



MSRD 2015
UAB School of Medicine

Medical Student Research Day
October 27, 2015

MSRD JUDGES 2015

Dr. Omotomilayo F Akinyemiju
Dept. of Epidemiology

Dr. Namasivayam Ambalavanan
Dept. of Pediatrics

Dr. James Banos
Dept. of Academic Support

Dr. Santiago Borasino
Dept. of Pediatrics

Dr. Ayesha Bryant
Dept. of Surgery

Dr. Tiffany Carson
Dept. of Medicine

Dr. Do-Yeon Cho
Dept. of Surgery

Dr. Marilyn Crain
Dept. of Pediatrics

Dr. Jeremy Day
Dept. of Neurobiology

Dr. Ricardo Franco
Dept. of Medicine

Dr. Gregory Freidman
Dept. of Pediatrics

Dr. Catherine M Fuller
Dept. of Cell, Development, & Integrative
Biology

Dr. Shawn Gilbert
Dept. of Surgery

Dr. Samantha Giordano
Dept. of Medicine

Dr. Patricia Jackson
Dept. of Medicine

Dr. MiYoung Kwon
Dept. of Ophthalmology

Dr. Silvio Litovsky
Dept. of Pathology

Dr. Runhua Liu
Dept. of Genetics

Dr. Carmel McNicholas
Dept. of Cell, Development, & Integrative
Biology

Dr. Susan Nozell
Dept. of Cell, Development, & Integrative
Biology

Dr. Robert Oster
Dept. of Medicine

Dr. Leslie Rhodes
Dept. of Pediatrics

Dr. Elizabeth Sztul
Dept. of Cell, Development, & Integrative
Biology

Dr. Lizhong Wang
Dept. of Genetics

Dr. Qin Wang
Dept. of Cell, Development, & Integrative
Biology

Dr. Jason Warram
Dept. of Surgery

Dr. John Waterbor
Dept. of Epidemiology

Dr. Roger White
Dept. of Medicine

Dr. Martin Young
Dept. of Medicine

Dr. Nabiha Yusuf
Dept. of Dermatology

Oral Presentations
Lecture Room E

Short Term Research

- 10:00 – 10:15 am **Jordan Harper (MS4)**
Knowledge and Attitudes in an Open-Access Online Cultural Competency Training
Mentor: Dr. Carlos Estrada
- 10:15 – 10:30 am **Edward W. Ference, III (MS3)**
Learning-Related Changes in the Functional MRI Response to Fear Conditioning after Acute Medical Trauma
Mentor: Dr. Amy Knight
- 10:30 – 10:45 am **Salmaan Z. Kamal (MS2)***
Understanding the Primary Care Experience for Vulnerable Patients in a Student-Run Free Clinic
Mentor: Dr. Stefan Kertesz
- 10:45 – 11:00 am **Ross L. Pearlman (MS2)**
Plumbagin Reduces Proliferation and Induces Apoptosis in Melanoma Cells by Inhibiting PI3K/AKT Signaling
Mentor: Dr. Farrukh Afaq
- 11:00 – 11:15 am **Christopher A. Ray (MS2)**
Impact of Deceased Donor Allocation Changes on Outcomes among Pediatric Kidney Transplant Recipients
Mentor: Dr. Jayme Locke
- 11:15 – 11:30 am **Brandon A. Sherrod (MS2)**
Incidence, Risk Factors and Associated Complications of Blood Transfusion in Surgical Treatment of Pediatric Hip Dysplasia
Mentor: Dr. Shawn Gilbert

*indicates winner

Oral Presentations
Lecture Room A

Intermediate Term Research

- 10:00 - 10:15 am **Marshall C. Pritchett, III (MS2)**
Is Social Support Associated with Diabetes Distress and Glycemic Control in African Americans with Type 2 Diabetes?
Mentor: Dr. Andrea Cherrington
- 10:15 – 10:30 am **James Heath Pelham (MS3)**
Analysis of Dyslipidemia in Children with Type 2 Diabetes Mellitus
Mentor: Dr. Ambika Ashraf
- 10:30 – 10:45 am **Fenil Patel (MS3)**
Post-Operative Outcomes Following Elective Colorectal Surgery in the Obese Population
Mentor: Dr. Melanie Morris
- 10:45 – 11:00 am **Morgan L. Locy (MSTP-GS2)***
Modifications of Tyrosine are Increased in Plasma of Human subjects with Interstitial Lung Disease
Mentor: Dr. Victor Thannickal

Long Term Research

- 11:00 – 11:15 am **Anna Joy Graves Rogers (MSTP-GS3)***
Barriers and enablers to repeat HIV testing during pregnancy in Kenya: A quantitative study
Mentor: Dr. Janet Turan
- 11:15 – 11:30 am **Vincent A. Laufer (MSTP-GS3)**
Genetic Influences on Rheumatoid Arthritis and its Severity in African Americans
Mentor: Dr. Louis Bridges

*indicates winner

Group A

A-1 Alley, Wilson (MS2)

Short Term

Generating Improved Breadth and Potency of Antibodies Against Weak HIV Immunogens

Mentor: Dr. Hui Hu

A-2 Boppana, Sushma (MSTP-MS2)

Short Term

Compromised perforin production represents a possible mechanism of CD4 T cell-mediated HIV Immune Escape

Mentor: Dr. Paul Goepfert

A-3 Dean, Emma (MSTP-MS1)

Short Term

Utilizing Ex Vivo ATAC-seq to Understand the Differential Transcriptional Landscape between IL10+ and IL10- Regulatory T cells from a Murine Multiple Sclerosis Model

Mentor: Dr. Casey Weaver

A-4 Dennis, Evida (MSTP-GS2)

Intermediate Term

Cytomegalovirus Potentiates Inflammation in the Gastrointestinal Mucosa

Mentor: Dr. Phillip Smith

A-5 DiToro, Daniel (MSTP-GS4)

Long Term

Insulin-like Growth Factors Drive the Pathogenic CD4 T cell Response in Multiple Sclerosis

Mentor: Dr. Casey Weaver

A-6 Moseley, Carson (MSTP-GS5)

Long Term

A transcriptional regulatory mechanism governing Th17-driven autoimmunity

Mentor: Dr. Casey Weaver

A-7 Pope, Brandon (MSTP-MS2)

Short Term

The Role of Protein Kinase CK2 in the Function of Th17 Cell Polarization and EAE.

Mentor: Dr. Tika Benveniste

A-8 Singer, Jeff (MSTP-GS4)

Long Term

Postnatal Colonization Shapes the Immunologic Development of the Intestinal Barrier

Mentor: Dr. Casey Weaver

A-9 Stone, Sara (MSTP-GS4)

Long Term

T-bet regulates memory B cell and long-lived plasma cell development in an influenza model

Mentor: Dr. Fran Lund

Group B

B-1 Busing, Jordan (MS2)

Short Term

Eosinophilic esophagitis: Sampling of the Esophageal Microbiome

Mentors: Dr. Nick CaJacob and Dr. Reed Dimmitt

B-2 Flippo, Hilary (MS2)

Long Term

Factors Associated with Herpes Simplex Virus Type 2 Asymptomatic Shedding

Mentor: Dr. Nicholas Van Wagoner

B-3 Headrick, Andrew (MS3)

Intermediate Term

Individual and Family Perception of Living with Chronic Disability Secondary to Human T-lymphotropic Virus 1 (HTLV-1) Infection in Peru

Mentor: Dr. Marin Rodriguez

B-4 Jariwala, Ravi (MS2)

Short Term

Clinic Utility of Non-Invasive Liver Disease Staging in Patients with HCV and HIV/HCV CO-Infection

Mentor: Dr. Ricardo Franco

B-5 McClanahan, Taylor (MS4)

Intermediate Term

Creation of an Antibioqram for Kijabe Hospital in Kijabe, Kenya

Mentor: Dr. Annalise Sorrentino

B-6 Nadendla, Kavita (MS4) (Not Presenting)

Intermediate Term

Predictors of Central Line Venous Infection Salvage in Patients with Intestinal Failure

Mentor: Dr. Colin Martin

B-7 Olson, Kristin (MSTP-GS1)

Intermediate Term

Comparisons of Vaginal Floral Patterns among Sexual Risk Behaviors Groups of Women- Implications for the Pathogenesis of Bacterial Vaginosis

Mentor: Dr. Christina Munzy

B-8 Turner, Hannah (MS2)

Short Term

Screening, prevalence, and risk factors for cervical cancer/lesions in HIV positive women in Swaziland

Mentor: Dr. Pauline Jolly

B-9 Vachhani, Raj (MS3)

Short Term

Rapid Antigen Group A Strep Test

Mentor: Dr. Carlos Estrada

Group C

C-1 Carlisle, Matthew (MS3) (Not Presenting)

Intermediate Term

Amelioration of halogen-induced injury during pregnancy

Mentor: Dr. Sadis Matalon

C-2 French, Hunter (MS2)

Short Term

3D Model Printing of Mouse Airway Development

Mentor: Dr. Namasivayam Ambalavanan

C-3 Hoffman, Kyle (MS2)

Short Term

Protective Properties of Nanodisk-Amphotericin B (ND-AMB) over commercially available Amphotericin B in Human Nasal Epithelia

Mentor: Dr. Do-Yeon Cho

C-4 Iannuzzi, Luke (MS2)

Short Term

The impact of caregiver well-being on infant pulmonary function in Cystic Fibrosis

Mentor: Dr. William Harris

C-5 Jiang, Kevin (MS2)

Short Term

Immunopathogenic mechanisms associated with fungal colonization and sensitization in individuals with cystic fibrosis and asthmatics

Mentor: Dr. Chad Steele

C-6 Keeley, Jordie (MS2)

Short Term

Nitrites as a Biomarker of Bronchopulmonary Dysplasia (BPD) Diseases in Extremely Preterm Infants

Mentor: Dr. Charitharth Lal

C-7 Lam, Adam (MS3) (Not Presenting)

Intermediate Term

Heme mediates mitochondrial dysfunction and cellular toxicity in bromine injury

Mentor: Dr. Sadis Matalon

C-8 Phillips, Caroline (MS3) (Not Presenting)

Short Term

CT-determined Airway Size and Severity of Obstructive Sleep Apnea

Mentor: Dr. Mark Tafazozli

C-9 Smith, Andrew (MS4)

Intermediate Term

Implementation of the National Emergency Airway Registry at UAB

Mentor: Dr. Henry Wang

Group D

D-1 Sherrod, Brandon (MS2)

Short Term

Risk Factors for unplanned readmission within 30 days after pediatric neurosurgery: a nationwide analysis of 9,799 procedures from ACS-NSQIP

Mentor: Dr. Brandon Rocque

D-2 Atchley, Travis (MS2)

Short Term

Surgical Outcomes of Single Ventricle Patients with Heterotaxy Syndrome: A 15-year retrospective study

Mentor: Dr. Robert Dabal

D-3 Gans, Asaf (MS2)

Short Term

Early Ventilator Variables and Outcomes are Associated with Prolonged Mechanical Ventilation in Infants after Cardiac Surgery with Cardiopulmonary Bypass

Mentor: Dr. Santiago Borasino

D-4 Kim, Sanghun (MS2)

Short Term

Sarcopenia as predictor TIPS procedure outcomes

Mentor: Dr. Ahmed Kamel Adel Al

D-5 Parker, Cameron (MS2)

Short Term

Effect of Conditioned Media on Adipose-Derived Stromal Cells in Wound Healing using 3-Dimensional Skin Organotypic Cultures

Mentor: Dr. Sherry Collawn

D-6 Patel, Fenil (MS3)

Intermediate Term

Racial Disparities in Length of Stay Among Patients Undergoing Lower Extremity Revascularization

Mentor: Dr. Daniel Chu

D-7 Young, Bradley (MS3)

Intermediate Term

Risk Factors for Increased Morbidity Following Thoracic Outlet Syndrome Surgery

Mentor: Dr. Brent Ponce

Group E

E-1 Payne, Alaina (MS3)

Short Term

Patient Outcomes after a protocol of preliminary external fixation and staged conversion in distal radius fractures

Mentor: Dr. Nileshkumar Chaudhari

E-2 Davis, Benjamin (MS4)

Short Term

Does surgeon specialty training influence postoperative outcomes in hand and wrist fractures?

Mentor: Dr. Brent Ponce

E-3 Hess, Matthew (MS2)

Short Term

The Influence of Tranexamic Acid on Blood Loss During Acetabulum Fixation

Mentor: Dr. Jason Lowe

E-4 Laskay, Nicholas (MS2)

Short Term

The Perioperative Outcomes of Spinopelvic Fixation following Unstable Sacral Fractures with Spinopelvic Dissociation

Mentor: Dr. Jason Lowe

E-5 Read, Connor (MS2)

Short Term

Outcomes Following Anterior Cruciate Ligament Reconstruction to Defensive Players in the National Football League

Mentor: Dr. Glenn Fleisig

E-6 Real, Kelsey (MS2)

Short Term

Implementing Virtual ACE on Two Orthopedic Surgery Units: A Feasibility Study

Mentor: Dr. Kellie Flood

E-7 Terry, Charles (MS2) (Not Presenting)

Intermediate Term

Outcomes of fixation on Calcaneus through small incisions

Mentor: Dr. Michael Johnson

E-8 Sherrod, Brandon (MS2)

Short Term

Complications and 30-day Outcomes Associated with Venous Thromboembolism in the Pediatric Orthopaedic Surgical Population

Mentor: Dr. Shawn Gilbert

Group F

F-1 Bourgeois, Claire (MS2)

Short Term

A national survey of INTERMACs centers' institutional characteristics and specialist and generalist palliative care practices in patients with mechanical circulatory support devices

Mentor: Dr. Marie Bakitas

F-2 Jani, Aditi (MS2)

Short Term

For Homeless Veterans Entering Care, does Co-Existent Addiction and Chronic Pain Influence Housing Outcomes?

