicator dye. Detection was done on a cultured monolayer of glioma cells using a spinning disk confocal microscope. We first tested different concentrations of FMRF ligand and found fluorescent spikes (F/F_0) ratios ranging from 1.06-1.9 above baseline at 15 nM, 150 nM and 1.5 μM FMRF concentrations. These spikes could be repeated in narrow time frames upon repeated application of the ligand. We then tested the role of Ca^{2+} in glioma cell physiology, including migration (via transwell filters) and proliferation (via Coulter Counter) and found that high concentrations of FMRF (and subsequently large Ca^{2+} spikes) might actually inhibit both migration and proliferation, suggesting that there is an optimal Ca^{2+} concentration and exceeding this maximum might arrest the glioma cells.

Ejem, Stacy Ifeoma (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Kathy Harrington
Abstract Approved By Advisor:	Yes
Co-Authors:	Oluwasubomi Akindoju, Kathy Harrington, William C Bailey
Title:	Smoking Cessation in Hospitalized Patients

Smoking is the leading cause of preventable morbidity and mortality: it claims about half a million lives a year. It is also the number one preventable risk factor for coronary artery disease. In patient hospitalizations create a teachable moment for smokers, as they provide a smoke-free environment for patients. Smoking-related illnesses and hospitalizations can potentially increase smokers' motivation to quit. The Joint Commission on the Accreditation of Healthcare Organizations requires that every hospitalized patient who smokes be offered some smoking cessation counseling, pharmacotherapy, and post-hospitalization follow-up. The purpose of this study is to determine the attitudes, perceptions, and smoking habits of patients at UAB hospital. Patients whose smoking status was identified upon admission were approached by Lung Health Center staff and given a very brief smoking cessation intervention. Interested and eligible patients were enrolled in the study. Our data shows that patients are highly motivated to quit. There needs to be an institutionalized smoking cessation services to help patients succeed.

Ellenburg, James Luke (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Colin Martin
Abstract Approved By Advisor:	Yes
Co-Authors:	Scott Tanner, Dava Sue Cleveland, and Colin Martin
Title:	The Role of AhR Signaling in the Pathogenesis of Necrotizing Enterocolitis

Introduction: Necrotizing enterocolitis (NEC) is a leading cause of neonatal intestinal morbidity and mortality. Recently, the aryl hydrocarbon receptor (AhR) has been implicated for its role in attenuating T cell mediated immune responses and intestinal inflammation in an adult colitis model. However, the role of AhR activation in the setting of the neonate's immature mucosal immune system is unknown. We hypothesize that activation of AhR in the setting of an immature mucosal immune system is one mechanism of intestinal injury in premature infants.

Methods: To correlate the level of activation and location of AhR, and its downstream effector, CYP1A1, with the clinical severity of NEC, immunohistochemistry (IHC) and fluorescent microscopy were used on tissue sections taken from perforated and intact segments of small bowel of babies with NEC. Each tissue sample underwent a blinded analysis and scoring to quantify the intensity of AhR and CYP1A1 staining and the percentage of villus involvement. Clinical data on these patients was also gathered to compare the clinical severity of NEC to the IHC staining scores. The student's t- test was used to determine significance.

Results: The average CYP1A1 staining score was significantly lower in perforated segments than in intact bowel segments. Villus staining in the perforated segments was less uniform, with lower percentages of villus involvement than the intact segments. CYP1A1 staining was low in the crypts compared to the villi in all IHC samples.

Conclusion: AhR signaling may play a role in human NEC pathogenesis. Future studies will compare staining in non-NEC human controls and animal NEC models. The knowledge gained from this project will aid in clarifying a novel mechanism of AhR activity and the clinical manifestations of NEC.

Eustace, Nicholas James (MSTP)

Project Length:	Short
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Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Ardie Steyn
Abstract Approved By Advisor:	Yes
Co-Authors:	Nicholas Eustace, Jennifer Rowland, John Adamson, Bridgett Cummings, Deepak Almeida, Adrie JC Steyn
Title:	Ergothioneine levels in <i>Mycobacteria tuberculosis</i> infected lung tissue

Background: Ergothioneine (ET) is a unique antioxidant produced by a small number of fungi and bacteria such as *Mycobacteria tuberculosis*, that humans actively absorb from their diet using the organic cation transporter novel type 1(OCTN1). ET's purpose in humans is not well understood; however, it has been shown to be concentrated in organs and tissue experiencing oxidative stress. ET possesses properties of a redox buffer, copper chelating agent, moderator of intracellular signaling – DNA, RNA and protein synthesis, and more recently has been shown to inhibit TNF- α induced NF- κ B activation and IL-8 release in lung epithelial cells. These characteristics made understanding ET's potential role in *Mtb* infection of specific interest.

Hypothesis: Ergothioneine levels are elevated in *Mtb*-infected lung

Methods: Balb/C mice were independently infected with *Mtb* for three days (acute model) or four weeks (chronic model) before drug treatment with isoniazid (INH) or rifampicin (RIF) for four weeks. The mice were sacrificed, their lungs harvested and then homogenized in a BSL3 lab using both mechanical and enzymatic means. The lung lysate was processed to determine the ET concentration using multiple-reaction monitoring mass spectrometry (LC-MRM) as well as cultured for CFU data.

Results: Our data shows that ET concentrations increase with *Mtb* organ burden and this change correlate with the drug treated mice in both the acute and chronic models

Conclusions: *Mtb* infection changes ET levels in the surrounding lung rapidly and suggests a new potential role for ET in the pathogenicity of *Mtb*.

Evans, John Macarthur (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Jean-Francois Pittet
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Sarah Christiaans and Dr. Jean-Francois Pittet
Title:	Pseudomonas Aeruginosa Pneumonia in the ICU: Outcomes in ExoY+ Strains and Elevated Risk of Development in TBICU

Pseudomonas aeruginosa is a gram negative bacterium that frequently causes pneumonia in ventilated intensive care unit (ICU) patients. *P. aeruginosa* can possess up to at least four exoenzymes that are injected into host cells. ExoY has been shown to contribute to pulmonary edema but it is not known what its importance is in the overall severity of *P. aeruginosa* infection.

We hypothesize that the presence of ExoY in cultures grown from respiratory tract of patients who developed pneumonia while in the ICU will be associated with poorer outcomes.

Patients who develop pneumonia in a UAB Hospital ICU and test positive for *P. aeruginosa* are enrolled in the study. Patients are prospectively observed and clinical data is recorded. In addition, the cultures are sent to a laboratory for exoenzyme genotyping.

Currently, clinical data has been collected on 44 patients and the first 24 cultures have been genotyped. Of those, 22 of the 24 genotyped cultures were positive for ExoY. In summary, 2.61% of all Trauma Burn ICU patients (>21) have been enrolled in the study since data collection began and this rate is significantly larger than the rate from any other ICU.

There are too few patients enrolled to draw any conclusions on the role of ExoY in the severity of infection. However, preliminary data suggests a significantly higher incidence of *P. aeruginosa* pneumonia in the TBICU vs. any other ICU unit. A chi-square test for independence shows that which ICU a patient is admitted to is likely related to their risk of developing *P. aeruginosa* pneumonia. This is a significant but not surprising finding given that there is a known association between trauma / burn patients and *P. aeruginosa* pneumonia.

Farmer, Zachary Luke (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	
Faculty Advisor:	Dr. Cynthia J. Brown
Abstract Approved By Advisor:	Yes
Co-Authors:	Farmer ZL, Brown CJ, Ritchie CP
Title:	Beyond pain: A Description of Symptom Burden among Hospitalized Older Adults

BACKGROUND Research on patient reported symptoms historically has not accounted for chronic disease. While studies have evaluated symptoms in community dwelling adults, little is known about symptoms experienced during hospitalization.

OBJECTIVE To explore symptoms experienced and their bothersomeness among a population of hospitalized older adults.

DESIGN, SETTING, AND PARTICIPANTS 100 patients who were ≥ 65 years of age, newly admitted to the medical ward of the Birmingham VAMC, with a Mini Cognitive Assessment Score and Confusion Assessment Method score = 0, and able to walk in the 2 weeks prior to admission were enrolled. After informed consent, patients were randomly assigned to either a walking program (WP) or usual care (UC) group. All patients were asked daily to report the presence and bothersomeness of fourteen symptoms using the Condensed Memorial Symptom Assessment Scale (CMSAS). Four weeks after hospital discharge, CMSAS was reassessed via telephone. Chart review was used to determine comorbidities.

RESULTS The walking intervention had no significant impact on frequency or bothersomeness of symptoms. On hospital day 2, the most common symptoms were dry mouth (84.9%), pain (60.5%), lack of energy (59.3%), drowsiness (59.3%), and shortness of breath (53.5%). The bothersomeness of symptoms provided slightly different results with more patients being bothered by lack of energy than by pain (44.6% versus 41.3%, respectively). Hospitalization led to decline in patients' sleep hygiene and ability to concentrate, as these became increasingly bothersome by day 5. Patients with multimorbidity were most likely to have bothersome symptoms. The five most common chronic illnesses reported were diabetes (53.3%), CHF (34.8%), COPD (32.6%), CKD (31.5%), and history of CVA/TIA (22.8%).

CONCLUSION Symptoms experienced in the hospital are dynamic and evolving. As the number of patients with multimorbidity grows, researchers and clinicians must collaborate in establishing symptom specific palliation models that transcend single disease, guideline-based care.

Fawal, Marc Joseph (MS2)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)

Faculty Advisor: Dr. Reed Estes

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Evaluating Risk Factor for Overuse Injuries in Baseball Athletes: A Prospective Study of UAB Baseball Team

The young athlete has an immature skeleton with open growth plates and weaker bones, making them prone to failure with excessive stress leading to more frequent fractures and cartilage injuries. The majority of these injuries heal without sequelae if they are properly identified and managed early. The goal of this research project is to identify individuals and risk factors for overuse injuries. It is hypothesized that physical characteristics pertaining to range of motion and duration, intensity and frequency of activity contribute to the risk of overuse injuries. In preseason, the players will undergo physical evaluations that will monitor the ROM of the hip, knee, shoulder and elbow joints as well as isokinetic testing of these joints. In addition, athletes will complete questionnaires evaluating their previous and preexisting injury history as well as the time spent in strength training and practice. As the season progresses, players will be monitored as injuries occur. Continuous strain on the growing body creates opportunities for injuries to develop, but a better understanding of the risk factors of overuse will allow for stronger preventive measures to be put in place. The goal would be to modify training factors (ie, duration, intensity, and frequency of sports participation) and to correct improper biomechanics (alignment, laxity, inflexibility, and muscle imbalance) as part of the management plan.

Figge, David Anthony (MSTP)**Project Length:** Short**Prior Research Experience:** Yes**Source of Funding:** NIH Medical Scientist Training Program**Faculty Advisor:** David Sweatt**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** Epigenetic Regulation of the Insulin-Like Growth Factor System in Memory Consolidation

Memory loss is a common symptom of normal aging as well as many neurological diseases. Thus, to more fully be able to treat and improve these patient's lives, understanding the basic mechanisms of memory function are pivotal to providing future treatments. Consolidation processes following learning help to stabilize and control the strength of memory retention. Recent work has shown that expression of insulin-like growth factor 2 (IGF2) is induced in the dorsal hippocampus during the consolidation and extinction of contextual fear memories in rodents. This induction is regulated by the transcription factor CCAAT enhancer binding protein β (C/EBP β), and is required for long-term memory formation. Furthermore, recombinant IGF2 has been shown to be able to enhance these memory processes and induce multiple cellular correlates of neural plastic change. Epigenetic alterations, including DNA methylation, are known to be of pivotal importance in long term cellular memory, and have been shown to be specifically involved in the development of neuroplasticity and long term memory formation. IGF2, as a classically imprinted gene, is known to undergo significant epigenetic regulation throughout the body and specifically within the central nervous system. Thus, we sought to determine whether IGF2 and other members of the IGF system underwent dynamic epigenetic alterations during memory consolidation that are essential to memory formation. To address this hypothesis, Sprague-dawley rats were trained in contextual fear conditioning and 24 hours later dorsal hippocampi were collected to investigate the epigenetic status of IGF2. Additionally, in vitro models with specific inhibitors of epigenetic enzymes were used to determine neuronal specific regulation of IGF2. Alterations in epigenetic regulation were assessed using a combination of methylated DNA immunoprecipitation, western blot, and QPCR. Our preliminary results indicate that IGF2 is dynamically regulated by epigenetic processes and the IGF system may provide important contributions to memory consolidation.

Foppe, Sara Elizabeth (MS4)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	John Woods, MD
Co-Authors:	John Woods, M.D., Julie Covarrubias, EdD, MEd, David Ellington, M.D., Robert Holley, M.D., Holly Richter, M.D., Robert Varner, M.D.
Title:	Development of an Anatomically Realistic, Low-Cost Transvaginal Hysterectomy Surgical Model for Obstetrics and Gynecology Resident Training

Background: According to the American Council of Graduate Medical Education (ACGME) published statistics, the number of transvaginal hysterectomy (TVH) procedures performed in residency training has declined by 38% between 2006 and 2012, with only 50% of graduating residents completing an average of eighteen TVH procedures. This decrease has been primarily attributed to the adoption of alternative procedures/approaches. In patients with benign disease, TVH, when applicable, is preferred over laparoscopic and abdominal approaches due to better outcomes, fewer complications and lower cost (ACOG Committee Opinion #444, Nov 2009). Of concern is that only 28% of graduating residents report preparedness to perform TVH and only 38% of Program Directors report that graduating residents are “completely prepared” to perform the procedure (Burkett et al, 2011). The 2012 Residency Review Committee requirements for OBGYN residency program accreditation include performance of at least 15 transvaginal hysterectomies for graduating residents. We developed a simulated TVH model for use in our formal resident TVH curriculum. Our goal is to provide an anatomically realistic, low-cost TVH surgical model to facilitate training and improve vaginal surgical competency of our OBGYN residents.

Description/Methods: Design includes: a) Re-usable, suspensory plywood box for the uterine model - Total cost - \$30.00, b) Uterine Model – polystyrofoam form with black spandex material covering (including simulated peritoneal reflections), acrylic cord simulating supportive structures (uterosacral, round and infundibulopelvic ligaments) and 0.125 inch fuel line tubing to simulate uterine vasculature - \$7.00, c) Simulated Vaginal Mucosa (8" x 8") (Smooth-On Ecoflex 0030/Ecoflex Gel Silicone – \$6.00. Total cost of a single-use uterine model with vaginal mucosa –\$13.00. Construction time for uterine suspensory box was 1.5 hours, 20 minutes per uterine model and 30 minutes per vaginal mucosa insert.

Discussion: Accrediting organizations continue to require valid and reliable documentation of surgical competency in specific procedures. Along with focused assessment from faculty in the operating room, we anticipate that our simulated TVH model and the other components of our TVH curriculum will prepare our trainees to meet this qualification. The end result will be trained practitioners who are aware and confident of the benefits of transvaginal hysterectomy. Our plans are to integrate this simulated TVH surgical model into a “Comprehensive Transvaginal Hysterectomy Curriculum” for our Obstetrics and Gynecology residents this academic year (2013-2014).

Foster, Robert Campbell (MS3)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Eben Rosenthal
Abstract Approved By Advisor:	Yes
Co-Authors:	Asher M. Krell, Dr. Kurt Zinn,
Title:	Characterizing Fluorescent Imaging Properties of Antibodies Conjugated to IRDye800CW for Use in Cancer Imaging

Introduction: Proteins conjugated to near infrared (NIR) moieties for detection of a variety of disease states are being translated to the clinic. However, little is known about the fluorescent properties of IRDye800CW after conjugation to antibodies. We investigated factors that may alter the real-time observed fluorescence of antibody conjugated dye and the rate of fluorescent signal decay.

Methods: Dye decay was examined using three FDA approved monoclonal antibodies conjugated to IRDye800CW (LI-COR) over a period of 15 days. Temperature effects on fluorescence were examined for conjugated dye in both solution and a mouse tumor model. Samples were cooled to -20°C then warmed to predetermined temperatures up to 60°C with imaging performed using the PEARL Impulse (LI-COR) and LUNA (Novadaq) systems.

Results: Fluorescence was shown to increase linearly with increasing concentration of antibody-conjugated dye ($R^2=0.995$). Short term dye decay (< 1 hour) was linear, while long term decay (15 days) was exponential with significant increases in decay seen with light exposure and increased temperatures. Cooling of tumor tissue at -20°C was shown to significantly increase tumor fluorescence on both imaging modalities when compared to room temperature ($p=0.008$, $p=0.019$). Concurrently the ratio of tumor to background fluorescent signal (TBR) increased with decreasing temperature with statistically significant increases seen at -20°C and 4°C ($p=0.0015$, $p=0.03$). The effects of temperature on tumor fluorescence were shown to be equivalent for each antibody tested.

Conclusions: Decay of fluorescence for antibodies labeled with IRDye800CW occurs rapidly but predictably over time, and is more rapid with elevated temperatures and light exposure. TBR is inversely related to sample temperature, suggesting that the clinical exam of fluorescently labeled tissues may be improved at cooler temperatures. The rate of decay and the change in fluorescence with temperature observed for IRDye800CW are independent of the antibody to which it is conjugated.

Franklin, Danielle Sheree (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Marjorie Lee White, MD

Abstract Approved By Advisor: Yes

Co-Authors: Nancy Tofil, MD; Lynn Zinkan, RN; Amber Youngblood, RN; Dawn Taylor Peterson, PhD

Title: Procedural Skills Training For New Pediatric Interns.

Skills training has traditionally involved the “see one, do one, teach one” model. However, with the increasing focus on patient safety this is no longer acceptable. Simulation is increasingly being utilized in pediatric residency programs as a modality for procedural education. All UAB Pediatric Interns (PGY-1) actively participate in a 2½ hour skills lab training during orientation. This project evaluated the usefulness of this training as perceived by the residents. During the skills lab training, residents were divided among stations in the Pediatric Simulation Center, each with a content expert to teach the skill. Workshops included hands on practice on the following skills: Lumbar Puncture (LP), Intubation, Intraosseous, Nasal Gastric Tube, IV Placement, Arterial Stick, and Umbilical Artery and Vein Catheterization (UAC/UVC). A survey was developed to collect the number of observed and performed procedures by PGY-1 residents in their first month and second year (PGY-2) residents after their first complete year of residency. They also rated each skills lab procedure on its usefulness in preparation for clinical practice and were offered space to give feedback on the skills that were most recalled and skills that they wished they had focused on more. Twenty-Five residents were surveyed, PGY-1 (n=11) and PGY-2 (n=14). All of the PGY-1 residents surveyed rated the training to be helpful for the procedures learned but most helpful for UAC/UVC and LP. Procedures performed most by the PGY-2 residents included: LPs, Intubation and UAC/UVCs. Simulation procedural skills training was seen to be an effective method of teaching pediatric procedures as perceived by the learner. It allows a safe environment to prepare to take on more responsibility with clinical performance. Evaluations show that time and focus can be redirected for PGY-1 residents to focus on the more likely performed skills in order to improve clinical performance and confidence.

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Fryberger, Charles Theodore, III (MS2)

Project Length:	Short
Prior Research Experience:	No
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Brent Ponce
Abstract Approved By Advisor:	Yes
Co-Authors:	Chuck Fryberger, John Killian
Title:	Pilot Study: Virtual Interactive Presence in teaching a Manual Task

A recently developed virtual interactive presence (VIP) technology has the potential to improve educational outcomes of arthroscopic minimally invasive surgical techniques. The VIP system creates an augmented reality for the local user by virtually integrating an instructor's hands, gestures and models into the local video monitor, thus allowing the instructor to virtually interact with elements in the local user's field of view.

Since little research has been done on the efficacy of this novel teaching interface, the aim of this study is to evaluate the effectiveness of the VIP system in teaching a manual task. The manual task is defined as building a Lego™ model in an arthroscopic surgical trainer provided by the UAB surgery department. The surgical trainer blocks direct view of the subject's hands and the Lego™ model, but relays a minimally-invasive surgical perspective to a video monitor. The VIP system was evaluated by comparing teaching effectiveness to Skype™ (an audio-video telecommunication program) based instruction and self-study based learning. Subjects were split into 3 matched-groups based on a pre-test scores evaluating baseline skill in constructing Lego™ models. Each group then underwent a 30-minute instructional session utilizing either the VIP, Skype™, or self-study design protocol. These sessions taught the subject how to build the Lego™ model inside the surgical trainer. Subjects were then timed over multiple attempts to assess speed in building the model.

Initial results were inconclusive due to flaws in the study design. The Lego™ model originally selected proved too difficult for many of the subjects to learn resulting in failed build attempts and a failure to accurately assess building speed. In addition, due to a methodological error, the matching strategy did not produce similarly skilled groups, introducing bias. The study protocol has since been modified to address these flaws and continued research is underway.

Fung, Russell KinShun (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Nabil Elkassabany
Abstract Approved By Advisor:	Yes
Co-Authors:	Siya Bhatt, Jennifer Gaertner, Nabil Elkassabany, M.D
Title:	Predictors of Post-operative Pain After Shoulder Arthroscopy

Background:

Single injection peripheral nerve blocks are instrumental in reducing postoperative pain after shoulder surgeries that can ultimately impact patient satisfaction and their overall quality of recovery (QoR). This study aims to reveal more precise information on the correlation between catastrophizing scores and postoperative rebound pain scores (RPS), exploring both procedure and patient related characteristics as predictors of the severity of post-operative pain after shoulder arthroscopy.

Method:

After patients are consented for enrollment, demographic information are obtained from their records. Before surgery, the patients will complete a 13-Question PCS Survey for initial evaluation. Patients will be given a packet after the surgery containing a 9-Question Quality of Recovery (QoR-9) Surveys to be filled out at 24 Hours, 48 Hours and 1 weeks' time after surgery, an American Pain Society Patient Outcome Questionnaire (APS-POQ) Survey filled out at 24 hours after surgery and a pain diary. Variables from the intraoperative course will also be measured.

Results:

Preliminary data is presented for the first 4 patients enrolled in the study with completed survey packets returned. In the first 24 hours after surgery, patients with High-PCS scores, scored lower on the QoR-9 survey when compared to that of patients with Low-PCS scores. The results from APQ-QOR-R reinforces this trend as patients have shown to experience higher pain scores, pain duration, and lower percentage of relief.

Conclusion:

As we continue to enroll more patients in our study, we will be able to explore any correlation between patients' PCS score and the severity of postoperative pain. We will be able to predict if patient or procedure related characteristics have any negative impact on the patient quality of recovery. Prediction of the development of rebound pain after the nerve block recedes may help design a more aggressive pain management regimen targeting this specific patient group.

Gautney, Joshua Thomas (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. J. Edwin Blalock
Abstract Approved By Advisor:	Yes
Co-Authors:	Joshua Gautney, Mike Wells, Patricia Jackson, J. Edwin Blalock
Title:	“PGP Mediated Pulmonary Vascular Remodeling via Rho-kinase Activation”

Objectives:

Chronic airway exposure to Proline-Glycine-Proline (PGP), a collagen breakdown product and potent neutrophilic chemoattractant, results in findings consistent with development of emphysema and resultant cor pulmonale. Additionally, RhoA/Rho kinase mediated regulation of intracellular Ca^{2+} has been recently identified as a potential mechanism for hypoxic pulmonary vasoconstriction mediated development of pulmonary hypertension. Our objectives are to first, determine if chronic systemic PGP administration results in development of pulmonary hypertension, second, to ascertain the effect of PGP on the G-protein Rho kinase, and third, to evaluate the role of Rho kinase inhibitors on ameliorating the effects of chronic PGP induced pulmonary hypertension.

Methods:

This was accomplished by administration of AcPGP or a control with or without a Rho kinase inhibitor via intraperitoneal (IP) injection, with subsequent bronchoalveolar lavage (BAL) analysis. Additionally, we proceeded with fixation of lung tissues for histology and immunohistochemistry for evaluation of Rho and AcPGP activity as well as vascular occlusion and remodeling.

Results:

While the immunohistochemistry results are still pending, the results showed trending of increased Rho kinase activation via activation of its down-stream intermediate myosin phosphatase 1 (MYPT-1) with increasing dosages of PGP when compared to a control, though the result were not statistically significant. Additionally, and statistically significant, was the effect of Fasudil, a Rho kinase inhibitor, on MYPT-1 levels and hence Rho kinase activation when given with PGP when compared to a control.

Conclusions:

At first assessment it appears that increasing dosages of PGP did result in an up regulation of the Rho kinase down-stream target MYPT-1 when compared to control mice, as well as that the addition of the Rho kinase inhibitor, Fasudil, in conjunction with PGP did have a significant effect in decreasing the amount of MYPT-1 activation suggesting vasculature remodeling through Rho kinase activation may be through PGP activation.

George, David McNease (MS4)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Marjorie Lee White

Abstract Approved By Advisor: Yes

Co-Authors: ML White, P. Scalici, S. Gilbert, DT Peterson, N. Tofil, A. Youngblood, J. Zinkan

Title: An Exploratory Study of Fatigue and Alertness Among Attending Physicians

Background/Objective: Sleep deprivation in humans is associated with a variety of deficits in cognitive performance and is a mounting societal problem that affects performance regardless of career and social status.¹ Vigilance is a term used synonymously with alertness or sustained attention and reflects arousal and cognitive performance. After a period of extended wakefulness there is an increase in subjective feelings of fatigue and sleepiness, usually accompanied by a marked decrease in physical and mental performance, including reduced vigilance and slower reaction times.² A report from the Institute of Medicine estimates that approximately 100,000 people die in hospitals each year due to preventable medical errors – 60% to 80% of the errors have been partially attributed to fatigue.³ Using the Psychomotor Vigilance Test (PVT), a validated alertness tool, we sought to investigate the impact of various schedules on attending physician fatigue and alertness.

Setting and Participants: Subjects were selected from pediatric attending physicians in emergency medicine, hospital medicine, and orthopedics who practice at Children's of Alabama.

Description/Methods: Participating physicians were informed of the research study and verbal consent was obtained. Participation consisted of completing the PVT and a post-test questionnaire. The PVT is a 3-minute alertness test designed to assess changes in psychomotor speed, lapses of attention, wake state instability, and impulsivity induced by fatigue and other performance-degrading factors. The participant will click a box on the screen to begin the test and will click each time they see a flash or box appear on the screen. Response times to valid clicks and response times of false start clicks are automatically recorded on the data sheet embedded in the PVT software, as well as the start and stop time of each test. Physicians were asked to complete a 14-item questionnaire after using the PVT that collected information related to the number of hours worked during the service rotation as well as demographic information, strategies used to combat fatigue, area of subspecialty, and number of years in their subspecialty. Participants completed the PVT when they had not worked over the past 24 to 48 hours to establish a baseline, and then again during their next service rotation or at times when they were likely to be most fatigued. The participants answered the same questionnaire following the administration of each test. Once participants completed the PVT tests and the questionnaire, data was correlated to see if work schedules have an impact on physician fatigue and alertness. PVT data was analyzed using SPSS statistics. The study was IRB approved.

Evaluation/Results: A total of 44 attending physicians participated in the study including 35 pediatric emergency medicine physicians, 5 pediatric hospitalists, and 4 pediatric orthopedic surgeons. Of that number, 20 completed both the baseline and sleep deprived PVT test and post-test questionnaire. The mean age of attending physicians was 44 ± 7 years. The mean number of years in subspecialty was 11 ± 7 . There was a slight trend toward longer reaction times in the PVT when comparing baseline versus sleep deprived data (290 ± 36 versus 302 ± 36 ms [$p=0.14$]). Forty percent of attending physicians utilized sleep aids greater than 5% of the post call days/nights. Caffeine consumption (i.e., caffeinated drink consumption) rose from 1.9 ± 1.3 at baseline to 2.7 ± 1.6 ($p=0.1$) when sleep deprived. The median self-assessed performance when sleep deprived was 55 ± 19 percent of their self-assessed baseline performance. The average number of hours of sleep was $6.9 \pm .7$ at baseline versus 6.5 ± 1.1 when sleep deprived. However, the median self-assessed optimal need for sleep was $7.8 \pm .9$ for both data points.

Discussion/Reflection: According to our study, there was no statistically significant difference between average PVT reaction time among attending physicians at their baseline and when sleep deprived. However,

attending physicians do tend to sleep less than they feel is optimal both during baseline and fatigued periods. Additional testing would be needed to further evaluate the impact of various schedules on attending physician fatigue and alertness.

Gibson, Lauren Marie (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Kevin A. Roth, MD, PhD
Abstract Approved By Advisor:	Yes
Co-Authors:	Lauren Gibson, Niroop Kaza, Barbara Klocke, Christopher Graham, Kevin A. Roth
Title:	Analysis of the effects of AT101 on the CXCL12-CXCR4/CXCR7 axis in GBMs

The CXCL12-CXCR4/CXCR7 chemokine signaling axis has been reported to play a significant role in the progression of glioblastoma. Activation of this pathway correlates with more aggressive phenotypes; therefore, it represents a novel target for glioma therapy. The chemokine receptors, CXCR4 and CXCR7, are found to be overexpressed in glioma progenitor cells and differentiated glioma cells respectively. CXCR4 has been shown to promote proliferation, migration, angiogenesis and invasion, while CXCR7 prevents cells from undergoing apoptosis induced by cytotoxic drugs. The corresponding ligand, CXCL12, is produced by glioma cells and brain parenchyma. Its actions include activation of MAP-kinase and Akt pathways, which lead to increased survival and proliferation. Preliminary data from our lab indicates that Gossypol (AT101) downregulates CXCL12 gene expression in malignant peripheral nerve sheath tumor (MPNST) cells. We hypothesized that AT101 may elicit similar effects on the CXCL12-CXCR4/CXCR7 axis of GBMs. GBM cell lines U87 and LN229 were analyzed for alterations in protein levels and gene expression of the CXCL12-CXCR4/CXCR7 axis components, when treated with AT101. Receptor protein levels were analyzed using Western blot analysis, while gene expression was determined using real time PCR. We found that compared to MPNSTs, U87 cells demonstrated a slight upregulation in CXCL12 gene expression. Likewise, CXCR4 gene expression was increased in U87s. When CXCR4 protein levels were analyzed in T265, U87 and LN229 lines, they were found to decrease or remain constant. Robust increases in protein and gene expression of CXCR7 were observed in U87s, while similar effects were noticed for the protein expression of CXCR7 in T265s. While these results are preliminary, the data does indicate that AT101 affects the CXCL12-CXCR4/CXCR7 axis in glioma cell lines. However, further investigation is needed to confirm and validate this observed novel property of AT101 in GBMs.

Gleason, Michael Francis Flemming (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Shawn Gilbert
Abstract Approved By Advisor:	Yes
Co-Authors:	Richie Tanner, David Barrington
Title:	Investigation of DFO as a novel treatment for contaminated open fractures

Desferrioxamine (DFO), a hypoxia inducible factor pathway activator, is a pharmacologic agent that has been shown to increase bone vascularity and improve healing in acute fracture and distraction osteogenesis models. The goal of this research project is to determine the effectiveness of local application of DFO in the definitive management of open fractures with established infections. It is hypothesized that enhancing local vascularity following severe extremity injury will improve the local tissue environment and help prevent the development of complications such as failure of bone and muscle healing. Open fractures were created in the lower extremity of 60 adult male brown Norway rats. The wounds were then contaminated with methicillin resistant *Staphylococcus aureus* and *Acinetobacter baumannii* complex and temporarily fixed. Four days following the initial injury, wounds were irrigated and debrided, and definitively fixed with an intramedullary K-wire and composite scaffold. Either tobramycin or a combination tobramycin and DFO were administered to the scaffold. Following the surgery 40 subjects were euthanized at 6 weeks post-op and 20 subjects were euthanized at 12 weeks. The muscle and femur segments were harvested at the time of euthanasia and were examined for the following: bacterial burden, muscle and bone histology, and CT angiography. It is expected that local antibiotic delivery will decrease but not completely eradicate infection in this model. The application of DFO in addition to Tobramycin will increase vascularity and thus improve local environment that will result in further clearance of infection, improved muscle and bone repair, or both. MicroCT will detect increased vascularity and bone healing and decreased muscle fibrosis in the treatment group receiving both Tobramycin and DFO in comparison to the group that is treated with only Tobramycin.

Goyal, Shubhi (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Christina K. Ullrich, MD, MPH

Abstract Approved By Advisor: Yes

Co-Authors: Nita Bhatia, MA

Title: Caring for Children with Life-Threatening, Primary Neurological Conditions at the End-of-Life

Background: Children with life-threatening conditions characterized primarily by neurologic impairment comprise the majority of children receiving pediatric palliative care (PPC). Most PPC research, however, has focused on children with cancer and their families. Little is known regarding the specific needs and experiences of children with life-threatening, primary neurological conditions, including those at end-of-life (EOL).

Objectives:

- 1) Describe the demographic and clinical characteristics of children with life-threatening, primary neurological conditions who received PPC consultation;
- 2) Describe the nature of their PPC consult;
- 3) Describe the child's experience and patterns of care during EOL.

Methods: We are retrospectively reviewing the medical records of all children with a life-threatening, primary neurological condition who received PPC consultation at Boston Children's Hospital between January 1, 2006 and May 31, 2013, and have since died (n=239). Data collected includes demographic and clinical characteristics, symptoms, treatments and interventions, and location of care at the time of consultation and within the last month of life. Medical records will also be reviewed for documentation of advance care planning and EOL discussions. Characteristics of the PPC consultation, including reason for referral, timing and outcome of consultation will also be collected.