Mentor: Dr. Stefan Kertesz

F-3 Joshi, Madhura (MS2) (Not Presenting)

Short Term

Exploring stress as a contributor to racial and gender disparities

Mentor: Dr. Tiffany Carson

F-4 Mahalingam, Mythreyi (MS2)

Short Term

Frailty and Risk of Sepsis: A prospective analysis of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort

Mentor: Dr. Monika Safford

F-5 Patel, Dhruv (MS2) and Thomas, John (MS4)

Short Term

Child Life Services Lessens the Emotional Response of Children During Laceration Repair in the Emergency Department

Mentor: Dr. Christopher Pruitt

F-6 Paulsen, Alex (MS2)

Short Term

Associations between changes in gut microbiota composition and psychosocial outcomes in breast cancer survivors participating in a randomized controlled physical activity trial

Mentor: Dr. Laura Rogers

F-7 Pynes, Malissa (MS2)

Short Term

Chronic Pain in the ambulatory palliative care setting: a distinct entity from acute pain?

Mentor: Dr. Jessica Merlin

F-8 Shuford, Rebecca (MS2)

Short Term

Racial Disparities in Sexual Function after Radiation Therapy for Gynecological Malignancies

Mentor: Dr. Robert Kim

F-9 Worth, Anna (MS3)

Short Term

Factors influencing life-space recovery in non-surgical hospitalized patients

Mentor: Dr. Cynthia Brown

F-10 Zeiger, Herbert (MS2)

Short Term

Subdural Hematoma in the Elderly (SHE) Study: Management and Clinical Course

Mentor: Dr. James Markert

Group G

G-1 Bares, Jennifer (MS3)

Intermediate Term

Comparing Incoming Residents' Inpatient and Outpatient Oral Presentation Structures

Mentor: Dr. Ryan Kraemer

G-2 Bouldin, John (MS4)

Short Term

The Use of a Sports Metrics App in the Recording of In-Situ Mock Code Data

Mentor: Dr. Marjorie Lee White

G-3 Colon, Chad (MS4) (Not Presenting)

Intermediate Term

Comparing High Risk Exposure disclosure among medical students and residents following intervention between 2002-2015

Mentor: Dr. Craig Hoesley

G-4 Cox, Kathryn (MS2)

Long Term

Experiences that Strengthen and Weaken Enthusiasm for Primary Care in First Year Medical Students: A Nominal Group Techniques Evaluation

Mentor: Dr. Carlos Estrada

G-5 Davis, Ann (MS3)

Intermediate Term

Improving Cardiopulmonary Resuscitation by Implementing First Five Minute Training

Mentor: Dr. Nancy Tofil

G-6 Love, Ashley (MS4)

Short Term

Pediatric Cardiology Simulation: When to Give Fluids and Oxygen and When Not

Mentor: Dr. Leslie Rhodes

G-7 Rana, Amaad (MS3) (Not Presenting)

Long Term

Kaizen-UME: Utilization patterns and educational outcomes of a software application to improve medical knowledge among medical students.

Mentor: Dr. James Willig

G-8 Smith, Walter (MS2)

Short Term

Using Medical Students as Hypertension Patient Educators in the Emergency Department Setting

Mentor: Dr. Charles Khoury

G-9 Sweeney, Mary Katherine (MS2)

Short Term

What Do Primary Care Physicians Offer that Others Do Not?: A Nominal Group Technique

Mentor: Dr. Carlos Estrada

Group H

H-1 Chung, Sebastian (MS2)

Short Term

Hospital Adherence to Evidence-Based Severe Traumatic Brain Injury Management Guidelines

Mentor: Dr. Leslie Hayes

H-2 Craig, Carlyne (MS4)

Short Term

Development and Implementation of a Standardized Sedation Weaning Guidelines in a Pediatric ICU

Mentor: Dr. Leslie Hayes

H-3 Hoepfner, Lauren (MS2)

Intermediate Term

Validity of the Braden Scale in Grading Pressure Ulcers in Trauma and Burn Patients

Mentor: Dr. Jeffrey Kirby

H-4 Junkin, Elizabeth (MS4) (Not Presenting)

Intermediate Term

Primary Care towards Patient-Centered Medical Home Qualifications through a Diabetes Self-Management Program

Mentor: Dr. Lea Yerby

H-5 Kasanagottu, Koushik (MS2)

Intermediate Term

Development and Assessment of a Video Health Education Program

Mentor: Dr. Monika Safford

H-6 Kennel, Tim (MSTP-GS1)

Intermediate Term

An OpenInfoButton and I2B2 Merger: Bringing Buttons to the translational research tool I2B2

Mentor: Dr. James Cimino

H-7 Lewis, Justin (MS2)

Short Term

Living Well with Diabetes

Mentor: Dr. Monika Safford

H-8 Riley, William (MS2)

Short Term

Medical Students as Diabetes Educators in the Emergency Department Setting

Mentor: Dr. Todd Peterson

H-9 Sheets, Ryan (MS4) (Not Presenting)

Intermediate

Getting on the Bandwagon Improving Code Status Identification

Mentor: Dr. Winter Williams

H-10 Payne, Alaina (MS3)

Intermediate Term

An analytical study of the Alabama Rural Physicians Tax Credit Law

Mentor: Dr. William Coleman

Group I

I-1 Allen, Sarah (MS4) (Not Presenting)

Intermediate Term

Use of Multiple Antihypertensive Agents to Achieve Blood Pressure Control Associated with Adverse Pregnancy Outcomes?

Mentor: Dr. Lorie Harper

I-2 Antipenko, Sergey (MSTP-GS3)

Long Term

The Effect of Inflammation on Cardiac Stem Cells

Mentor: Dr. Tim Townes

I-3 Berry, Ryan (MSTP-GS3)

Long Term

Differential tissue and time-of-day response to hGH in C57 Black 6 male mice

Mentor: Dr. Stuart Frank

I-4 Bray, Alexander (MSTP-GS4)

Long Term

Mitochondrial Genetic Background Influences Susceptibility to Atherosclerosis

Mentor: Dr. Scott Ballinger

I-5 Chiu, Sherwin (MS2)

Short Term

Is Pulse Pressure in the Early Postoperative Period a Predictor of Morbidity After the Norwood Procedure

Mentor: Dr. Jeffrey Alten

I-6 Dowla, Shima (MSTP-GS2)

Short Term

Does Providing Fresh Fruits and Vegetables to Children and Adolescents Reduce Weight? Designing a Randomized Control Trial

Mentor: Dr. Tapan Mehta

I-7 Erwin, William Clinton (MS2)

Short Term

Does arterial-venous CO₂ gradient correlate with other known markers of low cardiac output?

Mentor: Dr. Leslie Rhodes

I-8 Hackney, Andrew (MS2)

Short Term

MAP Management and Acute Spinal Cord Injuries

Mentor: Dr. Neway

I-9 Ives, Chris (MS2)

Short Term

Estrogen reduces inflammation in postmenopausal women through modulation of macrophage phenotype

Mentor: Dr. Suzanne Oparil

I-10 McMongle, Ryan (MSTP-MS1)

Short Term

Mitochondrial Influence on Gene Expression

Mentor: Dr. Scott Ballinger

I-11 Pepin, Mark (MSTP-GS1)

Long Term

The Diabetic Heart: GABA signaling and Heart Failure

Mentor: Dr. Adam Wende

I-12 Reddy, Alex (MS2)

Short Term

Biotinylation: Novel Mechanism Linking the Cardiomyocyte Circadian Clock to Cardiac Metabolism

Mentor: Dr. Martin Young

I-13 Youngstrom, Mallory (MS4) (Not Presenting)

Long Term

Outcomes in Women with a History of Chronic Hypertension by Normal Blood Pressures in Pregnancy

Mentor: Dr. Lori Harper

Group J

J-1 Crowson, Cole (MS2)

Short Term

Induction of Immunosuppression Regimen and the Odds of Acute Rejection by Race in Pediatric Kidney Transplant Recipients

Mentor: Dr. Jayme Locke

J-2 Deas, Dale (MS2)

Short Term

Interleukin-6 and interleukin -8 as acute kidney injury biomarkers in cardiac surgery in infants

Mentor: Dr. David Cleveland

J-3 Fox, Brandon (MSTP-GS3)

Intermediate Term

Endothelial-Derived Endothelin-1 Contributes to Renal Dysfunction and Mortality in Sickle Cell Mice

Mentor: Dr. Jennifer Pollock

J-4 Hu, Muhan (MSTP – GS1)

Short Term

Mechanisms of TGF β signaling critical for C. elegans fertilization

Mentor: Dr. Michael Miller

J-5 Lever, Jeremie (MSTP-GS1)

Short Term

Characterization of renal inflammation in a model of ischemic Acute Kidney Injury Leading to Chronic Kidney Disease

Mentors: Dr. Anupam Agarwal and Dr. James George

J-6 Ma, Elizabeth (MSTP-GS3)

Intermediate Term

Urinary F2-Isoprostanes Do Not Reflect Oxidative Stress Operative in Human Insulin Resistance, but are correlated with Lean Mass and Serum Lipids

Mentor: Dr. Tim Garvey

J-7 Mosher, Zachary (MS2)

Short Term

Renal function during and after prophylactic peritoneal dialysis after cardiopulmonary bypass surgery in infants

Mentor: Dr. Santiago Borasino

J-8 Neu, Matthew (MSTP-MS2)

Short Term

De novo variant analysis in whole genomes

Mentor: Dr. Greg Cooper

J-9 Smith, Burke (MS1)

Short Term

Dosing eculizumab for antibody mediated rejection in kidney transplantation: a case report

Mentor: Dr. Jayme Locke

J-10 Turner, Eric (MS2)

Intermediate Term

Validation of Bosniak Classification for Contrast Enhanced Ultrasound and Introduction of a New Classification System

Mentor: Dr. Jessica Zarzour

J-11 West, Janelle (MS4)

Intermediate Term

The Use of Contrast-Enhance Ultrasound in the Diagnosis of Indeterminate Small Renal Lesions

Mentor: Dr. Jessica Zarzour

J-12 Zou, Sylvia (MS2)

Short Term

Macrophage polarization in acute kidney injury: macrophage differentiation into M2 phenotype in IL-4 and IL-13 knockout mice

Mentor: Dr. Raymond Harris

Group K

K-1 Bevans, Stephanie (MS2)

Short Term

Fluorescence guided surgery in aggressive odontogenic tumors using Cetuximab-IRDye800

Mentor: Dr. Jason Warram

K-2 Brinkley, Garrett (MSTP-MS2)

Short Term

Following treatment with bortezomib, myeloma cells secrete exosomes with altered proteins composition that enhance chemoresistance and tumor proliferation

Mentor: Dr. Ralph Sanderson

K-3 Dussaq, Alex (MSTP-GS3)

Long Term

Mechanistic parameterization of the kinomic signal using PamGene peptide arrays

Mentor: Dr. Christopher Willey

K-4 Etikala, Deepa (MS2)

Short Term

The Identification of FOXP3 Isoforms in Human Cancer Cell Lines

Mentor: Dr. Lizhong Wang

K-5 Griswold, Gage (MS2)

Short Term

Frequency of skeletal surveillance in primary carcinomas at high risk for metastasis to bone

Mentor: Dr. Nichole Behnke

K-6 Harris, David (MS3)

Intermediate Term

The Importance and Risks of CBCT Alignment for Prostate Cancer Radiotherapy

Mentor: Dr. John Fiveash

K-7 LeGrand, Jason (MSTP-GS5)

Long Term

Identification of Cytogenetically Normal Human CD34⁺CD34⁻ Hematopoietic Stem/Progenitor Cells from inv(16⁺) Leukemic Bone Marrow

Mentor: Dr. Christopher Klug

K-8 McCaw, Tyler (MSTP-GS1)

Short Term

Solid Tumor Targeting with T cells, Linker Proteins, and Precise Gene Editing

Mentors: Dr. Troy Randall and Dr. Tim Townes

K-9 Prince, Andrew (MS2)

Short Term

Dual-Modality Approach to Improving Surgical Intervention in Head and Neck Cancer Using ⁸⁹Zr and IRDye800 Labeled Panitumumab

Mentor: Dr. Jason Warram

K-10 Ramesh, Tushar (MS2)

Intermediate Term

Evaluation of optical imaging agents in a fluorescence-guided surgical model of head and neck cancer

Mentor: Dr. Jason Warram

K-11 Singireddy, Ramya (MS2)

Short Term

Vitamin D receptor polymorphism status and the association of osteopontin and vitamin D receptor expression in skin tumors

Mentor: Dr. Nabiha Yusuf

K-12 Weaver, Alice (MSTP-GS3)

Long Term

Activation of Notch signaling pathway is associated with poor prognosis in oral cavity squamous cell carcinoma

Mentor: Dr. Eddy Yang

Group L

L-1 Birchall, Betsy (MS2)

Short Term

Imaging and Analysis of Dendritic Spines

Mentor: Dr. Jeremy Herskowitz

L-2 Eustace, Nicholas (MSTP-GS2)

Intermediate Term

MARCKS has a critical role in the growth and proliferation of Glioblastoma multiforme

Mentor: Dr. Christopher Willey

L-3 Evans, John (MS4)

Intermediate Term

Fractional tumor burden calculation using perfusion MRI can predict progression-free survival and overall survival in glioblastoma multiforme patients treated with bevacizumab

Mentor: Dr. Asim Bag

L-4 Figge, David (MSTP-GS4)

Long Term

Role of Dynamic DNA Methylation in Levodopa-Induced Dyskinesia

Mentor: Dr. David Standaert

L-5 Gragg, Stephen (MSTP-GS1)

Short Term

CDC42, ID2, and SIRT6 are promising targets for regulation of microRNA-31

Mentor: Dr. Tika Beveniste

L-6 Guzman Karlsson, Mikael (MSTP-GS5)

Long Term

Genome-wide transcription profiling in an APP mouse model of Alzheimer's disease.