A Research Electronic Data Capture database was designed to capture specifically the data above. Analyses, conducted via the SAS statistical software package, will be primarily descriptive in nature. Associations between variables and outcomes of interest will be explored using a two-tailed Fisher's Exact Test or t-test for categorical or continuous variables, respectively.

Anticipated Results and Significance

These findings will be the first to describe the experience of children with life-threatening, primary neurological conditions, as well as the role of PPC in their care. Such insight is imperative for the development of PPC interventions aiming to relieve suffering and maximize quality of life for these vulnerable children and their families.

Gragg, Stephen Douglas (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Victor Thannickal
Abstract Approved By Advisor:	Yes
Co-Authors:	Bernard K, Thannickal VJ
Title:	Characterizing the effects of CLU expression on matrix synthesis by lung fibroblasts

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, fibrosing lung disease that has an incidence of 6.8-17.4 per 100,000 individuals a year in the United States. It is uniformly lethal, with an average survival time of 2.5-3.5 years. An important factor in the progression of IPF is profibrotic signaling in myofibroblasts. Recent evidence indicates that mechanical properties of the extracellular matrix (ECM), in particular matrix stiffness, regulate extrinsic and intrinsic pro-fibrotic signaling in myofibroblasts. In preliminary experiments, we have shown that mice deficient in clusterin (CLU), an extracellular chaperone, are more susceptible to fibrosis in a bleomycin lung injury model. Since extracellular chaperones are thought to selectively target misfolded ECM proteins for endocytosis and degradation, we wanted to test whether deficiencies in CLU caused measurable changes in the composition and biomechanical properties of the ECM. We developed a method to culture lung fibroblasts from wild type and CLU deficient mice and isolate the de-cellularized ECM. The extracted ECM from wild-type and CLU-deficient mice could later be solubilized and analyzed by mass spectrometry. These studies will elucidate mechanisms of ECM composition and dynamics in fibrotic lung disease, including IPF.

Graves, Anna Joy (MSTP)**Project Length:** Short**Prior Research Experience:** Yes**Source of Funding:** NIH Medical Scientist Training Program**Faculty Advisor:** Nir Menachemi**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** The Impact of the Intrauterine Environment on Offspring Metabolic Outcomes: A Systematic Review

The fetal origins of disease (FOD) hypothesis posits that maternal exposures prior to and during pregnancy impact the intrauterine environment, leading to fetal compensatory mechanisms that may predispose offspring to short- and long-term metabolic disease. For this systematic review, we examined nearly 3,000 articles that fall within the scope of the project; of these, a preliminary 200 articles were reviewed and 71 identified to have all characteristics necessary for inclusion. A coding sheet was designed and abstracts were reviewed with key information extracted for a meta-analysis. The purpose was to determine the study factors that affected the likelihood of finding support for the FOD hypothesis. Of all studies examined, 83% gave support for the FOD hypothesis. Maternal exposures examined included insulin resistance ($n = 25$), obesity (8), diet (22), serum markers (11), placental insufficiency (6), and toxins/drugs/viruses (14). In the absence of maternal exposures, 15% of studies used postnatal indicators of the intrauterine environment, including placental characteristics, intrauterine growth restriction, size for gestational age, birth weight, and anthropomorphic measures. Studies using maternal exposures had 1.8 times the odds (95%CI: 0.9 – 3.7) of reporting an association with a metabolic outcome than studies that used a surrogate indicator for the maternal exposure. Because experimental study designs of maternal exposures are unethical in human populations, animal models provide a viable alternative. Although only 37% of the articles studied animals, they were significantly more likely ($p = 0.006$) than human studies to demonstrate an association. In this sample, only 19% of studies examined epigenetic and “organ programming” mechanisms for long-term offspring disease risk, and only 7% reported sex as a modifier. However, examining these associations holds great promise for further understanding the nature of the association between maternal exposures and offspring outcomes. Furthermore, we are lacking longitudinal data on maternal exposures, as evidenced by the fact that the majority of studies only examined exposures in utero. These preliminary results will form the basis of a larger systematic review aimed at identifying gaps in the literature.

Guzman Karlsson, Mikael Carl Gustav (MSTP)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	J. David Sweatt
Abstract Approved By Advisor:	Yes
Co-Authors:	Alejandro Monteon, Sarah Strange
Title:	Transcriptional Regulation of Intrinsic Excitability and Memory Allocation

Sparse ensembles of neurons encode a given memory. Understanding the molecular mechanisms that allocate memories to specific cells in a given neural circuit is becoming increasingly studied. Previous research suggests that the levels of the transcription factor cyclic adenosine 3', 5'-monophosphate response element binding protein (CREB) may predispose certain groups of neurons to encode a memory by modulating their intrinsic excitability. CREB-mediated gene transcription is well established in the learning and memory field as it serves a fundamental role in the consolidation of long-term memory and the regulation of synaptic plasticity. However, how CREB-mediated gene transcription regulates intrinsic excitability and memory allocation are less understood. Our central hypothesis is that CREB-mediated modulation of excitability and memory allocation occurs via transcriptional regulation of voltage- and/or calcium-gated ion channels. To characterize the transcriptional profile downstream of CREB, we overexpressed CREB with a modified herpes simplex virus in embryonic cortical mouse cultures. Preliminary data indicates that overexpression of CREB downregulates specific voltage-gated K⁺ channels. These findings indicate that modulation of K⁺ channel transcript level may underlie the increased excitability necessary for CREB-mediated memory allocation.

Hadley, Jennifer Ann (MSTP)**Project Length:** Long**Prior Research Experience:** Yes**Source of Funding:** NIH Medical Scientist Training Program**Faculty Advisor:** Adrienne C. Lahti**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** Graph Theoretic Analysis of Network Interactions in Schizophrenia

Patients with schizophrenia experience the insidious onset of symptoms including hallucinations, delusions, and cognitive decline. Antipsychotic drugs can alleviate some of these symptoms, but response is variable and up to 30% of patients do not experience a reduction in symptoms. Current clinical guidelines recommend at least a six-week trial of new medication before determining efficacy; on average, it takes nine months to identify an effective antipsychotic. A major predictor of a patient's long-term prognosis is the duration of untreated symptoms, and so there is a need for a biomarker to identify non-responders so that they can be changed to a different treatment. Relatively little is known about the etiology of schizophrenia, but a number of neuroimaging studies have provided evidence in support of the hypothesis that impaired functional interactions between brain regions are responsible for its symptoms. Unfortunately, the effect of antipsychotics on these interactions has not been explicitly studied. We hypothesize that interactions between brain networks are impaired in unmedicated patients with schizophrenia (SZ0) compared to controls (HC) and that specific alterations will predict symptom severity and treatment response. 32 SZ0 and 32 HC received a resting-state fMRI scan; afterwards patients began antipsychotic treatment. After six weeks, patients received a second fMRI scan (SZ6). The interactions between brain networks were compared using graph theory methods of fMRI data. Compared to HC, SZ0 showed increased clustering in the default mode, salience, and precuneus networks; clustering in SZ6 and HC in these networks did not differ. SZ0 also showed decreased global efficiency compared to HC, which was also normalized with treatment. Severity of alterations correlated with symptoms and response to medication. This suggests that network interactions may be useful biomarkers of symptom severity, and lends support to the theory that impaired interactions between brain networks underlie the symptoms of schizophrenia.

Hall, Jason Durwood (MS3)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Meredith Robbins
Abstract Approved By Advisor:	Yes
Co-Authors:	Cary DeWitte, BS; Timothy Ness, MD, PhD; Meredith Robbins, PhD
Title:	Systemic administration of 5-HTP has opposing effects on visceral and somatic nociceptive processing

5-hydroxytryptophan (5-HTP) is a biosynthetic intermediate in conversion of L-tryptophan, an essential amino acid, to serotonin (5-HT). 5-HT released from the descending pain modulatory pathway plays an important role in spinal nociceptive processing, either inhibiting or facilitating nociception depending on the type of pain and which 5-HT receptors are involved. Little is known about the role of serotonergic systems in nociceptive processing related to the bladder or the effect of 5-HTP on somatic and visceral nociception. We investigated effects of systemic administration of 5-HTP on somatic and visceral nociceptive processing and sought to identify 5-HT receptors involved in bladder hypersensitivity.

Methods. One group of female Lewis rats received subcutaneous 5-HTP or vehicle and after 15min, was anesthetized with inhaled isoflurane. Another group was anesthetized immediately, received 5-HTP or vehicle, and after 15min, was treated with a selective 5-HT receptor antagonist (ondansetron or WAY-100635) or vehicle. Bladder distention was achieved using a 22-gauge angiocatheter placed via the urethra. Silver electrodes in the external oblique musculature immediately superior to the inguinal ligament recorded electromyographic (EMG) activity.

Somatic sensation following administration of 5-HTP or vehicle was evaluated using Hargreaves' method, which measures hindpaw withdrawal latency to a thermal stimulus. Serum and CSF ELISA was performed to measure levels of 5-HT and its principal metabolite, 5-hydroxyindoleacetic acid (5-HIAA).

Results and Conclusions. 5-HTP significantly enhanced UBD-evoked EMG activity, indicating that it produces visceral hypersensitivity. This effect was attenuated by administration of WAY-100635 but not by ondansetron, suggesting the 5-HT1A receptor is directly involved in serotonergic modulation of bladder hypersensitivity. In contrast, 5-HTP produced somatic analgesia as revealed by increased hindpaw withdrawal latency. ELISA results suggest that 5-HTP induces somatic analgesia and visceral hypersensitivity through peripheral serotonergic mechanisms as both effects were observed within 30min of 5-HTP administration and dissipated by 2h.

Hardigan, Andrew Alexander (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Dr. Richard Myers
Abstract Approved By Advisor:	Yes
Co-Authors:	Kevin Bowling, Marie Kirby, Todd Burwell
Title:	Identification of Novel Transcripts Associated with Neuropsychiatric Disorders

Neuropsychiatric disorders such as bipolar disorder (BD), schizophrenia (SZ), and major depressive disorder (MDD), are complex pathologies resulting from interaction between genetic, epigenetic and environmental factors; these interactions are not well understood. Recent studies have implicated brain region dependent gene expression changes as functional causes of these disorders, though the role of biologically relevant but currently unannotated novel transcripts identified by RNA sequencing remains to be determined.

The primary goal of this project is to use next-generation sequencing technology to measure the transcriptome of patients who suffered from MDD, SZ or BD and identify previously unknown novel transcripts that associate with disease pathology. Human post-mortem brain tissue was collected from control, MDD, SZ, and BD patients (n=22-24 for each group) from three regions that have been previously implicated in psychiatric phenotypes: dorsolateral prefrontal cortex (DLPFC, n=94), anterior cingulate cortex (AnCg, n=96), and the nucleus accumbens (nAcc, n=91). Using RNA-sequencing, we generated 281 RNA-seq libraries with ~46,743,480 reads per library of which 74% aligned to the GENCODE reference. We identified 8,634 novel transcripts present in at least one sample that did not overlap with known transcripts. We performed negative binomial regression analyses of normalized raw counts with inclusion of sample covariates, yielding differential expression of two transcripts in the DLPFC SZ group, one transcript in AnCg BD group, and 30 transcripts in the AnCg SZ group. These 30 transcripts were chosen for further analyses and filtered to ensure they were intergenically located, did not reside in a segmental duplication and sufficiently distant from transcriptional start sites. In order to facilitate future functional analyses we performed RACE-PCR to determine the 3' and 5' ends of one transcript, chr10:71802762-71804532. Future studies will focus on verification and further characterization of the potential functional roles these differentially expressed novel transcripts play in neuropsychiatric disorders.

Harvey, Evan Matthews (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	American Heart Association Fellowship
Faculty Advisor:	Dr. Jeffrey Alten, Dr. David Cleveland, Dr. Santiago Borasino, Dr. Stephen Robert
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Jeffrey Alten, Dr. David Cleveland, Dr. Santiago Borasino, Dr. Stephen Robert
Title:	Impact of Fluid Overload and Kidney Injury on Outcomes after the Arterial Switch Operation

Background: The arterial switch operation (ASO) for repair of transposition of the great arteries in the neonatal period is associated with significant morbidity. Duration of mechanical ventilation is a surrogate of morbidity after ASO; aggressive fluid removal is one of the proposed strategies to decrease morbidity. The purpose of this study was to determine factors associated with increased mechanical ventilation duration, focusing on fluid management in this population.

Methods: Single-center retrospective chart review of all ASO patients from 2006-2013.

Results: 78 patients underwent an arterial switch operation (ASO) at this institution. Mean age at surgery was 9.7 ± 11.9 days. 75% were male. 36.8% had other cardiac anomalies, including VSD. The mean duration of mechanical ventilation was 98 ± 116 hours. More positive fluid balance at 24 hours post-operation was correlated with increased duration of mechanical ventilation ($r= 0.385, p = 0.001$). Transfusion of packed red blood cells and platelets was also significantly correlated with duration of mechanical ventilation ($r=0.42, p\leq 0.001$ and $r=0.62 p\leq 0.001$), as well as 5% albumin administration in the first 24hrs ($r=0.36, p=0.002$). Cardiopulmonary bypass and aortic cross-clamp times, and concurrent VSD closure did not correlate with duration of mechanical ventilation. Fluid balance at 24hrs was significantly more negative with the use prophylactic peritoneal dialysis (-2.8ml/kg vs. -35.2ml/kg, $p=0.028$).

Conclusion: Increased positive fluid balance, blood product administration, and albumin boluses in the early postoperative period are associated with increased duration of mechanical ventilation following the ASO.

Hicks, Stephen Bradley (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Bradford Woodworth, MD

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Characterization of Primary Porcine Nasal Epithelium Model in Transepithelial Ion Transport and CFTR Function

Background Transgenic cystic fibrosis (CF) murine models have greatly facilitated studies of CF pathogenesis and treatment. However, small rodents do not reproduce key aspects of human airway physiology. Notably, murine models do not develop spontaneous lung and pancreas disease, two of the major causes of morbidity in human CF patients. The objectives of the current experiments were to develop primary porcine nasal epithelial (PNE) cultures and evaluate their usefulness as a model of transepithelial transport and CFTR function.

Methods PNE derived from the septum or turbinates of WT and CFTR^{-/-} neonatal pigs were cultured at an air-liquid interface on filter supports. Differentiation occurred within 14 days and all inserts attained resistance >500 Ω/cm². Epithelial monolayers were mounted in Ussing chambers to investigate pharmacologic manipulation of ion transport. Ciliary beat frequency (CBF) and SEM images of the monolayers were used to indicate degree of ciliation and cell differentiation.

Results Stimulation of CFTR-mediated anion transport was significantly greater in epithelia derived from the septum when compared to turbinates. CFTR-mediated Cl⁻ secretion was absent in CFTR^{-/-} epithelia. Blockade of epithelial sodium channels was more robust and forskolin-stimulated Isc more inhibited by CFTR_{INH}-172 in septal epithelia. Calcium-activated Cl⁻ Channel (CaCC) secretion was increased in septum vs. turbinate cultures following the administration of UTP, however, overall Cl⁻ transport through CaCCs was very low. Degree of ciliation and CBF in response to UTP and forskolin were similar among groups.

Discussion The porcine nasal septum is a superior source of primary nasal epithelia when compared to turbinates as the cells exhibit a more robust ion transport phenotype. Porcine CFTR^{-/-} airway disease could be attributable to diminished alternative pathways for Cl⁻ transport as calcium-activated Cl⁻ transport is very low when compared to other species. Overall, porcine nasal epithelia have similarities to human respiratory epithelia not exhibited in murine cells and represent useful models for studying CFTR activity.

Hingorani, Neha (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Dr. Theresa Strong
Abstract Approved By Advisor:	Yes
Co-Authors:	Steven Walker
Title:	The Role of Sp17 in Genetic Instability in Breast Cancer

Sperm protein 17 (Sp17, gene name SPA17) is a cancer-testis antigen highly expressed in many cancers, including over 70% of breast and ovarian cancers. Sp17 has limited expression in somatic tissues, making it a suitable candidate for cancer imaging and targeted therapeutics; however, Sp17's role in oncogenesis is poorly understood. Previous research performed in our lab has shown that Sp17 expression may be up regulated early in oncogenesis and promote several characteristics of genetic instability: multinucleation, aneuploidy, and centrosome amplification, but overexpression of Sp17 did not result in increased cell proliferation in vitro. Here, we examined the consequences of enforced overexpression of Sp17 in the breast epithelial cell line, MCF-10A. The MCF-10A cell line was chosen to represent the early stages of oncogenesis. To gain a better understanding of Sp17's role in genetic instability, we altered functional motifs in Sp17's protein coding sequence. Specifically, we mutated DBOX, a mediator for protein degradation necessary for cell cycle progression, and deleted IQ, a calmodulin-binding motif that orchestrates cellular cascades via calcium sensing. MCF-10A cells with altered motifs were grown in 3D culture instead of 2D to better mimic in-vivo growth, and we found that in 3D culture, cells with a DBOX mutation grew uninhibited in large, stacking acini clusters whereas cells with an IQ mutation formed smaller, distinct acini more consistent with normal cellular morphology. This contrasts previous experiments in our lab in which cells with a DBOX mutation grown in 2D culture did not cause signs of oncogenesis, including increased cell proliferation. Thus, we conclude that 3D culture suggests DBOX may be a key factor in SP17's role in genetic instability while affirming that the normal morphology seen with an IQ deletion in both 2D and 3D culture indicates calmodulin-based signaling may play a key role as well.

Honasoge, Avinash Vinayak (MSTP)**Project Length:** Long**Prior Research Experience:** Yes**Source of Funding:** Other**Faculty Advisor:** Harald Sontheimer**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** Autocrine regulation of glioma cell proliferation via pHe-sensitive K⁺ channels

Since the seminal studies of Otto Warburg in the 1920s it has been widely recognized that cancers grow glycolytically even in the presence of oxygen. This generates an abundance of protons in a gradient across most solid tumors with an acidic core and an alkaline rim. Whether and how this proton gradient may also serve in an autocrine fashion on glioma cells is unclear. Here we demonstrate that human glioma cells form spheroids which act as a viable three-dimensional tumor model, forming physiologically relevant extracellular pH (pH_e) and cell proliferation gradients. Using fluorescent cell cycle trackers we determined that the rate of cell proliferation is directly dependent on pH_e, and that cells adjust their growth rate according to their position within the pH gradient. We further show that glioma cells sense pH via H⁺-sensitive K⁺ channels that translate changes in pH into changes in membrane voltage. These channels are tonically active and blocked by acidic pH_e, quinine, and ruthenium red. Blockade of this K⁺ conductance either by acidic pH_e or drug inhibition depolarized both glioma cells and tumor spheroids and prevented them from passing through the hyperpolarization-dependent G₁-to-S phase cell cycle checkpoint, thereby inhibiting cell division. In this way, pH_e directly determines the proliferative state of glioma cells.

Hu, Muhan (MSTP)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Daniel Gorelick
Abstract Approved By Advisor:	Yes
Co-Authors:	Daniel Gorelick
Title:	Characterization of G-Protein Coupled Estrogen Receptor Expression in Zebrafish Embryos

Estrogens act on diverse tissues by binding to multiple estrogen receptors. Studies have focused on the characterization of the classical estrogen receptors ($ER\alpha$, $ER\beta\Box$, which are ligand-dependent transcription factors. Less is known about the more recently discovered G-protein coupled estrogen receptor, which is a membrane associated estrogen receptor. In adult rodents, GPER may influence heart rate and protect the heart following ischemia. However, less is known about GPER expression and function during embryonic development. Two previous studies reported widespread *gper* expression in zebrafish embryos, including in the heart. However, specific localization of *gper* in the heart was not reported. In this study, we examined the expression of *gper* more closely to identify the specific areas of the heart that express GPER (e.g. heart valves, myocardial cells). This will help us generate a hypothesis about its role in the heart during embryonic development. We performed whole mount *in situ* hybridization on wild type zebrafish embryos at 25 – 96 hours post fertilization. Surprisingly, we did not detect *gper* expression in the embryonic heart. Unlike the widespread *gper* expression reported previously, our results showed restricted *gper* expression in discrete regions in the brain. *gper* transcripts were observed in the presumptive hypothalamus. Bilaterally symmetric *gper* mRNA labeling was also observed in the olfactory bulb and preoptic area in the forebrain. Our results suggest that GPER expression in embryos is not as extensive as previously thought, and that GPER does not act on the heart directly during embryonic development. We hypothesize that GPER activation mediates embryonic heart function via the GPER expressing cells in the brain. Future studies will identify the specific cell types that express *gper* by performing double-label *in situ* hybridization using *gper* and cell-specific probes. We will also identify GPER function by generating *gper* mutant zebrafish.

Hubbard, Meredith Gene (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. Tim Townes
Abstract Approved By Advisor:	Yes
Co-Authors:	Chia-Wei Chang
Title:	Differentiation of Induced Pluripotent Stem Cells from the Skin Cells of Immunodeficient Patients to T-Lymphocytes

T lymphocytes (T-cells) are one of the main components of a functional immune system with an essential role in systemic immunity against foreign pathogens. Generation of induced pluripotent stem cells (iPS) has the potential to create a diverse selection of renewable T Lymphocytes and a better therapeutic option for patients with diseases such as Severe Combined Immunodeficiency (SCID) and Wiskott-Aldrich Syndrome (WAS). SCID and WAS iPS lines derived from patients with mutations in Jak3 (nonsense point mutation in amino acid 613) and WASP (T45M) are used in this study. The iPS cells were generated by a “Hit and Run” lentiviral plasmid or episomal plasmid method. We corrected the Jak3 point mutation utilizing a precise genome editing technology called the CRISPR/Cas system (clustered regularly interspaced short palindromic repeats). CRISPR has been shown to facilitate RNA guided site-specific DNA cleavage to facilitate in homology-directed repair with minimal mutagenic activity. The repair sequence was then introduced into SCID iPS cells to correct the mutation. Corrected iPS cells will be plated on OP9 stromal cells for hematopoietic differentiation. After purification of CD34+ cells and plating them on OP9 expressed with Notch ligand (OP9-DL4), the cells will be measured by the expression of CD4, CD8, CD7, intracellular CD3, and surface CD3. The goal of this study was to create genetically corrected induced pluripotent stem cells from dermal cells of patients with immunodeficiency to be differentiated into hematopoietic stem cells that will produce a diverse repertoire of T lymphocytes to be used as a potential therapy.

Hull, Travis David (MSTP)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	American Heart Association Fellowship
Faculty Advisor:	James F. George and Anupam Agarwal
Abstract Approved By Advisor:	Yes
Co-Authors:	A Agarwal and JF George
Title:	Heme Oxygenase-1 Expression Prevents Doxorubicin-Induced Delayed Onset Heart Failure

Background: heme oxygenase-1 (HO-1) is an inducible enzyme that degrades pro-oxidant heme into carbon monoxide, biliverdin, (both antioxidants) and iron. We have previously shown that cardiac-specific HO-1 expression prevents acute cardiac injury. Doxorubicin (DOX) is a highly effective and widely utilized chemotherapeutic agent. However, its clinical utility is limited because it causes delayed onset cardiac failure (DOCF) in a dose dependent manner.

Hypothesis: expression of HO-1 in cardiomyocytes protects against DOX-induced DOCF by preventing cardiomyocyte death secondary to mitochondrial toxicity.

Methods and Results: we used DOX to develop a model of DOCF in mice (18 mg DOX per kg of body weight, administered IV as three 6 mg/kg doses separated by two days). This treatment protocol does not cause acute cardiac dysfunction, but results in DOCF as determined by echocardiography at days 14 and 60 after treatment. HO-1 overexpression in humanized transgenic (HBAC) mice prevents body weight loss (4% vs 15% in WT, P < 0.05, n=10) and systolic dysfunction (ejection fraction 67% vs 51% in WT mice, P<0.05, n=5) at day 14 after DOX treatment. DOX-induced DOCF, characterized by dilation of the left ventricle (3.22 mm vs 3.55 mm in WT mice, P<0.05, n=5) and wall thinning (0.89 mm vs 0.61 mm in WT mice, P<0.05, n=5), is also prevented by HO-1 overexpression. Examination of H&E stained sections demonstrated that HO-1 overexpression prevents cardiomyocyte necrosis, evidenced by cytoplasmic vacuolization and loss of myocyte striations, as well as secondary inflammation in necrotic foci. DOX increases the proportion of CD45⁺ cells in the heart of WT mice relative to vehicle treated controls (1.42% vs 0.62%, P < 0.01, n=5), while HO-1 expression inhibits the infiltration of CD11b⁺ mononuclear phagocytes (P < 0.05, n=5).

Conclusion: HO-1 expression prevents delayed onset cardiac failure caused by DOX.

Huynh, Thy Nhat (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Naveed Sami
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Bruce Korf, Dr. Amy Theos, Dr. Michael Crowley, Dr. David Crossman, and Dr. Kristopher McKay
Title:	WHOLE EXOME SEQUENCING IN FAMILY WITH UNSPECIFIED GENODERMATOSIS OF SCLERODERMOID FEATURES

Objectives/Specific Aims: Genodermatoses consist of inherited dermatologic disorders with associated single-gene mutation. We have identified a family with unique sclerodermod features. Diagnosis has remained inconclusive due to mixture of clinical features consistent for scleroderma, palmoplantar keratoderma (PPK), or Huriez. Our objective is to elucidate genetic mutation associated with this undiagnosed genodermatosis.

Methods/Study Population: Informed consent was obtained from all subjects and approved by IRB. History, physical exam, and family pedigree were performed (n=4). Skin biopsies were taken from affected members (n=3). Genomic DNA was isolated from peripheral blood samples. Next generation sequencing (NGS) with exome capture is conducted prior to data processing, variant discovery, genotyping, and integrative analysis. Sanger sequencing was performed to validate variants of suspected for disease.

Results: Affected members had varying degrees of hyperpigmented macules on acral surfaces; firm indurated plaques around mouth and distal fingers; and erythematous, scaly plaques with some fissuring on bilateral hands and feet. Calcinosis, Raynaud's phenomenon, sclerodactyly, and dysphagia were exhibited. Though some clinical features were consistent for scleroderma-type disease, members were negative for anti-nuclear, anti-centromer, and anti-SCL-70 antibodies. Biopsies for affected members showed stratum corneum with hyperorthokeratosis and alternating parakeratosis. Keratinocytes in spinous layers had eosinophilic inclusions. Mutations FBN1 15q21.1 for familial scleroderma and AAGAB 15q22 for PPK were not generated in this family. Novel genetic mutations included variants for 11 genes, such OLFML2B, TGOLN2, STK11IP, HJURP, ATP6V1B2, OR1N1.

Discussion/Significance of Impact: Exome sequencing has the potential to provide diagnostics and genetic pathology for uncharacterized genodermatoses. We have found 11 novel variants likely involved in causing disease manifestation. Further study would involve genetic analysis of a similar phenotype in a different kindred family to confirm mutations as this the first family with characterized disease.

Hyndman, LaKeshia Nicole (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	CaRES Program
Faculty Advisor:	Dr. Laura Q Rogers

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Taraneh Soleymani; Dr. Sunil Daniel; Courtney Blair, Chaundra Hall, Dr. LQ Rogers

Title: Weight Loss Barriers: Cancer Survivors versus Non-cancer Controls

Multiple cancer types have been linked to obesity. Furthermore, cancer survivors frequently remain (or become) overweight or obese after their cancer diagnosis, increasing their risk of cancer recurrence and mortality. Because weight loss barriers faced by cancer survivors are not well understood, our study focused on determining these barriers and whether they differed for cancer survivors and with non-cancer controls. We reviewed medical records of patients seen in an Academic Medically Supervised Weight Management Clinic. Fifteen patients with a history of cancer documented in the medical record were age and gender matched to a control patient. The 30 participants had a mean age = 55 ± 11 years, initial visit body weight = 240 ± 69 lbs, and initial body mass index 37 ± 10 (no statistical difference for cancer versus controls). For race, 16 were White, 10 were African-American, and 4 were other. Cancer type for the cancer survivors included skin (n=7), breast (n=3), prostate (n=1), gynecologic (n=1), and other (n=3). Using Fischer's exact, barriers for cancer survivors versus control were: junk food (e.g. alcohol, snacks, non-nutritious foods) [5 (33%) versus 3 (20%), p = .68]; lack of motivation [3(20% versus 3(20%), p=1.0], health problems [3(20%) versus 1(7%), p= .60], social (eating alone, family celebrations, holidays) [4(27%) versus 0(0%), p = .10], other [1(6.7% versus 3 (20%), p = .60], life stress [2(13% versus 2(13%), p = 1.0], physical inactivity [2(13%) versus 1(7%), p = 1.0]. Using independent groups t-test, the mean for total barriers was 2 ± 1.3 for cancer survivors versus $1.1\pm.64$ for controls, p=.024. While individual barriers didn't differ for cancer compared with controls, the higher mean for total barriers for cancer survivors suggests that program focusing on the aforementioned barriers are needed. Further research is needed to determine if social barriers warrant greater attention in cancer survivors.

Isbell, Jonathan Andrew (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Herrick J. Siegel, M.D.

Abstract Approved By Advisor: Yes

Co-Authors: Andrew C. Morris, M.D., Jonathan A. Isbell, M.S., MS-2

Title: Road map past the lateral femoral cutaneous nerve during the direct anterior hip approach: a cadaver study

Background: During the surgical anterior approach to the hip, damage to the lateral femoral cutaneous nerve (LFCN) is the main complication. Our aim is to identify where the nerve is most likely injured, in what way, and how to prevent this.

Hypothesis: When using the modified Hueter anterior hip approach, by staying inside the tensor fascia lata fascial sheath, the distance of retractor placement and plane of exposure will be greater resulting in less risk of damaging the LFCN compared to traditional anterior hip approaches will be decreased.

Study Design: Anatomical cadaver study

Materials and Methods: Four hip cadaveric prosections were dissected in a lab using variations in incision, approach, and retractor replacement. The distance from the LFCN to the retractors and exposure were measured during these variations.

Results: Currently being analyzed

Conclusion: Our hypothesis is that the modified Hueter approach using the bikini transverse incision will result in the farthest distance from the LFCN to both the medial retractor and the dissection plane.

Isbell, Kayla Danielle (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Spencer J. Melby and James F. George

Abstract Approved By Advisor: Yes

Co-Authors: Kyle Bess, Spencer J. Melby, James F. George

Title: Levels of Pro-Oxidant and Inflammatory Molecules in Postoperative Pericardial Fluid are Related to Atrial Fibrillation

Purpose: Atrial fibrillation (AF) after cardiac surgery has been linked to inflammation. Studies have evaluated serum markers but not pericardial fluid (PCF) for its contribution. We hypothesized that post-operative PCF is a distinct cellular compartment from the serum, is pro-inflammatory, pro-oxidant, and that myocytes are oxidatively damaged in this environment, which contributes to postoperative AF.

Methods: Plasma and PCF from 18 adults was obtained at the start of CABG and/or valve surgery and at 4, 12, 24, and 48 hours post-surgery. Cell-free methemoglobin (metHgb), cell phenotypes, myocardial breakdown products and cytokines were measured at each time point by spectrophotometry, flow cytometry, and multiplex bead assays. The student t-test was used for statistical analyses. Values are mean \pm standard error.

Results: At all time points measured post-surgery pro-inflammatory (IL-6, IL-8, myeloperoxidase) and myocardial damage markers (troponin-I, CK-MB, myoglobin) were significantly increased in PCF vs serum. Flow cytometry showed that $93.9 \pm 2.2\%$ ($n=4$) of cells in the PCF were neutrophils at 24 hours. Most remaining cells were monocytes $2.3 \pm 1.4\%$ ($n=4$). Kinetic measurements showed AF patients with significantly increased pro-oxidant MetHgb at 12 hours vs patients without AF (83.7 ± 10.4 μ M, $n=4$ vs 44 ± 6.7 μ M, $n=8$; $p=.005$). This preceded the markers of elevated Troponin-I at 48 hours [$217,600 \pm 25,300$ pg/mL in AF pts ($n=4$) vs $91,000 \pm 25,400$ pg/mL in non-AF pts ($n=8$), $p=0.01$].

Conclusion: The presence of highly pro-oxidant and pro-inflammatory factors in the postoperative PCF was found to be predictive of atrial fibrillation. These markers of postoperative AF are distinct from markers found in the serum, and provide new insights into mechanisms of its onset and may allow for new directed treatment modalities to be developed for cardiac surgery patients.

Johnston, Lucy Baldwin (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: CaRES Program

Faculty Advisor: Warner Huh, MD

Abstract Approved By Advisor: Yes

Co-Authors: Plash, Madison Huh, Warner

Title: The Efficacy of Using Indocyanine Green for Sentinel Lymph Node Biopsy in Endometrial and Cervical Cancer.

Background: The sentinel lymph node is the first lymph node that cancer cells spread to from a primary tumor. Sentinel lymph node biopsy has been proven to be effective and advantageous to stage breast cancer and melanoma. **Objective:** Though sentinel lymph node biopsy is performed in some gynecological cancer cases, there is no consensus among Gynecology Oncologists on how to assess lymph nodes. This study was designed to generate data to support sentinel lymph node biopsy as the standard of care for endometrial and cervical cancer staging. **Methods:** Women with endometrial or cervical cancer are chosen for the study. We use indocyanine green (ICG), a safe dye that has been used for more than 50 years for medical diagnostics, in a new innovative way. We inject the dye directly into the cervix of the patient, and wait for the dye to travel through the lymph channels. The dye pools in the sentinel node and it lights up bright green under a laser with a wavelength of 780nm. With the lymph node illuminated, it is better visualized for removal via robotic surgery. We collect preliminary data in the operating room, including patient demographics, BMI, if the sentinel node can be visualized, and the specific time points in which it is visualized. Other crucial data points include the volume and concentration of the dye, depth of injection into the cervix, and type of needle used. We hope to collect data on 25-30 women in order to determine the optimal dosing of dye and how much time should be allowed for the lymph nodes to be visualized. **Conclusion:** By exploring how to identify the sentinel lymph node in endometrial cancer, we can improve the morbidity and mortality of treatment for endometrial and cervical cancer.

Jones, Andrew Lloyd (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Masako Shimamura, M.D.

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Influence of CsA upon antiviral immune responses in a murine model for renal transplantation

Background: In human renal transplantation, CMV infection has been associated with increased graft loss due to activation of antiviral immune responses. Cyclosporine (CsA), an immunosuppressant, has been used to decrease the alloimmune response in transplant recipients and is associated with decreased graft loss, but its effect upon antiviral immune responses has not been thoroughly examined. CsA could either lower the frequency of immune populations, particularly T-cell lineages, in MCMV infected mice, or alternatively could prevent immune control of viral infection, leading to increased inflammation and allograft damage.

Methods: Using a mouse model (BALB/c), the immune populations in mouse spleens were measured using flow cytometry under stimulated and unstimulated conditions to determine how the populations changed in response to MCMV infection and MCMV infection in the presence of CsA, compared to uninfected controls.

Results: Variable responses to MCMV and MCMV/CsA conditions in BALB/c mice were observed. As compared to the control group and MCMV group, the frequency of T-cells including CD4+/TH17 and T-regulatory cells increased in the presence of MCMV/CsA while the frequency of NK cells decreased. The frequency of CD4+/Th1 cells increased in both groups compared to the control, and the frequency of CD4+/Th2 cells remained similar between all groups. Additionally, the frequency of CD8+ cells including cytotoxic T-cells and T-effector memory cells were similar between the three groups.

Conclusions: These results show that CsA did not effectively immunosuppress T-cell lineages and may contribute to increased T-cell responses in MCMV-infected BALB/c mice. However, CsA reduced the frequency of NK cells, a part of the innate immune system on which it has not been traditionally believed to have a significant effect. Based on this small sample size, it is hard to draw any well-defined conclusions, which could be addressed by analyzing a larger sample size.

Jordan, Melissa Rae (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Elizabeth Richardson

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Identifying Differences in Spinal cord Injury-related Neuropathic Pain:Virtual Illusion Treatment Outcomes as a Function of Subtype of Pain

Introduction: Studies have shown differences in response to virtual walking as a form of pain treatment depending on location of pain (below or at-level) as well as hyperexcitability at the dermatomes of the level of injury. This study's aims were to determine the effect of location of spinal cord injury-related neuropathic pain (SCI-NP) on pain outcomes following exposure to virtual walking as well as demonstrate a relationship between neuronal hyperexcitability, as measured by Quantitative Sensory Testing (QST), and pain reduction following virtual walking exposure.

Methods: Participants recruited from a larger project of the UAB SCI Model System examining virtual walking in SCI-NP underwent QST on each of their pain sites and a nonpainful area. Five domains of QST were tested: brush allodynia, punctate hyperesthesia, innocuous cool, noxious cold, pressure pain.

Results: A total of 11 pain sites were obtained. The 2 at-level pain sites were subjected to the control (wheeling). The mean pain reduction was recorded as 1.0. Of the 9 below-level pain sites that were subjected to the control, there was a mean reduction by 0.5. Those that were given treatment (walking), had a mean reduction of 0.0.

One participant who had no response to QST was given treatment and had 0.0 reductions in pain. The other participant who did not respond to QST was given the control and had a reduction in pain by 0.5. The one participant who showed response to QST was also given the control and had a reduction in pain by 2.0.

Discussion: This study is still in its early stages of recruitment and enrollment. Further data is needed to clarify if there is a difference in responsivity depending on pain sites, as well as, differences between those with below level pain who responded to QST versus those who had no hypersensitivity.

Kapadia, Akash A. (MS4)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Sunil Sudarshan

Abstract Approved By Advisor: Yes

Co-Authors: Dustin Gayheart, M.D.

Title: Pyruvate dehydrogenase kinase-1 inhibitors potentiate the anti-tumor activity of Sorafenib against renal cell carcinoma cells via activation of the tricarboxylic acid

Introduction and Objectives: Sorafenib is one of the tyrosine kinase inhibitors with proven anti-tumor activity against renal cell carcinoma (RCC) cells, as evidenced by its efficacy in patients with advanced RCC. However, of those patients that initially respond to treatment, most invariably develop resistance. One of the proposed mechanisms underlying the acquired resistance is the propensity of RCC to utilize glycolysis in lieu of oxidative phosphorylation for rapid growth, a phenomenon known as the Warburg effect. Dichloroacetate (DCA), a known pyruvate dehydrogenase kinase-1 (PDK-1) inhibitor, has been shown to potentiate the effect of Sorafenib in treatment-resistant hepatocellular carcinoma *in vitro*. The objective of this study is to investigate whether PDK-1 inhibitors dichloroacetate and phenylbutyrate (PB) potentiate the anti-tumor activity of Sorafenib against RCC cells.

Methods: RCC cell lines A498 and 786-O were exposed to Sorafenib only and PDK-1 inhibitors DCA and PB only in order to determine the drug-response relationship. Minimally inhibitory doses of PDK-1 inhibitors were then used in combination with increasing doses of Sorafenib. MTS assays were performed in each experimental design in order to determine cell proliferation and viability.

Results: Sorafenib alone showed lower growth suppression in 786-O cells with increasing doses than when combined with DCA ($p<0.05$). Similarly, Sorafenib alone showed decreased growth suppression in both A498 and 786-O cells with increasing doses than when combined with PB ($p<0.05$). Furthermore, the differences in cell viability between control groups (no treatment) and DCA alone/PB alone were not statistically significant.

Conclusions: Activation of the tricarboxylic acid (TCA) cycle via inhibition of PDK-1 potentiates the anti-tumor activity of Sorafenib. Although further characterization of the role of PDK-1 inhibitors in tumor growth suppression is required, our preliminary data suggests an important role of the Warburg effect demonstrated by RCC in the development of treatment resistance. Furthermore, unlocking the metabolic pathways associated with this phenomenon may be the key to a novel therapeutic approach in the treatment of RCC.

Kennell, Timothy Irving, Jr. (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Selvarangan Ponnazhagan

Abstract Approved By Advisor: Yes

Co-Authors:

Title: A Novel Approach to Targeted Gene Therapy

The adeno-associated virus (AAV) has become increasingly useful as a vector for gene therapy due to its site-specific integration, low immunogenicity, and wide range of tissue hosts. However, one of the major disadvantages of AAV is that, even though eleven serotypes have been discovered, all have general non-specificity for tissue infection. Recently, several systems have been developed for creating targeted gene therapy with the AAV, including the use of bispecific antibodies, biotin-avidin ligand linkers, and recombinant AAV coat proteins conjugated to antibodies specific for tissue type. However, all of these methods are either complex in their development or modify the AAV coat proteins, creating undesirable effects. Our objective was to characterize the epitope of a 37 kDa single-chain fragment antibody (scFv) that binds to an AAV coat protein for use in building a linker between the AAV and the tissue type. Use of a ligand bound to the scFv specific for the tissue type could allow AAV tissue targeting. Specifically, the bacterial cell line XL1 Blue was used to express, via IPTG induction, the scFv gene that had been cloned into the pOPE101 vector. However, multiple attempts yielded no scFv expression based on comparison between uninduced and induced cells in a SDS-PAGE. Therefore, the plasmid that contained the scFv gene was restricted in order to confirm the gene's presence and was then transformed into an alternate cell line BL21 (DE3), an *E. coli* strain specifically designed for high yield protein expression. The c-Myc tag that was engineered into the vector for recombinant protein detection was used for a western blot. However, the results showed non-specific binding of the antibody to a protein approximately 37 kDa in both uninduced and induced cells, indicating no expression of the scFv.

Killian, John Thomas, Jr. (MS2)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Alan Percy

Abstract Approved By Advisor: Yes

Co-Authors: Jane Lane, Alan Percy

Title: Pubertal Development Deviates from Norm in Rett Syndrome

Background: Rett syndrome, a unique neurodevelopmental disorder that affects approximately 1 in 10,000 live female births, is associated with reduced height, weight, and BMI overall.

Objectives: The aim of this study was to characterize pubertal trajectories in a population of females with Rett syndrome. Our hypothesis was that pubertal trajectory deviated from the general female population: onset of puberty was early and menarche was delayed.

Methods: To assess pubertal trajectory, we used data from the Rett Natural History Study, and performed survival analysis on the milestones of thelarche, adrenarche, and menarche, Cox proportional hazard analysis to study the relationships between BMI, mutation type, and pubertal milestones, and Chi-squared analysis to analyze pathway synchrony.

Results: Over one-fourth of participants initiated puberty early, before the age of 8. Menarche was delayed compared to the general female population with the median age being 13.0 years. The median length of puberty, from thelarche to menarche was 3.9 years, also greater than the interval typically seen in the general female population. Higher BMI was associated with early adrenarche and thelarche, but not menarche.

Mutation type was not related to pubertal trajectories. 52% of participants entered puberty in synchrony, 15% led with thelarche, and 32% led with adrenarche, a finding that also differs from that in females generally.

Conclusions: Pubertal trajectories in Rett syndrome differ from those in a normal population, entering puberty early and reaching menarche later. As expected, BMI predicts pubertal timing; however, it is less clear that specific mutations may affect the neuroendocrine pathology of Rett syndrome.

Kulkarni, Abhay Krishnaji (MS4)

Project Length: Short

Prior Research Experience: No **Source of Funding:**

Faculty Advisor: Chris Pruitt

Abstract Approved By Advisor: Yes

Co-Authors: Pallavi Ghuge, M.D.; Chris Pruitt, M.D.; Michele Nichols, M.D.

Title: Unintentional Opioid Poisoning in the Pediatric Population

Background: Opioid medications, prescribed for their analgesic properties, have numerous adverse effects such as vomiting, drowsiness, respiratory depression, and even death. Unfortunately, improper storage or therapeutic errors can lead to unintentional overdose. Currently, there is limited descriptive data about unintentional opioid ingestions presenting to the emergency department (ED).

Purpose: The purpose of this retrospective epidemiologic study was to describe unintentional opioid exposures in children 0-6 years of age reported to the regional Poison Control Center (PCC) over a three-year period.

Methods: Information was collected from the database of the Birmingham, Alabama PCC from July 2010 to June 2013. Data included patient age, gender, ingested drug, presence of symptoms, ED referral, therapeutic interventions, and in-hospital outcomes.

Results: Four hundred thirty one patient charts met inclusion criteria. Fifty seven percent of patients were male and 43% were female. One hundred forty (32%) patients were symptomatic and 113 (80%) of these symptomatic patients presented to the ED. A total of 235 (55%) patients were seen in the ED. In the ED, 152 (66%) patients required observation only, 9 (4%) patients received oxygen, 29 (12%) patients received intravenous fluids, 30 (13%) received naloxone, and 41(17%) patients were treated with activated charcoal. One hundred sixty one (69%) patients were discharged directly from the ED, while 65 (28%) patients were admitted to the hospital. Disposition for three patients was unable to be obtained from the documentation. There were no fatalities.

Conclusion: Unintentional opioid exposure in young children is a frequently encountered problem. While most cases are referred for emergency evaluation, these patients do not usually require therapeutic intervention, and most are discharged from the ED. Admitted patients generally have favorable outcomes.

Kumar, Sandhya Lekshmi (MS3)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Andrea Cherrington, MD MPH

Abstract Approved By Advisor: Yes

Co-Authors: Jeremy Walker (MS3); Dr. Amanda Willig, PhD; Dr. Dennis Pillion, PhD

Title: "Examining Perceived Barriers to Good Nutrition in Birmingham's Urban Homeless Women"

Background: Poor health is well-recognized for its relationship to homelessness as both a cause and an effect. Many of today's food-insecure homeless suffer from obesity-related complications, including hypertension and diabetes. Homeless individuals who regularly access meals provided by charitable services are at the mercy of well-meaning food-providers, and seemingly have minimal control in their food choices. The main aim of this study is to identify perceived barriers to good nutrition in a subset of Birmingham's homeless.

Methods: In this mixed-methods study, 11 women in a transitional housing program took part in a semi-structured interview focused on perceived barriers to good nutrition and an 83-item questionnaire on demographics, health status, extent and accuracy of nutrition knowledge, food security, and determinants of healthy food choices. Another 38 women recruited from the same institution's "Day Center" participated in the survey alone.

Results: Mean age category is 41-50 years. 20% report diagnosis of diabetes and 53% report hypertension. Data analysis reveals a significant relationship between self-reported health status and dietary intake. 63% of participants express a desire for a "special diet", 81% citing for health concerns. Thematic analysis of interview scripts reveals food concepts (good versus bad foods, utility versus consequences), desired nutrition knowledge (food budgeting, how to shop, components of food), and influences on food choices (availability, access, competing demands, social reciprocity).

Conclusion: This subset of homeless experiences a high rate of hypertension and diabetes. Many desire more information and more control over what they eat. Nutrition-based education and lifestyle modification is a practical and desired avenue of chronic disease management in this population. Life-skills courses focused on nutrition education involving practical shopping and preparation skills appropriate for the individual's living context is an investment that will help redefine concepts of food and benefit health status, financial status, and future generation's health-promoting behaviors.

Landham, Jonathan Barton (MS4)

Project Length:	Intermediate
Prior Research Experience:	No
Source of Funding:	Departmental or Mentor Funds
Faculty Advisor:	Duraid Younan
Abstract Approved By Advisor:	Yes
Co-Authors:	Duraid Younan, Russell Griffin, Jerry Bradley, Donald Reiff, Loring Rue, III
Title:	Penetrating Limb Injuries: A 5 year Retrospective Analysis from a Level 1 Trauma Facility

Introduction: Penetrating limb injuries (PLI) commonly result from firearm, industrial, and stabbing incidents. However, little information is available regarding the functional outcome, mean hospitalization, and mortality of these patients. Presented is a five year retrospective analysis on PLI from a level 1 trauma facility.

Methods: A retrospective analysis was conducted on 1,218 patients presenting with penetrating limb injuries from 2005 – 2009. Information collected included year of injury, sex, race, age, mechanism, associated injuries, ISS, hospital stay, mortality, insurance, and functional outcome. Patients without the required components were excluded. The data was analyzed utilizing ANOVA and chi-square test for continuous and categorical variables respectively. Mortalities were reviewed to determine cause and location.

Results: A majority of the patients with PLI were male (86.7%) with an average age of 34.2 ± 12.1 years. The most common mechanism of injury was firearm assault (60.1%) followed by stab assault (16.7%) with an average ISS of 10.4 ± 11.3 on admission. Location was evenly divided between upper and lower extremity at 45.2% and 42.3% respectively, with 12.6% of the patients sustaining insults to both. The average hospital stay was 6.4 ± 13.5 days and was not significantly different among types of trauma ($p=0.7769$). Overall mortality irrespective of mechanism and associated limb was 5.3%, with 83.5% of patients being discharged to home. Functional outcome scores at discharge for upper, lower, and combined extremity were 11.6 ± 1.0 , 11.3 ± 0.8 , and 11.2 ± 1.2 respectively ($p < 0.001$). Mortality (5.3%) was rare, 58% of that due to exsanguination from other injuries. Only 4.8% of patients required amputations, and less than 10% required a vascular operation.

Conclusions: The mean ISS, functional outcome, and length of hospitalization differed little between upper, lower, or combined extremity injuries. Most patients were discharged home with good functional capacity. Overall morbidity and mortality were low, the majority expiring by exsanguination from associated injuries.

Langston, Bradley Robert (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Lawrence Sincich

Abstract Approved By Advisor: Yes

Co-Authors: Bradley Langston, Kady Bruce

Title: Contribution of intraretinal scatter to single photoreceptor threshold discrimination

Background: The purpose of this research is to increase our understanding of how individual cone photoreceptors contribute to overall visual perception. Using an adaptive optics scanning laser ophthalmoscope (AOSLO) outfitted with separate imaging and stimulation channels, we measured increment thresholds when cone-sized stimuli were delivered to individual photoreceptors. It is not known whether responses to these stimuli are influenced by immediately surrounding cones. Our experiments seek to uncover if intraretinal scatter of light onto these surrounding cones contributes to a subject's threshold performance.

Methods: A group of 8-10 cones are spectrally identified as long-, medium-, or short-wavelength sensitive using specific wavelength stimuli and background conditions that elicit responses from only one spectral type of cone. Once a group is identified by spectral type, the threshold of two of the cones situated in the middle of the group are measured using a staircase procedure, and these thresholds are analyzed in the context of their respective surrounding cone compositions.

Results: We have characterized multiple cone clusters by spectral type and are now poised to compare the thresholds of cones surrounded by mixtures of cone types.

Conclusion: We have shown that cones are identifiable by their spectral type using an AOSLO and have evidence that stimulation is cone specific. Further experiments will reveal the contribution of surrounding cone types to the threshold measured at single cones.

Lantrip, Brittney Renee (MS2)

Project Length: Intermediate **Prior Research Experience:** Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Meredith Hitch

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Kimberly Coveney

Title: Epidemiology of Pediatric Inflammatory Bowel Disease- A tertiary Pediatric Hospital Experience from 2000-2010

Background: Inflammatory bowel disease (IBD) is a condition characterized by chronic inflammation of the digestive tract, which includes ulcerative colitis and Crohn's disease. Ulcerative colitis and Crohn's disease are thought to develop from genetic and environmental factors that influence the host immune system. Epidemiological studies have previously shown that the incidence of IBD is greatest in northern areas, and that smoking and appendectomy are a deterrent to ulcerative colitis yet a risk factor to developing Crohn's disease.

Objective: To our knowledge, this is the first study of the epidemiology of Pediatric IBD in the state of Alabama. We aimed to investigate the environmental, demographical, and geographical associations with the incidence of IBD to further understand the interplay between risk factors, known and state specific, and the occurrence of IBD in the children of Alabama and our referral territories.

Methods: ICD-9 code search for "IBD, ulcerative colitis, Chrons disease, and indeterminate colitis," identified 498 patients in the Children's Hospital of Alabama health system electronic medical records between the years 2000-2010. From a retrospective chart review, we gathered information about geographic locations, demographics, diagnostics, comorbidities, and treatments of the 498 patients with confirmed IBD.

Results: Our preliminary data suggests that certain environmental exposures, such as eosinophilia and microbial infection, induce an immune response predisposing patients to IBD.

Conclusions: This project aims to identify potential environmental "hot spots" for IBD in Alabama.

Laufer, Vincent Albert (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Jonas Almeida and Dr. Robert Kimberly

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Reclassification of Autoimmune Disease by Applying Machine Learning Algorithms to Genetic Variants used as Essentially Bayesian Priors

Nearly a decade of Genome Wide Association Studies (GWAS) has succeeded in demonstrating variants associated with a colorful variety of complex diseases, among them aetiologically complex idiopathic autoimmune conditions like Rheumatoid Arthritis (RA) and Systemic Lupus (SLE). Despite the limitless possibilities for powerful forms of statistical analysis, in practice these large-scale studies are most often analyzed using a single-SNP-association approach. Paradoxically, this approach is neither the most statistically powerful nor well-suited to ask certain biological questions, for example “who will get Lupus?” As such, the number of studies focusing on biological pathways or the single human genome as a relevant level of analysis lags far behind such SNP-centered foci.

We hypothesize that the use of Machine Learning algorithms founded on certain forms of Bayesian and Frequentist statistics will enable diagnosis of autoimmune conditions such as Systemic Lupus Erythematosus or Rheumatoid Arthritis in advance of the first clinical symptoms.

In order to test this hypothesis, we plan to several large datasets on RA and SLE. The first approach is to take all the known variants associated with RA and SLE (compiled from GWASCentral.org, ClinVar, dbSNP, and dbGAP). Both supervised and unsupervised learning algorithms will then be used to classify people into “Disease” or “Control.” Future approaches will consider a greater number of SNPs, and a long-term goal is to classify any genome into “high risk of autoimmune disease” or “low-risk.” Along the way, we will remain open-minded with respect to what the term “SLE” or “RA” might actually mean.

As the amount of Immunochip, GWAS, and NextGen data begins to accumulate on dbGAP, we anticipate that this approach could provide clinicians with low-cost means by which to diagnosis autoimmune and related diseases greatly.

Related research goals include use of microarray data and adjacency matrices to model biological networks more accurately than literature curation can.

LeGrand, Jason Nathaniel (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Christopher Klug

Abstract Approved By Advisor: Yes

Co-Authors: Stephanie C. Heidemann, C. Scott Swindle, and Christopher A. Klug

Title: Identification of cytogenetically normal human CD34+CD38- hematopoietic stem/progenitor cells from inv(16)+ leukemic bone marrow

Transplant experiments of primitive CD34⁺CD38⁻ bone marrow cells from leukemia patients into immunodeficient mice have shown that leukemogenic mutations are often present at the hematopoietic stem/progenitor cell level and that these cells can function as leukemia-initiating cells (LIC). A significant challenge to understanding and targeting these cells has been that LIC share many of the same cell-surface markers as their normal counterparts, thus making it difficult to purify and functionally characterize this important leukemic subset from bulk bone marrow. To directly identify cell-surface markers that are differentially expressed on the LIC of the inv(16) subtype of acute myeloid leukemia (AML), we first used Affymetrix microarray to identify changes in cell-surface proteins on highly purified murine hematopoietic stem cells (HSC) that transiently expressed the inv(16) fusion protein for 24 hours. Changes in mRNA expression were then validated at the protein level using flow cytometry. With this approach, we were able to identify significant changes in the cell-surface expression of a number of proteins, including CD55, CD200R, FceRI, CD27 and CD93. These changes were validated on FACS-purified HSC isolated from mice reconstituted with cells expressing the inv(16) fusion protein from a retroviral vector. Importantly, many of the expression changes noted on murine HSC were not observed on human bone marrow CD34⁺CD38⁻ cells isolated from inv(16)⁺ bone marrow samples. Analysis of a number of additional markers found differentially expressed on human AML bone marrow samples showed that TIM-3 and CLL-1 could significantly enrich for a population of CD34⁺CD38⁻ cells that lacked the inv(16). These results have important implications for therapeutic targeting of inv(16)⁺ hematopoietic stem/progenitor cells in patients with relapsed and refractory disease and for purification of normal HSC from leukemic bone marrow samples.

Lester, Davis Page (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Fadi Hage

Abstract Approved By Advisor: Yes

Co-Authors:

Title: The prognostic value of transient ischemic dilation of the left ventricle with regadenoson myocardial perfusion

The work ups for cardiac patients with chest pain thought to secondarily to CAD usually involve a stress test. These tests may provide evidence to suggest that these pains are related to cardiac problems. Exercise stress testing is the preferred method; however, sometimes this is not an option (e.g., when you think the patient is unable to exercise or when you don't think they can reach 85% of their age – predicted heart rate and five metabolic equivalents). In these cases drugs are used to conduct the test. The classically used drug is adenosine but regadenoson is a new drug being used that is more selective therefore having less side effects . Secondly transient ischemic dilation (TID) is a good predictor of poor outcomes for cardiac patients. TID is measured by dividing the diameter of the left ventricle during stress by the diameter of the left ventricle during rest. Little research has been conducted concerning the regadenoson stress test and those patients who appeared to have TID. Dr. Fadi Hage's laboratory is trying to demonstrate the outcomes of patients that had a TID with regadenoson stress test at UAB in July of 2008 to March of 2009. We hypothesized that TID with regadenoson will add to the prognosis derived from stress testing. We also tested the hypothesis that TID will only be associated with increased risk if it occurs in conjunction with abnormal myocardial perfusion. To achieve this outcome images were retrieved from an archive and analyzed using the 4DM-SPECT. Also certain variables were extracted from patient records such as patient demographics, heart failure, comorbidities, prior percutaneous coronary intervention and coronary artery bypass grafting. The impact of this study will be that it could add to what cardiologists learn from a pharmacological stress test performed with regadenoson.

Lever, Jeremie Matthew (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Michael Niederweis

Abstract Approved By Advisor: Yes

Co-Authors: Axel Siroy

Title: Mycobacterium tuberculosis nanocompartments and copper toxicity resistance

Mycobacterium tuberculosis (Mtb) has the highest mortality rate of any bacterial pathogen worldwide. In 2011, tuberculosis caused 1.4 million deaths. Mtb must maintain levels of oxidative nutrients, such as copper, which are vital for growth but are toxic at high concentrations. Macrophages phagocytose Mtb, where the engulfed pathogens are subject to oxidative stress. One strategy of the oxidative macrophage response to Mtb infection is to raise copper concentration in the phagosome to toxic levels. Mycobacteria possess a gene encoding a Dye-decolorizing Peroxidase (DyP), a member of a class of heme-containing peroxidases that may be involved in oxidative stress response. In Mtb the gene dyP is localized in an operon with cfp29 (Culture Filtrate Protein of 29 kDa). The encapsulin, a homolog to CFP29 found in Thermotoga maritima, oligomerizes into nanocompartments likely involved in redox metabolism. The presence of a homologous gene in Mtb suggests that it may utilize a similar nanocompartment. It has been proposed that DyP and CFP29 together form a functional nanocompartment and play a role in Mtb resistance to copper-related oxidative stress during phagocytosis. We investigated the link of these proteins to copper metabolism in Mtb. I cloned the dyP-cfp29 operon of Mtb into an extrachromosomal vector, under the control of the inducible Acetamidase operon. The genes were conditionally expressed in *Mycobacterium smegmatis*. I tested the viability of *M. smegmatis* harboring these genes in the presence of increasing amounts of copper sulfate using a drop assay on agar plates. The recombinant strain expressing DyP and CFP29 showed a growth advantage over wild type when challenged with copper. I undertook the cloning of the genes encoding DyP_{Mtb} and CFP29_{Mtb} into *Escherichia coli* overexpression vectors with the goal of producing recombinant protein for the generation of polyclonal antibodies. I was able to purify recombinant DyP_{Mtb} to 72% purity.

Lewis, Lauren Elizabeth (MS4)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. ML White

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Nancy Tofil

Title: 3rd Year Resident Self Reporting of Lumbar Puncture Success in Attempt to Quantify Baseline Success Rates

Background: Pediatric residents have not been well studied when it comes to competency in procedural requirements. Depending on the program, there is a wide variability when it comes to which procedures are considered important.³ For lumbar puncture alone, there are very few studies for residents that clearly indicate preferred methods and techniques to assure the highest success rates. In 2009, members of Pediatrics Outcomes in Simulation Education (POISE) developed comprehensive training and evaluation of interns performance of lumbar punctures³. This study found that interns who are documented to be competent in initial training and just-in-time refreshers are more likely to have procedural success. However, the average success rate for first time LP in this population is 37%.

Objective: The goal of this survey was to quantify 3rd year resident success rates of performed lumbar punctures as well as to assess which lumbar puncture techniques were preferred for the residents at 10 participating sites.

Description / Methods: We conducted a survey-based inquiry of 23 upper level pediatric residents to explore their experience both supervising and performing infant and other pediatric lumbar punctures throughout the three years of residency. This survey asked if they participated in a lumbar puncture training course as a PGY1 and whether or not they found that the training was helpful. We also asked to upper levels to breakdown the number of lumbar puncture attempts by residency year, the age of the patient, and whether they were directly supervised for each procedure. Inquiries were made regarding their most recent infant LP about whether anesthesia was used and which type, the quality of the CSF fluid obtained, and whether family members were present. We questioned them about patient positioning, who was assisting in holding the patient, and stylet technique. Lastly, we asked them to assess their performance and whether or not they felt prepared for the procedure. This survey was seeking to quantify baseline success rates for this cohort.

Evaluation / Results: Seventeen out of 23 upper level pediatric residents completed the survey. The average number of lumbar punctures performed intern year was 22.88, average during PGY2 year was 15.35, and average during PGY3 year was 12.24. Of the total number punctures, the residents averaged 38.12 infants, 8.76 children, and 3.06 adults. The assessment in the confidence of infant lumbar punctures, 16 of 17 were confident in their ability. The residents were asked to provide details on their most recent lumbar puncture and described an overall success rate of 87% (82% were not supervised). It was found that half of this surveyed group used anesthesia and of that group, 67% used topical anesthesia. There was no family present during the procedure for 81% of the surveyed group. Only 1 out of 17 preferred the patient in a sitting position and 94% used the early stylet removal technique. Overall, 87.5% of the upper level residents felt they were proficient in clinical infant lumbar punctures.

Discussion/Reflection: Upper level pediatric residents were found to be confident in their ability to perform infant lumbar punctures. This confidence is probably due to the volume of opportunities to practice and perfect

this procedure in this age group. Reported success rate for these PGY3 residents is 87%. The optimum combination of training and refreshers has likely not yet been achieved.

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Li, Zan Catherine (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Judy Creighton, Ph.D.

Abstract Approved By Advisor: Yes

Co-Authors: Paul Wolkowicz, Ph.D.

Title: Transient Receptor Potential (TRP) proteins: Novel targets of AMP-activated Kinase in pulmonary endothelial barrier function

Introduction: Maintaining tight contact among vascular endothelial cells (EC) is critical for blood vessel patency as loss of contact increases vessel permeability, causing edema. While adenosine monophosphate-activated protein kinase (AMPK) regulates and maintains cell energy homeostasis, we have shown that EC cell-cell network formation also requires AMPK. We sought to identify how AMPK might influence the important physiological task of maintaining EC barrier integrity.

Hypothesis: Calcium signals arising from the plasma membrane are critical for maintaining or disrupting EC barrier integrity. TRP proteins are transmembrane ion channels that generate most cell calcium signals. Thus our hypothesis states that AMPK phosphorylates one or more TRP as part of the process of EC barrier repair and/or injury.

Approach & Results: Two studies tested our hypothesis.

(i) Analysis of amino acid sequences of canonical (TRPC) and Vanilloid TRP (TRPV) using the MotifScan algorithm revealed conserved likely AMPK phosphorylation sites at serine residues S24TRPC1, S195TRPC4, and TRPV4 S162 and S319. Algorithm-identified TRP sites exhibited comparable stringency for phosphorylation as HMG-CoA reductase and Acetyl-CoA carboxylase, known targets of AMPK.
(ii) RT-PCR analysis of pulmonary artery (PA), microvascular (PMV), and smooth muscle (PVSM) cell total RNA demonstrate that PAECs and PMVECs express TRPC1 and TRPV4. By contrast, only PVSMCs express TRPC4. Western blot analyses verified these results.

Conclusions & Future Studies: ECs express TRPC1 and TRPV4 which may generate calcium signals important in EC barrier function. Both transporters are promising targets of AMPK.

We have established an immunoprecipitation protocol for TRPV4 and are completing one for TRPC1. We will then use (i) back-phosphorylation to establish whether these two channels are AMPK targets, and (ii) site-directed mutagenesis to assess how their phosphorylation by AMPK affects EC barrier function.

Lin, Helen (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Richard Allman; Dr. Patricia Sawyer
Abstract Approved By Advisor:	Yes
Co-Authors:	Richard M. Allman MD; Patricia Sawyer PhD; Richard E. Kennedy MD, PhD; Michael Crowe PhD; Courtney P. Williams MPH
Title:	The Association Between Health Literacy and Medication Self-Management in Community-Dwelling Older Adults

Only 1% of adults aged 75+ have proficient health literacy. Despite associations between low health literacy and worse health outcomes, few studies have examined it among community-dwelling adults aged 75+. This study examines the association between health literacy and medication self-management among community-dwelling adults aged 75+. Medication self-management difficulty (MSMD) was determined as self-reported receipt of assistance with medications. Health literacy was assessed using the revised Rapid Estimate of Adult Literacy in Medicine (REALM-R) and two single-item questions (SIQs) about filling out medical forms (SIQ1) and reading medical documents (SIQ2). Sociodemographics and health measures were also collected.

Multivariable logistic regression analyses were conducted to examine the significance and independence of the association between inadequate health literacy and MSMD. The study participants ($N = 395$; 33% African-American, 57% female) had a mean age of 81.6 ($SD = 4.7$) with 19% having MSMD. Comparing persons receiving medication assistance versus those not receiving assistance, the mean REALM-R (SD) was 3.9 (3.2) versus 6.4 (2.5); 60.0% versus 18.1% were not confident filling out medical forms alone; and 76.0% versus 21.6% needed help reading medical information ($p < 0.001$ for all 3 measures of health literacy).

Controlling for sociodemographics and health, the REALM-R, SIQ1, and SIQ2 each remained significant and independent correlates of MSMD ($p = 0.016$, 0.003 , and <0.001 respectively). For each point lower REALM-R, participants were 16% more likely to report MSMD ($OR (95\% CI) = 0.84(0.73, 0.97)$). The area under the curve (AUC) of the receiver operating characteristic (ROC) of the 3 measures were comparable (REALM-R = 0.876, SIQ1 = 0.879, SIQ2 = 0.892). After controlling for sociodemographics and health, older adults with inadequate health literacy were more likely to have MSMD. The SIQs are a viable alternative for clinical health literacy screening and, unlike the REALM-R, can be easily incorporated into a social history.