Mentor: Dr. David Sweatt

L-7 Hardigan, Andrew (MSTP)

Long Term

Blocking of targeted microRNAs from next-generation sequencing libraries

Mentor: Dr. Richard Myers

L-8 Pacl, Hayden (MSTP-MS1)

Short Term

Effects of Alzheimer's Disease Risk Factor BIN1 on Amyloid Plaque Deposition in a Mouse Model of Alzheimer's Disease

Mentor: Dr. Erik Roberson

L-9 Patel, Bhavika (MS2)

Short Term

Assessing binocular function in glaucoma

Mentor: Dr. MiYoung Kwon

L-10 Patterson, Kelsey (MSTP-GS2)

Long Term

Motor and Behavioral Phenotypes in a Novel Rate Model of Rett Syndrome

Mentor: Dr. Michelle Olsen

L-11 Raman, Fabio (MSTP-MS2)

Short Term

Unraveling Mechanisms and Treatment Options of Glioblastoma Multiforme Progression

Patterns: A Computational Analysis

Mentor: Dr. Hassan Fathallah-Shaykh

L-12 Stoyka, Lindsay (MSTP-MS2)

Short Term

G2019SLRRK2 May Lead to Increased Alpha-Synuclein Aggregation in Parkinson's Disease

Mentor: Dr. David Standaert

Group M

M-1 Black, Ryne (MS2)

Short Term

Activation of neurons within PVN in Wistar and Wistar-Kyoto rats following the forced swim test

Mentor: Dr. Ilan Kerman

M-2 Bolis, Ramy (MS2)

Short Term

A Predictive Algorithm of Citalopram Efficacy

Mentors: Dr. Nita Limdi and Dr. Richard Shelton

M-3 Cohen, Joshua (MSTP-GS3)

Long Term

12 Things you didn't know about high responder/low responder rats, stress coping, and microRNA in the dorsal raphe. Number 5 will blow your mind!

Mentor: Dr. Sarah Clinton

M-4 Duke, Corey (MS2)

Short Term

Experience Dependent Epigenomic Reorganization

Mentor: Dr. Jeremy Day

M-5 Ramaker, Ryne (MSTP-GS2)

Intermediate Term

Comparative transcriptomic and metabolomic profiling of psychiatric disorders across three brain regions

Mentors: Dr. Sarah Cooper and Dr. Rick Myers

M-6 Souder, Paige (MSTP-MS2)

Short Term

Expression and Function of Astrocytic Connexin-43 in a Model of Pediatric Traumatic Brain Injury

Mentor: Dr. Michelle Olson

M-7 Webb, William (MSTP-GS2)

Long Term

Histone methylation and NK- κ B methyl-lysine signaling in the hippocampus and entorhinal cortex during memory formation

Mentor: Dr. Farah Lubin

M-8 Zipperly, Morgan (MSTP-MS2)

Short Term

Assessment of Neuronal Activity in Reward-Associated Behavioral Circuits

Mentor: Dr. Jeremy Day

Allen, Heather Elizabeth

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: David G Standaert

Co-Authors: Heather E Allen Reish, Ashley S Harms, PhD, David G Standaert MD PhD

Title: C3 is not required for alpha-synuclein-induced neuroinflammation and neurodegeneration in the AAV-SYN model of Parkinson disease

Prior Research Experience: Yes

Abstract Approved: Yes

Parkinson disease (PD) is a common neurodegenerative movement disorder that induces selective dopaminergic neuron loss in the substantia nigra (SN). There is no known neuroprotective treatment. Pathologic and genetic studies indicate a causal role for the protein alpha-synuclein in the pathogenesis of PD. However, how alpha-synuclein mediates its toxic effects on dopaminergic neurons is still unclear. One leading hypothesis is the induction of toxic neuroinflammation by aggregated or otherwise abnormal forms of alpha-synuclein. Here, we hypothesized that complement component 3 (C3) was required for the neuroinflammation and neurodegeneration induced by alpha-synuclein in PD.

Wildtype and C3^{-/-} mice were stereotaxically injected with an adeno-associated virus that selectively overexpresses alpha-synuclein in the substantia nigra (AAV-SYN) or a control virus (AAV-GFP). To assess neuroinflammation, mice were sacrificed 4 weeks post-injection. Brains were either processed for qPCR or sectioned and stained for C9, MHCII, and IgG immunofluorescence. Sections were scored by blinded rating. To assess neurodegeneration, wildtype and C3^{-/-} mice were sacrificed at 4 weeks and 6 months post-injection; brains were sectioned and stained for tyrosine hydroxylase (TH) and counted using unbiased stereology.

C3 mRNA was upregulated 4.7 fold, and C9 deposition was significantly increased in AAV-SYN-injected mice, indicating an upregulation of complement system components in the AAV-SYN model 4 weeks post-injection. Surprisingly, deletion of C3 did not ameliorate AAV-SYN-induced MHCII⁺ microglial activation or IgG deposition 4 weeks post-injection. Furthermore, deletion of C3 did not prevent AAV-SYN induced neuron loss. At 6 months post-injection, AAV-SYN induced an 18% TH⁺ neuron loss in both wildtype and C3^{-/-} mice, indicating no role for C3 in either the neuroinflammatory or the neurodegenerative pathway of the AAV-SYN model of PD.

Together these results indicate that although alpha-synuclein induces C3 expression, C3 is not involved in the downstream neuroinflammatory or neurodegenerative pathways of the AAV-SYN model of PD.

Allen, Sarah Elizabeth

Project Length: Intermediate

Source of Funding: Other

Faculty Advisor: Dr Lorie Harper

Co-Authors: Tita, Anderson, Nadeau, Biggio, Harper

Title: Is Use of Multiple Antihypertensive Agents to Achieve Blood Pressure Control Associated with Adverse Pregnancy Outcomes?

Prior Research Experience: Yes

Abstract Approved: Yes

While requiring multiple antihypertensive agents to achieve a normal blood pressure (BP) is a surrogate marker of chronic hypertension (HTN) severity, it is unclear whether the number of agents required to achieve BP control is associated with adverse pregnancy outcomes. We assessed whether requiring >1 medication for BP control is associated with adverse pregnancy outcomes.

The study is a retrospective cohort of all singletons complicated by HTN at UAB from 2000-2014. Subjects initiated on >1 agent were compared to those on 1 agent < 20 weeks gestation age. Because BP is tightly linked to pregnancy outcomes, only subjects achieving a BP<140/90 mmHg were considered. Subjects with major medical comorbidities, baseline renal disease and fetal anomalies were excluded. The primary maternal outcome was preeclampsia (PE). Secondary maternal outcomes were severe PE, cesarean delivery (CD) and antepartum hospitalizations to rule out PE. The primary neonatal outcome was small for gestational age (SGA). Secondary neonatal outcomes were preterm birth (PTB, <35 weeks) and a composite of perinatal death, assisted ventilation, umbilical cord pH <7, 5-minute Apgar \leq 3 and neonatal seizures. Exposure groups were compared with Student's t-test and χ^2 ; logistic regression adjusted for confounding variables.

Of 634 women, 122 (19.2%) used >1 agent. Among women with BP <140/90 mmHg, those on >1 agent had similar odds of PE (AOR 1.3, 95% CI 0.7-2.5), severe PE (AOR 1.4, 95% CI 0.6-2.9) and CD (AOR 0.9, 95% CI 0.5-1.6). Women on >1 agent had increased risk of antenatal admission to rule out PE (AOR 3.2, 95% CI 1.6-6.6). Neonatal outcomes were similar between groups. When comparing those with BP \geq 140/90 mmHg, requiring >1 agent was not associated with increased risk for any outcome studied. Initiation of >1 antihypertensive agent prior to 20 weeks was not associated with an increased risk of adverse outcomes when a normal BP is achieved.

Alley, Wilson Edward

Project Length: Short

Source of Funding: T35

Faculty Advisor: Hui Hu

Co-Authors: Jianlin Geng, Hairong Wei, Xueri Luo, Hui Hu

Title: Generating Improved Breadth and Potency of Antibodies Against Weak HIV Immunogens

Prior Research Experience: Yes

Abstract Approved: Yes

HIV evades the host immune system by gene mutation and genetic diversity, and many HIV potential targets are weak antigens. Creating antibodies to a given weak antigen by host cell manipulation may help overcome the evasiveness of the virus towards host humoral responses. T20 is one such conserved peptide located on the GP41 region of HIV. Foxp1 is a negative regulator of follicular T helper cells (Tfh), and downregulation of this gene is necessary for germinal center b-cell function. When Foxp1 is deleted, naïve T cells preferentially differentiate into Tfh cells augmenting antibody production, isotype switching, and increased kinetics. Our goal was to use a foxp1 conditional knock out mouse model to create antibodies to T20, which would serve as a proof of principle that manipulation of Foxp1 can improve breadth and potency of B cell responses. The foxp1 cko mice were inoculated with OVA (ovalbumin) - T20 and serum was collected. This serum was then analyzed for antibody production with both an enzyme linked immunosorbant assay (ELISA) and a viral inhibition assay. The ELISA revealed positive antibody production to ovalbumin; however, T20 antibody production was negative. The HIV viral inhibition assay was done using a serial dilution of mouse serum on a human CUCY cell line. This test showed sustained viral inhibition with all serum concentrations including the control mouse serum. This project was unable to serve as a proof of principle that manipulation of the Foxp1 pathway can result in improved breadth and potency of B cell responses.

Antipenko, Sergey

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: Tim Townes

Co-Authors: Sumanth Prabhu, Tim Townes

Title: The Effect of Inflammation on Cardiac Stem Cells

Prior Research Experience: Yes

Abstract Approved: Yes

Objective: Several populations of stem cells exist in the heart and have been shown to be able to in vitro differentiate into cardiomyocytes, endothelial cells, fibroblasts, and others. In the context of heart injury this multipotency does not present itself. We wanted to investigate the role of inflammation in abrogating differentiation potential.

Methods: Stem cells were isolated from minced hearts and grown in explant culture. These cells were sorted for a Sca1+/CD31-/DDR2- population. Cells were subjected to either TGF β (10 ng/mL), TNF α (20ng/mL), or a combination of the two for a total of 4 days. Collagen gel contraction assay and PCR for fibrotic markers were performed after stimulation.

Results: Sca1+ cells in the presence of TGF β take on a more contractile and fibrotic phenotype. The addition of TNF α in the presence of TGF β ameliorates some of this effect.

Conclusions/Broader Impacts: The inflammatory milieu that cardiac stem cells reside in after heart injury may affect their differentiation potential and cause them to take on a more fibrotic phenotype.

Acknowledgments: UAB MSTP, UAB Training Program in Cardiovascular Pathophysiology (5T32HL007918-12)

Atchley, Travis James

Project Length: Short

Source of Funding: T35

Faculty Advisor: Dr. Robert Dabal

Co-Authors: David Cleveland, Robert Dabal, Ayesha Bryant, Santiago Borasino, Jeffrey Alten, Krissy Hock

Title: Surgical Outcomes of Single Ventricle Patients with Heterotaxy Syndrome: A 15-year retrospective study

Prior Research Experience: Yes

Abstract Approved: Yes

Heterotaxy syndrome is a disorder in the left-right body axis resulting in multiple congenital anomalies, especially of the heart and gastrointestinal system. Single ventricle with heterotaxy patients have worse surgical outcomes than single ventricle patients without heterotaxy despite undergoing the same palliative procedures. In recent years, computed tomography angiography has been used to diagnose heterotaxy syndrome and determine if pulmonary artery (PA) reconstruction is necessary. Since 2012, we have had greater access and usage of CTA and have since adopted a more aggressive PA reconstruction approach. In a retrospective study of heterotaxy patients diagnosed between 200 and 2015, we compared outcomes between patients that underwent PA reconstruction at first palliation to those who received only a neonatal shunt. We found that there has been little difference in surgical mortality between these two groups; however, there has been improvement of outcomes in patients diagnosed with heterotaxy after 2012.

Bares, Jennifer Cushing

Project Length: Intermediate

Source of Funding: Other

Faculty Advisor: Ryan Kraemer

Co-Authors:

Title: Comparing Incoming Residents' Inpatient and Outpatient Oral Presentation Structures

Prior Research Experience: Yes

Abstract Approved: Yes

Background/Study Aims

During medical school, students learn to present to a preceptor through Introduction to Clinical Medicine courses and clerkship rotations. Our study aimed to compare the oral presentation structure taught to medical students in outpatient vs. inpatient settings.

Methods

60 incoming residents from 40 medical schools were asked to complete an anonymous written survey at orientation. The survey asked residents if they were taught a standard oral presentation format for 4 different patient situations (initial hospital admission H&P, subsequent day hospital rounds, acute outpatient problem, and outpatient follow-up visit for a patient with several chronic problems). Participants were also asked to write the headings of each section used when presenting an admission H&P, a subsequent day inpatient, and a routine follow-up outpatient.

Results

100% of responders indicated they were taught hospital admission oral presentations, 98% subsequent day follow-up inpatient oral presentations, 83% for acute outpatient presentations, and only 71% reported being taught a presentation structure for a chronic outpatient follow-up presentation.

When listing the headings of each section used for follow-up hospital presentations, 44 of 54 responses listed SOAP (Subjective, Objective, Assessment, Plan) and 10 responses had no common pattern. For follow-up outpatient presentations, 10 of the 53 responses listed SOAP and 43 responses listed a mixture of common presentation elements in various orders without a discernable pattern.

Conclusions

Our survey showed that incoming PGY-1 residents perceived being taught outpatient presentation structures less often than inpatient presentation structures. In addition, our survey revealed one common inpatient follow-up presentation structure (SOAP), while no common structure for chronic outpatient follow-up presentations was identified. Our study of new residents from 40 different medical schools indicates that current curricula do not provide a uniform presentation structure to guide medical students' outpatient presentations.