Lockhart, Jonathan Russell (MSTP)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	NIH Medical Scientist Training Program
Faculty Advisor:	Thomas M. Ryan
Abstract Approved By Advisor:	Yes
Co-Authors:	Yongliong Hou and Thomas M. Ryan
Title:	Allogeneic Bone Marrow Transplantation Without Cytoreductive Conditioning to Cure Cooley's Anemia

β -thalassemia is a heterogeneous group of inherited blood disorders marked by defects in β -globin chain production. Cooley's anemia (CA), or β -thalassemia major, is the most severe form of the disease and results in a complete absence of β -globin and thus the major adult hemoglobin (HbA). Currently, allogeneic hematopoietic stem cell transplantation (HSCT) is the only cure for CA. Successful HSCT requires a non-affected, HLA-matched hematopoietic stem cell (HSC) donor. Furthermore, the procedure entails potentially lethal myeloablation and immunosuppression, which carry a high risk of complications. High-risk patients only have a 53% chance of event free survival of this procedure; adverse events include death, graft rejection (GR), graft versus host disease (GVHD), and infection.

Our lab has developed a preclinical humanized mouse model of CA in which novel transplantation methodologies can be tested. In this model the adult mouse α -globin and β -globin genes have been replaced with human α -globin and a human α - to α^0 -globin hemoglobin switching cassette, respectively. These mice survive on 100% human fetal hemoglobin (HbF) at birth before completing their fetal-to-adult hemoglobin switch post-natally to their nonfunctional α^0 -globin allele at which time they succumb to their lethal anemia at around two weeks of age.

We hypothesized that by exploiting the naivety of the newborn immune system and survival advantage of healthy donor erythroid cells, stable HSC engraftment could be achieved by transplant in a non-conditioned neonate. In this study, HSCT was performed on neonatal humanized CA mice in the absence of any cytoreductive conditioning. We show that the low levels of donor hematopoietic chimerism achieved were sufficient enough to rescue the animals from their lethal anemia with no evidence of GVHD. Importantly, donor derived RBC and hemoglobin levels were over 90 and 95%, respectively. These experiments are the first steps in developing safer therapeutics for patients with CA.

Locy, Morgan Lee (MSTP)**Project Length:** Short**Prior Research Experience:** Yes**Source of Funding:** NIH Medical Scientist Training Program**Faculty Advisor:** Anupam Agarwal

Abstract Approved By Advisor: Yes

Co-Authors: Subhashini Bolisetty and Anupam Agarwal

Title: Heme Oxygenase 1 Deficiency Exacerbates Cisplatin Induced JNK Activation in Kidney Proximal Tubule Cells

Acute tubular necrosis is one of the most common causes of acute kidney injury and is characterized by proximal tubular epithelium necrosis. Cisplatin, a commonly used chemotherapeutic agent, causes dose-dependent nephrotoxicity by accumulating in the proximal tubule cells (PTC). Heme oxygenase 1 (HO-1), a protective antioxidant, is induced by cisplatin in the kidney. The present study tests the hypothesis that cisplatin causes c-Jun N-terminal kinase (JNK) activation that is exacerbated by HO-1 deficiency in PTC. WT and HO-1 deficient (KO) murine transformed PTC were seeded at equal densities and treated with 50 μ M cisplatin or vehicle for 0.5-48 h. Cell protein lysate was collected at the respective time point and assessed by western blot. JNK activation assessed by phospho-JNK protein expression was observed as early as 1 h post cisplatin treatment and sustained through 24 h in both WT and HO-1 KO cells. In comparing WT and HO-1 KO cisplatin-treated PTC at 2, 4, and 24 h, a 2.24-fold ($n=2$), 1.47-fold ($n=3$), and 1.19-fold ($n=3$) increase in phospho-JNK expression was observed respectively. Cleaved caspase 3 expression was increased in HO-1 KO compared to WT PTC 24 h post cisplatin treatment. In preliminary experiments, activation of p38 assessed by phospho-p38 expression was not altered in WT or HO-1 KO cisplatin-treated PTC. In conclusion, these studies support that JNK activation and apoptosis signaling occurs in PTC treated with cisplatin. Additionally, these studies support that HO-1 upregulation is vital in attenuating both JNK activation and apoptosis during cisplatin toxicity. These studies further support the idea that HO-1 targeted therapies could yield substantial clinical benefit in preventing cisplatin-mediated nephrotoxicity.

Lopker, Michael John, Jr. (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: George Shaw

Abstract Approved By Advisor: Yes

Co-Authors: Maness, NJ; Li, H; Warrier, RJ; Wang, S; Vidnovic, K; Kreider, TF; Hahn, BH; Watkins, DI; Veazey, RS; Shaw, GM.

Title: Cryptic Epitope in the 5' Leader of SIVmac239

Background: Studies in rhesus macaques have defined the activity and temporal associations of the expansion of cytotoxic T-lymphocyte (CTL) responses to the decline in peak viremia between 3-4 weeks post infection (w.p.i.). The breadth and magnitude of CTL responses to MHC-1 restricted peptides across the viral proteome are believed to be important in constraining viral replication. Recently, our laboratory made the surprising discovery in ten out of ten Mamu-B*29 macaques acutely infected with SIVmac239, of a novel site of hypermutation and rapid virus selection in the 5' leader. The 5' leader is the most highly conserved region of the viral genome and serves critical viral functions including RNA dimerization, packaging, and transcriptional and translational regulation. Here, we show evidence for a cryptic epitope in this essential region that is selected against by CTL's as early as 4 w.p.i.

Methods: We used single genome sequencing (SGS) to perform a detailed molecular analysis of viral hypermutation across longitudinal time-points in SIVmac239 infected macaques.

Results: By 4 w.p.i. greater than 97% of the viral sequences demonstrated striking hypermutation in stem loop 1 (SL1) of the 5' leader, and by 12 w.p.i. a majority of the viral sequences had purified to a single best mutation. Hypermutation was only seen in animals with the Mamu-B*29 allele, suggesting selection is MHC restricted and allele specific. The timing, pattern, and concentration of nucleotide substitutions within a potential 9mer peptide suggests CTL selection.

Conclusions: SGS is uniquely suited to follow immune escape over time and provides strong evidence for early CTL pressure in Mamu-B*29 rhesus macaques, leading to hypermutation and escape in a cryptic epitope in the 5' leader of SIVmac239. We have observed similar, discrete regions of hypermutation across the 5' leader of SIVsmE660, diverse natural SIVsmm lineages, and HIV-1 patients suggesting that peptide expression from the 5' leader is a ubiquitous feature of primate lentiviruses. These results expand the number of epitopes potentially contributing to SIV and HIV containment to the most highly conserved region of the genome.

Luckie, Cory Allen (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Adrienne Milner

Abstract Approved By Advisor: Yes

Co-Authors: Adrienne Milner, Elizabeth Baker, Ashley Sanders, Zachary Sanders

Title: Walking buses for adults: a pilot program to decrease obesity.

OBJECTIVE: Our aim is to create a community walking bus program and to evaluate the effects of this program on obesity by monitoring participants' physical activity levels.

METHODS: This summer, we conducted a survey that was confined within a 2-mile radius of The University of Alabama at Birmingham. Surveys were distributed both electronically and physically in mailboxes. The survey included questions that aim to determine the specific motivations for participating or not participating in this study. Also, the survey included questions that will help determine the best routes for the program. Lastly, the survey collected general demographic data. The second phase of the study will include 50 willing participants whose physical activity will be monitored over a 6-month period. Physical activity will be measured by a pedometer and will be quantified by the number of steps taken per week. Also, biweekly physical measurements and BMI calculations will be taken to track the physical changes that arise due to the increase in physical activity. The final phase of the survey will be to assess how race/ethnicity impact the effect of walking buses. Motivations, monetary incentive, and physical changes will be compared between different race/ethnicity groups.

RESULTS: At this time, phase one of the study is still in progress. Data analysis of the surveys is underway and reports are expected soon. We expect to gather at least 50 participants for the pilot study.

CONCLUSIONS: We hope to find an improvement in the physical activity levels and obesity levels of the participants. Also, we hope to create habits that will continue to improve these factors after the study is completed.

Luke, Elizabeth Waud (MS4)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Nancy M. Tofil, MD
Abstract Approved By Advisor:	Yes
Co-Authors:	Marjorie Lee White, MD, MPPM, MEd, Dawn Taylor Peterson, PhD
Title:	Pediatric Resident Survey of their Self-Perceived Competency and Knowledge Regarding Anaphylaxis and Epinephrine Auto-Injectors

When reflecting on ways to improve patient care and resident training, there is no formal way to assess what trainees know regarding anaphylaxis treatment and the use of epinephrine auto-injectors. Residents need to understand how auto-injectors work and details about the medication so they may effectively treat patients in an acute situation as well as effectively educate patients, families and peers on the use of auto-injectors. This survey is the first step towards understanding knowledge gaps that may exist among Pediatric Residency trainees regarding anaphylaxis treatment. Pediatric residents were asked to complete an anonymous paper survey containing 29 multiple-choice questions. Frequency of answers to each question was calculated and aggregate results were compared using variables such as level of training, trainees' confidence in their answers, and type of training (Pediatrics or Medicine-Pediatrics). Seventy Pediatric Residents completed the survey including 26 PGY-1s, 14 PGY-2s, 10 PGY-3s and 20 recent residency graduates. The results of this survey indicated knowledge gaps in Pediatric Residency trainees regarding treating anaphylaxis with epinephrine. Statistical analysis showed average test scores of trainees positively correlated with the length of time they had spent in training, with an overall correct average of 40% +/- 20% ($p=0.061$). The results of the survey showed no statistical difference between those being trained in Pediatrics versus combined Internal Medicine-Pediatrics training. Fifty-four percent of the respondents reported experiencing confusion regarding the dosing of epinephrine during an anaphylaxis event. Only 34% of residents knew that an anaphylactic reaction would not automatically result in the calling of a code. These preliminary findings suggest interventions such as a training module or simulation sessions need to be implemented to help close the knowledge gaps that currently exist among Pediatric residents. Such training would likely improve the treatment of and education regarding anaphylaxis by Pediatric trainees.

Ma, Elizabeth Yean (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: W. Timothy Garvey

Abstract Approved By Advisor: Yes

Co-Authors: Qinglan Liu, W. Timothy Garvey

Title: Novel Small-Molecule Agonists of the Orphan Nuclear Receptor NR4A3 Increase Glucose Transport and Uptake in Skeletal Muscle Cells and Adipocytes

NR4A3 (also known as NOR1) is an orphan nuclear receptor that has been shown to promote insulin-stimulated glucose uptake in adipocytes through increases in insulin signaling and GLUT4 translocation. Additionally, insulin resistant rodent models were found to have reduced gene expression of NR4A3. Thus, NR4A3 may be a potential drug target for treatment of diseases related to insulin resistance. Previously, our laboratory screened 130,000 small-molecule compounds for potential NR4A3 activating ligands, and identified 430 with high activity. 33 of these were selected due to their unique chemical structures, and 3 of them (#12, 14, and 15) were discovered to significantly increase glucose transport activity and GLUT4 translocation in L6 muscle cells. Injection of these compounds in hyperglycemic db/db mice also showed improved glucose tolerance and insulin sensitivity. Since previous data indicated that #15 was toxic to cells at higher doses, we defined dose-response relationships to determine whether #15 could effectively stimulate glucose transport at doses that were devoid of cell toxicity. In L6 muscle cells, we observed that even small doses of #15 could effectively augment glucose transport in the absence of insulin (2.5-10 μ M) without evidence of cell toxicity. At these lower doses of #15, glucose uptake rates were further increased by insulin. We also assessed #15's effects on GLUT4 translocation and found a similar dose-responsive induction in L6-GLUT4myc cells, a muscle cell line expressing GLUT4 modified to contain an immunoreactive exofacial epitope. In further studies, we assess bioactivity of the 3 small molecule NR4A3 transactivators in adipocytes, another important cell type in metabolism. Our results show that all 3 increase glucose transport under basal conditions (i.e., in the absence of insulin), with statistically significant results recorded for compounds 12 and 15 ($p<0.05$). These findings constitute proof-of-principle that small molecule agonists of NR4A3 can augment glucose uptake into metabolically active cells, and underscore the significance of NR4A3 as a novel drug target for treatment of insulin resistance and Type 2 Diabetes.

Machemehl, Hannah Caroline (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. van Wagoner

Abstract Approved By Advisor: Yes

Co-Authors: Hook III, EW; Holman, K; Harbison, H., Eloppe, L.; Hellwege, S.

Title: Improving Patient Referral Partner Notification: Delivering a Sexual Health Centered Message

Partner referral is paramount to preventing transmission of sexually transmitted infections. Current standard of care offers a disease-centered education message to patients at the time of diagnosis, including an appeal to refer all recent sex partners to be screened. This study seeks to explore a novel, sexual- health centered education message in men diagnosed with urethritis. In this 1:1 randomized control trial, participants receive either a health-centered or disease-centered education message at the time diagnosis. Both the intervention and control groups listened to a brief counseling message, received printed information appropriate to their intervention, and completed a short survey. The primary outcome is intention to refer partners, as reported by patients immediately after hearing the education message. Current analysis shows no significant difference between the two groups (n=17). Secondary and tertiary outcome measures and analyses are still underway.

Mahdi, Elaa Mohamed (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Jeffrey Alten Abstract

Approved By Advisor: Yes

Co-Authors: Jeffrey Alten, MD; Santiago Borasino, MD; David Cleveland, MD;

Title: Mediastinal Infection in Children Undergoing Cardiac Surgery

Mediastinitis is a rare complication of cardiac surgery involving a median sternotomy. Although its incidence is thought to be between 0.2-3.3% of all cardiothoracic surgeries (small studies), it is associated with high morbidity and mortality. Currently, there is inadequate data regarding risk factors as well as limited data on the association of lymphopenia with post-operative mediastinal infection. Previous studies have limitations including single center studies, limited sample size, and non-specific focus just on post-operative mediastinal infections. The objective of this study was to describe the clinical characteristics of postoperative mediastinitis. The clinical characteristics include presenting signs and symptoms, most common pathogens, and management. The second objective was to determine whether lymphopenia is associated with worse clinical outcomes in patients with postoperative mediastinitis. It was hypothesized that in post-operative mediastinitis patients, lymphopenia is associated with delay in sternal closure, prolonged ICU and hospital stay, increased time on mechanical ventilation, increased mortality. A retrospective chart review was performed on patients under 19 years old diagnosed with mediastinitis following cardiac surgery between 2008-2012. Those with superficial surgical site infection only and transfers from outside institution with infection within 30 days of primary cardiac surgery were excluded. Patient data collected included patient demographics, pre-operative data, ICU length of stay before & after surgery, details about primary surgery, co-morbidities, presenting signs and symptoms, laboratory data (lymphopenia: <3000/microL), and therapy. The measured outcomes included length of ICU stay, length of hospital stay, time spent on mechanical ventilation, and hospital mortality (mortality due to mediastinitis). Expected results are increased length of ICU and hospital stay, longer duration on mechanical ventilation, and increased mortality in post-operative mediastinal patients. Additional expected results include worse outcomes associated with post-operative mediastinitis in patients with lymphopenia.

Manikonda, Neha Rao (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Marsha S. Sturdevant

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Nefertiti Durant

Title: Correlates of Condom Knowledge, Skills and Intent to Use Condoms in Incarcerated Adolescents

Purpose:

Incarcerated adolescents are at increased risk for exposure to sexually transmitted diseases and HIV due to their participation in high risk behaviors including sexual activity. Use of condoms decreases the risk of transmission of sexually transmitted diseases in this high risk, underserved population. Few studies have investigated correlates of condom knowledge, skills and intent to use condoms in incarcerated adolescents. The aim of this study to assess condom knowledge, attitudes and behaviors in a diverse population of incarcerated adolescents.

Methods:

Sociodemographic, psychosocial, and sexual behavior data were collected and analyzed on 1198 incarcerated adolescents ages 13-18 participating in an HIV/STI education intervention in a detention facility in Alabama. Univariate analyses, t-tests and anova tests were conducted. Items were taken from a newly created scale designed to assess condom attitudes, condom skills knowledge, and intent to use condoms in incarcerated adolescent populations.

Results:

Adolescent girls reported a higher intent to use condoms than adolescent boys $p = 0.033$. Beliefs about the use of condoms varied significantly by age and race ($p=0.003$ and 0.017 respectively). Anova tests showed that condom skills knowledge and positive beliefs about condom use increased significantly with age ($p<.05$, $p=0.003$ respectively).

Conclusions:

Differences in the intent to use condoms vary by gender and age. Incarcerated adolescent girls are more likely than boys to endorse the intent to use condoms. The intent to use condoms, condom skills knowledge and positive beliefs about condoms does increase with age. Future programs for incarcerated adolescents should explore developing innovative programs that target adolescent boys and younger adolescents to improve skills, knowledge and beliefs around condom use.

Mann, Steven Alexander (MS3)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Jill Adamski, MD, Ph.D.

Abstract Approved By Advisor: Yes

Co-Authors: Jill Adamski, MD, Ph.D.

Title: Therapeutic Apheresis use at UAB: A ten-year analysis

Therapeutic Apheresis (TA) consists of the separation of the blood into each of its components and the treatment or removal of the particular component implicated in the disease of the patient. Efforts to detail how TA is used, as well as the outcomes of such use, are both important and necessary. We have created a simple database and compiled basic information from all TA procedures scheduled at our center over a recent ten-year span. From January 1, 2003 to December 31, 2012, 1068 unique patients were treated by the transfusion medicine service at our institution. Over this period, 11,850 procedures were recorded. The number of patients treated with TA at our center has been trending up, with a low of 116 patients in 2003 and a high of 174 patients in 2012. About 55.1% of the procedures from 2003 to 2012 were therapeutic plasma exchange (TPE) and about 43.6% of them were extracorporeal photopheresis (ECP) procedures. The remaining three procedure types accounted for less than 2% each of the total number of procedures for the ten years. The most common indications for TPE, in order, were thrombotic thrombocytopenic purpura at 26.8%, myasthenia gravis (MG) at 16.5%, solid organ transplant rejection at 14.6%, focal segmental glomerulosclerosis at 7.2%, chronic inflammatory demyelinating polyneuropathy at 5.7%, and Guillain-Barre at 4.5%. In the ten-year span, ECP was used as a treatment type for four indications. In the more recent years, our TA center has significantly increased the use of TPE for MG, ECP for graft versus host disease, and red blood cell exchange for sickle cell patients. By analyzing the trends of TA use at our institution, we hope to validate continued TA services for current patients, contribute to a better understanding of current practices, and help discover new options for future patient populations.

Marks, Margaret Pollard (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Etty Benveniste

Abstract Approved By Advisor: Yes

Co-Authors:

Title: The Potential Role of JAK1 Inhibitor AZD3715 in Glioblastoma Therapy

The Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway is involved in activating genes important for inflammation, cell survival, and cell proliferation. Aberrant activation of the JAK/STAT pathway has been implicated in glioblastoma (GBM) progression. Despite surgical resection and aggressive treatment with chemotherapy and radiation, GBM patients have a median survival of only 12-15 months. We have evaluated the potential therapeutic effects of AZD3715, a pharmacologic JAK1 inhibitor, on the sustained activation of STAT-3 that is characteristic of GBM. The *in vitro* efficacy of AZD3715 was tested using the patient-derived GBM xenograft model, which consists of patient GBM tumors that are serially passaged in the flanks of immune compromised mice instead of cell culture. This method has been shown to retain the *in vivo* genetic alterations and invasive phenotypes seen clinically. STAT-3 is constitutively active in all of the xenograft tumors, but the level of activation varies, which is consistent with the heterogeneity of GBM. The xenograft tumors can be removed from the flank, disaggregated into cells and propagated as neurospheres for *in vitro* analysis. Herein, we found that AZD3715 treatment blocked constitutive and stimulus-induced STAT-3 phosphorylation as well as downstream gene expression in these xenograft tumors *in vitro*. Moreover, AZD3715 treatment resulted in a decrease in secretion of IL-6, a STAT-3 driven cytokine. To determine functional anti-tumor effects of AZD3715, proliferation assays were performed. We found that AZD3715 as a single agent only modestly inhibited proliferation of the xenograft cells. However, when combined with temozolomide (TMZ), a standard chemotherapeutic, or Gefitinib, a potent EGFR inhibitor, AZD3715 synergistically inhibited proliferation of the xenograft cells when compared to single agent therapies. Therefore, the effectiveness of AZD3715 in inhibiting STAT-3 activation as well the potential for combination therapies indicates that AZD3715 should be considered for the treatment of GBM patients.

Mathews, Eleanor Katherine Isbell (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Robert Russell, MD

Abstract Approved By Advisor: Yes

Co-Authors: Russell Griffin, Vincent Mortellaro, Elizabeth Beierle, Carroll M. Harmon, Mike K. Chen, and Robert T. Russell

Title: Clinical Predictors of Perforated Appendicitis: the Utility of Immature Granulocyte Percentage

Background: Acute appendicitis is a common surgical condition in the pediatric population. The diagnosis of appendicitis and differentiation between acute and perforated appendicitis is often challenging. Many adjuncts are utilized to help clinicians predict acute or perforated appendicitis, which may affect the course of treatment. Newer automated hematologic analyzers may perform more accurate automated differentials including immature granulocyte percentage (IG%). Elevated IG% has been shown to be more accurate for predicting sepsis in the neonatal population than traditional immature to total neutrophil count (I/T) ratios. We intended to assess the additional discriminatory ability IG% may add to traditionally assessed parameters in differentiating acute and perforated appendicitis.

Methods: After IRB approval, we retrospectively identified all patients with appendicitis from July 2012 to June 2013 by ICD-9 code. Charts were reviewed for relevant demographic, clinical, radiographic, and outcome data. We defined perforated appendicitis as the surgeon's interpretation based on operative findings. Standard statistical methods were utilized.

Results: 251 patients with appendicitis were included in the analysis. Those with perforated appendicitis had a higher mean white blood cell count ($p=0.0063$), c-reactive protein (CRP) ($p<0.0001$), and IG% ($p=0.0299$). Laboratory variables were put into an adjusted logistic model predicting odds of perforated appendicitis. In the adjusted model, only elevated CRP (OR 3.46, 95% CI 1.40-8.54) and presence of left shift (OR 2.66, 95% CI 1.09-6.46) were significant predictors of perforated appendicitis. The c-statistic of the final model was 0.70, suggesting fair discriminatory ability of this model to predict perforated appendicitis.

Conclusions: IG% did not provide any additional benefit to elevated CRP and presence of a left shift in the differentiation between acute and perforated appendicitis.

Matin, Tasnia (MS4)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Charles Leath, MD, Britt Erickson, MD

Abstract Approved By Advisor: Yes

Co-Authors: Britt Erickson, MD, Bin Zhang, PhD, Jovana Y. Martin, MD, Monjri S. Shah, MD, Christen L. Walters, MD, J. Michael Straughn Jr., MD, Charles A. Leath, III, MD

Title: The Charlson Comorbidity Index predicts survival in women with epithelial ovarian cancer independent of surgical debulking status

Objective: Our objective is to determine if patient comorbidities negatively impact progression free survival (PFS) and overall survival (OS) in patients with epithelial ovarian cancer (EOC).

Methods: Eligible subjects for this retrospective cohort study included women diagnosed with EOC between 2004-2009 who received primary treatment and follow-up at our institution. After IRB approval, records were reviewed for demographics, tumor characteristics, recurrence, survival, and comorbidity as quantified using the Charlson Co-morbidity Index (CCI). The CCI is a validated predictor of hospital mortality and includes 19 medical conditions that are weighted based on their association with hospital mortality. For our analysis, patients were separated into 3 categories based on a CCI of 0, 1, or 2+. Survival was calculated using Kaplan-Meier estimates and compared with the log-rank test.

Results: 367 women were included. 225 women (61.3%) had a CCI of 0, 99 (27.0%) had a CCI of 1 and 43 (11.7%) had a CCI of ≥ 2 . Compared to women with a CCI ≥ 1 , women with a CCI of 0 were more likely to be younger, white, and have private insurance. Women with a CCI of 0 were more likely to receive NCCN standard of care (RR 1.95; 95% CI 1.3-2.9). A CCI of 0 was not associated with an increased rate of optimal debulking (RR 1.01; 95% CI 0.71-1.42). PFS and OS varied significantly based on CCI. Median PFS for women with a CCI of 0, 1, or 2+ was 18.8, 12.1, and 9.7 months ($p < .005$). Median OS for women with a CCI of 0, 1, or 2+ was 46.5, 33.1, and 20.4 months ($p < .005$). On multivariable analysis adjusting for age, race, grade, stage, and debulking status, a CCI ≥ 1 was independently associated with a greater hazard for progression (HR 1.16; 95% CI 1.04-1.28 and death (HR 1.19; 95% CI 1.07-1.34).

Conclusions: Patient comorbidities, as measured by the CCI, are independently associated with a lower PFS and OS in women with EOC. Future clinical trials may need to include the CCI or other predictor of outcome as a stratification variable.

Mays, Melissa Ann (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Sztul

Abstract Approved By Advisor: Yes

Co-Authors: Melissa Mays, Jay Bhatt, John Wright, and Dr. Elizabeth Sztul

Title: Probing for Novel Interactions of the Homology Downstream of Sec7 3 (HDS3) domain in the ARF-GEF GBF-1

GBF1 is a Golgi-localized guanine nucleotide exchange factor (GEF) that catalyzes GDP to GTP exchange on the ADP-ribosylation factor (ARF) family of GTPases. ARFs regulate vesicle formation in intracellular traffic and are only active in the GTP-bound state. GBF1-mediated ARF activation is essential for Golgi biogenesis and for ER-Golgi trafficking. GBF1 consists of a multiple conserved domains, most of which are poorly characterized. It is understood that the Sec7 domain is catalytically active in GBF1, but several other domains are also conserved: DCB and HUS domains upstream from Sec7 and HDS1, HDS2, and HDS3 domains downstream. Many of these domains have been studied in the past, but HDS3 has not been previously examined. We hypothesize that by performing HDS3 assays we will be able to assess its contribution to the overall function of GBF1. Through our studies we have gathered evidence that the HDS3 domain is, in fact, functionally relevant with regard to establishing and maintaining Golgi homeostasis. We base this conclusion on the comparison of our HDS3 mutants with wild-type GBF1 in cells depleted of GBF1. In these cells, the Golgi does not maintain its structure as well when HDS3 mutants are present. Given the known role of GBF1 in the maintenance of Golgi homeostasis, this strongly suggests that these mutants are functionally compromised. Our results suggest that GBF1 targeting to the Golgi is not affected by HDS3 mutation, indicating that HDS3 plays a minimal role in protein targeting. However, we demonstrated that with a mutated or absent HDS3, the Golgi is not functional. The question remains as to how exactly the HDS3 domain is involved in GBF1 function. Given the predicted fold of HDS3, we speculate that HDS3 may serve as an interaction interface and plan to identify potential interactors for this domain in future experiments.

McCaw, Tyler Robert (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Christopher Klug

Abstract Approved By Advisor: Yes

Co-Authors: Tyler McCaw, Dr. Christopher Klug

Title: Sequestration of Oxidized Lipids, Immunomodulation, and Tumor Progression in Pdx1-Cre;Kras^{G12D/+}; p53^{-/-} Mouse Model

Pancreatic cancer is currently the fourth leading cause of cancer deaths in the United States and, in contrast to nearly all other forms of cancer, has seen an increase in mortality rates since 1990. Hence, it is critically important to understand the potential of the immune response in combating this disease. Oral administration of 4F, a synthetic polypeptide with a high affinity for oxidized lipids, was recently reported to reduce inflammation and inhibit cancerous lesion formation and growth. This study was therefore initiated to determine the potential anti-tumorigenic properties of 4F for suppressing the development and progression of pancreatic ductal adenocarcinomas in the Pdx1-Cre;Kras^{G12D};p53^{R172H} mouse model. Interestingly, however, we have shown that a 4F diet greatly accelerates the timeline of lesion progression from low grade to tumor in the Pdx1-Cre;Kras^{G12D} cohort. Our next step is to repeat these experiments and characterize the immune response of both normal diet and 4F diet mice to early and late stage lesions as well as to compare these response profiles to what has been previously reported for pancreatic ductal adenocarcinomas.

McFalls, Kristen Ann (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Namasivayam Ambalavanan, M.D.

Abstract Approved By Advisor: Yes

Co-Authors: Drs. Martha Bidez, PhD, Donald Burke, PhD, Namasivayam Ambalavanan, MD

Title: Neonatal Patient Safety

Medical errors are a major cause of morbidity and mortality, and little advancement has been made in eliminating serious medical errors. This research study was designed to explore and expose medical errors within the setting of a regional neonatal intensive care unit (NICU). The first step of this project was to create a list of common medical errors occurring within the NICU using a random patient safety audit process. This was accomplished using 2 standard questionnaires, one for nurses and one for physicians, listing possible causes of adverse outcomes. Data consisted of responses collected from 50 of each survey. We found that 30% of the nurse surveys and 66% of the physician surveys identified potential or actual patient safety issues. The main safety issues were radiology studies and equipment/medical devices for nurses and intermittent suction not set to ≤ 80 as well as inability to locate consultations for physicians. Future steps are to construct a plan of action to eliminate the potential for errors happening in the NICU and improve patient safety. This technique may be useful in other health-care settings.

Meadows, Jarrod Phillip (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: J. David Sweat and John J. Hablitz

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Epigenetic Regulation of Synaptic Scaling via DNA Methylation

Homeostatic plasticity refers to cellular changes, synaptic and intrinsic, that allow neurons to maintain relatively stable firing rates; thus mediating one of the most salient and paradoxical characteristics of neuronal networks: robust stability in the face of remarkable plasticity. A form of homeostatic plasticity, synaptic scaling, involves bidirectional compensatory changes in global post-synaptic receptor density in response to chronically elevated or depressed activity. Theoretical models suggest scaling provides negative feedback to positive feedback Hebbian processes, such as LTP and LTD, and also serves to maintain information acquired through synapse-specific changes in strength acquired during these processes by maintaining relative synaptic weights. Importantly, synaptic scaling occurs via a highly coordinated, cell-wide program that multiplicatively adjusts post-synaptic weights across all synapses. This program is initiated in a cell-autonomous manner, as neurons respond robustly to fluctuations in their own spiking rates by sensing concomitant changes in intracellular Ca^{2+} entry through somatic L-type voltage-gated channels. The coordinated, global expression of synaptic scaling suggests an equally coordinated and integral role for transcriptional and epigenetic regulation. Indeed, we have shown synaptic scaling requires the activity of DNA methyltransferases (DNMTs), a group of enzymes that add a methyl group to cytosine residues within DNA; an epigenetic mechanism with a well-documented history of regulating gene expression. Scaling down of excitatory strength in response to chronically elevated activity can be blocked with the DNMT inhibitor, RG108, and chronic RG108 treatment alone mimics the physiological changes associated with scaling up. Furthermore, we have demonstrated DNMTs regulate scaling in an activity-dependent manner, as silencing network activity blocks the scaling up effects of RG108 treatment. Together, our results show the regulation of gene expression via DNA methylation represents a critical point of control in the induction and expression of synaptic scaling.

Merriman, John Wesley, III (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: American Heart Association Fellowship

Faculty Advisor: Dr. David Cleveland

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Franco Diaz

Title: Correlation between sublingual small vessel density and blood lactate levels in the neonatal cardiac surgical patient

Infants with congenital heart disease display complex hemodynamic properties and physiology as an adaptive response to abnormal blood flow. These changes are often reflected in microvasculature, which provides a unique perspective on pathology and physiology of tissues and related blood flow. Current technology allows for bedside monitoring and secondary quantitative analysis of microcirculation via Sidestream Dark Field (SDF) imaging technology. Real time minimally-invasive video is collected across mucosal surfaces with a small handheld videomicroscope: stroboscopic green light emission from the device is capable of high-contrast imaging of small blood vessels less than 100 μ m in diameter.

This prospective observational study aims to qualitatively and quantitatively describe sublingual vessel density in post-operative cyanotic infants during cardiac catheterization procedures compared to healthy, non-cyanotic infants undergoing routine procedures not affecting overall cardiovascular function. General anesthesia and intubation during these procedures will be noted for comparison to microcirculatory changes. External video analysis will be conducted to prevent researcher bias: total vessel densities and total perfused vessel densities will be averaged over 5 video samples collected from each infant. Research is currently ongoing and analysis will be completed at a future time.

Ultimately, this project will be aimed at investigating possible correlations between sublingual small vessel density changes and blood lactate levels in perioperative neonatal congenital heart surgery patients as a prognostic indicator. Constant monitoring will also improve response time to acute negative sequelae.