Berry, Ryan D.

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: Stuart J. Frank

Co-Authors: Martin E. Young

Title: Differential tissue and time-of-day response to hGH in C57 Black 6 male mice.

Prior Research Experience: Yes

Abstract Approved: Yes

The circadian clock is critical for the optimal timing of important signaling and metabolic processes throughout the body. The central circadian clock resides in the suprachiasmatic nucleus of the brain and synchronizes intrinsic peripheral clocks located in nearly every cell of the body to the environmental light-dark cycle. This mechanism provides the body with the advantage of being able to anticipate regularly occurring events (e.g. waking, sleeping, and food intake) and optimize signaling and metabolism. Disruption of this synchronization process eliminates the anticipatory advantage and allows or causes ill-timed signals and metabolic processes. Chronic disruption of the circadian clock predisposes individuals to diabetes, metabolic disease, obesity, depression, cancer and cardiovascular disease. It has been clearly shown that secretion of numerous endocrine factors (e.g. growth hormone (GH), melatonin) varies with the time of day (TOD). However, few have discussed TOD dependent variations in tissue sensitivity. Here we analyzed the sensitivity of numerous organs from 16 week old C57 B6 male mice to intravenously administered GH at ZT0 (lights on) and ZT12 (lights off). We found that cardiac and skeletal muscle sensitivity to a GH bolus, as represented by the phosphorylation level of signal transducer and activator of transcription (STAT) 5 relative to total STAT5 protein, was increased by four fold at ZT0 compared to ZT12. We also found that the response to GH varied between tissues. This is the first work to show a differential TOD dependent response to GH in the heart.

Bevans, Stephanie Leigh

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Jason Warram

Abstract Approved: Yes

Co-Authors: Hope Amm, Lindsay Moore, Mary McDougal, Anthony Morlandt, Jason Warram

Title: Fluorescence-guided surgery in odontogenic tumors using Cetuximab-IRDye800

Introduction:

Odontogenic tumors are benign, yet invasive, making their localization and surgical removal difficult. We hypothesize fluorescence-guided imaging using Cetuximab-IRDye800 can provide adequate tumor contrast for applications in intraoperative surgical removal as demonstrated in novel patient derived xenograft and secondary cell line models of odontogenic tumors. A temporal study was performed using 200 μ g/mouse of Cetuximab-IRDye800 in SCID and athymic mouse groups, each group containing mice bearing keratocystic odontogenic tumor, ameloblastoma, and patient derived xenograft ameloblastoma models.

Methods:

Fluorescence imaging was performed once every 4 days beginning at time of infusion using commercially available open-field near infrared (NIR) and closed-field NIR imaging systems. On day 14 the mice were sacrificed and subcutaneous tumors were imaged with skin removed to compare the detectability of the tumor using brightfield imaging and open-field NIR imaging. Tumors for 2 mice were resected and progressively smaller fragments were re-introduced into the wound bed in order to determine the smallest cancerous mass detectable using both open- and closed-field NIR imaging systems.

Results:

Intraoperative imaging effectively differentiated tumor from normal tissue in all SCID and athymic mouse models known to have tumor at time of imaging. Tumor-to-background ratios peaked on day 11 for SCID mice, with values of 3.8, 3.0, 2.0, and 1.4 for (AB-20 PDX-1), (AB-20 PDX-2), (KCOT-3 cells), and (AB-17 cells), respectively; and peaked on day 11 for athymic mice, with values of 4.1, 2.6, and 2.6 for (AB-20 PDX-1), (AB-20 PDX-2), and (KCOT-3 cells), respectively. Tumor sections as small as 0.5mg were visualized with TBRs of greater than 2.1 in SCID and athymic mice using open- and closed-field NIR imaging systems.

Conclusion:

Fluorescence-guided imaging showed potential for use in fluorescence-guided surgical applications for odontogenic tumors as demonstrated in keratocystic odontogenic tumor, ameloblastoma, and patient derived xenograft ameloblastoma models in SCID and athymic mice.

Birchall, Elizabeth Langford

Project Length: Short

Source of Funding: T35

Faculty Advisor: Jeremy Herskowitz

Co-Authors: Erik Gentry

Title: Imaging and Analysis of Dendritic Spines

Prior Research Experience: No

Abstract Approved: Yes

Alzheimer's disease, the most prevalent form of dementia in the United States, is classically defined by the presence of amyloid β plaques and neurofibrillary tangles. While it is known that dendritic spines, which play a key role long and short term memory, change throughout the disease, little is known about the extent of change or the characterization of these changes. Furthermore, few experiments have previously been conducted that effectively examine dendritic spines in human tissue preserved in 4% paraformaldehyde. The goal of this project is, first, to determine a method to stain neurons, quantify and qualify dendritic spines and, second, to analyze and classify the differences seen in human tissue from symptomatic Alzheimer's patients, asymptomatic Alzheimer's patients and a control group. Initially, we attempted to use fluorescent tracing with lipophilic substances like Dil and confocal microscopy in human and mouse tissue. Despite numerous variations of protocols, fluorescent tracing is not feasible in human tissue, presumably due to membrane degradation during the post-mortem interval. Alternatively, we used FD Rapid GolgiStain kit, and were able to efficiently and reliably stain neurons in human tissue. Software programs like ImageJ and Reconstruct have been vital in the post imaging analysis of the size, shape and quantity of the spines. The future aims of the project are to continue staining human tissue of different cohorts and to analyze the data using Reconstruct and ImageJ.

Black, Jeffrey Ryne

Project Length: Short

Source of Funding: T35

Faculty Advisor: Ilan Kerman

Co-Authors: Black, J. R., Nam, H., Kerman, I. A.

Title: Activation of neurons within PVN in Wistar and Wistar-Kyoto rats following the forced swim test

Prior Research Experience: Yes

Abstract Approved: Yes

Depression impacts millions of patients worldwide, but little is known about the neurobiological processes involved in these disorders. The Wistar-Kyoto (WKY) rat exhibits physiological and behavioral characteristics consistent with depression and is an established pre-clinical model of depression. A particularly striking aspect of WKYs' behavior is their pronounced immobility during the forced swim test (FST), which assesses behavioral despair, a core feature of depression. Previous studies have documented distinct patterns of corticosterone secretion in WKYs in response to a variety of stressors. In the current study we hypothesized that WKYs exhibit a distinct pattern of neuronal activation within the paraventricular nucleus of the hypothalamus (PVN), a key region in the hypothalamic-pituitary-adrenal axis, in response to FST exposure. To test this notion we exposed WKY and the genetically-related Wistar (WIS) rats to the FST and then examined patterns of neuronal activation within the PVN using immunocytochemistry for c-Fos. While most PVN subregions showed no differences in c-Fos expression, the dorsal part of the medial parvocellular area (PVNmpd) exhibited significantly higher activation for WIS rats on Day 2 of the FST. This finding parallels our observation in the A1 noradrenergic cell group, which provides excitatory tone to the PVN, and may underlie this difference. It also suggests that the radically different coping strategy of the WKY rats on the FST may serve an adaptive purpose. Future investigations will involve quantifying the neuronal activation of other regions that receive noradrenergic innervation from the A1, and the related A2, cell group.

Bolis, Ramy Ahdy

Project Length: Short Prior

Research Experience: No

Source of Funding: T35

Faculty Advisor: Dr. Nita Limdi and Dr. Richard Shelton

Abstract Approved: Yes

Co-Authors:

Title: A Predictive Algorithm of Citalopram Efficacy

Major depressive disorder (MDD) is a common mental disorder that manifests as “low mood” that is pervasive and persistent. According to the World Health Organization, MDD is the leading cause of disability worldwide. For men, there is a 7% to 12% lifetime risk for developing MDD. For women, there is a 20% to 25% lifetime risk for developing MDD.

For many patients, the first line treatment is Citalopram (Lexapro), a Selective Serotonin Reuptake Inhibitor (SSRI). The resultant increase of serotonin attenuates depression symptoms in about 50% of the patients. However, it causes nausea, agitation, insomnia, drowsiness, tremor, dry mouth, weight gain or loss, and sexual dysfunction. Moreover, 33.5% experience relapse of depression.

Predicting a patient’s response to Citalopram was the focus of my research. To do so, we planned to leverage the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. The study provides a wealth of information aimed at determining which subsequent treatments are most effective following non-remission or intolerance to an initial SSRI treatment.

I proposed to analyze the data from the STAR*D study to identify demographic, clinical, and genetic predictors of Citalopram response. As defined by STAR*D, “remission” was defined as a score of 5 or less on the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) and “response” was defined as a 50% or more reduction in baseline QIDS-SR score.

My hypothesis was there are patient-specific characteristics and genetics that can predict the efficacy of Citalopram.

Currently, the NIMH distribution agreement for our data request has been finalized. I have compiled a ZIP file with all the forms required for the NIHM data request. The ZIP file will be submitted to the NIMH in the near future in hopes of receiving the STAR*D data soon.

Boppana, Sushma

Project Length: Short

Source of Funding: NIH MSTP

Faculty Advisor: Paul Goepfert, MD

Co-Authors: Victor Y Du, MS

Title: Compromised perforin production represents a possible mechanism of CD4 T cell-mediated HIV Immune Escape

Prior Research Experience: Yes

Abstract Approved: Yes

Purpose: Recently, cytotoxic CD4 T cells have been shown to exert immune pressure on HIV, forcing viral escape. While we previously detected differences in immunogenicity between adapted and non-adapted HIV forms, the mechanism underlying this difference remains unknown. We hypothesized that CD4 T cells are less responsive to adapted HIV epitopes (AE), and produce less cytotoxic molecules as compared to the non-adapted epitopes (NAE).

Methods: This project aimed to determine: 1) whether AE-specific effector CD4 T cells have lower antigen sensitivity than their NAE counterparts, and 2) if NAE and AE specific CD4 T cells express different phenotypes that could influence T cell function. For antigen sensitivity, we measured CD4 T cell responses to serial dilutions of NAE/AE pairs in HIV seropositive samples using ELISpot assays. To assess cellular phenotype, we performed intracellular cytokine staining (ICS) flow cytometry to evaluate the cytokine production of CD4 T cells stimulated with NAE and AE antigens.

Results: We detected no significant difference between CD4 T cell responses to NAE and AE at any antigen concentration; However, we discovered a trend ($p=0.08$) towards a lower percentage of perforin-expressing CD4 T cells when stimulated by AE as compared to NAE stimulated cells.

Conclusion: CD4 T cells targeting adapted epitopes exhibit no significant differences in antigen sensitivity but show a trend towards decreased perforin production. This represents a potential mechanism of immune escape whereby HIV may provoke a less cytotoxic response due to viral escape mutations. These results warrant further investigation into the differences between NAE and AE stimulated cell populations and serve as a springboard into additional research involving the clinical and vaccine implications of these CD4 T cell-mediated escapes.

Bouldin, John Bradley

Project Length: Short

Source of Funding: Other

Faculty Advisor: Marjorie White, MD

Co-Authors: April Belle, RN, MSN; Marjorie White, MD

Title: The Use of a Sports Metrics App in the Recording of In-Situ Mock Code Data

Prior Research Experience: No

Abstract Approved: Yes

Background:

For the past two years, the Office of Interprofessional Simulation (OIPS) has been performing in-situ mock codes to test UAB Hospital's response to code situations. Data points from these events are recorded and reported to the nation-wide Simulation Data Registry Project. Originally, these metrics were recorded on paper, causing many near-simultaneous data points to be missed, and transferring captured data points from paper to a tracking spreadsheet was a generally time-consuming activity. For these reasons, OIPS looked for novel recording solutions and to see if a sports metrics application could help with this process.

Methods:

OIPS developed data points to test the code response system for each in-situ mock code. These data points consisted of times to completing key ACLS algorithm steps and the arrival times of various team members.

A sports metrics recording software application, Sportstec's iCoda, was introduced in an attempt to streamline the recording process. The app allowed OIPS to record time-based metrics with taps of on-screen buttons. After the mock code is over, the results are saved in a format that can be quickly copied and pasted into a tracking spreadsheet.

Evaluation and Discussion:

Evaluation of the process after use in three mock codes showed a general improvement in data gathering. Using the app provided higher accuracy of time-based metrics, faster conversion from collection to recording, helped the recorder miss fewer events, and increased the number of data points captured. Overall, recorders reported experiencing less difficulty in data collection and increased ability to focus on the actions being performed in the mock code.

In conclusion, it was determined that the use of a sports metrics application as a novel method of recording mock code performance data increased the fidelity and amount of data collected while also streamlining the process of recording and transferring that data.

Bourgeois, Claire Elizabeth

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Marie Bakitas

Abstract Approved: Yes

Co-Authors: Marie A Bakitas, Rodney Tucker, Keith Swetz, Dio Kavalieratos, J. Nicholas Dionne-Odom, Jackie Palmore, Peggy Blood, Kristen R Allen, Gisella Mancarella, Salpy V. Pamboukian

Title: A national survey of INTERMACS centers' institutional characteristics and specialist and generalist palliative care practices in patients with mechanical circulatory support devices

Mechanical circulatory support device (MCS) placement is a high-risk medical procedure requiring treatment by an interprofessional team. The International Society for Heart and Lung Transplantation recommends inclusion of a palliative care (PC) specialist in pre-placement patient evaluation of MCS as destination therapy.

Study goals were to (1) identify INTERMACS centers' MCS and PC program characteristics, (2) identify timing and frequency of PC involvement with MCS patients, and (3) describe clinicians' attitudes regarding integration of PC into MCS patient care.

We conducted a population-based survey of PC and MCS coordinators/clinicians at North American INTERMACS centers. Using literature, expert panel, and MCS guidelines, we developed three surveys: Survey 1-MCS (15 items) included MCS institutional characteristics, Survey 1-PC (23 items) included PC program characteristics, and Survey 2 (31 items) assessed cardiology and PC clinicians' perceptions of PC use in MCS and cardiology clinicians' comfort with PC activities (7 additional items). We collected responses via Qualtrics™ web-based software or by phone.