Mitchell, Chase Matthew (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Frank Skidmore

Abstract Approved By Advisor: Yes

Co-Authors: Myers J, Marstrander J, Standaert D, Anthony T & Skidmore FM

Title: Disease Subtype in Parkinson Disease is Associated with Specific Changes in the Cerebellum and Thalamus

Parkinson's disease (PD) is a neurodegenerative disorder with a wide clinical spectrum. Over time, various PD subtypes have been categorized. One of the more common ways of subtyping PD has been to classify the disorder into the subset of tremor dominant (TD), and a subtype dominated by postural instability and gait disorder (PIGD). A number of imaging differences have been shown to be associated with these clinical subtypes. The aim of this study is to determine if there are consistent differences in diffusion tensor imaging-fractional anisotropy (DTI-FA) in individuals with tremor predominance (TD subtype), compared to those with predominant symptoms of postural instability and gait disorder (PIGD subtype). Our results show that individuals with the TD subtype of PD have increased DTI signal in the Uvula of the Cerebellum (Midline Lobule IX) and decreased signal in the medial dorsal nucleus of the thalamus compared with individuals with the PIGD subtype of PD. Lobule IX, particularly the vermis, is intimately connected with motor functions associated with the leg. Conversely, aberrant thalamic activity is known to be associated with tremor in PD, and the thalamus is a target for deep brain stimulation in individuals with tremor. Our findings therefore suggest that disease specific classifications in PD have a functional basis. Further research will be required to determine if these changes can be used to predict disease course and severity in idiopathic PD.

Moseley, Carson Edward (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Casey Weaver

Abstract Approved By Advisor: Yes

Co-Authors: Craig L. Maynard, Robin D. Hatton, Casey T. Weaver

Title: The Regulation of Interleukin 10 Transcription in Autoimmunity

Interleukin-10 (IL-10) is cytokine with potent anti-inflammatory activities that are critical for restraining immune-mediated pathology to self-tissues. Notably, patients with nullifying mutations in *IL10* or either chain of the IL10 receptor develop a severe inflammatory bowel disease (IBD) in the first years of life. Despite the non-redundant function of IL-10 in preventing autoimmunity, an understanding of the complex transcriptional regulation of *IL10* remains in its infancy.

Here, we identified the transcription factor Growth Factor Independent 1 (Gfi1) as a repressor of *IL10* transcription in multiple lineages of CD4⁺ T cells. T cells from mice deficient in *Gfi1* produce excess *IL10* mRNA and IL-10 protein upon *in vitro* stimulation. Chromatin Immunoprecipitation (ChIP) experiments identified binding of Gfi1 in several highly conserved regions of *IL10*, including two regions previously found to contain mutations that lead to increased susceptibility to Crohn's Disease and Ulcerative Colitis. *Gfi1*-deficient T cells also contained epigenetic marks indicative of a more active *IL10* locus following stimulation.

Finally, we found that mice conditionally deficient in *Gfi1* in the T cell compartment are highly resistant to mouse models of IBD and Multiple Sclerosis, and that this reduced disease is dependent upon their increased expression of IL-10. Thus, we have identified a previously unknown mechanism of *IL10* repression that should lead to a deeper insight into the complexities of cytokine gene regulation and may inform future therapeutic targeting in autoimmunity.

Musgrove, John Larkin, Jr. (MS4)

Project Length: Short

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Carlos Estrada

Abstract Approved By Advisor: Yes

Co-Authors: Jason Morris, Ryan Kraemer, Carlos Estrada

Title: UTILIZING ITERATIVE CASE PRESENTATION TO DEMONSTRATE CONCEPTS OF CLINICAL REASONING

In the medical education literature, clinical problem solving exercises have emerged as a means of exploring the nuances of clinical reasoning. In this format, a case is iteratively presented with commentary from an expert clinician. We aim to characterize the clinical reasoning concepts of published clinical problem solving exercises.

First, we identified four nationally-distributed per-reviewed journals which regularly publish clinical problem solving exercises. Articles published between January of 2010 and May of 2013 were included. **Second**, two authors compiled an extensive list of clinical reasoning concepts from seminal reviews. Twenty core concepts were selected by seven independent reviewers. **Third**, an automated approach was used to objectively identify the core concepts mentioned in each article. Batch searches were conducted on standardized plain text versions of each article. Redaction of superfluous text characters was conducted using a regular expression text editor. **Fourth**, the main outcome was the presence of each clinical reasoning concept in each article. We examined differences between journals with the Chi-square test.

We identified 79 clinical problem solving exercises: 41 (52%) in the *New England Journal of Medicine*, 22 (28%) in the *Journal of Hospital Medicine*, 11 (14%) the *Journal of General Internal Medicine*, and 5 (6%) in the *American Journal of the Medical Sciences*. The five most commonly mentioned clinical reasoning concepts were *diagnosis* (100%), *context* (25.3%), *bias* (16.5%), *illness script* (13.9%), and *problem representation* (12.7%). We observed differences between journals on all but five of the domains (all $p <= 0.005$).

Clinical problem solving exercises represent a highly accessible learning tool capable of detailing the clinical judgments of an expert clinician. Supplementing such exercises with discussion of relevant clinical reasoning concepts further reveals the nuance of these cognitive skills. Identifying core domains may allow educators to consider the role of these exercises in teaching clinical reasoning.

Nadendla, Kavita Devi (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Judy Creighton

Abstract Approved By Advisor: Yes

Co-Authors: Tao Yu, Judy Creighton

Title: Changes in circulating levels of AMPK correlate with pulmonary dysfunction in hypertension

Progression of pulmonary hypertension (PH) involves a series of complex processes culminating in pulmonary vascular remodeling, increased resistance, and sustained hypertension, primarily from dysfunction in lung endothelium and smooth muscle. Such vascular changes indicate an imbalance between growth inhibitors and mitogenic factors, suggesting a common mechanistic thread: loss of cellular homeostasis. AMP-activated kinase (AMPK) was originally described as a molecular sensor for maintaining metabolic homeostasis and responds to metabolic stresses (e.g. hypoxia, oxidants, humoral mediators, and hypoglycemia) which alter energy (ATP) levels. More recently, AMPK function has been associated with a broader range of physiological functions that occur independently of ATP levels. However, little information exists regarding AMPK function in pulmonary vascular processes. We hypothesized AMPK has the potential to become an effective biomarker that will allow consistent detection of pulmonary vascular disease, indicate its severity, and identify the location of affected tissue, with the benefit of being easily measured using non-invasive methods through blood and bronchoalveolar lavage fluid. Using hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC), we studied the morphology of the lung to identify pathology associated with a hypertensive rat (SHR) model compared with healthy controls, as well as a change in expression of different isoforms of AMPK contributing to the progression of PH in these animals. H&E staining showed both hypertrophy of smooth muscle in proximal vessels and a disruption of normal alveolar architecture in SHR animals. IHC demonstrated an increase in expression of both AMPK α 1 and AMPK α 2 primarily in regions of proximal vessel smooth muscle hypertrophy. These findings support the overall hypothesis that AMPK contributes to the pathogenesis of pulmonary vascular disease, with the exciting potential to become a novel drug target in the treatment of PH. Supported by HL102296 and HL 110803.

Oak, Si Won (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: American Federation for Aging Research MSTAR Fellowship

Faculty Advisor: Christine A. Curcio

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Subretinal Drusenoid Deposit: Further Characterization by Lipid Histochemistry

Two extracellular lesions associated with age-related macular degeneration (AMD) are drusen and subretinal drusenoid deposits (SDD), distinguishable by their laminar locations and topographical predilections relative to the fovea. Lesion composition provides important clues to affected biological pathways. Among lipids, only unesterified cholesterol (UC) has been localized to SDD. We stained cryosections from 11 AMD eyes of 11 donors (mean age=83.9 yr) retained from previous studies. We utilized Oil Red O (ORO) to stain esterified cholesterol (EC), in addition to triacylglycerol, free fatty acids, and retinyl esters. We also used filipin, which reveals either EC or UC depending on tissue pre-treatment. Sections were counterstained with hematoxylin. High-resolution sections stained with toluidine blue were used to examine SDD's morphology.

SDD was rich in UC, and poor in EC and other neutral lipids. SDD's fine texture and compact architecture made it discriminable from other subretinal materials. These findings support the 2- lesion, 2-compartment model of AMD lesion biogenesis, which posits retinal pigment epithelium secretion of a UC-rich high-density lipoprotein apically and an EC-rich very low-density lipoprotein basolaterally.

Obert, John Everett (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Edgar A Jaimes

Abstract Approved By Advisor: Yes

Co-Authors: Gabriel Rezonzew, Phillip Chumley, Edgar A Jaimes

Title: Understanding the Role of Nicotine in the Progression of Kidney Disease in Diabetics

Kidney damage is a major complication of both type I and type II diabetes. Tobacco and/or nicotine use among diabetics is a risk factor for the progression of kidney disease. With more than 285 million diabetics and 1 billion tobacco users worldwide, understanding the mechanisms by which nicotine damages the kidney is critical to improving our understanding of the disease process and to develop strategies to minimize harm to the diabetic population. We hypothesize that tobacco related kidney damage is mediated in large part by specific nicotinic acetylcholine receptors (nAChRs), in particular the $\alpha 7$ nonneuronal nAChR, which is present in large amounts in the kidney. To test this hypothesis, we administered nicotine to commercially available C57/BL6 mice lacking the $\alpha 7$ nAChR and to wild type C57 mice, both diabetic and nondiabetic. Preliminary data suggests that at nicotine induced kidney damage is mitigated by the lack of the $\alpha 7$ nAChR, with both proteinuria and albuminuria relatively decreased in the $\alpha 7$ nAChR $-/-$ animals on nicotine. After euthanasia, further analysis will be conducted to characterize and determine the extent of kidney damage, and the degree to which lack of the $\alpha 7$ nAChR protects the kidney from nicotine.

Omar, Nidal Bassam (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Mamerhi Okor

Abstract Approved By Advisor: Yes

Co-Authors: Benjamin J. Ditty, MD, Nidal Omar, Paul Foreman, MD, Patrick R. Pritchard, MD, and Mamerhi O. Okor, MD

Title: The non-surgical nature of patients with subarachnoid or intraparenchymal hemorrhage associated with mild traumatic brain injury

Object Mild traumatic brain injury (Glasgow Coma Score $>/= 13$) is a common problem in the United States and worldwide, estimated to affect more than 1 million patients yearly. When associated with intracranial hemorrhage it is a common reason for consult to neurosurgical services and transfer to tertiary care centers. The authors' goal is to demonstrate the non-surgical nature of SAH and/or IPH associated with mTBI in hopes of reducing the frequency of neurosurgical consult or transfer for these minor injuries.

Methods We performed a retrospective review of patients admitted to a Level One Trauma Center in Alabama between September, 2004 and May, 2013 with mTBI and SAH and/or IPH. We performed a review of medical records to confirm the diagnosis, determine neurological condition at admission, and assess for episodes of neurologic decline including altered mental status, seizures, hyponatremia, etc.

Results Of the 414 patients reviewed, 251 (60.6%) were male and 163 (39.4%) were female. Average age was 46.3 years. 45 patients (10.9%) sustained isolated IPH, 349 (84.3%) were found to have isolated SAH, and 20 (4.8%) had radiographic evidence of both IPH and SAH. 125 patients (30.2%) were transferred an average distance of 64.7 miles. We identified no patients who experienced neurological worsening during their hospital course. One patient experienced hyponatremia which required treatment with sodium supplementation.

Conclusions Patients with the constellation of SAH and/or IPH and mTBI do not require neurosurgical consultation and these findings should not be used as the sole criteria to justify transfer to tertiary referral centers.

Oruc, Vedran (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Molly Bray

Abstract Approved By Advisor: Yes

Co-Authors: Vedran Oruc, Carroll M. Harmon, David K. Crossman, Matthew P. Herring, Beverly Haynes, and Molly S. Bray

Title: Familial and Genetic Components of Early Onset Obesity

Introduction: While it is accepted that the obesity phenotype results from a combination of influences, extreme early onset obesity has a strong genetic component. Currently, there are limited diagnostic genetic tests available for children with extreme obesity. Use of whole exome sequencing (WES) allows for rapid analysis of DNA sequence variation and can serve to identify new candidate genes associated with disease.

Methods: Probands were ascertained at the Children's Center for Weight Management. Participant evaluation began the construction of pedigrees in order to evaluate segregation of obesity. Following consent, a family gathering was held to perform physical measurements and collect buccal samples for DNA extraction. WES was performed using next generation sequencing on the Illumina platform. Data quality was checked using FastQC software, and sequences with low quality (Q-score <20) were removed. Raw reads were aligned to the human reference genome hg19 using the Burrows-Wheeler aligner tool, followed by re-calibration of the aligned reads and called variants using Genome Analysis Tool Kit.

Results: Here we report results for a single family with a 3-yr-old male proband weighing 64.5 kg (BMI=48.7 kg/m²). Variants common to both the proband and unaffected father were removed from further evaluation. We then identified variants common to the proband and affected maternal family members. Six unique variants were found residing in or near the following genes: IGSF3, TPGS2, HRC, KRTAP19-3, SCUBE1, GPRASP1. Common features of these novel variants include expression primarily in brain, skeletal muscle, adipocyte, thyroid, and adrenal glands and reported associations with body composition.

Conclusions: Although analysis of the identified variants is still ongoing, these findings may provide potential new gene targets for children at risk for early onset obesity. The common pattern of tissue expression seen in the variants may suggest the need for a multiple hit model for predicting early onset obesity.

Parks, David (MS4)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Nancy Tofil

Abstract Approved By Advisor: Yes

Co-Authors: A. Nicki Sims, MD; Kristin Dietiker, MD; Daniel Feig, MD; Marjorie Lee White, MD, MEd, MPPM; Dawn Taylor Peterson, PhD; David Parks, MSIII; J. Lynn Zinkan, RN, MPH; Nancy M. Tofil, MD, MEd

Title: A Novel Teaching Mechanism in Nephrology of the Dangers of Hypocalcemia in Chronic Renal Failure.

Simulation allows standardized exposure to rare but crucial scenarios that are important to specialties. This case was designed to illustrate the important pathophysiologic interaction of sodium bicarbonate (NaHCO_3) and ionized calcium levels in a hyperkalemic, chronic renal failure patient. The goal of the simulation was to standardize resident exposure to this complex case scenario and enhance resident learning. All pediatric residents completed a pre-test prior the simulated case. They then participated in groups of 2-3 in the case and completed the post-test and demographic form immediately after the debriefing. Twenty-one pediatric residents (16 females and 5 males, mean age = 28.2 ± 2.5 , mean year in residency = 2.0 ± 1.0) participated in the simulation as part of their nephrology rotation. One major finding was that mean percentage of correct responses increased from pretest (66% $\pm 24\%$) to posttest (97% $\pm 7\%$, $p < 0.0001$). There was no statistically significant association, however, between pretest performance and year in residency or number of times on nephrology service. All ten teams ordered and administered calcium. Four groups also gave NaHCO_3 . In each of these groups, calcium was ordered prior to NaHCO_3 by an average of 130 ± 108 s. Based on pretest responses, many residents were unaware that NaHCO_3 can cause life-threatening dysrhythmias and should not be given as a treatment for hyperkalemia when ionized calcium is low. Even fewer were aware of the underlying mechanism. Expansion of the simulation to pediatric emergency medicine and intensive care fellows may be important as there appears to be a lack of knowledge of this physiology and many children in extremis will present to one of these two locations.

Partain, Paige Ivey (MS4)

Project Length:

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Mark H. Thomas, MD

Abstract Approved By Advisor: Yes

Co-Authors: Ilya Gutman, Mark H. Thomas, MD

Title: The Associations Between Health Risk Behaviors, Executive Function Deficits, and ADHD Symptoms in University Students

Purpose: (1) Demonstrate the association between Attention-Deficit Hyperactivity Disorder (ADHD) and Health Risk Behaviors (HRBs), (2) Determine if an association exists between questionnaire-based reports of Executive Function Deficits (EFDs) and HRBs, and (3) Determine if an association exists between questionnaire-based EFDs and ADHD. **Method:** University students (N=422) completed an online survey consisting of questions from the Barkley Adult ADHD Rating Scale- IV (BAARS-IV), the Barkley Deficits in Executive Functioning Scale (BDEFS), the Barkley Functional Impairment Scale (FIS), and the 2011 Youth Risk Behavior Survey (YRBS) created by the CDC. Data were analyzed using SPSS software to ascertain if an association exists between ADHD symptoms, EFDs, and HRBs. **Results:** We found statistically significant differences between ADHD and non-ADHD groups for 9 (ADHD Symptom Group) and 11 (Total ADHD Group) HRB questions. In all cases, the ADHD group was more likely to engage in risky behaviors. There were 10 statistically significant questions found when comparing EFD and non-EFD groups. For all 10 questions, individuals at risk for EFDs were more likely to engage in risky behavior. Finally, we found that a large proportion of patients in the ADHD subgroups also qualified as having EFDs (48.4 % - 60.7%, depending on ADHD group). **Conclusion:** It seems that the presence of ADHD symptoms as well as EFDs place patients at increased likelihood of engaging in risky health behaviors. Also, many patients with ADHD also have clinically significant EFDs. This information could help guide clinicians as they assess and counsel patients with ADHD and EFDs.

Patel, Shaan Suresh (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Brent Ponce MD

Abstract Approved By Advisor: Yes

Co-Authors: Shaan S. Patel BA, Evan D. Sheppard BS, Herrick J. Siegel MD, Brent A. Ponce MD

Title: Evaluating the readability of online patient education materials related to bone and soft-tissue sarcomas.

Cancer patients rely on patient educational materials (PEMs) to gather information regarding their disease and treatment options. Patients who are better informed with regards to their illness have been shown to have better health outcomes. With more cancer and orthopaedic patients searching the Internet for PEMs, it is important for the reading level of online PEMs to match the health literacy level of cancer and orthopaedic patients. The National Institutes of Health (NIH) recommends PEMs to be written at a 6th to 7th grade reading level. The purpose of this study was to evaluate the readability of online PEMs related to bone and soft-tissue sarcomas and related conditions.

Relevant online PEMs were identified from the following websites: American Academy of Orthopaedic Surgeons, academic training centers, sarcoma specialists, Google search hits, bonetumor.org, Sarcoma Alliance, Sarcoma Foundation of America, and Medscape. Ten separate readability instruments were used to evaluate the reading level of each websites' PEMs.

72 websites and 774 articles were evaluated. None of the websites had a mean readability score at or below 7 (seventh grade). Collectively, all websites had a mean readability score of 11.4 and the range of scores was grade level 8.9 to 15.5.

All PEMs in this study related to bone and soft-tissue sarcomas and related conditions did not meet the NIH's recommendation for the reading levels of PEMs. Concerted effort to improve the reading level of orthopaedic oncologic PEMs is necessary.

Patel, Shyam Arvind (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. John Mason

Abstract Approved By Advisor: Yes

Co-Authors: Shyam Patel, BS; Ryan Burton, MD; Duncan Friedman, MD; Carrie Huisinigh, MPH; John Mason, III, MD

Title: Correlation Between Hemoglobin A1c and Response to Bevacizumab Therapy in Diabetic Macular Edema

Objective: To determine if there is a correlation between pretreatment Hemoglobin A1c (HbA1c) levels and efficacy of intravitreal Bevacizumab therapy in diabetic macular edema.

Methods: We reviewed the charts of 573 patients, who received intravitreal Bevacizumab injections for diabetic macular edema from January 2011 to October 2011. Inclusion criteria included having a recorded HbA1c value within three months of treatment initiation, recorded best corrected visual acuity (BCVA) and central subfield macular thickness (CSMT) values at treatment initiation and at follow-up visits, and approximately one year of Bevacizumab therapy not interrupted by laser, surgery, or injection of other intravitreal agents. Sixty-one eyes from sixty-one patients were included in this study.

Results: Thirty-five patients (57.3%) were female, and thirty-four patients (55.7%) were Caucasian. The average age was 63.0 (SD 11.8) years. A majority of patients had non-proliferative diabetic retinopathy (83.6%) and insulin dependent diabetes mellitus (65.6%). Average HbA1c was 8.1% (5.8-13.8%). At baseline, mean BCVA was 20/55 (20/20-20/400), and the average CSMT was 352 µm (171-655 µm). Correlation coefficient comparison revealed essentially no correlation between HbA1c values and response to Bevacizumab treatment in terms of BCVA or CSMT. Comparison of patients with HbA1c greater than and less than 7% showed no statistically significant difference between the change in BCVA ($p=0.43$) or CSMT ($p=0.96$) with Bevacizumab therapy. There was an overall improvement with therapy in mean logarithmic BCVA and mean CSMT across all patients.

Conclusions: Bevacizumab is useful for macular edema regardless of the level of diabetic control based on HbA1c values. No correlation existed between HbA1c and response to Bevacizumab therapy for diabetic macular edema.

Patterson, Kelsey Claire (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Harald Sontheimer

Abstract Approved By Advisor: Yes

Co-Authors: Ian Kimbrough, Harald Sontheimer

Title: Human glioma cells in tumors of varying size differentially associate with blood vessels

Glioblastoma multiforme (GBM) is the most common primary brain cancer in adults, affecting about 5 in 100,000 people, and is associated with significant morbidity and mortality. GBM lethality is characterized by the unique invasive abilities of the tumor, which produce large, unresectable masses. Cancer cells invade perivascularly along blood vessel tracts, co-opting existing vessels and eventually producing new vessels through various mechanisms of neovascularization. These processes continue throughout tumor progression, as cells spread and produce satellite tumors. The principal objective of this study was to identify characteristics, such as vessel type and vessel diameter, of the vascular structures with which glioma cells make associations. To do so, we used *in situ* confocal imaging techniques on fixed brain slices, which were prepared from a mouse model displaying salient features of the disease. We stereotactically implanted human glioma cells expressing enhanced green fluorescent protein (D54-EGFP) into immunodeficient (SCID) mice and allowed tumors to grow for several weeks before fixing, slicing, and staining brains. Antibodies and fluorescent dyes used to stain tissues were specific for either vascular endothelium or arteries >10 μ m in diameter. Image analysis revealed that, compared to smaller tumors, tumors with larger average areas encompassed a higher percentage of total vascular area and associated with larger, primarily arterial, vessels at their cores. Smaller tumors had less centrally located vessels, if any core vessels could be identified, and these vessels were less likely to be arteries and more likely to be veins. These findings indicate that the GBM-vascular interface is fluid, and cancer cells may preferentially associate with differing vessels in order to accommodate unique needs of the tumor at a particular stage of invasion or growth. Continued research into this vascular interface may reveal clinically targetable mechanisms that trigger preferential tumor cell associations contributing to tumor progression and severity.

Pepin, Mark Emile (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Marcas Bamman

Abstract Approved By Advisor: Yes

Co-Authors: Michael Stec

Title: Effect of paralysis on the sensitivity of human satellite cell differentiation

Self-renewal is a characteristic of all tissues that must be maintained to continue healthy functioning. Although previously considered important only during traumatic events (tears, lacerations, etc...), recent studies have shown that skeletal muscle progenitor cells (i.e. satellite cells) are vital in the normal functioning of skeletal muscle, even in daily maintenance and hypertrophy (Collins et al., 2005; Kuang, Kuroda, Le Grand, & Rudnicki, 2007; Olgun & Olwin, 2004; Wen et al., 2012; Zammit et al., 2004). An important unresolved issue is how the satellite cell population accomplishes this phenomenon of self-renewal. Recent studies have discussed the possibility of a number of pathways in response to growth factors, including Notch and TGF- β (specifically myostatin in skeletal muscle). Others still have considered the importance of mechanical loading on self-renewal, assessing the focal adhesion kinase (FAK) signaling cascade.

Of clinical relevance is the effect of severe disuse on the systemic contribution of skeletal muscle on overall health, in addition to the more obvious mobility. Recent studies have shown that, in **spinal cord injured (SCI) patients**, the deleterious onset of insulin resistance in SCI patients is a result of severe muscle disuse atrophy (Yarar-Fisher et al., 2013). However, the severity of insulin resistance was attenuated with neuromuscular electrical stimulation (NMES), which resulted in hypertrophy of the muscle and translocation of Glut-4 to the plasma membrane. These data pose an interesting scenario, wherein disuse atrophy of 20+ years has caused significant decline in skeletal muscle function. However, a single bout of NMES exercise significantly improves the ability to accommodate high glucose loading. What properties of skeletal muscle are maintained even after 20+ years of inactivity? An hypothesis presented by the current study is somewhat counterintuitive, in that the local skeletal muscle progenitor cells, termed satellite cells, are responsible for the enhanced sensitivity of skeletal muscle, allowing for detection of both mechanical and hormonal stimulation.

In this seminal study, satellite cells from SCI (n=3) and able-bodied controls (n=3) were cultured in vitro. The cell population were subjected to mechanical stretch with flexcell apparatus, and treated with varying concentrations of insulin. The cellular responses to these stimuli were recorded by quantifying FAK, IGF-1, AKT, and mTORC-1 activation using Western Blotting, with analyses set relative to GAPDH protein concentration. The SCI satellite cells are expected to be higher in response to insulin and stretch (previous results have shown that MAPK, FAK, SAPK all increase more than control) when compared to controls. This may be a compensatory effort due to atrophied myocyte population. The real question becomes, which signaling pathway is up-regulated in SCI muscle: mTORC1 via AKT (i.e. growth factor sensitive) or p38 (mechanically sensitive) (Yarar-Fisher et al., 2013)?

Plash, Madison Louise (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: CaRES Program

Faculty Advisor: Warner Huh

Abstract Approved By Advisor: Yes

Co-Authors: Lucy Johnston

Title: The Efficacy of Using Indocyanine Green for Sentinel Lymph Node Biopsy in Endometrial and Cervical Cancer.

Background: The sentinel lymph node is the first lymph node that cancer cells spread to from a primary tumor. Sentinel lymph node biopsy has been proven to be effective and advantageous to stage breast cancer and melanoma. **Objective:** Though sentinel lymph node biopsy is performed in some gynecological cancer cases, there is no consensus among Gynecology Oncologists on how to assess lymph nodes. This study was designed to generate data to support sentinel lymph node biopsy as the standard of care for endometrial and cervical cancer staging. **Methods:** Women with endometrial or cervical cancer are chosen for the study. We use indocyanine green (ICG), a safe dye that has been used for more than 50 years for medical diagnostics, in a new innovative way. We inject the dye directly into the cervix of the patient, and wait for the dye to travel through the lymph channels. The dye pools in the sentinel node and it lights up bright green under a laser with a wavelength of 780nm. With the lymph node illuminated, it is better visualized for removal via robotic surgery. We collect preliminary data in the operating room, including patient demographics, BMI, if the sentinel node can be visualized, and the specific time points in which it is visualized. Other crucial data points include the volume and concentration of the dye, depth of injection into the cervix, and type of needle used. We hope to collect data on 25-30 women in order to determine the optimal dosing of dye and how much time should be allowed for the lymph nodes to be visualized. **Conclusion:** By exploring how to identify the sentinel lymph node in endometrial cancer, we can improve the morbidity and mortality of treatment for endometrial and cervical cancer.

Poholek, Catherine Helen (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Laurie E. Harrington

Abstract Approved By Advisor: Yes

Co-Authors: Catherine H. Poholek, Laurie E. Harrington

Title: Interleukin-21 Drives Intestinal Inflammation by Bridging the Adaptive and Innate Immune Compartments

OBJECTIVES/SPECIFIC AIMS

Th17 CD4 T cells have been cast as pathogenic in the context of many autoimmune diseases, including Inflammatory Bowel Disease (IBD); however, the mechanism for this pathogenicity has yet to be elucidated. Based on the observation that IL-21 expression is increased in biopsies from patients with ulcerative colitis compared to healthy controls and Genome Wide Association Studies have shown an association between the locus containing *il2/il21* and IBD, we posit that IL-21 produced by Th17 cells mediates inflammation in the intestine.

METHODS/STUDY POPULATION

We use mouse models of both spontaneous and CD4 T cell-dependent colitis to interrogate the role of IL-21 signaling on disease pathogenesis. Analysis is completed using a combination of flow cytometry, ELISA, quantitative-PCR, and histological techniques.

RESULTS/ANTICIPATED RESULTS

We show that a large number of IL-21-producing CD4 T cells are present in the intestines of mice with colitis and importantly, that IL-21 production is required for full disease progression. We find that although IL-21^{-/-} CD4 T cells are unable to initiate disease, they produce elevated levels of IL-17A and IL-17F and are not selectively converted into Foxp3+ regulatory T cells, indicating that IL-21 is both crucial to the induction of colitis and surprisingly, is not acting via effects on the activation and differentiation of T cells. In direct support of this idea, IL-21R^{-/-} CD4 T cells are capable of inducing disease unlike their IL-21^{-/-} counterparts. In fact, our data demonstrate that IL-21 has an impact on the innate lymphoid cell compartment, which has previously been implicated in IBD pathogenesis.

DISCUSSION/SIGNIFICANCE OF IMPACT

Taken together, our data show an important and previously unrecognized role for IL-21 that links CD4 T cells to innate lymphoid cells in the induction of chronic intestinal inflammation.

Powell, Jamie Leigh (MS3)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Susan Walley, M.D.

Abstract Approved By Advisor: Yes

Co-Authors: Jamie Powell, MPH, Karlene Walker, Susan Walley, MD, Chioma Chime, MPH, Jennifer Burczyk-Brown, MA, Robin Bates, MPH, Caroline Courville, MD, Kathy Monroe, MD, Ellen Funkhouser DrPH

Title: Using a DVD Intervention for Parents and Caregivers of Children Hospitalized for Respiratory Illnesses to Improve Knowledge and Reduce Secondhand and Thirdhand Tobacco Smoke Exposure

Purpose: A child hospitalized with respiratory illness with Tobacco Smoke Exposure (TSE) offers a unique opportunity to educate and counsel families. Our objective was to use a DVD intervention for caretakers of children hospitalized with respiratory illness to increase knowledge and change behaviors to reduce second- and thirdhand TSE.

Methods: Parents and caretakers of children hospitalized for respiratory illnesses at a tertiary care children's hospital with TSE were recruited between June and December 2012. These study subjects (SS) completed a self-administered questionnaire before DVD intervention to determine knowledge of effects of TSE and motivation for smoking cessation. The DVD reviews the health effects of TSE on children and provides strategies to reduce TSE. The SS were referred to the state tobacco quitline. The questionnaire was repeated after the DVD and a telephone follow-up was performed at one and three months post-intervention including knowledge questions, motivation for smoking cessation, and queried behavior changes. Paired t-tests were used to compare pre- and post-intervention knowledge scores.

Results: We enrolled 167 SS. 81% were parents with 19% other caretakers. The percentage of caretakers with perfect scores on the knowledge assessment were 62.0% pre-intervention, 91.0% post-intervention, 93.4% one month follow-up, and 97.2% three month follow-up ($p<0.0001$). 106 (63.5%) of the 167 SS completed one month and three month follow-up assessments. Of 69 SS who ever smoked, 19% reported smoking cessation, 77% decreased cigarette use (~9 cigarettes/day), 25% used nicotine replacement therapy, and 35% utilized quitline services. 91% and 86% initiated a smoking ban in the home or vehicle, respectively. Of all caregivers at follow-up, ($n=123$), 55% began changing clothes after smoking or encouraged others, 89% began discussing reducing TSE, and 90% began washing hands after smoking or encouraged others.

Conclusions: A low-resource DVD intervention yields sustained knowledge of the adverse effects of TSE and encourages behavior changes at one and three months follow-up in caretakers of children hospitalized for respiratory illnesses. Sustained behavior changes can lead to a decrease in second- and thirdhand tobacco smoke exposure among children.

Powell, Scharlene Hendrix (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Lorie M. Harper

Abstract Approved By Advisor: Yes

Co-Authors: Alan Tita, Joseph R. Biggio, Lorie M. Harper

Title: Impact of Obesity on Gestational Diabetes Mellitus

Introduction: Gestational diabetes mellitus (GDM) and obesity are associated with adverse maternal and neonatal outcomes. We investigated the impact of obesity on pregnancy outcomes in pregnancies with GDM compared to non-obese women with GDM.

Methods: Retrospective cohort of singleton pregnancies with GDM between 2007-2012. Comparisons were made between obese ($\text{BMI} \geq 30\text{kg/m}^2$) and non-obese women ($\text{BMI} < 30\text{kg/m}^2$). Secondary analysis classified subjects as normal weight ($\text{BMI} < 25\text{kg/m}^2$), overweight ($\text{BMI} 25\text{-}30\text{kg/m}^2$), obese BMI ($30\text{-}40\text{kg/m}^2$), and morbidly obese ($\geq 40\text{kg/m}^2$). Subjects were excluded if the pregnancy was complicated by major maternal illness, fetal anomalies, or if pre-pregnancy BMI was undocumented. Comparisons between obese and non-obese were made using t-test and χ^2 test as appropriate; a χ^2 test for trend was used in the secondary analysis. Maternal outcomes considered include: preeclampsia, A2DM, insulin use, and cesarean delivery. Neonatal outcomes considered were macrosomia ($>4000\text{g}$), shoulder dystocia, and a composite of stillbirth, neonatal death, birth injury, cord arterial pH <7 , or cord base excess ≥ 12 . Multivariable logistic regression models were used to adjust for possible confounders.

Results: The subjects included 320 non-obese and 396 obese women. Obese women were at an increased risk of preeclampsia (aOR 5.43, 95% CI 3.0-9.8), A2DM (aOR 2.84, 95% CI 2.05-3.94), insulin requirement (aOR 2.64, 95% CI 1.16-6.00), and cesarean delivery (aOR 1.72, 95% CI 1.26-2.34). Obese women had an increased risk of adverse neonatal outcomes, including the composite neonatal outcome (aOR 1.67, 95% CI 1.10-2.54), macrosomia (aOR 1.53, 95% CI 0.94-2.42), and preterm delivery (aOR 1.94, CI 1.19-3.16). As pre-pregnancy BMI increased, so also did the incidence of adverse maternal and neonatal outcomes.

Conclusion: Obesity significantly worsens outcomes in gestational diabetes and this risk increases as obesity worsens.