MCS coordinators (n=13), PC coordinators (n=24) and MCS/PC clinicians (n=36) completed the surveys. Of 44 INTERMACS centers represented, more than half of MCS and PC programs were established by 2003 and 2007, respectively. 74% of patients considered for MCS were referred to PC. All respondents agreed that PC involvement should occur during evaluation. No PC and 36% of cardiologists felt that cardiologists were able to manage patients' psychological symptoms as effectively as PC. Cardiologists reported high confidence in discussing goals of care, conducting family meetings, and addressing existential/spiritual distress.

Respondents agreed with ISHLT recommendations for including PC in MCS evaluation, however there was less consensus on clinicians' roles and confidence with providing PC during treatment. There is great need for PC/MCS clinicians' collaboration to increase consensus on the role of PC in MCS patient care.

Bray, Alexander Wendell

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Scott W. Ballinger

Abstract Approved: Yes

Co-Authors: Jessica L. Fetterman, David G. Westbrook, Kimberly J. Dunham-Snary, Scott W. Ballinger

Title: Mitochondrial Genetic Background Influences Susceptibility to Atherosclerosis

Cardiovascular disease (CVD) is the leading cause of mortality in the United States, and the majority of cases are due to atherosclerosis. Despite the widespread prevalence of this disorder, the contribution of inherited genetics to CVD susceptibility remains poorly understood. Furthermore, the cellular mechanisms through which defined CVD risk factors such as age, ethnicity, family history, hypercholesterolemia, and tobacco smoke converge to stimulate atherogenesis have yet to be clearly articulated. Mitochondria are multifunctional organelles that sustain oxidant-mediated damage following chronic exposure to these CVD risk factors. In addition, mitochondria possess their own maternally inherited genome that reflects maternal geographic origins and contains polymorphisms capable of influencing mitochondrial and cellular function. In the following study, we directly assessed the causal role mitochondrial genetics and function play in the pathogenesis of atherosclerosis. Utilizing novel Mitochondrial-Nuclear eXchange (MNX) mouse technology developed in our laboratory, apoE^{-/-} WT (apoE^{-/-} C57n:C57mt) and MNX (apoE^{-/-} C57n:C3Hmt) mice were generated in order to test the hypothesis that altering a mouse's mitochondrial genetic background would influence atherogenesis in this setting of genetically driven hypercholesterolemia. Our data has supported this hypothesis by demonstrating that apoE^{-/-} C57n:C3Hmt mice accumulate both atherosclerotic lesions and mitochondrial DNA damage at a significantly lower rate than their apoE^{-/-} C57n:C57mt counterparts. Moreover, studies performed on apoE^{-/-} C57n:C57mt and apoE^{-/-} C57n:C3Hmt aortic ring segments ex vivo revealed that the presence of the C3H mtDNA is associated with greater maintenance of both vascular mitochondrial reserve capacity and endothelial-dependent vessel relaxation in the face of pathogenic hypercholesterolemia. Together, these data are consistent with our hypothesis that mitochondrial DNA background is able to modulate the progression of atherosclerosis through its ability to influence development of mitochondrial dysfunction and cellular oxidative stress.

Brinkley, Garrett Joseph

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Dr. Ralph Sanderson

Abstract Approved: Yes

Co-Authors: Garrett Brinkley, Shyam Kumar Bandari, Anurag Purushothaman, Ralph Sanderson

Title: Following treatment with bortezomib, myeloma cells secrete exosomes with altered protein composition that enhance chemoresistance and tumor proliferation

Exosomes are small, 30-100 nm vesicles secreted by most cells. The contents of exosomes can contain a large number of proteins, RNA and DNA that can impact signaling pathways in cells that come in contact with the exosomes. In cancer, exosomes have been shown to influence tumor progression by promoting epithelial-to-mesenchymal transition, cancer stemness, angiogenesis, and metastasis. Using myeloma cell lines as a model, the purpose of the present study was to determine if the anti-myeloma drug bortezomib alters exosome composition thereby altering the function of exosomes secreted by those cells. Preliminary studies revealed that treatment with bortezomib increased exosome secretion by myeloma cells and that these exosomes when added to myeloma cells would enhance chemoresistance and proliferation. To determine if these effects were due to alterations in exosome composition resulting from bortezomib treatment, the exosomes secreted by cells treated with or without bortezomib were analyzed for their protein composition. Preliminary results revealed that of the 550 proteins detected in the exosomes, approximately 60 were significantly upregulated in exosomes derived from bortezomib treated cells compared to controls. Notably, two of the proteins showing a high increase in amount in exosomes from bortezomib treated cells were heat shock proteins HSP90beta and HSP70 1A/1B. Because HSPs can be associated with enhanced chemoresistance, these results provide a potential explanation as to how exosomes secreted following bortezomib treatment can enhance resistance to drug therapy.

Busing, Jordan Douglas

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Nick CaJacob, Dr. Reed Dimmitt

Abstract Approved: Yes

Co-Authors: Dr. Nick CaJacob, Department of Pediatric Gastroenterology

Title: Eosinophilic Esophagitis: Sampling the Esophageal Microbiome

Eosinophilic Esophagitis (EoE) is a chronic, allergen mediated disease characterized by clinical features of dysphagia, vomiting, and food impaction combined with pathologic evidence of an eosinophil rich inflammation of the esophagus. Recent studies have shown a link between altered esophageal microbiota, collected by esophageal brushings during upper endoscopy, and EoE. Further research is needed to investigate the role that the altered microbiome plays in EoE pathology. A key aspect in that research is the collection and processing of microbiome specimens from the esophagus. Esophageal brushing is not routinely done on upper endoscopies and therefore our group seeks to assess whether tissue biopsies that are routinely obtained for pathologic examination offer the same microbiome results as the esophageal brushings. The aim of this study was to analyze and compare the microbiome of the esophagus from two separate collection methods: esophageal brushing and tissue biopsy. We hypothesize that the bacterial composition from each type of collection method should be quantitatively and qualitatively similar. Once we obtain the results of our DNA processing and analysis, we will be able to ascertain if both sampling techniques produce the same microbiome profile. If so, it will open up a wide range of previously taken esophageal biopsies of patients with EoE to further study the link between the microbiome and EoE.

Carlisle, Matthew Alexander

Project Length: Intermediate

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Sadis Matalon

Co-Authors: Matthew Carlisle, Adam Lam, Saurabh Aggarwal, Tamas Jilling, Sadis Matalon

Title: Amelioration of halogen-induced injury during pregnancy

Prior Research Experience: Yes

Abstract Approved: Yes

Background: There have been no prior studies assessing halogen inhalation toxicity in vulnerable populations (pregnancy), which can occur in transportation/industrial accidents and terrorist acts. Halogen exposure inhibits endothelial nitric oxide synthase (eNOS) with a compensatory upregulation of inducible nitric oxide synthase (iNOS). Nitric oxide (NO) and endothelin-1 (ET-1), major regulators of pulmonary vascular resistance, are either beneficial (NO) or injurious (ET-1) to placental development and fetal growth. Data from animal models and human samples indicate that decreased endothelial NO and increased ET-1 production are key mechanisms of pulmonary hypertension, preeclampsia, and intrauterine fetal growth restriction (FGR). Therefore, we hypothesized that halogen exposure in pregnancy results in pulmonary hypertension, preeclampsia, and FGR. We further hypothesized that a phosphodiesterase type 5 inhibitor (tadalafil) reduces halogen-mediated pulmonary artery pressures and maternal mortality while improving fetal growth.

Methods: Pregnant mice (15-days gestation) were exposed to Br₂ gas (600ppm, 30min). Samples were collected (3-4-5 days) post-exposure. Mice were treated 1-hour post-exposure with tadalafil (2mg/kg) via gavage and once daily following exposure. Echocardiography was used to monitor fetal growth and pulmonary artery pressures in vivo.

Results: Br₂ exposed pregnant mice exhibit 85% mortality while exposed non-pregnant mice exhibit 25% mortality. Gene expression of fms-like tyrosine kinase-1 (sFlt1), a marker of preeclampsia, was increased in the placenta, and endothelin-converting enzyme was increased in the kidneys and lungs of Br₂ exposed pregnant mice. This correlated with profound intrauterine fetal growth restriction and echocardiographic evidence of pulmonary hypertension. Administration of tadalafil resulted in a significant decrease in maternal mortality (33% vs 85% without tadalafil), increase in fetal growth and viability, and decreased pulmonary artery pressures.

Conclusion: Pregnancy predisposes to increased maternal and fetal vulnerability to halogen inhalation injury. Tadalafil treatment following Br₂ exposure improves pulmonary circulation, reduces the degree of FGR as well as maternal and fetal mortality.

Chiu, Sherwin Shao-Yun

Project Length: Short

Source of Funding: Other

Faculty Advisor: Jeffrey Alten, MD

Co-Authors: Santiago Borasino, MD, MPH, Kimberly Jackson, MD, Jeffrey Alten, MD

Title: Is Pulse Pressure in the Early Postoperative Period a Predictor of Morbidity After the Norwood Procedure

Prior Research Experience: Yes

Abstract Approved: Yes

Background: Cardiac Surgery Associated-Acute Kidney Injury (CS-AKI) is a frequent complication after Norwood Procedure (NP) and leads to significant morbidity. Massive transfusions (MT) have been associated with multi-organ failure. We sought to understand the frequency of MT associated CS-AKI post-NP.

Methods: All patients who underwent NP with Sano modification between December 2008 and April 2014 were reviewed. Patients requiring extracorporeal membrane oxygenation (ECMO) in operating room and/or requiring a hybrid NP were excluded. CS-AKI defined as doubling of pre-operative serum creatinine and/or urine output less than 0.5 ml/kg/hr. MT defined as requiring >40 ml/kg of blood products within six hours from admission. Multinomial logistic regression with main effects model used to adjust for other important variables associated with AKI. Data represented as medians with interquartile range (IQR).

Results: 57 patients met criteria. Median age at operation 6 (IQR 5,7) days, median weight 3.2 (IQR 2.9,3.5) kg, median cardiopulmonary bypass (CPB) 169 minutes (IQR 133.5,198.3) and median aortic cross clamp (ACC) 69.5 minutes (IQR 61.8,91). 61.4% developed CS-AKI. 35.1% of patients required MT. Incidence of CS-AKI in non-MT vs MT was 51.4% and 80%, respectively ($p=0.047$). MT not associated with admission vasoactive inotrope score (VIS), admission lactate, post-operative open chest, or ECMO. Patients with MT had longer CPB 192 (IQR 158.8,214) vs 161.5 (IQR 124.8,181.8) ($p=0.007$), ACC 87.5 (IQR 72.5,96.8) vs 63 (IQR 53.8,77.8) ($p<0.001$), mechanical ventilation hours 161.5 (IQR 122.3,306.1) vs 92.2 (IQR 77.6,139.3) ($p=0.002$), and a non-significant increase in mortality 25% vs 13.5% ($p=0.298$). After adjusting for admission lactate, admission VIS, CPB and weight, MT was independently associated with development of CS-AKI: OR 26.3 (95% CI: 1.9-348).

Conclusions: MT is independently associated with development of CS-AKI in patients after NP. Larger studies are required to confirm this finding as a potentially modifiable risk factor in development of CS-AKI.

Chung, Sebastian King yin

Project Length: Short

Source of Funding: Cunningham Fellowship

Faculty Advisor: Leslie Hayes, M.D.

Co-Authors:

Title: Applying the Brain: Hospital Adherence to Evidence-Based Severe Traumatic Brain Injury Management Guidelines

Prior Research Experience: Yes

Abstract Approved: Yes

Background:

The evidence-based medicine movement has helped standardize and optimize the practice of medicine. However, there are few studies that have looked at the adherence to these evidence-based guidelines. This is especially true with the more complex processes such as the management of traumatic brain injuries (TBI).

Objectives:

We evaluated adherence to an existing Children's of Alabama (COA) algorithm derived from evidence-based guidelines for management of severe TBI. We also determined the agreement between the pediatric intensive care unit (PICU) team's estimates of adherence with the TBI algorithm and the actual calculated compliance.

Methods:

We performed a retrospective chart review of 85 COA patients admitted to the PICU for severe TBI not caused by child abuse from January 2013 to June 2015. Data was analyzed using excel with QI macros and Minitab16. Adherence to the TBI algorithm was determined by calculating the percent of time each patient reached the 10 management goals outlined in the COA TBI algorithm during the first 7 ICU days (cerebral perfusion pressure/mean arterial pressure, central venous pressure, sodium, hematocrit, sedation, temperature, oxygen and carbon dioxide, glucose, seizure, and enteral feeds).

We surveyed 27 PICU staff about their familiarity with the COA TBI algorithm and their adherence estimates to the algorithm.

Results:

Adherence with the COA severe TBI algorithm for the 85 patients was 27.53%, which is much lower than the PICU staff's estimated adherence of 72.64%. Adherence to each of the ten management goals ranged from 12.34% (sedation) to 75.29% (seizure prophylaxis).

Conclusions and next steps:

Self-reported familiarity with COA's severe TBI algorithm overestimated adherence to the algorithm. A process change has been identified to develop practical bedside algorithms for key elements: sodium, carbon dioxide, temperature and cerebral perfusion pressure control. Data monitoring for improvement is ongoing.

Cohen, Joshua L.

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Dr. Sarah Clinton

Abstract Approved: Yes

Co-Authors: Anoosha E. Ata, Nateka L. Jackson, Ilan A. Kerman, Sarah, M. Clinton

Title: 12 Things you didn't know about high responder/low responder rats, stress coping, and microRNAs in the dorsal raphe. Number 5 will blow your mind!

Purpose: Stress is a well-known environmental risk factor for the development of a variety of mental illnesses. However, not everyone who encounters stress develops a mental illness, or the same mental illness. Therefore it is necessary to understand how the neural circuits that respond to stress and how these circuits differ between individuals, especially between those vulnerable and resistant to stress-induced psychopathology.

Methods: To investigate the neurocircuit and molecular mechanisms underlying different stress coping styles, we utilized selectively bred high-responder (HR) and low-responder (LR) rats. HR/LR rats are a well-developed model for studying individual differences in emotionality and behavior. Animals underwent defensive burying testing, a test of stress coping style. Rats were placed in a chamber with bedding and exposed to an electric probe, which delivered a single shock upon interaction. Behavior following shock was recorded and classified as proactive, burying the probe with bedding, or reactive, freezing. Ninety minutes following testing brains were collected. Sections of brain were dual-label for c-Fos, a marker of neuronal activity, and tryptophan hydroxylase (TPH), a marker of serotonergic neurons, to determine if differences in serotonergic cell activation may contribute to stress coping style.

Results: HR rats spent more time burying the probe than LR rats, while LR rats spent more time immobile. HR rats displayed an increase in c-Fos activation in TPH cells of the midline dorsal raphe, while LR rats display a decrease.

Conclusion: HR and LR rats display proactive and reactive coping styles respectively. Differential activation in the midline dorsal raphe group may contribute to coping behavior. The midline dorsal raphe projects to regions involved in stress and emotionality, such as the central amygdala and dorsal hypothalamus, and regions involved in motor function, the sensorimotor cortex, motor cortex, and caudate putamen. Current work is investigating molecular mechanisms of the differential activation observed in the dorsal raphe. Sequencing of microRNAs isolated from the region has been performed, several promising miRNA species and downstream targets implicate epigenetic differences in the dorsal raphe of HRs and LR rats.

Colon, Chad Michael

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Craig Hoesley

Abstract Approved: Yes

Co-Authors: Patrick Rowan, Gary Cutter PhD, Mollie Deshazo MD, Craig Hoesley MD

Title: Comparing High Risk Exposure disclosure among medical students and residents following intervention between 2002 and 2015

Purpose: Previous research has estimated that the number of percutaneous injuries sustained annually by healthcare providers (HCP) was 384,325. Additionally, previous research has shown that hospital patient populations have higher rates of Hepatitis B, C and HIV than the general population. Despite this increased risk, unreported exposure amongst HCP has been shown to be as high as 53%. Previous work by Dr. Deshazo showed similar rates of unreported exposure and methods were implemented at the University of Alabama Hospital, in Birmingham, Alabama (UAB) to encourage awareness and reporting. The purpose of this study was to resurvey medical students and residents to assess the effectiveness of those efforts and to understand the current environment of exposure and exposure reporting.

Method: An anonymous survey was distributed to medical students and residents in internal medicine, emergency medicine, obstetrics and gynecology, and surgery at UAB between February 13 and April 30, 2015. The exposure rate, disclosure rate, method and circumstance of exposure, reason for not reporting, and method of exposure were recorded and analyzed.

Results: The new survey showed that 28 of the 77 (36%) accidents went unreported in 2015, compared to 57 of 128 (45%) accidents in 2002. Additionally, the new survey found participants were more likely to be aware of the viral status of the patient they were exposed to, 52 Yes, 25 No, compared to 36 Yes, 92 No in the 2002 survey.

Conclusions: Implementing an orientation lecture that focused on awareness and reporting protocols of exposure, as well as creating a streamlined method of ordering a comprehensive workup in the electronic medical record, increased reporting rates among medical students and residents and increased awareness of patient viral status.

Cox, Kathryn Elyse

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Carlos Estrada MD, MS

Abstract Approved: Yes

Co-Authors: Michael Belue, MA, William Curry, MD, Carlos Estrada, MD, MS, H. Hughes Evans, MD, PhD, B. Earl Salser, MD, Erin Snyder, MD

Title: Experiences that Strengthen and Weaken Enthusiasm for Primary Care in First Year Medical Students: A Nominal Group Technique Evaluation

Background/Objectives: Primary care physicians are in short supply. To better cultivate careers in primary care, the University of Alabama School of Medicine (UASOM) established the Dean's Primary Care Scholars Program (DPCSP) – a merit-based scholarship – aimed at decreasing the educational debt burden and increasing exposure to primary care leaders. In this report, we examined experiences of first year medical students that strengthen or weaken enthusiasm in primary care.

Methods: DPCSP medical students participated in May of their first year (Classes of 2016-2018). In a cross-sectional design, we used the nominal group technique (NGT) to examine experiences. NGT permits equal participation, eliminates the effects of dominant or shy personalities, and allows the efficient acquisition of ranked responses. The NGT has four steps, participants: i) individually recorded responses to a question posed by an experienced facilitator ("During medical school, what sorts of experiences strengthen your enthusiasm to become an excellent primary care physician?"), ii) provided responses in a round-robin manner without discussion, iii) clarified responses, and iv) weigh their top three responses (3 = most important, 1= least important). We then repeated the process with another question: "During medical school, what sorts of experiences weaken your enthusiasm to become an excellent primary care physician?" We present the top five responses from each class and categorized them using an iterative consensus agreement process among the authors.

Results: All 20 students participated. Experiences that strengthen the enthusiasm include patient interactions (percent weight, 35%), physician interactions/ role models (29%), community interactions (23%), and health care finances (13%). Experiences that weaken the enthusiasm include the hidden curriculum (percent weight, 40%), poor role models (32%), healthcare system/finances (18%), and patient interactions (10%).

Discussion: Interacting with patients in the context of community service was the most important experience for students interested in primary care, further supporting the significance of service learning.

The perceived prestige and glorification of specialties, the 'hidden curriculum,' was the greatest deterrent. Poor role models were also of significant concern. Physicians advising against own career path or faculty commenting on shortcomings of primary care suggest dissatisfaction or lapses in professionalism. We highlight the importance of student experiences in undergraduate medical education in promoting primary care careers.

Craig, Carolyne Marie

Project Length: Short

Source of Funding: Other

Faculty Advisor: Dr. Leslie Hayes

Co-Authors: Leslie Hayes MD, Kristen Waddell NP, Ashley Penn NP, Lucy Daniel PharmD

Title: Development and Implementation of a Standardized Sedation Weaning Guideline in a Pediatric ICU

Prior Research Experience: Yes

Abstract Approved: Yes

Introduction: The pediatric ICU at Children's of Alabama sees over 1400 children each year, approximately 30% of whom require sedation and mechanical ventilation.

However, there is no standardized method to wean children from sedation, and ICU physicians use various medications and doses. The dosing and number of days to wean a patient from IV sedation is unpredictable. A paucity of protocols and guidelines has been published about pediatric analgesic and sedation medication weaning. Withdrawal from sedation medications is a potentially life-threatening condition.

Hypothesis: A standardized sedation weaning guideline for a pediatric ICU will result in more predictable number of days on oral weaning medication and less risk of withdrawal from medications, as measured by the Withdrawal Assessment Tool Score (WATS).

Methods: Charts of all patients who were on mechanical ventilation and sedation for five or more days between August 2014 and March 2015 were reviewed (n=100). Data concerning IV sedation medications and oral weaning medications was obtained, along with documented WATS. Quality analysis was performed using statistical process control charts and pareto charts using Minitab 16 statistical software program. We then created an evidence-based, practical sedation weaning protocol.

Results: Chart review showed both massive variation in practice and inconsistent documentation. WATS scores were only recorded for 52% of patients at risk for withdrawal, with scores ranging from 0-9. After implementation of our new sedation weaning guideline, our pilot patient had WATS scores within the evidenced-based target range (0-3), consistent with no symptoms of withdrawal.

Conclusion: Implementation of a standardized sedation weaning guideline in the pediatric ICU resulted in more predictable weaning medication dosing, more predictable number of days of weaning, and less evidence of withdrawal. Currently, spread of this sedation guideline is ongoing throughout the ICU with data collection underway.

Crowson, Cole Nathaniel

Project Length: Short

Source of Funding: Other

Faculty Advisor: Dr. Jayme E. Locke

Co-Authors: Rhiannon D. Reed, Brittany Shelton

Title: Induction Immunosuppression Regimen and the Odds of Acute Rejection by Race in Pediatric Kidney Transplant Recipients

Prior Research Experience: Yes

Abstract Approved: Yes

Background: The use of induction immunosuppression has been associated with a reduction in the risk of acute rejection (AR) among adult kidney transplant recipients (KT). However, data on type of induction regimen and AR are lacking among the pediatric KT population.

Methods: We examined outcomes among 7808 first time pediatric KT recipients using Scientific Registry of Transplant Recipients data (2000-2011). Recipient and donor characteristics were compared across induction immunosuppression regimen using the Kruskal Wallis test for continuous and chi-square tests for categorical variables. Odds of acute rejection were estimated using logistic regression models, stratified by recipient race and adjusting for recipient age, gender, and donor type.

Results: Odds of AR within one year were lower in AA recipients receiving lymphocyte-depleting induction (antithymocyte globulin or alemtuzumab) (Odds ratio [OR], 0.68; 95% confidence interval [CI], 0.49-0.93; $P=0.02$) compared to AA recipients receiving anti-interleukin-2 receptor antibody (IL-2) induction. This difference was not seen in non-AA recipients receiving lymphocyte-depleting induction (OR, 0.87; 95% CI, 0.73-1.04, $P=0.12$) as compared to their IL-2 induction counterparts (Figure 1). AA recipients were also more likely to receive lymphocyte-depleting induction or IV steroids as compared to Non-AA recipients ($P<0.0001$). Non-AA recipients were more likely to receive IL-2 induction as compared to AA recipients (Table 1).

Conclusions: These findings support a role for lymphocyte-depleting induction agents in AA pediatric patients undergoing KT. In addition, these findings support the continued use of IL-2 inhibitor induction in non-AA pediatric kidney transplant recipients.

Davis, Ann Elizabeth

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Nancy Tofil

Abstract Approved: Yes

Co-Authors: Kandi Wise, Amber Youngblood, Chrystal Rutledge, Lynn Zinkan, Nancy Tofil

Title: Improving Cardiopulmonary Resuscitation by Implementing First Five Minute Training

The first five minutes (FFM) of cardiopulmonary resuscitation are the most influential in the outcome of the coding patient. Proper technique and response time are critical in these emergent settings. While all nurses and physicians are trained in Basic Life Support (BLS), without regularly practicing these skills, they may not be able to provide necessary care. Children's of Alabama began an initiative through the simulation center to provide FFM training to all nurses on a regular basis on their units (in-situ). Our hypothesis was that providing regular BLS training would improve parameters of CPR success including time to chest compressions, bag valve mask use, backboard use and time to epinephrine administration during our 1-2 times monthly mock codes. In each session, a dedicated nurse educator from the Pediatric Simulation Center provided in-situ training for participants. The session started with a pre-brief describing the features of the simulator and goals of the session. Following this, the simulator would experience a cardiopulmonary arrest. Participants practiced recognizing the event, starting BVM ventilation and chest compression, obtaining a backboard and requesting epinephrine. We evaluated 33 hospital wide mock codes conducted from January 2013 through May 2015. The time to chest compression improved significantly after FFM training from 93 ± 72 seconds pre to 26 ± 38 seconds post ($p=0.043$). The time to epinephrine has not improved $5:26 \pm 3:22$ minutes pre-FFM training versus $5:49 \pm 1:51$ minutes post-FFM training ($p= 0.79$). Backboard use and BVM use were very high both before and after the intervention. Because the time to administration of epinephrine has not improved and still averages over 5 minutes (the target goal of the American Heart Association), future efforts including rapid cycle deliberate practice will focus on attempting to improve this parameter.

Davis, Benjamin Joseph

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Brent Ponce

Abstract Approved: Yes

Co-Authors: Dustin Baker, Dr. Brent Ponce

Title: Does surgeon specialty training influence postoperative outcomes in hand and wrist fractures?

Purpose. The purposes of this study are to (1) evaluate whether orthopaedic surgery versus plastic surgery specialty training influences the outcomes after hand and wrist fracture surgery and (2) evaluate baseline demographics and comorbidities of patients treated between the 2 specialties using a large national database.

Methods. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database from years 2011-2013 was used to retrospectively review all patients who underwent select hand and wrist fracture related procedures. Cohorts were compared for procedural distribution. Univariate analysis was used to compare demographics, comorbidities, operative characteristics, and postoperative complications between the two specialties. Multivariate analysis was utilized to determine any independent factors for postoperative complications.

Results. There were 3,217 patients included for analysis. Orthopaedic surgeons performed 72.8% of these procedures compared to 27.2% performed by plastic surgeons. Orthopaedic patients had a higher number of comorbidities. Complication rates were similar between specialties for severe adverse events, surgical site infection, DVT/PE, readmission, and reoperation. Complication rates for any adverse event were 1.7% and 0.6% for orthopaedics and plastic surgeons, respectively. Multivariate analysis revealed that surgeon training in either orthopaedic or plastic surgery does not influence overall complication rates for hand and wrist fracture surgery.

Conclusions. Surgeon specialty training in either orthopaedic or plastic surgery is not a risk factor for increased postoperative complications after hand or wrist fracture surgery.

Dean, Emma Caitlin

Project Length: Short

Source of Funding: NIH MSTP

Faculty Advisor: Casey Weaver

Co-Authors: Carson E Moseley, Robin D Hatton, Duy Pham, Casey T Weaver

Title: Utilizing Ex Vivo ATAC-Seq to Understand the Differential Transcriptional Landscape between IL10+ and IL10- Regulatory T Cells from a Murine Multiple Sclerosis Model

Prior Research Experience: Yes

Abstract Approved: Yes

Interleukin 10 (IL10) is an immunosuppressive cytokine produced by effector T cells, namely regulatory T cells (Tregs), to limit inflammatory responses to both antigen and self. In the murine multiple sclerosis model—experimental autoimmune encephalomyelitis (EAE)—IL10 has been shown to play a mitigating role. Although this role has been well characterized, the delayed onset of IL10 production is not well understood. We isolated Tregs from 10BiT-Thy1.1/Foxp3-GFP reporter mice that were immunized with myelin oligodendrocyte glycoprotein (MOG). These cells were then used to assay transposase-accessible chromatin with high throughput sequencing (ATAC-Seq). ATAC-Seq is a method wherein a hyperactive, mutated transposase is used to identify nucleosome-free regions of the genome. This assay generates an enrichment of regions in which transcription is most likely occurring. Using this method, we were able to determine key transcriptional differences between Tregs that produce IL10 and those that do not. We hope these data can be used in developing therapies that allow for earlier disease intervention in multiple sclerosis.