Powelson, Julia Ann (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Susan Bellis

Abstract Approved By Advisor: Yes

Co-Authors: Fenil Patel, Matthew Schultz,

Title: Role ST6Gal-I expression in cell survival in ascites

ST6Gal-I is a sialyltransferase which adds α 2–6 sialic acid to N-linked glycans on selected receptors. ST6Gal-I has been shown to be upregulated in human tumor cells and correlated with poor prognosis. Previously published work demonstrates that TNFR1 and Fas sialylation confers resistance to apoptosis. In the setting of ovarian cancer, ascites fluid is present that is rich in TNF and immune cells that express Fas-L. Immunohistochemistry done on ascites cell pellets showed ST6Gal-I expression in these cells. These experiments attempted to determine if ST6Gal-I expression inhibits ascites-mediated cell death. Tumor cells were tested for activation of survival pathways of sialylated and non-sialylated cells from SKOV-3 and ID8 pancreatic cell lines. Cells were treated with ascites fluid at 1 and 6 hours and subsequently lysed. Western blots performed on the resulting lysate showed expression of phospho-Erk was increased in ST6Gal-I expressing cells after treatment with ascites. These experiments, along with previous work, indicate that ST6Gal-I expression may be protective to tumor cells in ascites against TNFR1 and Fas mediated apoptosis.

Rainey, Katherine Louise (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Leon S. Dure, M.D.

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Parents' attitudes toward pediatric genetic testing and incidental findings

Abstract

In the last two decades, advancements in genetic sequencing technology have rapidly propelled the field of genetics. While innovative techniques such as Whole Genome Sequencing (WGS) are now identifying the genetic basis of many diseases, commercial use is also available. In the foreseeable future, as costs decline, the use of WGS as a routine clinical test will likely become a reality. While the science and technology of genetic testing are improving, little is being done with regard to the ethical questions it poses, such as finding the appropriate way to handle incidental findings. Information about patients' opinions and perspectives is lacking, especially in the field of pediatrics, where parents make decisions for the patients.

This study seeks to establish parents' general attitudes toward genetic testing, and more specifically, how they would handle the opportunity to have whole genome sequencing done for their child. Pediatrics is the opportune setting to address this topic, because patients can be accessed for potential genetic effects before their physiological manifestations appear. However, it also imposes extra ethical dilemmas, such as the fact that parents could be making severely life-altering decisions for their children, thereby limiting the actual patient's autonomy.

Research was conducted in the pediatric neurology clinic at Children's Hospital of Alabama, where surveys were verbally given to parents of children diagnosed with epilepsy. Results show some generalized, yet important trends. Of 151 participants, greater than 88% said that they would agree to genetic testing in which results would include incidental findings concerning major, life-long diseases. 18.5% agreed to conduct the same test on their child in a direct-to-consumer form, showing that the majority of parents would rather rely on medical personnel to conduct the testing. This and other important trends are outlined in this study regarding WGS in the field of pediatrics.

Ramaker, Ryne (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Sara Cooper

Abstract Approved By Advisor: Yes

Co-Authors: Karen Bosma

Title: Applying Metabolomics to Pancreatic Cancer

Pancreatic adenocarcinoma (PDA) is the 5th leading cause of cancer death. While other lethal cancers have experienced improvements in survival rates, PDA mortality has remained dismal with a five year survival rate of 3% and a median survival of six months. The best treatment for PDA remains surgical resection, yet less than 20% of patients diagnosed are eligible for surgery upon diagnosis. New drug development and mechanisms for earlier detection are required to improve these outcomes, as recent studies have shown that PDA tumorigenesis begins an average of 17 years prior to diagnosis.

The primary goal of this project is to use untargeted metabolomic analysis of serum and urine to identify small molecule metabolite profiles unique to PDA patients. Using two-dimensional gas-chromatography with mass spectrometry, we analyzed samples from PDA patients ($n=46$), healthy controls ($n=18$), and chronic pancreatitis patients ($n=79$). Data analysis with the open source software Metaboanalyst identified signatures unique to PDA patients and metabolic changes consistent with disease progression. Initial analyses revealed urine 2-piperidine carboxylate and asparagine to be the most significantly elevated metabolites in PDA patients compared to healthy controls. Interestingly, serum asparagine was significantly decreased in PDA patients indicating high levels of kidney filtration. In urine of PDA patients, we observed decreases in TCA cycle metabolites near amino acid synthesis branch points. Chronic pancreatitis patients had lower urine oxovaleric acid than PDA patients. PDA tumor stage progression correlated directly with increasing urine glycine and glutamate, while the opposite was true in serum. Urine palmitate was significantly elevated with metastatic compared to local tumors. Our preliminary findings indicate that metabolomic analysis of serum and urine shows promise in assisting diagnosis, staging, and drug development for PDA. Future work will focus on verifying these trends in additional patient samples and exploring the differences observed between serum and urine.

Ranganath, Neel Kiran (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Bradford Woodworth

Abstract Approved By Advisor: Yes

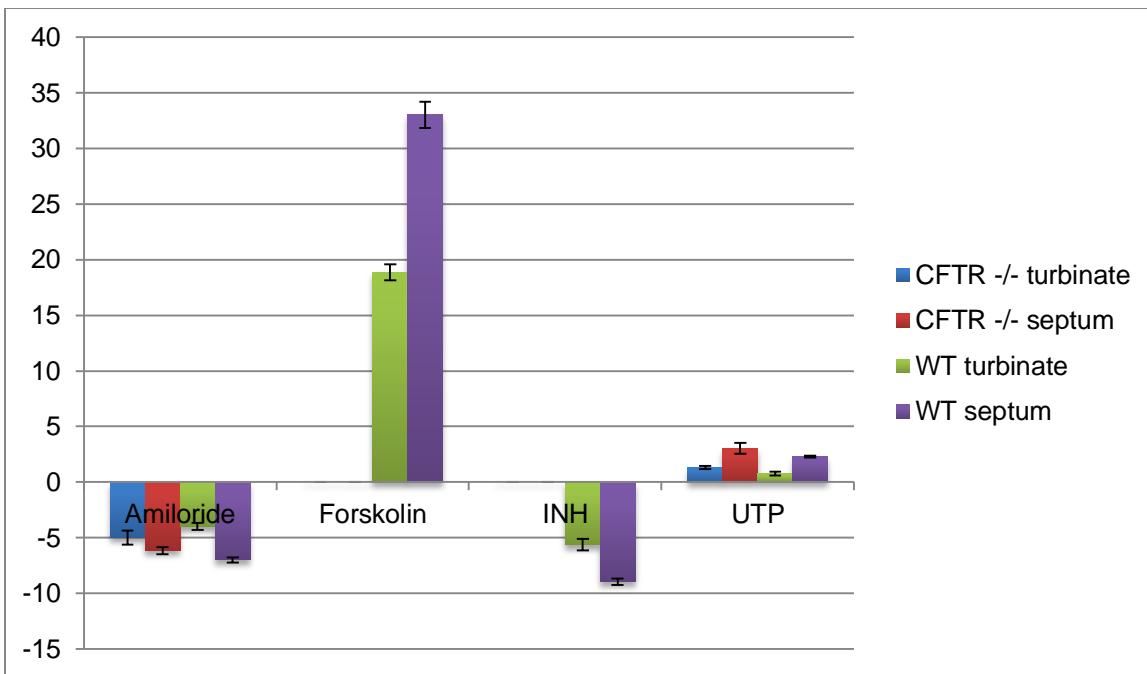
Co-Authors: Nichole Dean, James Phillips, Shaoyan Zhang, Dan Skinner, Eric Sorscher, Bradford Woodworth

Title: Porcine nasal epithelial cultures for studies of cystic fibrosis sinusitis

Background Transgenic cystic fibrosis (CF) murine models have greatly facilitated studies of CF pathogenesis and treatment. We recently described and characterized a primary cell culture model of murine nasal septal epithelium (MNSE) grown at an air-liquid interface that demonstrates excellent differentiation, and robust, physiologic ciliary beat frequency stimulated by ATP and other agonists. However, small rodents do not reproduce key aspects of human airway physiology. Notably, murine models do not develop spontaneous lung and pancreas disease, two of the major causes of morbidity in human CF patients. Because of these limitations, pig and ferret transgenic CFTR-/- models have been developed and are currently being characterized. These CF animal models have phenotypes more closely resembling that of human CF patients. The objectives of the current experiments were to develop and characterize primary porcine nasal epithelial (PNE) cultures and evaluate their usefulness as a model of transepithelial transport and CFTR function.

Methods PNE derived from the septum or the turbinates of WT and CFTR-/- neonatal pigs were cultured at an air-liquid interface on filter supports to confluence and full differentiation. Optimization of culture conditions was conducted to achieve approximately 80-90% ciliated cells. Differentiation occurred within 14 days and all inserts attained resistance > 500 Ω/cm². Epithelial monolayers were mounted in Ussing chambers to investigate pharmacologic manipulation of ion transport. Ciliary beat frequency (CBF) and SEM images of the monolayers were used to indicate degree of ciliation and cell differentiation.

Results Stimulation of CFTR-mediated anion transport [forskolin-stimulated short-circuit current (Δ Isc in μ A/cm²)] was significantly greater in epithelia derived from the septum when compared to turbinates (33.04 +/- 1.17 vs. 18.9 +/- 0.73, respectively; p<0.0005). CFTR-mediated Cl⁻ secretion was absent in CFTR-/- epithelia. Forskolin-stimulated Isc was inhibited by CFTR_{INH}-172 to a greater extent in septal cells as well (-9.0 +/- 0.29 vs. -5.63 +/- 0.54; p<0.0056). Blockade of epithelial sodium channels (ENAC) was also greater in septal cells (-7.0 +/- 0.24 vs. -4.0 +/- 0.31; p<0.0016). Interestingly, calcium-activated Cl⁻ transport was very low with the administration of UTP (2.3 +/- 0.08 vs. 0.76 +/- 0.16; p<0.001). Degree of ciliation and CBF in response to UTP and forskolin were similar among groups. The total yield per porcine septum is 2×10^6 vs. 6×10^5 per murine septum.



Discussion The results of the current study indicate the nasal septum of the pig is the best source for primary nasal epithelia as the cells exhibit a more robust ion transport phenotype when compared to the cells derived from turbinates. The development of porcine CFTR^{-/-} airway disease could be attributable to diminished alternative pathways for Cl⁻ transport as calcium-activated Cl⁻ transport is low.

Thus, porcine nasal septal epithelia have similarities to human nasal epithelia not exhibited with murine nasal cells and represent useful models for studying CFTR activity.

Reeve, Nathaniel Harrison (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Corinne Griguer

Abstract Approved By Advisor: Yes

Co-Authors: T Markert, C Oliva and CE Griguer

Title: CD13 is a potential novel cancer stem cell marker for malignant glioma

Glioblastoma multiforme (GBM) is a very deadly and highly vascularized tumor, but targeting glioma angiogenesis by vascular endothelial growth factor inhibition has been minimally successful. Thus, understanding the molecular mechanisms that control glioma angiogenesis and progression could lead to significant new therapies. We previously described that mitochondrial DNA (*mt*DNA) depletion induces increased tumor angiogenesis, decreased mouse survival, increased resistance to chemotherapy, and an increase in CD133 (a well-known stem cell marker). Because glioma enriched with brain tumor stem cells (BTSCs) share similar properties with *mt*DNA depleted glioma cells, we hypothesize that genes up-regulated in mitochondrial depleted cells could be signature markers of BTSCs. Thus, *mt*DNA could be essential for the maintenance and expansion of BTSC populations. We ran an RT Profiler PCR array for angiogenesis on both U251 p° cells depleted of *mt*DNA and on the parental, isogenic U251 glioma cells. CD13 mRNA expression was increased 200 fold in p° cells over U251 cells. Using fluorescence-activated cell sorting and immunocytochemistry we found that CD13 is significantly increased in p° cells over U251 cells, and is not regulated by hypoxia (1% O₂). Purification of the CD13+ population by magnetic-activated cell sorting revealed that these cells form neurospheres when cultured in Neurobasal (NB) medium. In addition, 60% of CD13+ cells were also CD133+ in NB medium, while only 10% of CD13+ cells were also CD133+ in DMEM/F-12 medium. These findings suggest CD13 may be a marker of cancer stem cells in GBM. Further elucidation of the molecular mechanisms controlling the expression of CD13 may reveal novel therapeutic targets capable of improving the treatment of GBM.

Reid, Daniel Keith (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr Shawn Gilbert

Abstract Approved By Advisor: Yes

Co-Authors: Lindsey N Dietrich, David Doo, Daniel Reid, Naomi S Fineberg, Joseph G Khouri, Shawn R Gilbert

Title: Factors Predicting MRSA vs. MSSA in Pediatric Acute Hematogenous Osteomyelitis

Background: The incidence of acute hematogenous osteomyelitis(AHO) due to community acquired Methicillin Resistant *Staphylococcus aureus* (MRSA) has been rising and presents significant challenges for management. With this increase of MRSA, there has been an increase in the use of broad-spectrum empiric antibiotic coverage in pediatric patients with AHO. There is growing concern in the medical community that empiric antibiotic coverage may contribute to antibiotic resistance in the long term. Recently, a diagnostic algorithm was proposed that may help differentiate MRSA versus MSSA in pediatric patients with AHO. However, the patient population in these studies had a majority of MSSA and minority of MRSA. The purpose of our study was to evaluate the utility of clinical predictors in a setting where the majority, rather than the minority of cases of AHO are caused by MRSA.

Materials and Methods: Retrospective chart review of consecutive patients between 1-18 years of age with culture-proven *Staphylococcus aureus* AHO was completed. Data for twenty-one variables were collected at initial presentation. These variables were age at onset, duration of symptoms, history of prior hospitalization, antibiotic use at presentation, weight, weight bearing status, affected site, subjective history of fever, temperature, respiratory rate, heart rate, systolic and diastolic blood pressure, white blood cell count, absolute neutrophil count, hematocrit and hemoglobin levels, platelet count, erythrocyte sedimentation rate (ESR), CRP, and oxygen saturation. Between 2006 and 2012, 68 patients met criteria for inclusion. Univariate comparisons were used to evaluate each variable between the MRSA and MSSA AHO groups. Comparisons between the two groups used t-tests for continuous variables and Fisher's Exact Test for discrete variables. Logistic regression was performed using a forward stepwise regression in order to determine a model for predicting MSSA osteomyelitis based on initial clinical and laboratory parameters.

Results: Patients with MRSA AHO presented with statistically significantly increased: temperature, respiratory rate, heart rate, white blood cell count, ANC, ESR and CRP as well as a decreased platelet count as compared to those with MSSA AHO. Three variables were identified as co-predictors of MRSA: Temperature, CRP and absolute neutrophil count (ANC). The use of these three variables combined correctly predicts MRSA in 92% of patients and also correctly predicts MSSA in 79% of the sample population with an 87% overall correct classification of MRSA versus MSSA osteomyelitis. In 2011, Ju et al identified four independent predictors of MRSA osteomyelitis that include temperature, hematocrit, white blood cell count, and CRP. However, only 9% of that study population was MRSA and the remaining 91% were MSSA. When compared they found a sensitivity of 91% and specificity of 79%. We would not expect their criteria to do as well in our population. When compared, if they have ≥ 2 criteria, 22% will not have MRSA. If they have < 2 criteria, 35% will have MRSA.

Conclusions: We were able to develop a formula that incorporates patients' Temperature, CRP, and ANC. In our clinical practice setting where MRSA predominates in cases of AHO, this prediction algorithm can be used to correctly predict methicillin sensitivity and resistance with 87% accuracy when applied to our cohort retrospectively. Further work is needed to determine whether the model would perform well prospectively. This could be useful to guide empiric therapy, which at our institution typically is selected to treat MRSA.

Reynolds, Jackson Averett (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Nathaniel Robin

Abstract Approved By Advisor: Yes

Co-Authors:

Title: The Utilization of Genetic Evaluation and Services by Family Medicine Physicians in Rural Alabama

Advances in genetic testing and knowledge have pushed modern medicine towards a greater understanding of what causes many diseases and how to predict and treat them. However, accessing genetic services and its benefits may be difficult for many patients in Alabama who reside outside of the major population centers. Compounding the lack of access to services is the relatively small number of medical geneticists and genetic counselors in Alabama. Alabama's primary care physicians will be at the forefront of integrating genetic services into patient care in rural areas. Therefore, assessing the current perspectives, attitudes, and utilization of genetic services by these primary care physicians will be beneficial. In addition, this study will draw conclusions on the level of interest in genetic services from patients, how comfortable physicians are with integrating genetic services into their practice, and what role physicians see genetic services playing in primary care. Responses to these questions will be coupled with demographic information from the physicians including their proximity to an academic medical center or genetic testing center, number of patients in their practice, and how long they have been in practice to determine if any correlations can be made. We will use the data from this survey to find areas for improvement in the utilization of genetic services either through better access or education.

Rhyne, Robert Rhett (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Mary T. Hawn

Abstract Approved By Advisor: Yes

Co-Authors: L. A. Graham, J. S. Richman, T. M. Maddox, M. T. Hawn

Title: Adverse Cardiac Events: The Risky Business of non-cardiac surgery for patients with a prior cardiac stent

I. Introduction: Perioperative adverse cardiac events are more likely for cardiac stent patients undergoing non-cardiac surgery and the incremental surgical risk is not well characterized.

II. Methods: Patients with a cardiac stent implanted in the VA from FY2000-FY2010 were identified by ICD-9 diagnosis codes. Non-cardiac surgeries within 24 months of stent placement occurring in VA and Non-VA hospitals were identified using CPT codes. Patients with subsequent surgery were defined and matched to two non-surgery controls by age, race, stent type, stent year, and several cardiac comorbidities. Cardiac endpoints of MI, death, and/or repeated revascularization (MACE) within 30 days of surgery were compared to matched non-surgery controls during the same 30 day time period following stent. The risk difference of MACE and the changes in risk over time following stent placement were estimated using generalized linear models.

III. Results: The cohort consisted of 22,501 surgery and 45,002 non-surgery patients, 53% of which had DES and 37% had a history of MI within 6 months prior to stent. Most surgeries were integumentary (17%), with a median RVU of 6.6(IQR 2.2-11.7), and 65% were outpatient. While MACE rates decreased over time since stent placement, the overall MACE rate among cases was 4.5% compared to 1.3% in the non-surgery controls. This resulted in an overall risk difference across of 3.2%(2.9%-3.5%) with surgical cases being more likely to experience MACE in the postoperative period [(RR=3.4(3.1-3.7)]. Overall, cases were more likely to experience MI [RR=4.2(3.1-5.6)] or death [RR=1.7(1.1-2.5)] but not more likely to experience revascularization [RR=1.2(0.9-2.5)]. After adjusting for surgical characteristics, the risk difference decreased across time to a point of no significant incremental cardiac risk for surgery 6 months after stent.

IV. Conclusions and Relevance: In both cohorts, adverse cardiac events following coronary stenting decrease over time since stent. Furthermore, we found no differences in MACE risk beyond 6 months after adjusting for surgical characteristics.

Robert, Stephanie Marie (MSTP)

Project Length:	Long
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Harald Sontheimer
Abstract Approved By Advisor:	Yes
Co-Authors:	Stephanie Robert, MS, Sue Buckingham, PhD, Susan Campbell, PhD, Kenneth T. Holt, Michael Berens, PhD, Harald Sontheimer, PhD
Title:	Brain tumor-associated excitotoxicity and seizures as a result of System xc- expression

Glioblastoma multiforme (GBM) is the most prevalent and aggressive malignant brain tumor. Past research has identified an important role for the cystine/glutamate exchanger, system x_c^- (SXC) in the growth of these tumors providing cellular uptake of cystine for synthesis of the endogenous antioxidant glutathione. More recently SXC-mediated glutamate release has been found to cause excitotoxic neuronal injury and tumor-associated seizures. When we evaluated tissue micro-arrays of matched GBM and uninvolved brain from 45 patients, we found heterogeneous SXC expression, with 54% expressing high levels and 46% expressing low/undetectable levels. This heterogeneity was also observed in mouse-propagated xenolines by Western blot, where only 5/9 showed prominent SXC expression. When implanted intracranially, 60–80% of high SXC expressing xenolines cause seizures in mice, compared to <15% of low SXC expressing tumors. High SXC expressing tumors release larger amounts of glutamate, cause increases in neuronal excitability and intracellular Ca^{2+} on Fura-AM Imaging, and create marked neuronal glutamate toxicity when co-cultured with cortical neurons. A dramatic decrease in viable neurons peritumorally is seen in high SXC expressing tumor implanted mice, but not in mice implanted with low SXC expressing xenolines. Additionally, survival of mice implanted with high SXC expressing xenolines is decreased ~2x versus low SXC tumor implanted mice. This survival trend also holds in the patient population. Using the NCI's REMBRANDT database we compared survival data for patients with upregulated versus downregulated expression of the SXC gene, SLC7A11, and found a decrease in survival with upregulation of this gene. These findings suggest that high SXC-expressing tumors comprise an excitotoxic and more malignant glioma subtype, and that high SXC expression may be associated with a poorer prognosis and increased incidence of glioma-associated seizures. Defining subpopulations of gliomas is an important first step for a personalized medicine approach to treatment of these devastating tumors.

Roth, Christen Thigpen (MS4)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Marjorie Lee White

Abstract Approved By Advisor: Yes

Co-Authors: White ML, Tofil N, Batemen L, O'Neal L, Youngblood A, Zinkan L, Roth C, Dure L, Needham B.

Title: Use of High-Fidelity Simulation to Explore Pediatric Critical Care and Emergency Physicians Communication Surrounding End-of-Life Care

Approximately 500,000 children in the US have life-threatening conditions. Research on pediatric end-of-life care (ELC) indicates that good communication between a child's medical team and family is necessary to ensure that the family's wishes regarding the use of life-prolonging treatments are understood and respected. We sought to demonstrate that the simulated setting could be used to explore physician communication surrounding end of life care.

21 pediatric critical care or emergency physicians took part in our study at the Children's of Alabama Pediatric Simulation Center. The physicians responded to a simulated emergency involving a chronically ill child with signs of impending respiratory failure. We developed a mixed methods study surrounding the interaction between the physician and the simulated patient and simulated parent and structured interviews with the physician after the simulation to study the physician communication of ELC. Participants in the case were assigned a quantitative communication score ranging from 1 to 4, where 1 represents a treatment decision made after extensive discussion of available options while 4 indicates a treatment decision made without discussing available options. Qualitative data was collected from the sessions and from structured, scripted debriefings which were audiotaped, transcribed, and coded using grounded theory.

We found there to be differences in communication related to race, gender, experience, and fatigue. We did not find differences in parental status. Malpractice fear approached statistical significance.

The simulated setting can be used to examine individual-level physician characteristics associated with doctor-parent communication. To our knowledge this represents the first attempt to combine the use of sociological assessment tools with high-fidelity pediatric simulation to better understand barriers to communication regarding ELC. Participatory physician-parent communication may not consistently occur in EOL pediatric care. Addressing this issue is crucial to improving care for children who are at the end of life.

Rowan, Patrick David (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Yang Yang

Abstract Approved By Advisor: Yes

Co-Authors: Timothy N Trotter, Mei Li, and Yang Yang

Title: Heparanase induces EMT-like phenotype in human myeloma cells

Multiple myeloma is the second most common hematological malignancy after non-Hodgkin's Lymphoma. A hallmark of myeloma cells is their predominant localization in the bone marrow of the patients and metastasis from primary bone sites to new sites in distant bone. Bone metastases occur in 90% of patients with myeloma, but the mechanisms of myeloma metastasis remain unclear. Studies have demonstrated that myeloma cells expressing high levels of the enzyme heparanase induce more bone destruction and metastasis to bone than myeloma cells expressing low levels of heparanase. Epithelial to mesenchymal transition (EMT) is a process where cells lose their epithelial characteristics and acquire more migratory, mesenchymal properties. When cells undergo EMT, they down-regulate E-cadherin and up-regulate other surface proteins such as vimentin and N-cadherin, which aid them in migration. EMT is known to occur in some malignancies of epithelial origin, allowing the cells to become more invasive. Myeloma cells are not of epithelial origin; however, a recent study suggests that they can undergo an EMT-like phenotype, allowing the myeloma cells to constantly invade new areas within the bone marrow. Very little is known about an EMT-like process occurring in myeloma cells. The present study investigates the influence heparanase expression has on the induction of an EMT-like phenotype in CAG myeloma cells. Using methods of flow cytometry, immunoblotting, and immunohistochemistry to quantify levels of EMT-associated proteins, we support the hypothesis that overexpression of heparanase in CAG myeloma cells leads to an increase in mesenchymal markers N-cadherin and vimentin *in vitro* and *in vivo* and a decrease in epithelial marker E-cadherin. In addition, heparanase inhibitor SST1 can inhibit heparanase-mediated EMT, suggesting heparanase enzymatic activity is important for this EMT induction. Our findings reveal new insights into the role of heparanase in multiple myeloma and provide a novel strategy for the treatment of myeloma.

Saini, Reshu (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Heidi Umphrey

Abstract Approved By Advisor: Yes

Co-Authors: Marshal Mahoney, Kenneth Hoyt, Heidi Umphrey

Title: An Evaluation of Contrast Enhanced Ultrasound Imaging in Patients with Breast Cancer: A Feasibility Study

Breast cancer is the most common type of cancer in women (29% of cases) with the second highest mortality rate (14% of cancer deaths each year). Angiogenesis is a process by which new blood vessels develop to replenish a growing tumor. This process is a fundamental step for tumor growth, metastasis, and prediction of behavior of certain cancers. Recently, the use of ultrasound (US) and US contrast agents (termed microbubbles) to characterize tumor angiogenesis has been demonstrated in both murine animal models and human breast cancer models. In this study, we observe the utility of US contrast agents in characterizing early response to neoadjuvant therapy in breast cancer. Eight female patients with estrogen and progesterone positive operable breast cancers were followed over an 18 wk period with concurrent neoadjuvant chemotherapy (letrozole and bevacizumab). A baseline US with and without contrast agents was performed with a follow up imaging session every 3-5 wk for each patient during the course of therapy. Tissue perfusion parameters were extracted utilizing offline image processing with MATLAB. Preliminary results show a decrease in tissue perfusion parameters, especially area under the curve (AUC) and the wash-in-rate (WIR), between the baseline and first follow-up, highlighting a good response to the neoadjuvant therapy. The use of US and US contrast agents in monitoring chemotherapy can provide a prognostic tool and can prevent toxic side effects for non-responders in the early stages of therapy.

Sands, Claire Elizabeth (MS3)**Project Length:** Short**Prior Research Experience:** No**Source of Funding:** Other**Faculty Advisor:** Candace Floyd, Ph.D**Abstract Approved By Advisor:** Yes**Co-Authors:****Title:** A novel catalytic oxidoreductant improves functional outcomes in spinal cord injured rats

Spinal cord injuries (SCI) are devastating injuries that often result in neuropathic pain and reduced locomotor ability. Secondary tissue injury results from the formation of reactive oxygen species (ROS) and activation of nuclear factor kappa B (NF- κ B) signaling. This cascade leads to inflammation and expansion of the damaging lesion. A novel therapeutic catalytic oxidoreductant compound, Mn-TnBuOE-2-PyP⁵⁺ (BuOE), is a potent superoxide dismutase (SOD) mimetic known to dissipate ROS and inhibit NF- κ B activation. With efficient CNS bioavailability and decreased toxicity, BuOE is undergoing active research in the area of neuropathic pain. However, this compound has yet to be investigated in terms of functional motor and sensory recovery. This study investigates whether post-SCI administration of BuOE, in conjunction with exercise rehabilitation, increases function and decreases neuropathic pain.

Thirty adult male rats received a moderate contusion SCI at the T10 level. Each animal was blindly assigned to one of four groups: BuOE administration only, BuOE + rehabilitation, rehabilitation only, or no subsequent therapy. BuOE was administered one hour post injury, then twice per day for the next 7 days. Weekly functional recovery tests included the Basso, Beattie, Bresnahan (BBB) open field test, von Frey filaments for mechanical allodynia, and acetone for cold allodynia. The rehabilitation consisted of swimming exercise four times per week with weekly assessment using the Louisville Swim Scale (LSS). These tests continued for 7 weeks post-SCI.

Animals treated with BuOE show a trend toward increased locomotor ability, independent of any rehabilitation effect. There was no difference between groups with regards to mechanical allodynia post-injury. Both the BuOE and the BuOE + rehabilitation groups showed decreased cold allodynia post injury. Rehabilitation-only animals exhibited a less robust decrease in cold allodynia.

These data suggest that BuOE may be beneficial after SCI by increasing locomotor ability and reducing cold allodynia. Given these promising trends, and the pressing need for therapeutics aimed at improving functional outcomes, further studies investigating the beneficial effects of BuOE in spinal cord injury models is warranted.

Sauer, Paul Frederick, Jr. (MS2)**Project Length:** Short**Prior Research Experience:** No**Source of Funding:** MSSRP (NIH T35)

Faculty Advisor: Devin Eckhoff MD

Abstract Approved By Advisor: Yes

Co-Authors: Derek DuBay MD, Jack Crawford MD, PhD, Andrew Chou

Title: Intraoperative Predictors of Liver Transplant Outcomes

Background: Surgical transplantation of the liver is a treatment option for end stage liver disease, acute liver failure, hepatocellular carcinoma, and some pediatric metabolic liver diseases. There are two main surgical techniques used for orthotopic liver transplantation, the bicaval or conventional caval reconstruction technique (CV) and the piggyback technique (PBT). CV involves surgical clamping of the recipient's suprahepatic and infrahepatic inferior vena cava, while the PBT preserves the recipient's retrohepatic vena cava by surgical dissection of the native liver off of the cava. An end-to-side or side-to-side anastomosis is then created from the donor to the recipient's cava during the PBT.

The aim of this study was to examine how intraoperative periods of hypotension, defined as a mean arterial pressure (MAP) below 60 mm Hg, affected liver transplant outcomes. Outcomes included patient survival, hospital length of stay (LOS), intensive care unit LOS, and acute kidney injury (AKI) following liver transplantation.

Hypothesis: As the piggyback technique better maintains venous return during liver transplantation because of only partial occlusion of the inferior vena cava, it is hypothesized that this surgical technique will be associated with shorter intraoperative periods of hypotension and better outcomes when compared to the conventional caval reconstruction technique.

Methods: The UAB liver transplant database was used to identify those patients that had received a liver transplant. The electronic medical record was used to identify hospital course and operative technique variables. The separate anesthesia database recorded intraoperative hemodynamic data. This data will be analyzed to identify predictors of liver transplant outcomes using statistical analysis.

Results and Conclusions: Once the data is analyzed by a statistician, the results may inform intraoperative and post-operative management of patients undergoing surgical transplantation of the liver.

Sawyer, Kristine Campbell (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Marjorie Lee White
Abstract Approved By Advisor:	Yes
Co-Authors:	Dr. Laura Lindsay
Title:	Pilot Survey of Components of EMS Emergent Handoffs

Purpose of study: Many patients arrive to the Emergency Department (ED) via Emergency Medical Services (EMS); the information provided by EMS personnel can expedite the care given to critically ill children. Communication errors are the root cause in up to 70% of sentinel events and cause treatment delays in 84% of cases (Cheung et al. 2010). No studies have been done evaluating from an EMS perspective what information should be included.

Methods: A paper survey was distributed to EMS providers who transport pediatric patients to Children's of Alabama. Questions focused on demographics, approaches to emergent handoff, education for emergent handoffs, components important to an emergent handoff, and situations that affect handoff quality. For the purpose of this survey an emergent hand off was defined as the handoff that occurs between providers upon transfer of a patient to a higher level of care specifically the information given when transferring an unstable or decompensating patient. IRB approval was obtained by the University of Alabama at Birmingham.

Results: A total of 105 surveys were collected from 22 (21%) EMT basic, 1 (1% EMT Advanced and 80 (76%) Paramedics. Sixty-three percent had greater than 10 years experience; 15% had 5-10 years; 13% had 1-5 years; and 9% had less than 1 year. Seventy-two percent reported that their agency encourages standardization but only 40% report receiving training. Of those receiving training 79 % indicated that their training was effective or highly effective. Respondents described completeness of their handoff as complete 35% of the time and containing some or very little of the information 15% of the time. Sixty-five percent of respondents organized their handoffs chronologically. Fifty percent agreed that emergent handoffs are fundamentally different from non-emergent handoffs. Handoffs are reported strongly or somewhat affected by high noise level (84%), multiple interruptions (91%), and interactivity (72%). The most essential components rated by EMS providers include chief complaint, mechanism of injury, medications given, response to medications, and physical interventions. Components rated lowest in priority by EMS providers were name, sex, weight, comorbid factors, and lab results (ie glucose).

Conclusions: To our knowledge, despite significant attention to the importance of handoffs in improving patient care this is the first survey to query EMS providers about the content and structure of emergent handoffs. This study provides prospective on EMS provider priorities and can serve as the basis for development of a standardized handoff tool. Future steps will be to match physician and EMS providers priorities' to develop a standardized handoff approach to maximize communication.

Scanlon, Nicholas (MS2)

Project Length:	Short
Prior Research Experience:	Yes
Source of Funding:	Department of Medicine Fellowship
Faculty Advisor:	Steffanie Sabbaj and Paul A. Goepfert

Abstract Approved By Advisor: Yes

Co-Authors: Steffanie Sabbaj and Paul A. Goepfert

Title: Allogeneic Responses as an Explanation for Higher Risk of Transmission of HIV-1 in HLA-B Matched Individuals

Human leukocyte antigen (HLA) class I alleles have been associated with different outcomes of HIV progression, and epidemiologic studies have demonstrated that HLA class I homozygosity accelerates HIV-1 progression. Additionally, it has been shown that discordant couples sharing HLA-B class I alleles are more likely to transmit HIV-1. More importantly, children who shared HLA class I alleles with their mother were more likely to acquire HIV-1 via vertical transmission and progress to AIDS, while maternal homozygosity at class I HLA increased the risk of vertical HIV-1 transmission and was associated with higher pre-HAART viral load. We hypothesized that individuals who match at both HLA-B alleles should have a reduced mixed lymphocyte reaction (MLR) than those who are not matched. To test this hypothesis, we performed a variation of the MLR by incubating peripheral blood mononuclear cells (PBMCs) matched for both copies of any of the three class I HLA alleles, HLA-A, HLA-B, or HLA-C and measuring cytokine production from proliferating cells.

Furthermore, we did the same for PBMCs matched at both HLA-B alleles in addition to either one -A or one -C allele. Proliferation and production of IFN- γ , perforin, or granzyme-B by CD8 $^{+}$ T cells matched at both HLA-B alleles and one -C allele was significantly decreased when compared to that of CD8 $^{+}$ T cells not matched at any HLA allele. Furthermore, proliferation and production of IFN- γ by CD4 $^{+}$ T cells was significantly decreased when compared to that of CD4 $^{+}$ T cells not matched at any HLA allele. Linkage disequilibrium may account for the finding that a matching HLA-C allele in addition to matching HLA-B alleles is necessary to see a difference in production of these effector molecules. These findings support the hypothesis that reduced allogeneic responses may be an explanation for higher risk of transmission in HLA-B matched couples.

Scogin, Mallory Ann (MS4)

Project Length: Long

Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Jeffrey Blount

Abstract Approved By Advisor: Yes

Co-Authors: Brandon Rocque MD MS, Ralee' Bishop, Mallory Scogin, Betsy Hopson, Anastasia Arynchyna MPH, Christina Boddiford MPH, Chevis N Shannon, MBA, DrPH, Jeffrey Blount, MD

Title: Assessing Health-Related Quality of Life in Children with Spina Bifida

Introduction: The purpose of this study was to explore various aspects of health-related quality of life (HRQOL) in children with spinal dysraphism.

Methods: We enrolled a prospective cohort of 159 patients from the multi-disciplinary spina bifida clinic. Surveys were distributed to caregivers of spina bifida patients age 5 and older. Data were collected using the HUI-3 health-utilities index focusing on vision, speech, hearing, dexterity, ambulation, cognition, emotions, and pain. Each participant received an overall HRQOL utility score and subscores. These were correlated with demographic and treatment variables. Analysis was done using SPSS Statistics (V21).

Results: There were 125 patients with myelomeningocele, 25 with lipomyelomeningocele, and few other dyraphisms. Among patients with myelomeningocele, 107 (86%) had CSF shunts in place; 14 (11%) had undergone Chiari 2 decompression, 58 (46%) were community ambulators and 45 (36%) were non-ambulatory.

Patients with myelomeningocele had significantly lower overall HRQOL scores than patients with closed spinal dysraphism. Among patients with myelomeningocele, younger patients had higher HRQOL scores ($R^2=0.051$, $p=0.008$). History of VP shunt was associated with worse HRQOL (overall score, ambulation, and cognition subscores). History of Chiari 2 decompression was associated with worse overall and cognition scores. Patients who could ambulate in the community had higher overall and ambulation scores. History of tethered cord release was correlated with lower pain subscore. No association was found between gender, race, insurance type, bowel or bladder continence and HRQOL.

Conclusion: Patients with myelomeningocele have significantly lower HRQOL scores than other spinal dysraphism patients. History of shunting and Chiari decompression correlate with lower HRQOL scores.

Among myelo

No association with race (ANOVA), gender, insurance, bowel continence, bladder continence

Strong association with shunt (p<0.001 overall, 0.001ambulation, 0.028 cognition).

of shunts associated with overall by linear regression (p=0.008)

Considering only patients with shunts, # of shunts correlates with MAambulation.(persists with control for age)

Chiari 2 decompression (p=0.008 overall, 0.012 cognition)

Mobility (p<0.001 overall and ambulation) Community sig higher than non-amb and non func overall. Comm sig higher than all in ambulation subscore.

TCR history sig worse pain component.

Shafferman, Ashley Corinne (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Timothy Beukelman

Abstract Approved By Advisor: Yes

Co-Authors: Kevin R Fontaine, Randy Q Cron, Timothy Beukelman

Title: Changes in Body Mass Index in Children with Juvenile Idiopathic Arthritis Treated with Tumor Necrosis Factor Inhibitors

Objective. To evaluate changes in body mass index (BMI) among cohorts of children with juvenile idiopathic arthritis (JIA) with and without tumor necrosis factor inhibitor (TNFi) therapy

Methods. We performed a retrospective chart review of children with JIA who newly initiated TNFi therapy and had at least 1 year of subsequent follow-up (TNFi cohort). We also included children with JIA and at least 1 year of follow-up without any TNFi therapy (comparator cohort). Children with systemic arthritis were excluded. Age and sex specific BMI z-scores and their corresponding categories (normal, overweight, obese) were determined. We compared changes from a baseline visit to the last follow-up visit using t-test for BMI z-scores and chi square and Kruskal-Wallis tests for BMI categories.

Results. The TNFi cohort had 167 patients; the comparator cohort had 37. The median study follow-up was 2.8 and 2.2 years, respectively. The cohorts had similar age, sex, race, weight, and height distributions. The TNFi cohort had a statistically significant increase in BMI z-score from baseline (+0.15; p=0.02) that was not significantly different than the increase (+0.09) observed in the comparator cohort (p=0.7). There was no significant change in the proportions of overweight and obese children in the TNFi cohort compared to baseline (p = 0.4) or compared to the change in the comparator cohort (p=0.2).

Conclusion. Over more than 2 years of follow-up, we did not observe a significant increase in BMI among children with JIA receiving TNFi compared to those not receiving TNFi.

Singer, Jeffrey Robert (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Casey Weaver

Abstract Approved By Advisor: Yes

Co-Authors: Matthew Palmer, Henrietta Turner, Karen Janowski

Title: The HAT-BAC Mouse Model: Turning Statistical Association into Biological Relevance for Inflammatory Bowel Disease

Crohns disease and Ulcerative Colitis classified together as Inflammatory Bowel Disease (IBD) affect an estimated 1.4 million Americans and combine for over \$1.26 billion of direct and indirect costs to the US economy. While the complex origins of these debilitating autoimmune diseases are incompletely understood, the immunoregulatory cytokine Interleukin-10 (IL-10) plays an essential and non-redundant role in protection from IBD. Patients with coding mutations in IL-10 or its receptor and mice deficient in this protein get spontaneous and severe intestinal inflammation. Additionally, recent Genome Wide Association Studies have implicated two single nucleotide polymorphisms (SNPs) within conserved non-coding regions (CNRs) of the *IL10* extended locus that increase one's susceptibility to IBD.

Until recently, attributing a functional role to these polymorphisms would have been impossible, as they do not alter the protein coding sequence of *IL10*. Here we describe the development of a novel mouse model to study functional cis-regulatory elements in order to elucidate a role for these polymorphisms in *IL10* regulation. The strategy implements Phi-C31 integrase to selectively insert a single copy Bacterial Artificial Chromosome (BAC) transgene into a known location on the X chromosome of the mouse genome.

Using recombineering, we have engineered a BAC containing the entire human *IL10* locus with the ability to selectively knock out the CNRs housing both SNPs linked to IBD susceptibility in various cell types. Using this powerful new murine model in concert with clinical samples from IBD patients, our studies provide a system in which to functionally test hypotheses generated from genomic datasets and elucidate novel mechanisms of *IL10* regulation.

Sistani, Bobbak R. (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Edgar Jaimes

Abstract Approved By Advisor: Yes

Co-Authors: Ping Hua, Philip Chumley, Edgar Jaimes

Title: Effects of Nicotine use on expression of VEGF, ETS-1, and Nephron in a diabetes model

Tobacco smoking has proved to be an independent risk factor accelerating the progression of diabetic nephropathy, the most common cause of Chronic Kidney Disease in the United States. Among the numerous harmful substances found in tobacco, nicotine is one of the highly active compounds that maybe acquired through active and passive smoking. The db/db mouse strain has been used as a model of type 2 diabetes. In this study, we investigated the effects of nicotine on the levels and presence of nephron, VEGF, and ETS-1 in the kidney. Eight weeks old db/db mice (C57BLKS/Jlepr) and control non-diabetic mice (C57BLKSJ) were divided in 2 groups each: control mice on tap water, control mice on nicotine (100 ug/ml) in the drinking water, diabetic mice on tap water, diabetic mice on nicotine. The mice were maintained in their respective treatment groups for 10 weeks. Kidneys were then harvested and saved for histology and molecular biology. Western blot densitometry studies indicate a significant decrease in nephron levels with nicotine use. Levels of VEGF decreased, but were not significant. Immunofluorescence suggested ETS-1 presence in histologic samples taken from mice in the nicotine group. These observations will provide insight for the pathogenesis of diabetic nephropathy with nicotine use and future treatment options.

Smith, Andrew Franklin (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Dr. Carroll M. Harmon

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Pediatric Roux-en-Y Gastric Bypass: A single site study of long term outcomes in adolescents and teens

Introduction: Obesity among the pediatric and adolescent U.S. population is on the rise and predisposes those individuals to a lifetime of health problems. The health complications of obesity include diabetes mellitus, hypertension, dyslipidemia, and a host of others. From 2004-2012, Roux-en-Y gastric bypass has been performed on 26 adolescents and teens at Children's Hospital of Alabama. This is a risky procedure with lifelong complications. It was our goal to observe the long term outcomes in these children in terms of complications and changes in overall health.

Methods: All patients that have undergone Roux-en-Y gastric bypass at Children's Hospital of Alabama were included in the study. Criteria considered include postoperative complications and comorbidities such as: BMI, hypertension, obstructive sleep apnea (OSA), joint pain, polycystic ovarian syndrome (PCOS), dysglycemia, dyslipidemia, liver function/enzymes, nonalcoholic steatohepatitis (NASH), and depression. Patients were reevaluated postoperatively at 3 months, 6 months, 1 year, 2 years, and 5 years.

Results: The outcomes of 26 patients (17 female, 9 male) were observed. There were no deaths from the procedure. Strictures requiring balloon dilation was necessary in 4 patients (15.4%). A large decrease in weight and BMI was observed. At 3 months, 6 months, 1 year, 2 years, and 5 years, average change in weight from preoperative baseline was (respectively): -31.2 kg, -46.9 kg, -59.7 kg, -58.6 kg, and -57.2 kg; average change in BMI from preoperative baseline was (respectively): -10.0, -15.9, -19.9, -19.3, -19.5. There was also a large reduction in observed comorbidities.

Conclusion: Roux-en-Y gastric bypass is a risky yet effective tool for weight loss in adolescent and teen patients.

Smith, Cory Daniel (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Candace Floyd

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Evaluation of a Novel Catalytic Oxidoreductant to Confer Tissue Protection on the Brain after Concussion

Objective: The objective of this study was to investigate the effects of a novel pharmaceutical agent, a catalytic oxidoreductant, after concussions in a murine model. The oxidoreductant was a metalloporphyrin manganese (111)-tetrakis (*N*-ethylpyridinium-2-yl) porphyrin (MnTE-2-PyP). The overarching hypothesis was that post-concussion administration of this novel therapy would reduce secondary injury and thereby protect the brain after a single concussion or after multiple concussions. We tested the hypothesis that the oxidoreductant would detoxify reactive oxygen species and inhibit Nuclear Factor – kappa B (NF- κ B) signaling which would confer tissue protection and prevent cognitive deficits after concussion through inhibition of the inflammation pathway.

Design: We used an impact acceleration model to induce concussions/ mild TBIs in adult male mice with one contact to the head correlating to one concussion. The multiple concussion group received one concussion per day for 3 consecutive days, and uninjured animals made up the control group and underwent all procedures except for the impacts. The drug group received subcutaneous injections of the oxidoreductant 30 minutes after each impact and daily until the time of euthanasia. The mice were humanely euthanized at either 6, 24, 72 hours, or 7 days post-TBI, and the brains were extracted for histological evaluation of reactive oxygen species, NF- κ B activation, neuroimmune response, diffuse axonal injury, neuronal cell death, and gliosis.

Results: Preliminary results demonstrate the post-injury administration reduced activation of NF- κ B and associated neuroinflammation at all time points evaluated. Studies are on-going.

Conclusions: The data suggests that post-concussion administration of MnTE-2-PyP is protective after brain injury and further research should be done to fully elucidate these effects.

Stanley, Jennifer Anne (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Eddy Yang M.D., Ph.D.

Abstract Approved By Advisor: Yes

Co-Authors: Nowsheen S, Cooper T, Forero, A, LoBuglio, AF, Yang ES

Title: Contextual synthetic lethality in human triple negative breast cancer cells involving EGFR, BRCA1, and PARP1

Background/Objectives

Few therapeutic options are effective for triple negative breast cancers (TNBCs). We previously published a novel therapeutic regimen combining inhibitors of poly(ADP-ribose) polymerase (PARP), which target homologous recombination repair deficient cells, and epidermal growth factor receptor (EGFR). We have extended these findings to encompass multiple subtypes of triple negative breast cancer and EGFR inhibitors. Additionally, we hypothesized that EGFR may be affecting DNA repair through interaction with repair proteins, PARP1 and BRCA1, and that this interaction is dependent on subcellular location, which may depend on the post-translational modification status of EGFR.

Methods

TNBC cells were assessed for cytotoxicity and cell viability following EGFRi, PARPi, or both. Protein-protein interaction and subcellular location was determined by immunoprecipitation and fractionation. To determine if interactions were dependent on DNA, lysates were treated with Ethidium Bromide before immunoprecipitation. Mass spectroscopy was utilized to confirm interaction data and post-translational modification data.

Results

EGFRi with lapatinib, cetuximab, or erlotinib induces a contextual synthetic lethality with the PARPi, veliparib, *in vitro* in multiple TNBC subtypes. EGFR inhibition also increases cytosolic BRCA1 and EGFR, shuttling them away from nuclear DNA repair substrates. However, PARP1 localization is unchanged and remains nuclear. Interestingly, EGFR, BRCA1, and PARP1 are in the same protein complex, which is reduced by EGFRi. This complex formation was verified by *in vitro* binding assay and mass spectroscopy. Additionally, these proteins were found to interact in the nucleus, independent of DNA. Finally, we observed a novel post-translational modification of EGFR, PARylation, in the context of EGFRi.

Conclusions

These results reveal a contextual synthetic lethality between combined EGFR and PARP inhibition in multiple subtypes of TNBC that occurs via novel regulation of HR repair, suggesting potential generalizability of this combination in patients with TNBC. Additionally, this combination may be effective in other EGFR-dysregulated cancers.

Stone, Sara Lynn (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Frances Lund

Abstract Approved By Advisor: Yes

Co-Authors: Andre Ballesteros-Tato, Betty Mousseau, Frances Lund

Title: T-bet and IFNyR signaling regulate germinal center responses and long-lived plasma cell development in an influenza model

Memory B cells (Bmem) and long-lived plasma cells (LLPC) arise from germinal center B cells (GCB). The transcription factor Bcl6 is required for GCB cell survival and the development of Bmem. By contrast, Bcl6 inhibits LLPC development by repressing the transcription factor Blimp1 that normally controls LLPC development. To date, it is not clear how these opposing transcription factors are regulated in GCB cells. Interestingly, in T lymphocytes, the transcription factor T-bet modulates the balance between Blimp1 and Bcl6 and controls their subsequent differentiation into memory and effector cells. When naïve B cells are activated in vitro with T helper 1 (Th1) cells, the B cells develop into antibody secreting cells in a T-bet and IFNy dependent manner. Therefore, we hypothesize that B cell T-bet expression will be necessary for the development of LLPC. To test this hypothesis we evaluated GCB and LLPC responses in a murine model of Influenza A (A/PR8 stain) infection. Using mixed bone marrow chimeric animals in which all B cells are T-bet-/-, IFNyR-/-, or WT we characterized the transcriptional profile of GCB cells by RT-PCR and the flu-specific LLPC responses using ELISPOT and antibody titers. Following influenza infection, WT GCB cells express T-bet. GCB cells which expressed CXCR3, a chemokine receptor known to be regulated by T-bet, had higher expression of Blimp1 and IRF4, suggestive of plasma cell commitment. GCB cells that were T-bet-/-, in our chimeric model, expressed lower levels of Blimp1 and IRF4, supporting our hypothesis that T-bet supports plasma cell development. Additionally, 60 days after infection, T-bet-/- or IFNyR-/- B cells exhibited reduced flu-specific LLPC responses by ELISPOT and reduced flu-specific antibody titers in the serum by ELISA. These results support a role for T-bet and IFNyR signaling in the development of antigen specific LLPC in influenza.

Stoyka, Lindsay Elizabeth (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Catherine M. Fuller

Abstract Approved By Advisor: Yes

Co-Authors: Arun K. Rooj, Zhiyong Liu, Catherine M. Fuller

Title: Psalmotoxin-1 Inhibits Phosphorylation of ERK 1/2 in Glioma Cells

Ion channels play a significant role in the proliferation and migration of glioma cells. We have previously shown that gliomas have an active inward sodium current not found in normal astrocytes. The ion channel underlying this current is composed of members of the Deg/ENaC superfamily, specifically ASIC1, α -, and γ ENaC. This channel can be inhibited with high specificity by psalmotoxin-1 (PcTX-1), an inhibitor cysteine knot peptide derived from the venom of a West Indies tarantula. Current inhibition by PcTx-1 reduces glioma cell proliferation and migration, processes highly regulated by the mitogen-activated protein kinase (MAPK) pathway. A key regulatory point in the MAPK pathway is phosphorylation of extracellular signal-regulated kinase (ERK 1/2). Following prolonged (24-48h) incubation, PcTX-1 decreased phosphorylation of ERK 1/2. The goal of the present study was to investigate the time course (30 min-24 h) of inhibition of ERK 1/2 phosphorylation due to PcTX-1 in cultures of D54-MG and U87-MG glioma cells. Cells were split onto 35 mm dishes and treated with 100 nM PcTx-1 the following day. After exposure, cells were lysed and a BCA protein assay was used to determine sample protein concentration. Samples were then subjected to 10% SDS-PAGE. Western blots were utilized to determine expression of pERK 1/2 and ERK 1/2, using actin as a loading control. We found that exposure to 100 nM of PcTX-1 inhibited ERK 1/2 phosphorylation after only 30 minutes of incubation. This study suggests that the glioma cation conductance is required to maintain the phosphorylation status of ERK1/2.

This study was supported by the NIH Grants #DK37206 and #T32 GM008361.

Tamimi, Iman (MS2)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Nabiha Yusuf

Abstract Approved By Advisor: Yes

Co-Authors: Michelle Chang, Purushotham Guroji, Israr Ahmad, Nabiha Yusuf

Title: Loss of *p16/INK4a* gene enhances UVB-induced inflammation-mediated cutaneous tumor development

Ultraviolet (UV) radiation can mutagenize several genes which are involved in tumor suppression, oncogenic, and cell-cycle regulatory signaling pathways resulting in tumor development. The tumor suppressor gene *p16/INK4a* is frequently inactivated in human tumors, including skin tumors. The mechanism by which inactivation of this tumor suppressor acts to promote tumor development is not well understood. *p16/INK4a* gene knockout (*p16/INK4a*-/-) mice develop a severe inflammatory response in many disease conditions. Since chronic inflammation is known to promote skin cancer development, we investigated the link between gene *p16/INK4a*, chronic inflammation and UVB-induced skin cancer development. We found that *p16/INK4a*-/- mice (on a C3H/HeN background) developed significantly more tumors than their wild type (WT) mice, when subjected to chronic UVB radiation (200mJ/cm²) for 30 weeks. The tumor latency was 22 weeks and the tumors grew rapidly in volume in *p16/INK4a*-/- mice. At 24 weeks, 100% of *p16/INK4a*-/- mice had tumors. There were no tumors in WT mice after similar exposure to UVB at 30 weeks. Increase in tumor development also correlated with a significant increase in cyclooxygenase-2 (COX-2) mRNA expression in UVB-exposed skin and UVB-induced tumors of *p16/INK4a*-/- mice. There was a significant increase in inflammatory cytokines (IL-6, TNF- α , and IL-1 β) in skin and serum samples of *p16/INK4a*-/- mice following treatment with chronic UVB radiation. Thus, our data suggest that *p16/INK4a* deficient mice are more susceptible to both UVB-induced inflammation and UVB-induced skin tumor development. This new information can be developed as a novel strategy for treating skin inflammation and inflammation-associated skin tumor development, and may be exploited to develop anti-inflammatory therapies for intervention in populations that carry this mutation.

Tanner, Richard Morrell, Jr. (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Shawn Gilbert, MD

Abstract Approved By Advisor: Yes

Co-Authors: Frank Gleason, David Barrington

Title: Investigation of DFO as a novel treatment for contaminated open fractures

Desferrioxamine (DFO), a hypoxia inducible factor pathway activator, is a pharmacologic agent that has been shown to increase bone vascularity and improve healing in acute fracture and distraction osteogenesis models. The goal of this research project is to determine the effectiveness of local application of DFO in the definitive management of open fractures with established infections. It is hypothesized that enhancing local vascularity following severe extremity injury will improve the local tissue environment and help prevent the development of complications such as failure of bone and muscle healing. Open fractures were created in the lower extremity of 60 adult male brown Norway rats. The wounds were then contaminated with methicillin resistant *Staphylococcus aureus* and *Acinetobacter baumannii* complex and temporarily fixed. Four days following the initial injury, wounds were irrigated and debrided, and definitively fixed with an intramedullary K-wire and composite scaffold. Either tobramycin or a combination tobramycin and DFO were administered to the scaffold. Following the surgery 40 subjects were euthanized at 6 weeks post-op and 20 subjects were euthanized at 12 weeks. The muscle and femur segments were harvested at the time of euthanasia and were examined for the following: bacterial burden, muscle and bone histology, and CT angiography. It is expected that local antibiotic delivery will decrease but not completely eradicate infection in this model. The application of DFO in addition to Tobramycin will increase vascularity and thus improve local environment that will result in further clearance of infection, improved muscle and bone repair, or both. MicroCT will detect increased vascularity and bone healing and decreased muscle fibrosis in the treatment group receiving both Tobramycin and DFO in comparison to the group that is treated with only Tobramycin.

Tapley, Jeffrey Lynn, Jr. (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Cynthia Owsley PhD

Abstract Approved By Advisor: Yes

Co-Authors: Gerald McGwin Jr PhD, Ambika Ashraf MD, Paul MacLennan PhD, Koula Callahan, Karen Searcey MSPH, Cynthia Owsley PhD

Title: Feasibility and Efficacy of Diabetic Retinopathy Screening in Children with Diabetes

Objective: The most common eye complication caused by diabetes is diabetic retinopathy (DR), which is now the leading cause of new cases of blindness in the United States. Screening for DR in adults with diabetes using a non-mydriatic (no dilating drops needed) fundus camera is accepted worldwide, but its use among children with diabetes has not been described. This project will determine the feasibility and efficacy of non-invasive, non-mydriatic diabetic retinopathy screening in children with type 1 and type 2 diabetes mellitus.

Methods: The population consisted of children with type 1 or type 2 diabetes mellitus, ranging from 8 to 18 years of age who were patients at the UAB Division of Pediatric Endocrinology Clinic. During the patient's regularly scheduled clinic exam, a non-mydriatic fundus camera (Nidek Model AFC-230) was used to obtain images of the fundus of each eye. Visual acuity for each eye was determined using the TitmusV2 Vision Screener. In addition, a brief survey was administered focusing on the child's diabetes and history of receiving eye care. Information was obtained from the medical record on HbA1c, urine microalbumin, and lipid profile. The fundus images were reviewed and graded by a UAB ophthalmologist specializing in retinal/vitreal disease using the UK National Health System's classification system for diabetic retinopathy.

Results: Data analysis will be completed in October 2013. 236 participants enrolled in the study -- 202 with type 1 diabetes and 34 with type 2 diabetes. 5/202 participants (2.5%) with type 1 diabetes screened positive for DR, and 1/34 participants (2.9%) with type 2 diabetes screened positive for DR. 78 participants (33%) were found to have decreased visual acuity, and 12 participants (5%) screened positive for other ocular abnormalities. 6 participants' images (2.5%) were determined unreadable.

Conclusions: Conclusions will be generated after data analysis is complete.

Thomas, John William (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Department of Medicine Fellowship

Faculty Advisor: Anath Shalev

Abstract Approved By Advisor: Yes

Co-Authors: Junqin Chen and Anath Shelev

Title: TXNIP Modulates miR-33a and SREBP-2 in Human Ventricular Cardiomyocytes

MicroRNAs are small (~22 nucleotides) non-coding RNAs that regulate gene expression by base pairing with mRNA transcripts, leading to translational repression or transcript degradation. Previous studies have shown that miR-33a, a micro-RNA within an intron of the sterol regulatory element binding protein-2 (SREBP-2) gene, works concurrently with the SERBP-2 transcription factor to maintain sufficient levels of intracellular cholesterol by inhibiting translation of cholesterol exporters and beta-oxidation enzymes such as carnitine O-octanoyltransferase (CROT) and the β subunit of the mitochondrial trifunctional protein (HADHB). CROT catalyzes the transfer of medium-chain fatty acids from CoA to carnitine, mediating their transport from peroxisomes to mitochondria for beta-oxidation. HADHB is responsible for the final thiolysis step of beta-oxidation by the mitochondrial trifunctional protein.

Thioredoxin interacting protein (TXNIP) is considered a regulator of cellular redox state that acts by binding to and inhibiting thioredoxins, antioxidant proteins necessary to keep proteins in homeostatic reduced states during periods of oxidative stress. Roles for TXNIP have been elucidated for insulin resistance, beta cell apoptosis, and cardiac cell apoptosis, as well as cardiac metabolism. Most recently, we discovered that TXNIP also regulates microRNA expression and hypothesized that TXNIP may modulate miR-33a and beta-oxidation.

We tested our hypothesis *in vitro* by transfecting AC16 human ventricular cardiomyocytes with an siRNA targeting TXNIP or scrambled control and then harvesting RNA for quantitative real-time reverse transcription PCR (qRT-PCR) analysis.

We discovered that transient TXNIP knockdown led to significant decreases in SREBP-2 and miR-33a expression. Subsequent qRT-PCR analysis revealed a decrease in CROT and HADHB mRNA levels, but initial Western blot data showed an increase in CROT protein levels in cells treated with siRNA-TXNIP.

In summary, our results suggest that TXNIP does regulate miR-33a and SREBP-2 expression in human ventricular cardiomyocytes. In addition, TXNIP may inhibit translation of the miR-33a target and beta-oxidation enzyme, CROT.

Vaid, Shalini (MS4)

Project Length:	Intermediate
Prior Research Experience:	Yes
Source of Funding:	Other
Faculty Advisor:	Dr. Ambika Ashraf
Abstract Approved By Advisor:	Yes
Co-Authors:	Russell Griffin, Dr. Ambika Ashraf
Title:	Determinants of Apolipoprotein B in Children with Type I Diabetes Mellitus

Background: Patients with Type 1 Diabetes Mellitus (T1DM) have an extremely high risk of cardiovascular (CV) disease and mortality. Even though LDL cholesterol (LDL) has been the cornerstone of CV risk assessment, it is now well recognized that apo B provides a direct measure of the number of atherogenic lipoprotein particles in the circulation as it includes all potentially atherogenic particles, including very-low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL), LDL, and lipoprotein(a) [Lp(a)].

Objective: The primary objective of this study was to analyze the type and nature of lipoprotein abnormalities prevalent in children with T1DM. The secondary objective was to evaluate the determinants of apo B concentrations among patients with T1DM.

Methods: A retrospective electronic chart review of 607 patients with Type I DM who underwent Vertical Auto Profile (VAP) testing. A total of 600 subjects were included, 123 African American (AA) and 477 Non-Hispanic White (NHW) subjects. Hispanic subjects were excluded.

Results: AA subjects had a higher hemoglobin A1C, total cholesterol, LDL, apo B, lipoprotein a, HDL 2 and 3. BMI was strongly associated with total cholesterol, LDL, apo B, non-HDL, VLDL, and VLDL-3. Multilinear regression analysis demonstrated that the negative determinants of apo B concentrations in children with T1DM were age, AA race, HbA1c, SBP, DBP, and male sex. The relationship persisted even after adjusting for covariates in race, BMI, A1C, duration of diabetes. The determinants of Lp(a) were AA race, LDL, apo B, and Non-HDL. The relationship persisted for AA race, LDL, non-HDL, but disappeared for apo B after adjusting for covariates.

Conclusion: AA with T1DM has a higher prevalence of abnormal lipoprotein profiles and poor glycemic control. BMI was associated with abnormal lipoprotein profiles in T1DM subjects and hence weight management may have bigger implications in T1DM. Apo B concentrations in subjects with T1DM were determined by age, HbA1C, and blood pressure (BP), pointing towards the importance of adequate glycemic control and BP control for better CV care.

Vankineni, Maya (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Stanford Massie

Abstract Approved By Advisor: Yes

Co-Authors:

Title: The Use of Reflection in Measuring Professionalism in Medical Education

Professionalism in medical education continues to be a growing topic of concern for medical institutions nationwide. Previous studies have addressed the need for implementing methods of measuring professionalism throughout medical school, but few have effectively integrated these ideas into medical curricula. The goal of this study was to determine the effectiveness of reflective exercises, to gauge students' ability to reflect upon professional behaviors, and to determine ways to reinforce humanism in medical education specifically during the third and fourth years of medical school.

Medical students in their third year of medical school (n=180) participated in an educational activity in 2011. As a part of this exercise, students were instructed to write reflection pieces anonymously based on examples of humanism displayed during their clerkship rotations. Reflection papers were de-identified, collected, and randomly assigned to four groups. Thematic analysis of all reflections conveyed significant overlap in the following topics: sensitivity to patient comfort, quality of time spent, basic communication skills, breaking bad news, and quantity of time spent.

The prompted reflective writing exercise followed by small group discussion serves as a means for students to acknowledge professionalism and humanism during clinical years. In several papers, students became cognizant of their own behaviors and commented on avenues for self-improvement. Students were also able to underscore and reevaluate key aspects of the physician-patient interview that were taught at the very onset of medical school. These exercises thus serve as a way to reintroduce those basic yet valuable skills that are not emphasized during clinical rotations. Implementation of such exercises after each core clinical clerkship would be a favorable addition to medical curricula. Such change will highlight the importance of professionalism and humanism in medical practice and also promote the use of self-reflection as an invaluable tool in monitoring professional behaviors throughout student's careers.

Vinyard, Ashlee Ann (MS4)

Project Length: Intermediate

Prior Research Experience: No **Source of Funding:** Other

Faculty Advisor: Dr. Spencer Melby

Abstract Approved By Advisor: Yes

Co-Authors: Jerald P Wallace, Desiree Picone

Title: The Use of a Moderate Dose of Recombinant Factor VIIa for Postoperative Hemorrhage is Not Associated with Thromboembolic Complications After Open Cardiac Surgery

Background: Excessive bleeding after cardiac surgery results in an increased risk of reoperation and mortality. Recombinant activated factor VII (rFVIIa) has been found to be effective for treatment of hemorrhage. However, small studies have suggested that there may be a dose-related increased risk of thromboembolic events. Our hypothesis was that low-dose rFVIIa is safe and effective for refractory bleeding after cardiac surgery.

Methods: From January 2009 through January 2012, 196 of 2472 adult cardiac surgery patients received low dose (25-35 μ g/kg) rFVIIa for postoperative bleeding. Propensity matching with untreated patients was successfully performed using a multivariable linear regression model with 25 demographic, pre-, intra-, and post-operative risk factors to calculate the probability of rFVIIa use. Outcomes were tested using 2x2 chi-square tables.

Results: A single dose of rFVIIa was given in 184 (94%) of patients, while 12 (6%) required 2 or more doses. Propensity matching yielded 160 rFVIIa patients matched with 160 controls. Reoperation due to bleeding was 23% for the rFVIIa group and 28% for the untreated group ($p=.35$). Both groups experienced a similar high risk for 30-day hospital mortality (rFVIIa 23% v 25%, $p=.8$). No significant differences were found for stroke (rFVIIa 9% v 6%, $p=.29$), pulmonary embolism (rFVIIa 1% v 0%, $p=.31$), peripheral embolism (rFVIIa 1% v 1%, $p=.56$), MI (rFVIIa 0% v 1%, $p=0.31$), or other thromboembolic event(rFVIIa 3% v 1%, $p=.17$). No difference was found for rates of infection in the sternum (rFVIIa 10% v 10%, $p=.95$) or other sites, including the extremities and septicemia (rFVIIa 11% v 11%, $p=.85$).

Conclusion: Patients who have postoperative bleeding after cardiac surgery have a high incidence of complications, including thrombotic and embolic events, and have high perioperative mortality. Use of low-dose rFVIIa did not increase the risk of thromboembolic events or operative death in patients with bleeding when compared to a similar high-risk group of patients with hemorrhage that did not receive rFVIIa. These results demonstrated that use of low-dose rFVIIa for postoperative hemorrhage in cardiac surgery patients is effective and poses minimal increased rates of morbidity and mortality for these high-risk patients.