Deas, Dale Shelton, Jr.

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. David C Cleveland

Abstract Approved: Yes

Co-Authors: Jeffrey A Alten, David C Cleveland, Santiago Borasino, Hayden J Zaccagni, Kristal M Hock

Title: Interleukin-6 and interleukin-8 as acute kidney injury biomarkers for cardiac surgery in infants

Background: Infants undergoing cardiac surgery are at risk for acute inflammation associated with cardiopulmonary bypass (CPB). Acute kidney injury (AKI) is common following CPB and has been shown to be associated with increased post-operative morbidities and mortality. We sought to determine the associations between pro-inflammatory cytokines interleukin-6 (IL-6) and interleukin-8 (IL-8) with AKI and other adverse clinical outcomes both prior to and following CPB in infants.

Methods: A total of 138 infants were identified in a prospectively maintained study undergoing CPB. Plasma concentrations of IL-6 and IL-8 were measured preoperatively and then again at 0, 4, 12, 24, and 48 hours postoperatively. AKI was defined as a doubling of serum creatinine concentration or a sustained urine output of less than 0.5 ml/kg/h for 12 or more hours following surgery.

Results: AKI was diagnosed in 61 (44.2%) infants and was associated with longer CPB time ($p < 0.001$) and ICU length-of-stay ($p = 0.021$). AKI group had significant elevations in IL-8 at 0 and 12 hours ($p = 0.015$ and $p = 0.002$, respectively) and IL-6 at 48 hours ($p = 0.026$). Interestingly, preoperative IL-6 was lower in infants with AKI ($p = 0.038$), and serum creatinine at 48 hours was not associated with AKI. Significant elevations in IL-6 and -8 at 0 hours were strongly associated with mortality ($p = 0.007$ and $p = 0.014$, respectively). Prophylactic hydrocortisone and IVIG infusion resulted in significantly lower IL-8 at 12 hours and IL-6 at 48 hours. Prophylactic IVIG also resulted in significantly lower IL-8 at 0 hours.

Conclusions: Postoperative IL-6 and -8 are strongly associated with AKI and mortality. Prophylactic hydrocortisone and IVIG infusion result in significantly lower serum concentrations of IL-6 and -8 postoperatively. Earlier identification of patients at high risk of developing AKI may lead to the development of novel therapeutic interventions to improve kidney function and reduce mortality following cardiac surgery requiring CPB in infants.

Dennis, Evida Adiko

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Phillip Smith

Abstract Approved: Yes

Co-Authors: Evida Dennis, Lesley Smythies, PhD, Masako Shimamura, MD, William Britt, MD and Phillip Smith, MD

Title: Cytomegalovirus Potentiates Inflammation in the Gastrointestinal Mucosa

Cytomegalovirus (CMV) is an important pathogen in immunosuppressed persons, including HIV-1-infected subjects, organ and stem cell transplant recipients, and persons with inflammatory bowel disease (IBD). Among immunosuppressed persons, the gastrointestinal tract is a major site of CMV inflammatory disease, often progressing to severe inflammation, ulceration, and ischemic necrosis in the presence of CMV infection. The lesions associated with CMV mucosal infection contain a large proportion of infected intestinal macrophages and macrophage-derived cytokines. Paradoxically, intestinal macrophages in normal mucosa, are uniquely and profoundly down-regulated for cytokine production (inflammation anergy) due to stroma-induced NF- κ B inactivation which prevents microbe-induced cytokine release when commensal bacteria breach the epithelial barrier. This unique feature is in sharp contrast to the exclusive precursor of intestinal macrophages, blood monocytes, which rapidly respond to pro-inflammatory stimuli. We hypothesize that CMV infects circulating monocytes and inhibits their differentiation into inflammation anergic intestinal macrophages by hijacking the NF- κ B signal pathway thereby potentiating bacteria-induced inflammation. To address this hypothesis, we used stroma-conditioned media (S-CM), generated from normal intestinal stroma, to differentiate monocytes into inflammation anergic intestinal macrophages. To determine whether CMV blocks inflammation anergy, monocytes were infected with CMV, treated with S-CM, then analyzed for flagellin-induced cytokines, expression of CD14 and TLR4/5, MyD88, and NF- κ B. Our results show that monocytes first infected with CMV and then S-CM differentiated produced significantly more cytokines and expressed higher TLR4/5 and MyD88 compared with mock-infected, S-CM-differentiated macrophages. CMV infection also blocked S-CM-induced NF- κ B inactivation. Our results indicate that systemic infection of monocytes by CMV before recruitment to the mucosa strategically positions pro-inflammatory macrophages to interact with bacteria via TLR4/5, leading to inducible cytokine responses by enhancing NF- κ B signal transduction.

DiToro, Daniel Francis

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: Casey Weaver

Co-Authors: Stuart Frank

Title: Insulin-like Growth Factors Drive the Pathogenic CD4 T cell Response in Multiple Sclerosis

Prior Research Experience: Yes

Abstract Approved: Yes

Multiple sclerosis (MS) is an auto-immune disorder of the central nervous system (CNS) characterized by axonal demyelination and sensory and motor impairment. Pro-inflammatory Th17-type CD4 T cells drive inflammation in the CNS, which can be resolved by anti-inflammatory Treg CD4s. Immunosuppressive therapies represent the most successful treatment modality for MS, but first line drugs are only modestly effective and the few second line drugs available are limited by toxicity. None of the approved therapeutics specifically modulates the balance of Th17 and Treg cells. Targeting these cells directly could offer improvements in both efficacy and toxicity.

Insulin-like growth factors (Igfs) are pleiotropic cytokines that function by binding the Igf1 receptor (Igf1R). These factors were shown to be essential for the normal development and proliferation of B and T lymphocytes, and to positively influence their proliferation and survival following activation. But early attempts to identify potential roles in T cell differentiation and function lead to conflicting results, and the field was largely abandoned. More recent advances in our understanding of T cell biology, including the discovery of Th17 and Treg CD4s, permit a more sophisticated approach. Our studies indicate that Th17 and Treg CD4s express Igf1R and insulin-like growth factor binding protein 4 (Igfbp4), a critical regulator of Igf activity, at significantly higher levels than other CD4 T cells. Exposure to Igfs promotes Th17 differentiation while suppressing Treg differentiation, while CD4s lacking Igf1R demonstrate a defect in Stat3 phosphorylation and IL17a production, and enhanced Treg differentiation. Mice lacking Igf1R on T cells (Igf1R cKO) are protected from Experimental Autoimmune Encephalomyelitis (EAE), a mouse model for MS, demonstrating substantially reduced clinical scores and a reduction in the relative and absolute numbers of CNS CD4s producing IL-17A, Ifn- γ , and GM-CSF. Lastly, this protection can be recapitulated through the administration of Igf1R blocking antibodies in-vivo.

Dowla, Shima Afroze

Project Length: Short

Source of Funding: NIH MSTP

Faculty Advisor: Tapan Mehta

Co-Authors: Kevin Fontaine

Title: Prevalence Trends in Cardiometabolic Prescription Medication Usage Among Obese Adults, 1987-2012

Prior Research Experience: Yes

Abstract Approved: Yes

Background: Recent studies have suggested that medical advances for obesity-associated cardiometabolic conditions (e.g. hypertension) have reduced the obesity-associated mortality burden. This has been attributed to recent advances in awareness and treatment of cardiovascular conditions such as hypertension. Given the economic barriers that exist in treating obesity directly, it is plausible that individuals with obesity are increasingly treated for co-morbidities using cardiometabolic medications.

Purpose: The purpose of this study is to evaluate the trend in cardiometabolic medications prevalence in obese individuals between 1987 and 2012. We hypothesize that the prevalence of these medications in the obese population has increased over time.

Methods: A repeated cross sectional analysis of nationally representative sample of younger to middle-aged (20 to <60) and older U.S. adults (60 or above) will be conducted using the National Health and Nutrition Examination Survey (NHANES), for the time period 1987 to 2012. Standard BMI categories will be used for the analyses (<18.5, 18.5 to <25, 25-29.9, >30). Level 2 therapeutic classifications of the medication data (cardiovascular and metabolic) will be used. A logistic regression model will be fitted with medication usage as a binary outcome. The model will include main effect terms for sex, race, age, smoking status, BMI, year (continuous variable) and an interaction variable between BMI and year. Change in prevalence rate ratios for obese categories between 1987 and 2012 will be estimated and tested using a significance level of 0.05.

Results: Results are pending.

Conclusions: We anticipate that our results will indicate that the prevalence rate ratio of cardiometabolic medications in obese individuals has increased over time.

Duke, Corey Grant

Project Length: Short

Source of Funding: T35

Faculty Advisor: Jeremy Day

Co-Authors: Andrew Kennedy, David Sweatt, Jeremy Day

Title: Experience Dependent Epigenomic Reorganization

Prior Research Experience: Yes

Abstract Approved: Yes

The formation and maintenance of new memories requires transcription and translation of genetic material, and epigenetic mechanisms such as methylation and demethylation serve as powerful regulators of this gene expression that is crucial to these processes. Moreover, aberrant DNA methylation has been identified in neurological and psychiatric disease states associated with impaired cognition, such as Alzheimer's disease, autism-spectrum disorders, schizophrenia, and drug addiction. Despite the clear necessity for epigenetic and transcriptional changes in memory formation, the precise nature of these phenomena has not been comprehensively explored. To illuminate this area, we harnessed whole-genome sequencing tools to systematically characterize memory-related changes in gene expression and DNA methylation status following a hippocampus-dependent memory acquisition experiment. In addition to providing the first transcriptome- and DNA methylome-wide maps following behavioral memory formation, these results shed new light on the dynamic nature of DNA methylation and demethylation in the adult nervous system. We observed thousands of significant gene expression and epigenomic changes in the rat hippocampus that are experience dependent. These modifications were evident as early as one hour following the learning experience, becoming more marked and pronounced after twenty-four hours. Furthermore, we integrated these datasets with previously characterized epigenetic and transcriptional changes in brain disease states to provide a comprehensive resource to aid in the identification of memory-relevant therapeutic targets. Our results shed new light on the gene expression and methylation changes involved in memory formation suggesting that this process is dynamic and experience dependent, in addition to providing a roadmap for future work to identify therapeutic targets.

Dussaq, Alex Maurice

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: Christopher Willey

Co-Authors: Alex Dussaq, Joshua Anderson, Christopher Willey, Jonas Almeida

Title: Mechanistic parameterization of the kinomic signal utilizing PamGene peptide arrays.

Prior Research Experience: No

Abstract Approved: Yes

Motivation: Kinases play a role in every cellular process involved in tumorigenesis ranging from proliferation, migration, and protein synthesis to DNA repair. While genetic sequencing has identified most kinases in the human genome, it does not describe the 'kinome' at the level of activity of these kinases against their substrate targets. An attempt to address that limitation and give the researcher a more direct view of cellular kinase activity and the kinome is found in the PamGene PamChip® system, which records and compares the phosphorylation of 144 tyrosine or serine/threonine peptides as they respond to cellular kinases. Accordingly, the kinetics of this type of time dependent kinomic signal needs to be well understood in order to transduce a parameter set into an accurate and meaningful mathematical model.

Results: Here we report on the analysis and mathematical modeling of these kinomic time series, which achieves a more accurate description of the accumulation of phosphorylated product than the current model by assuming a process dominated by enzyme-substrate kinetics. Its parameterization describes the underlying biochemical mechanism as being dominated by phosphorylation affinity and capacity. The reproducibility of the proposed solution was also object of particular attention. Specifically, the non-linear parameterization procedure is delivered as a public open source web application where kinomic time series can be accurately decomposed into the model's two parameter values measuring phosphorylation affinity and capacity. The ability to deliver model parameterization entirely as a client side web application is proposed as an important result on its own given the increasing preoccupation with reproducibility: the code is transferred to the browser client where it can be inspected and executed. There is also no need for a potentially transitory and opaque server-side component maintained by the authors, nor of exchanging potentially sensitive data as part of the model parameterization process.

Availability and implementation: Implementation example is available at <https://bit.ly/kinomic>.

Primary JavaScript libraries are available and documented at <http://bit.ly/fmincon> and

http://bit.ly/amd_cf.

Erwin, William Clinton

Project Length: Short

Source of Funding: T35

Faculty Advisor: Leslie Rhodes, MD

Co-Authors: Leslie Rhodes MD, Santiago Borasino MD, Jeffrey Alten MD

Title: Does arterial-venous CO₂ gradient correlate with other known markers for low cardiac output?

Prior Research Experience: No

Abstract Approved: Yes

Background: Low cardiac output (CO) following congenital cardiac surgery is a major concern in the neonatal population. Previous studies have shown a relationship between a widening arterial-venous pCO₂ difference (delta pCO₂) and low cardiac output, but to our knowledge there is no known correlation in neonates after cardiac surgery. We sought to correlate delta pCO₂ with other established methodologies for predicting low CO including central venous oxygen saturation (SvO₂) and arterial-venous oxygen saturation difference (delta HbO₂) in neonates after cardiac surgery. It has also been shown that SvO₂ and delta HbO₂ alone may not be sufficient predictors of CO because these factors are heavily influenced by pulmonary function and not solely by cardiac health. Delta pCO₂ has been shown to increase only in situations where blood flow is diminished, and not when oxygenation is compromised.