Vitta, Swaroop Pradeep (MS2)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Stefan Kertesz

Abstract Approved By Advisor: Yes

Co-Authors: Swaroop Vitta, Stefan Kertesz, Paul Wolff, Gerald McGwin, Renee Desmond, Davis Bradford, Garwen Chen, Shima Dowla, Zaki Yazdi, Shin Xu

Title: Assessing unmet need for medical care and safety net accessibility among Birmingham's homeless and the impact of major changes to the safety net

In Birmingham, Alabama previous reports (published in 2009 and currently in press) have shown that access to care for homeless persons is limited and has worsened over time. This study seeks to assess the impact on Birmingham's homeless of a rapidly changing health care safety net, drawing on methods developed in a study done by Kertesz, *et al.* (2010) that examined unmet medical needs for Birmingham's homeless. Unlike traditional access-to-care studies before it, the 2010 exemplar not only assessed access-to-care for those in need of medical care but also examined which safety net resources were used and how often, thus offering a portrait of safety net resource accessibility, as well as unmet needs for medical services. Since 2010, however, Birmingham's health care safety net has seen major changes. Many services offered by major public hospital sought by 51% of respondents in the 2010 survey closed due to a county debt crisis. More favorably, a student-run free clinic for the underserved population has opened since 2010. Through repetition, with modifications, of the 2010 homeless health care survey, this project aims to capture the changes to Birmingham's safety net since then. Specifically, we surveyed 200 homeless persons using a similar survey as that of the 2010 study. Though a full statistical analysis has not been run, preliminary results indicate access to care among the homeless has not improved in most areas. However, an unexpected increase in the number of homeless individuals reporting access to medications warrants further analysis. Using identical statistical methods, this study not only compares healthcare access for homeless individuals between now and 2010, it also illustrates the effect of the closure of a major safety net provider. Given the economic struggles facing much of the country, this could provide useful insight for communities facing similar economic difficulties.

Waits, George Sidney, IV (MS3)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Cynthia J. Brown

Abstract Approved By Advisor: Yes

Co-Authors: Lauren Stephens

Title: Evaluating Hospitalized Older Adults with the Acute Care Mobility Assessment

Background: Low mobility in older adults has been shown to be prevalent and associated with adverse outcomes, especially in the inpatient setting. Validation of a quick, bedside questionnaire to assess mobility level is a low-cost, practical way to inform diagnosis, target mobility-based treatments, and evaluate recovery in appropriate patient populations.

Methods: We recruited patients who were ≥ 65 years of age, newly admitted to the medical ward of the UAB Acute Care for Elders (ACE) Unit, with a Mini Cognitive Assessment score of > 3 , and able to walk in the 2 weeks prior to admission. Wireless accelerometers that record position every other second were attached to the thigh and ankle of consented patients in a standardized fashion. The monitor output was used to calculate the length of time patients spent at three different levels of mobility: lying, sitting, and standing or walking, using pre-defined criteria. The Acute Care Mobility Assessment (ACMA) questionnaire was used after 24 hours of wireless monitoring. The questionnaire asks the patient how frequently they sat up in a chair, and walked in their room, in the hall and off the unit. Data from the wireless monitors will be used to calculate the number of minutes lying, sitting, and standing or walking that occurred during the 24-hour observation period. Pearson correlation coefficients were used to assess the association between wireless accelerometer output and results from the ACMA.

Results: Patients questioned with the ACMA were shown to exhibit moderate activity levels, with an average score of 5.06 ± 1.67 (range 0-10), but correlation to the accelerometer data trended poorly.

Conclusion: Older hospitalized patients exhibited moderate activity levels as measured by the Acute Care Mobility Assessment. Future optimized algorithms for interpreting the accelerometer data may result in better correlation numbers.

Warmus, Brian Andrew (MSTP)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Erik Roberson

Abstract Approved By Advisor: Yes

Co-Authors: Dheepa R. Sekar, Gerard D. Schellenberg, Lori L. McMahon, Erik D. Roberson

Title: Mutant Tau Causes NMDAR-mediated Insulostratal Dysfunction and Behavioral Abnormalities in a Mouse Model of Frontotemporal Dementia.

Tau mutations cause frontotemporal dementia (FTD), a progressive and lethal disease that can present with personality changes, apathy, disinhibition, and repetitive behaviors. Patients have connectivity dysfunction and atrophy in a network of brain regions including insular cortex and ventral striatum. No mouse model with a tau mutation has demonstrated FTD-relevant behaviors, and it is unknown which brain regions or networks are impaired in a mouse model with FTD-relevant behaviors. We found that transgenic mice with the FTD-associated V337M human tau mutation (hTauV337M mice) have age-dependent repetitive grooming (severe enough to cause facial lesions), impaired nest building, and disinhibition. In a model demonstrating FTD-relevant behaviors, we hypothesized that tau mutations preferentially affect neurons in insulostratal regions. To test this hypothesis, we compared the biochemistry, anatomy, and physiology in insulostratal and anatomically similar control regions (motor cortex and dorsal striatum) of non-transgenic and hTauV337M mice. hTauV337M mice have decreased NMDA receptor (NMDAR) levels by western blot in insular cortex and ventral striatum at age of symptom onset (14 months), but NMDAR levels are not decreased in anatomically similar control regions. Consistent with decreased NMDAR function, hTauV337M mice have dendritic simplification of Golgi-stained neurons in insular cortex and ventral striatum, but not of neurons in anatomically similar control regions at 24 months. Electrophysiological recordings in acute striatal slices show hTauV337M mice have decreased excitatory transmission in ventral but not dorsal striatum at 14 months. In an effort to increase NMDAR function, acute treatment with the NMDAR co-agonist D-cycloserine (20 mg/kg, i.p.) decreased repetitive grooming and chronic oral treatment (20 mg/kg per day) reversed nest building impairments and disinhibition. These data suggest that FTD-associated tau mutations cause NMDAR dysfunction preferentially in neurons of insulostratal regions to cause behavioral abnormalities in a mouse model of FTD, providing a patient-relevant model for future therapeutic intervention.

Watson, John Deforest, IV (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Steven Rowe, MD MSPH

Abstract Approved By Advisor: Yes

Co-Authors: Hannah Bowers, Susan Birket PhD, Yao Li PhD

Title: Effect of a Novel Mucolytic on the Viscoelastic Properties of Cystic Fibrosis Mucus *In Situ*

Thick, hyperviscous mucus and delayed mucociliary clearance (MCC) are important elements underlying cystic fibrosis (CF) pathogenesis, but currently available therapeutics exhibit limited efficacy to combat mucus stasis. Our preliminary data suggests that PAAG, a soluble, nontoxic polycationic polysaccharide, reduces the viscosity of expectorated CF sputum. Therefore, we hypothesized that PAAG will improve viscosity of CF mucus *in situ*, ultimately improving MCC and abrogating CF progression. To test this hypothesis, we applied PAAG treatment to the air-liquid interface of well-differentiated primary human bronchial epithelial monolayers derived from CF donors, and then measured the viscosity of the mucus layer using particle tracking microrheology (PTM) of muco-inert 500 nm fluorescent beads *in situ*. PTM data showed a more than 100-fold decrease in static viscosity as compared to a vehicle control (3.05 +/- 0.57 PAAG vs. 470.70 +/- 131.00 Vehicle Control, 1.02 Hz frequency, n=4, p<0.05). Reduced viscosity was seen across all ranges of a frequency sweep (0.46 - 17.36 Hz), indicating the effect was robust and observed at shear rates likely to be encountered *in vivo*. These results mark the first demonstration of a pharmacologic reduction in CF mucus viscosity *in situ*. Subsequently, we used 1-μm resolution optical coherence tomography (μOCT) to simultaneously image the mucociliary transport (MCT) and ciliary beat frequency (CBF) of PAAG treated HBE monolayers (quantitative image analysis currently in progress). We expect that the decrease in viscosity will also be associated with an improved MCT and CBF, and this data will provide physiological significance to reduced viscosity conferred by PAAG. Further research in this area will examine the effect of PAAG on the MCC of living airway tissues *in situ*. These preliminary data indicate that PAAG markedly reduces the viscosity of CF mucus *in situ*, and represents a promising potential therapeutic agent for the treatment of CF lung disease.

Weaver, Alice (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Eddy S. Yang

Abstract Approved By Advisor: Yes

Co-Authors: Tiffiny Cooper, Hoa Q. Trummel, James A. Bonner

Title: DNA repair deficiency and sensitivity to PARP inhibition in HPV-positive head and neck cancer.

Incidence of human papillomavirus (HPV)-positive head and neck cancer (HNC) has risen sharply in recent years. These tumors significantly differ from their HPV-negative counterparts, including expression of HPV oncoproteins E6/E7 and increased response to both radio- and chemotherapy. Due to their favorable response rate, it is of great importance to identify de-intensified anticancer therapy to avoid excessive and unnecessary treatment-related toxicities in these patients. Poly (ADP-ribose) polymerase (PARP) inhibitors are exciting new agents that selectively target DNA repair-deficient cancers with only mild effects in normal tissue. As HPV E6 and E7 are known to degrade DNA damage response proteins p53 and Rb, we hypothesized that HPV-positive HNC has reduced DNA repair capability sufficient to be rendered sensitive to PARP inhibition. Consistent with our hypothesis, HPV-positive HNC demonstrated abnormal DNA damage resolution following radiation, as directly assessed by neutral comet assay. Additionally, this defect was specific to the homologous recombination (HR) pathway, as evidenced by reduced RAD51 foci-forming ability. This coincided with a significant response to PARP inhibition in *in vitro* and *in vivo* models, including a patient-derived HPV-positive xenograft. To further characterize the repair deficiency in HPV-positive HNC, we examined basal expression of a panel of DNA repair proteins. Interestingly, we found reduced expression of FANCD1/BRCA2 and FANCD2, two Fanconi anemia proteins that help initiate the DNA damage response and recruit HR factors to damage sites. Suspecting E6/E7 may be involved in regulating these proteins, we performed siRNA knockdown of E7 in HPV-positive HNC cell lines; re-assessment of HR proteins showed rescue of FANCD2 expression. In conclusion, HPV oncoprotein E7 reduces levels of FANCD2 in HNC by an as-yet unknown mechanism, correlating with a DNA repair defect and sensitivity to PARP inhibition. These studies identify PARP inhibitors as a potential agents for de-escalated anticancer therapy in HPV-positive HNC patients.

Webb, Justin James (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: American Heart Association Fellowship

Faculty Advisor: Lufang Zhou

Abstract Approved By Advisor: Yes

Co-Authors: Lufang Zhou, Qince Li

Title: Cardiac Optogenetics: Optical Pacing of Heart Tissue

Introduction: Optogenetics is an emerging technology that allows for the remote and precise optical control of specific cells in living tissue at high spatiotemporal resolution. Though widely employed in the field of neuroscience, the application of optogenetics in the study and therapy of cardiovascular diseases is still in its infancy. The primary objectives of this work are to examine whether optogenetic pacing is feasible in neonatal rat ventricular myocyte (NRVM) monolayers and to optimize the optogenetic pacing protocol.

Methods: Primary cultures of NRVMs were infected with lentivirus containing the ChR2 gene. Cells were stained with membrane potential (V_m)-sensitive dye (RH-237) and paced with short pulses of LED light (475nm) delivered via optical fibers of various diameters. V_m -sensitive fluorescence was excited at 580/40nm and mapped at >680nm using a photodiode mapping system. Pacing parameters such as light intensity, pulse duration, and the size of illuminated area that allow for successful pacing were determined.

Results: ChR2 can be stably and homogenously expressed in NRVM monolayers, although induction slightly affected monolayer confluence. ChR2-expressing NRVM cultures could be paced at frequencies ranging from 0.5-4Hz using even the smallest 300 μ m fibers, suggesting high level of ChR2 expression in NRVMs. Exposure of ChR2-expressing cells to V_m -sensitive mapping excitation light did not change the frequency of spontaneous cell beating, indicating such light did not activate ChR2 channels. Optical V_m mapping showed that light-induced wave velocities in ChR2-expressing monolayers were similar to wave velocities induced by electrical pacing but somewhat smaller than in control non-infected monolayers.

Conclusions: ChR2 can be stably expressed in cultures of NRVMs. Furthermore, the optogenetic pacing technology can be easily expanded to multi-site pacing, and thus has the potential to be developed into a novel optical-based pacing device that could be used for the re-synchronization therapy of end-stage heart failure.

Webb, William Mitchell (MSTP)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Joel Berry

Abstract Approved By Advisor: Yes

Co-Authors: Tim Fee

Title: Response of IPF Myofibroblasts to Mechanical Strain

Idiopathic pulmonary fibrosis (IPF) is a progressive disease of the lung with no known etiology and no effective treatments. In IPF, an aberrant fibrotic response is driven by mediators that induce the trans-differentiation of fibroblasts to myofibroblasts at fibroblastic foci. These cells secrete excess collagen matrix and express embryologically primitive contractile, smooth-muscle-like actin (α -SMA), a reliable indicator of disease progression.

This altered ECM, expression of α -SMA, and changing breathing dynamics in IPF constitute a unique mechanical microenvironment. Previous studies have shown that IPF myofibroblasts may be sensitive to the stiffness of their substrate, suggesting a mechanotransduction pathway within IPF myofibroblasts. However, despite characterized mechanotransduction pathways in other populations of fibroblasts, there exists a dearth of literature concerning the biophysical factors affecting IPF and the response of myofibroblasts to mechanical forces.

In order to examine the effects of mechanical strain on these cells, myofibroblasts were seeded onto collagen-coated electrospun PCL scaffolds and allowed to attach and grow for one hour before being subjected to strain or left as an unstrained control. A linear actuator/load cell bioreactor applied ~10% strain to test groups overnight. Using fluorescent nanospheres, DAPI, and phalloidin stains, fluorescent microscopy revealed viable myofibroblasts attached to their surface while a custom optical tracking program (MATLAB) confirmed dynamic strain. Relative expression of α -SMA was determined for both strained groups and controls via RT-PCR, revealing diminished α -SMA expression for strained groups.

These findings suggest a decreased pathologic response of myofibroblasts to mechanical strain, and further research into these mechanisms may elicit novel therapeutic targets for this devastating disease.

Wells, Derek Everett (MS2)

Project Length:	Short
Prior Research Experience:	No
Source of Funding:	MSSRP (NIH T35)
Faculty Advisor:	Dr. James Galbraith, M.D.
Abstract Approved By Advisor:	Yes
Co-Authors:	None
Title:	HCV Awareness, Risk Assessment, and Healthcare Utilization Among “Baby Boomers” Presenting to the UAB Emergency Department

Importance: Hepatitis C virus (HCV) is a challenging public health concern under-appreciated by most clinicians. Though treatable, HCV morbidity and mortality is expected to rise in coming decades due to the high prevalence of chronic HCV infection recently identified among the “baby boomer” birth cohort. This finding led to recommendations by the CDC and U.S. Preventative Services Task Force for a one-time HCV screening for all “baby boomers.” However, general understanding of HCV prevalence and risk among “baby boomers” presenting to emergency department (ED) settings is lacking. We therefore examined HCV infection knowledge, current HCV status, risk factors, and healthcare utilization practices among “baby boomers” seeking treatment at a large, urban-based ED.

Methods: A convenience sample of 150 consenting “baby boomers” participated in brief interviews prior to ED discharge. Interview questions focused on basic demographic and socioeconomic information; HCV knowledge, awareness and risk factors; and healthcare utilization practices. Responses were tabulated by HCV status, and chi-squared tests were performed to identify significant factors related to HCV status.

Results: Knowledge of HCV status was low among participants, with 68% unaware of their HCV status, 11.3% aware of their HCV+ condition, and 20.7% aware of their HCV- status. Of those unaware of their HCV status, many reported high prevalence of HCV risk factors. For example, 27.5% received a prior blood transfusion (42.9% before 1992) and 4.9% reported past intravenous drug use (2.9% prior to 1992). Only 10.8% were aware of recent HCV screening recommendations targeting “baby boomers,” and 35% of HCV+ participants were unaware that treatment existed for HCV infection.

Conclusions: The ED revealed a high rate of “baby boomers” with a high prevalence of HCV-related risk factors though unaware of their HCV status. These findings support the need to further evaluate ED settings as potentially successful HCV screening initiative sites.

Whisenhunt, James Dylan (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Barton L. Guthrie

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Mahesh Shenai, Dr. Harrison Walker, Dr. Bonita Agee

Title: MER-determined STN Width as a Predictor of Postoperative UPDRS Improvement

Background. DBS of the STN is an effective treatment for medically refractory Parkinson's Disease.

Intraoperative measurement of STN width through microelectrode recording (MER) is a common proxy for optimal electrode location.

Methods. Records were reviewed for 126 patients who underwent their first single-sided STN DBS placement for PD between 2005 and 2010 at UABMC. Patients lacking preoperative, intraoperative, or postoperative records were excluded. Reviews of preoperative and 3-month postoperative UPDRS Part III, intraoperative MER records, and postoperative MRI scans were conducted. Global UPDRS scores were split into ipsilateral, contralateral, and midline scores. The final cohort consisted of 67 patients (mean age = 60 yrs (\pm 11), length of disease = 13 yrs (\pm 5.6), baseline UPDRS global = 37 (\pm 11), contralateral = 15 (\pm 5.6), ipsilateral = 9.0 (\pm 4.2), midline = 4.2 (\pm 4.0)). STN widths were defined as depths associated with increased background activity and motor-driven, spiking action potentials on MER. Additionally, widths were normalized to AC-PC length (mean = 25.69 mm (\pm 1.65)). Relationships between STN width and UPDRS improvement were investigated using correlation and multivariate linear regression.

Results. Mean global and contralateral UPDRS improvements were 38% (\pm 24) and 58% (\pm 24). Mean STN width was 5.1 mm (\pm 1.6, min = 0.0, max = 8.7). There were no statistically significant relationships between STN width and UPDRS improvement, with and without AC-PC normalization ($R^2 < .05$). Stratification of STN widths failed to produce a statistically significant relationship.

Conclusion. This retrospective analysis raises questions about seeking maximal electrophysiological width of STN as a proxy for optimal outcome in DBS for PD. While a loose association exists, unknown factors involved in DBS warrant further refinement of operative techniques. We suggest that this strategy for DBS placement in PD be subject to more robust prospective investigation.

Wilson, Andrew Stuart, I (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Dr. Andrea Cherrington

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Trust in Physicians and Its Link to Intermediate Diabetic Outcomes

Trust in your physician has previously been linked to better glycemic control. We examined the relationship between general trust in physicians and diabetic outcomes as measured through blood pressure and glycemic control (A1c). This is a secondary data analysis using cross-sectional data from a community-based trial. Patients were mostly African Americans with diabetes living in southern, rural Alabama. Face-to-face interviews by a trained interviewer assessed general trust in physicians using a previously validated instrument (TMP-11). HbA1c and blood pressure were measured at baseline using a standardized protocol. Categorical variables were compared using chi square tests. Continuous variables were compared using bivariate linear regression. Multivariable analyses included general linear regression models adjusted for gender, income, education, insulin use, medication adherence, number of ambulatory visits, perceived discrimination, and depressive symptoms. 418 patients provided information for the trust scale (6 were missing). Mean age was 59, 75% were female and 87% were African American. High Trust ($\text{TMP} \geq 30$) was associated with older age, less perceived discrimination, and lower medication adherence. In bivariate analyses, hemoglobin A1c ($p=0.26$) and mean blood pressure ($p=0.64$) showed no significant association with provider trust. Multivariate adjusted analysis of both A1c and mean blood pressure again showed no association with general trust in physicians. General trust in physicians was not associated with change in glycemic control or blood pressure at follow-up in either unadjusted or adjusted analyses. Though it did not reach statistical significance, higher general trust was associated with higher systolic blood pressure. Future research should further explore these relationships.

Wilson, MacKenzie Leigh (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Cunningham Fellowship

Faculty Advisor: Wally Carlo, MD

Abstract Approved By Advisor: Yes

Co-Authors: Prem Fort, MD, Prabhu Viswanathan, MD, Jegen Kandasamy, MD, Namasivayam Ambalavanan, MD, Wally Carlo, MD

Title: Temporal Relationship between Administration of Antenatal Indomethacin and Steroids and Intestinal Perforation in Premature Infants

Intestinal perforation (IP) is the most common acute surgical emergency in preterm infants and is associated with a markedly high mortality rate. Two risk factors for the development of IP are necrotizing enterocolitis (NEC), ischemic bowel disease, and spontaneous intestinal perforation (SIP). The etiologies of NEC and SIP are controversial and are thought to be multifactorial. Drugs administered before birth (antenatal) or immediately after (postnatal) have been positively associated with the development of IP and are a preventable risk factor.

Maternal exposure to antenatal indomethacin (AI) for tocolysis and steroids (AS) for fetal lung development in preterm labor may play a significant role in the pathogenesis of IP in infants at UAB. Therefore, this historical cohort study aims to determine whether there is a relationship between maternal exposure to 1.) AI or 2.) AI and AS and development of IP in infants born at $22^{0/7}$ - $25^{6/7}$ GA. In addition, the number of hours from administration of 1.) AI or 2.) AI and AS to the development of IP will be recorded to determine whether the risk of IP is inversely related to this time period.

Data will be collected from a sample size of 275 infants (31 exposed v. 244 nonexposed) born at the aforementioned GA. These preterm infants must have been diagnosed with IP (from SIP or surgical necrotizing enterocolitis: Bell's Stage III) and had maternal exposure to 1) AI \leq 15 days prior to delivery or 2) AS + AI \leq 15 days prior to delivery. Infants with congenital malformations, genetic disorders, and/or diagnosis of abdominal diseases will be excluded.

Xu, Michael Yaxian (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: William Placzek

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Characterization of rBH3 specificity to anti-apoptotic Bcl-2 family members

In the intrinsic cell apoptotic pathway, Bcl-2 family proteins play an important role in suppressing apoptosis activation. Normally, stress and/or cellular damage activate cell death in order to prevent tumorigenesis. To circumvent this, cancer cells often overexpress anti-apoptotic Bcl-2 proteins and thereby suppress apoptotic response and facilitate chemoresistance. Previous research has shown that BH3 domains have the capacity to bind anti-apoptotic Bcl-2 family proteins, freeing pro-apoptotic BAX and BAK proteins to initiate downstream cell death signals. We hypothesized that the rBH3 motif of CDKN2C confers a similar ability to bind to anti-apoptotic Bcl-2 family proteins.

In this project a series of peptides were synthesized and purified, then their binding specificity to the anti-apoptotic Bcl-2 family member, MCL1, were then analyzed using *in vitro* fluorescence polarization assays. More specifically, we focused on the degree of interaction between the rBH3 motif of CDKN2C and mouse Mcl-1. To study this system we purified a series of peptides (synthesis, TFA cleavage, ether precipitation, HPLC purification, and MALDI) and recombinantly expressed protein (bacterial expression, Ni an GF chromatography); we used the resulting material to assess the binding between CDKN2C and MCL1. These studies confirmed a direct interaction between CDKN2C_{rBH3} and mMcl-1 protein. This project provides the foundation for future studies into the cross communication between cell-cycle progression, mediated by CDKN2C, and Bcl-2 family regulated apoptosis.

Xu, Shin (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Timothy Ness, M.D., Ph.D.

Abstract Approved By Advisor: Yes

Co-Authors: Buffie Clodfelter-Miller, Ph.D.

Title: The effects of nebulized drugs on lung injury due to chlorine gas in mice

Chlorine (Cl_2) is a popular chemical used in both industry and society alike, despite it being a highly irritant and reactive gas. Acute exposure can result in symptoms of airway obstruction such as wheezing, shortness of breath, mouth/nose/chest pain, and bronchospasm. Due to the pain and other symptoms associated with Cl_2 gas exposure, individuals are motivated to seek medical care for treatment. Currently, there is no known antidote for chlorine's poisoning effects. Potential treatments include topical exposure of the airways to nebulized drugs such as local anesthetics or sodium bicarbonate, which have been shown to improve the mobility of monitored animals after exposure to Cl_2 gas. In the current research project, we assessed the efficacy of the nebulized local anesthetic lidocaine (1% and 4%) and a nebulized 3.75% sodium bicarbonate solution following exposure to 400 ppm of chlorine gas. Biochemical measurements of injury to airway such as wet-to-dry lung weight ratios and bronchoalveolar lavage to examine protein and cytokine levels were performed. In mice exposed to 400 ppm Cl_2 gas, 1% lidocaine led to the greatest decrease of wet-to-dry lung weight ratio after 24 hours, indicating an anti-inflammatory effect. Treatment with 4% lidocaine increased wet-to-dry ratios compared to chlorine controls and lead to death in many cases. Lastly, sodium bicarbonate caused a slight decrease in wet-to-dry ratios compared to controls. This study indicates that nebulized 1% lidocaine is potentially a good treatment option after chlorine induced lung injury based on behavioral and biochemical data.

Yang, Jennifer Huasi (MS2)

Project Length: Short

Prior Research Experience: Yes **Source of Funding:** CaRES Program

Faculty Advisor: Harald Sontheimer

Abstract Approved By Advisor: Yes

Co-Authors: Jennifer Yang, Stefanie Robel

Title: The role of reactive astrocytes in tumor-associated epilepsy

Gliomas are brain tumors with very poor prognoses. Up to 70% of patients with primary brain tumors present with seizures although the underlying mechanism is largely unknown. One hypothesis is glutamate toxicity, where increased glutamate concentrations in the extracellular space released by the glioma cells disrupt the delicate balance between excitation and inhibition in the brain.

In the healthy brain, astrocytes, a glial cell type, are responsible for glutamate clearance after neuronal transmission through the use of glutamate transporters Glt-1 and GLAST and the enzyme glutamine synthetase (GS). Under pathological conditions, astrocytes become reactive, changing their morphology and gene expression. In this study, we were interested in the astrocytic response to gliomas, especially their role in seizure induction.

We used either D54 tumor cells expressing green or red fluorescent protein (GFP or TdTomato) or Jx22 patient-derived tumor cells that have been propagated in the flank of nude mice. These cells were injected into immunocompromised SCID mice or transgenic SCID mice expressing GFP in astrocytes. The latter allowed us to characterize the morphology, physiology and maturation states of peritumoral astrocytes.

Whole cell patch-clamp recordings of peritumoral astrocytes suggested that glutamate uptake is impaired. Using immunohistochemistry and western blotting, we found decreased levels of the high-affinity Glt-1, but increased low-affinity GLAST expression at the peritumoral border. GS levels remained unchanged. Since enhanced GLAST expression hints towards an immature phenotype, we next tested for the expression of the cell-cycle protein Ki67. Indeed, we found astrocytes surrounding the tumors, whereas astrocytes in normal and sham-operate brains did not proliferate at the time of analysis.

Together, these findings suggest that impaired glutamate uptake by peritumoral astrocytes contributes to the development of seizures in glioma patients and emphasize the importance of the tumor microenvironment for the course and comorbidities of the disease.

Yazdi, Siamak Mohammad Zaki (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr. Nathaniel Robin

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Nathaniel Robin, Dr. Edward Lose, Dr. Thomas Howard, Dr. Snehal Khatri, Wendy Piazza, Cara Donahue, Erin Flemming, Emily Rector

Title: Reproductive Decisions after Genetic Evaluation

Genetic testing has clearly improved diagnostic capabilities of physicians, yet the implementation of this technology has been accompanied by serious social and ethical implications. One area that genetic diagnosis directly affects is reproductive planning. Limited data exists regarding the reproductive behavior of couples that have given birth to a child with a known or suspected genetic condition. In an effort to explore this issue, we undertook a survey-based study of parents of children with defined or suspected-yet-unknown genetic disease. The goal of this study is to determine the manner in which genetic testing affects reproductive decision making in couples that have previously had a child with a genetic condition. We hypothesized that couples will exhibit a reproductive reduction following genetic diagnosis of a previous child, but that there will be some variation correlated with the recurrence risk and severity of the condition. Specifically, the conditions under study include Down Syndrome, Sickle Cell Anemia, Congenital Hearing Loss/Deafness, and Unknown Genetic Condition. Following an extensive literature review, we designed a pen and paper questionnaire that was distributed to these parents during clinic. To date, we have distributed questionnaires to parents of children with: Down Syndrome at Children's of Alabama and the Sparks Clinic; Sickle Cell Anemia at Children's of Alabama and UAB Montgomery; Congenital Hearing Loss/Deafness at the HEAR Center; and Unknown Genetic Condition at UAB Clinical Genetics. Data analysis is pending.

Youngstrom, Mallory Lynn (MS2)

Project Length: Short

Prior Research Experience: No

Source of Funding: MSSRP (NIH T35)

Faculty Advisor: Dr Lee Ann Reisenberg

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Systematic review of the literature for patient safety during handoffs

I have been doing a systematic review of the literature for patient safety, resident/ med student education, and protocol usage during handoffs. A list was generated by a librarian that used key words as mentioned above, This list generated about 6,000 articles. This list was reviewed by two separate reviewers where they selected about 2,000 articles. I have been finding these articles, and with another reviewer, we have been reading and including or rejecting these articles for all 3 different searches.

I have also been working on a different project that is also a systematic review that is further along in the process. This review is dealing with electronic solutions and handoffs. 36 articles were used after a rigorous selection process. A chart was made for all of these articles that includes what type of electronic record is used, what type of study was performed, and where the study was performed amongst many others.

Zhang, Mike Weng (MS2)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Eben Rosenthal

Abstract Approved By Advisor: Yes

Co-Authors: Sunny S. Khichi, P. Grant Cochran, Lisa K. Clemons, William R. Carroll, J. Scott Magnuson, Kirk P. Withrow, and Eben L. Rosenthal

Title: Investigating the effectiveness of the Dynasplint Trismus System

Objective: To investigate the effectiveness of the Dynasplint Trismus System (DTS) compared to tongue depressor therapy for treating trismus.

Design: Single-institution prospective randomized study

Setting: Academic tertiary care medical center.

Patients: A total of 53 patients with trismus as a complication of cancer treatment were enrolled in the study between 2007 and 2013. 27 patients were randomized to a treatment arm using the DTS, while 26 were randomized to a treatment arm that used tongue depressors to perform stretching exercises.

Main Outcome Measures: Examine the effectiveness of DTS and tongue depressors on improvement of trismus. Examine pretreatment characteristics and determine if any are associated with rate of improvement.

Results: DTS and tongue depressors both significantly increased the maximal intercisor opening (MIO) of patients at three and six months compared to baseline ($p<.01$ in both treatment arms). Patients who received only surgery and no radiation showed significantly more improvement in MIO from baseline to three months ($p=0.0036$) as well as six months ($p=0.012$). Improvement between timepoints was not found to be significantly higher between treatment arms.

Conclusions: Both DTS and tongue depressors were able to improve the trismus status for patients, especially in cases that arise as a result of single modality surgical therapy. Due to neither treatment being proven more effective, other factors such as ease of use and cost (approximately \$465 per month for DTS and \$12 for 1000 tongue depressors) must be considered for patients seeking relief from trismus to determine which treatment would be optimal.

Zimmermann, Terence Matthew Zwick (MS4)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Eben Rosenthal Abstract

Approved By Advisor: Yes

Co-Authors: Sweeny L, Burch MB, Rosenthal EL

Title: Expression of poor prognostic biomarkers in cutaneous squamous cell carcinoma of the parotid

BACKGROUND:

Extracellular matrix metalloproteinase inducer (EMMPRIN) and epidermal growth factor receptor (EGFR) are upregulated in cutaneous squamous cell carcinoma (cSCC), and increased expression is associated with poor outcomes. Our objective was to evaluate biomarker expression indicative of poor prognosis.

METHODS:

Patients who underwent a parotidectomy for cSCC at a tertiary care center between 2003 and 2012 were included (n = 218). Of these, 28 archived tumor samples were chosen for further molecular analysis. These 28 patients were separated into three cohorts: positive cervical lymph nodes (n=7), positive parotid and cervical lymph nodes (n=12), and neither cervical nor parotid lymph nodes positive (n=9). The expression of EMMPRIN, BMP-6, S100A9, and EGFR was examined by three blinded observers using immunohistochemistry techniques.

RESULTS:

The positive parotid cohort demonstrated high EGFR reactivity (2+-3+) (100%, n=12) compared to the positive cervical cohort (71%, n=5) and the lymph node negative cohort (67%, n=6). Few patients across all cohorts demonstrated high BMP-6 reactivity (29%, n=8). The positive parotid cohort demonstrated high S100A9 reactivity (75%, n=9), as did the lymph node negative cohort (89%, n=8). All cohorts demonstrated high EMMPRIN reactivity (86-92%, n=23). However, expression of EGFR, S100A9, BMP-6, and EMMPRIN did not differ significantly between the three cohorts. Increased EGFR expression did significantly correlate with increased levels of both EMMPRIN and S100A9 across all cohorts ($p=0.53$ and $p=0.06$, respectively). Furthermore, high EGFR reactivity was associated with decreased overall survival from the time of parotidectomy (24.7 months) compared to low EGFR reactivity (56.6 months) across all cohorts ($p=0.02$).

CONCLUSION:

Increased EGFR expression in cSCC of the parotid was associated with poorer outcomes, and correlated positively with both EMMPRIN and S100A9, suggesting a potential therapeutic target.