Methods: Retrospective study of all patients admitted to the cardiovascular intensive care unit (CVICU) from October 2012 to May 2015 who were ≤ 90 days and underwent cardiac surgery were included. Exclusion criteria were patients requiring extracorporeal membrane oxygenation before leaving the operating room. All central venous and arterial blood gas samples collected within the first 24 hours of admission to the (CVICU) were obtained from patient records. Arterial and venous blood gases were paired if they were drawn within 1 hour of each other and the pCO₂ difference was calculated.

Results and Conclusions: Delta pCO₂ is correlated with delta HbO₂ and SvO₂ within the first 24 hours after cardiac surgery in neonates. Because delta HbO₂ and SvO₂ are commonly used as surrogate markers for low CO, delta pCO₂ may also be an indicator of low CO, and may predict low CO even when delta HbO₂ and SvO₂ are unremarkable. Further analysis is required to determine if delta pCO₂ is a predictor of cardiac related morbidity and mortality in neonates.

Etikala, Deepa Melanie

Project Length: Short

Source of Funding: CaRES Program

Faculty Advisor: Dr. Lizhong Wang

Co-Authors: Jaimie Richards, Runhua Liu, Lizhong Wang

Title: The Identification of FOXP3 Isoforms in Human Cancer Cell Lines

Prior Research Experience: Yes

Abstract Approved: Yes

The FOXP3 gene plays an important role in cancer development by suppressing oncogenes and by inducing tumor suppressing genes. However, different cancer types have been known to show varying levels of FOXP3 expression. FOXP3 expression is downregulated in breast and prostate tumors but upregulated in pancreatic tumors. This conundrum led our research to focus on finding an answer to these varying rates of expression. During post-transcriptional regulation, the FOXP3 gene is often alternatively spliced, resulting in several isoforms. These isoforms, modified by the deletion or insertion of sequences, are important to understanding the differences in expression between cancer cell types. By cloning and sequencing cell lines from patients with prostate and pancreatic cancer, we were able to determine that all but the HPAC cell line showed a dominance of FOXP3 isoforms over the wild-type form. This suggests that isoforms play a key role in cancer development.

Eustace, Nicholas James

Project Length: Intermediate

Source of Funding: NIH MSTP

Faculty Advisor: Christopher Willey

Co-Authors: John S. Jarboe, Timothy D. Rohrbach, Patricia H. Hicks, Joshua S. Anderson

Title: MARCKS has a critical role in the growth and proliferation of Glioblastoma multiforme

Prior Research Experience: Yes

Abstract Approved: Yes

HYPOTHESIS: MARCKS is a key regulator of GBM growth and sensitivity, therefore, increasing levels of unphosphorylated MARCKS in combination with DNA damaging Temozolomide (TMZ) therapy in GBM cells, will further suppress cell growth.

Background: Glioblastoma multiforme (GBM) is the most common and deadly form of Glioma, with a median survival of 14 months. A loss of heterozygosity (LOH) of chromosome 10q has been found in 90% of GBM to date and a mutation in the tumor suppressor Phosphatase and Tensin Homolog (PTEN) is combined with this LOH in 60% of these cases [2]. PTEN has its tumor suppressor function by antagonizing PI3K/Akt signaling which begins when PI3K phosphorylates Phosphatidylinositol (4,5)-biphosphate (PIP2) into Phosphatidylinositol 3-kinase (PI3K) allowing for AKT activation. PIP3 recruits AKT to the plasma membrane where it phosphorylates and leads to changes in migration, invasion, angiogenesis, survival and proliferation. PTEN is responsible for dephosphorylating PIP3 back into PIP2; where-as Myristoylated Alanine Rich C-Kinase Substrate (MARCKS) electrostatically sequesters PIP2. It has been shown that activating mutations of PI3K[3], deactivating mutations of PTEN [4] and reduced levels MARCKS all correlate with a worsened GBM patient survival. MARCKS expression is strongly correlated with increased patient survival [5].

Methods: MARCKS mutants were created using a GBM cell lines with low native MARCKS expression (U87) using a tetracycline inducible lentiviral vector. We created a cell line that expresses MARCKS with a wild type (WT) effector domain(ED), a pseudo-phosphorylated (PP) ED, and non-phosphorylatable (NP) ED and one without an ED (deltaED). MARCKS effect on cell growth and signaling, clonogenic potential, DNA damage repair, and radiation and chemotherapy sensitivity were analyzed.

Results: Increasing WT and NP MARCKS levels resulted in significant tumor growth suppression.

Conclusions: Further investigation into the activity and function of MARCKS activity can aid the development of potential GBM combination therapies.

Evans, John Macarthur

Project Length: Intermediate

Source of Funding: Other

Faculty Advisor: Asim K. Bag

Co-Authors: Asim K. Bag, David Wever, Paula P Warren, John M Evans, Bradford Jackson

Title: Fractional tumor burden calculation using perfusion MRI can predict progression-free survival and overall survival in glioblastoma multiforme patients treated with bevacizumab

Prior Research Experience: Yes

Abstract Approved: Yes

Purpose: Imaging evaluation of glioblastoma multiforme (GBM) patients treated with bevacizumab is challenging using conventional magnetic resonance imaging (MRI) techniques due to bevacizumab induced profound changes in tumor vascularity. Perfusion MRI based fractional tumor burden (pMRI-FTB) calculation was originally described to be very effective in differentiating tumor progression from treatment related changes. In this study we have evaluated the prognostic significance of post-treatment pMRI-FTB in recurrent GBM patients treated with bevacizumab for prediction of progression free and overall survival.

Patients and Methods: Twenty-five glioblastoma multiforme patients who were treated with bevacizumab at first recurrence after standard initial treatment (biopsy/maximal safe resection followed by radiation with concurrent temozolomide followed by maintenance temozolomide therapy) and had MRI with perfusion imaging within 60 ± 15 days after starting bevacizumab were enrolled. pMRI-FTB was calculated by registering the normalized cerebral blood volume (nCBV) map with the post contrast T weighted sequence followed by segmenting the enhancing component of the tumor and categorizing the enhancing component as tumor based on optimized nCBV threshold. The Kaplan–Meier method was used to determine whether the post treatment pMRI-FTB was predictive of overall survival (OS) and progression free survival (PFS).

Results The overall survival and progression free survival were significantly longer if the fractional tumor burden, defined as $nCBV > 1$, at the first follow-up scan was $< 50\%$, $p = 0.01$ and 0.05 respectively.

Conclusion: Fractional tumor burden is predictive of OS and PFS in first time recurrent GBM patients treated with bevacizumab.

Ference, Edward William, III

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Amy Knight

Abstract Approved: Yes

Co-Authors: Nathaniel G. Harnett, Muriah D. Wheelock, Kimberly H. Wood, Martin R. Setliff,

Peyton C. Thetford, David C. Knight, Amy J. Knight

Title: Learning-Related Changes in the Functional MRI Response to Fear Conditioning after Acute Medical Trauma

Purpose: Little research has investigated changes in fear learning following acute trauma (i.e. < 1 month post event). These changes may be important to understanding Posttraumatic Stress Disorder (PTSD) susceptibility. The current study investigated the relationship between brain measures, behavioral measures, and PTSD symptom expression following acute medical trauma. We hypothesized that trauma exposure would be associated with elevated self-reported psychosocial risk factors and PTSD symptoms, as well as impaired Pavlovian fear conditioning.

Methods: 12 participants recruited from the Acute Trauma Unit at UAB Hospital completed self-reported surveys of psychosocial risk factors and PTSD symptoms, as well as a Pavlovian fear conditioning task during fMRI. Healthy controls (n=9) were recruited from an ongoing imaging study.

Results: PTSD symptom severity within 1 month of trauma correlated with symptom severity at 6 months post trauma ($p < 0.05$) and with psychosocial risk factors within 1 month of trauma ($p < 0.01$). During fear conditioning, healthy controls showed greater expectancy for threat during warning than safety cues. In contrast, trauma-exposed individuals showed equivalent threat expectations to warning and safety cues. Functional MRI revealed greater activation to warning and safety cues in the dorsomedial prefrontal cortex (dmPFC) in trauma-exposed compared to healthy control individuals ($p < 0.01$). Trauma-exposed individuals exhibited learning-related activity within left amygdala ($p < 0.01$), which was modulated by anxiety and depression symptoms. Finally, greater activity to warning than safety cues was observed within hippocampus for healthy controls; the reverse occurred in trauma-exposed individuals ($p < 0.01$).

Discussion/Conclusion: These data suggest initial psychosocial risk factors and PTSD symptom severity can predict future PTSD development. The trauma exposed group showed increased activity in the dmPFC, which is important for emotion regulation, but expected a threat after both the warning and safety cues. The group differences in the amygdala and hippocampus suggest that trauma can cause dysregulation in fear response pathways.

Figge, David Anthony

Project Length: Long

Source of Funding: NIH MSTP

Faculty Advisor: David Standaert

Co-Authors: Jaunarajs KE, Standaert DG

Title: Role of Dynamic DNA Methylation in Levodopa-Induced Dyskinesia

Prior Research Experience: Yes

Abstract Approved: Yes

Levodopa-induced dyskinesia (LID) develops after repeated levodopa (L-DOPA) exposure in Parkinson's disease patients, and is one of the primary obstacles to effective treatment. LID is a consequence of sustained changes in transcriptional behavior of striatal neurons. We used a LID rodent model to investigate the cellular mechanisms maintaining this state by inducing unilateral dopamine depletion via 6-hydroxydopamine followed by repeated L-DOPA administration. Immunoprecipitation of methylated DNA from the dyskinetic striatum demonstrated alterations in DNA methylation at promoter regions of several genes relevant to LID. Using reduced representation bisulfite sequencing, we found evidence for extensive dynamic changes in methylation following LID development. Treatment of animals with methionine (to enhance methylation) or RG-108 (a methyl transferase inhibitor) bi-directionally modulated dyskinetic behaviors. These results indicate a pivotal role for the reorganization of DNA methylation in the development of LID and modification of DNA methylation as a novel therapeutic target for LID.

Flippo, Hilary Morgan

Project Length: Long

Source of Funding: Other

Faculty Advisor: Dr. Nicholas Van Wagoner

Co-Authors: Dr. Nicholas Van Wagoner

Title: Factors Associated with Herpes Simplex Virus Type 2 Asymptomatic Shedding

Prior Research Experience: Yes

Abstract Approved: Yes

Introduction: Herpes Simplex Virus Type 2 (HSV-2) is the most common cause of genital ulcer disease worldwide. HSV-2 is characterized by both clinical (i.e. presence of lesions) and subclinical (i.e. absence of lesions) recurrences. Subclinical HSV-2 recurrence is defined as HSV-2 viral shedding from the ano-genital region. Factors influencing subclinical HSV-2 shedding are poorly understood, however, preliminary findings suggest that Caucasians may shed more than non-white persons, suggesting that genetic variation may predict asymptomatic shedding. The purpose of this study was (1) to compare HSV-2 viral shedding in white and non-white HSV-2 infected persons, (2) to design and prospective study to evaluate factors, including race, associated with HSV-2 viral shedding.

Methods: For objective 1, baseline shedding data from patients participating in randomized controlled clinical trials for a therapeutic HSV-2 vaccine were compiled. Prior to vaccination, participants collected daily ano-genital swab specimens for 28 days. Each swab was then analyzed to detect HSV-2 DNA. Rate of shedding was then calculated. Poisson analysis was used to determine rate ratios and 95% Confidence Intervals between comparison groups.

For objective 2, literature review in addition to the findings reported here, informed study questions. A study protocol has been created, and documentation has been prepared for the Institutional Review Board with a plan to initiate enrollment in the prospective study on November 1, 2016.

Results: A total of 24,638 ano-genital specimens were collected from 440 participants with known HSV-2. Persons who identified as non-white shed virus less often than persons who identified as white (White = 18.3%, Black = 14.6%, Other = 14.1%). Based on the above results, we have designed a case control study devoted to understanding factors associated with HSV-2 viral shedding, including race.

Fox, Brandon Michael

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Jennifer S. Pollock

Abstract Approved: Yes

Co-Authors: J. Brett Heimlich, Chiao-Wang Sun, Tim M. Townes, Masashi Yanagisawa, David M. Pollock, Jennifer S. Pollock

Title: Endothelial-Derived Endothelin-1 Contributes to Renal Dysfunction and Mortality in Sickle Cell Mice

Sickle cell disease (SCD) is a genetic hematologic disease that can cause progressive nephropathy. Endothelin-1 (ET-1) is elevated in plasma and urine of SCD patients and mice, and accumulating evidence suggests that ET-1 plays a role SCD pathophysiology. However, the cellular source of increased ET-1 production in SCD is unknown. We hypothesized that endothelial-derived ET-1 contributes to renal dysfunction and mortality in SCD mice. Vascular endothelial-specific ET-1 knockout (VEETKO) mice and genotype controls (flox) underwent bone marrow transplantation (BMT) with marrow from humanized SCD mice (HbSS). This resulted in the development of SCD in mice lacking endothelial ET-1 production (HbSS-VEETKOBMT) and mice with endothelial ET-1 production (HbSS-floxBMT). Full induction of the SCD phenotype requires approximately 12 weeks. The HbSS-VEETKOBMT group showed a significant survival advantage over the HbSS-floxBMT group ($p=0.026$) with all HbSS-VEETKOBMT mice surviving and only 58% of HbSS-floxBMT mice surviving at 18 weeks post-BMT. Dysfunctional urine-concentrating ability exists in SCD patients and mice, likely secondary to progressive renal injury. To determine whether endothelial-derived ET-1 participates in the SCD mediated loss of urine-concentrating ability, osmolality was measured in spot urines and 24-hour metabolic cage urine collections. At five weeks post-BMT, prior to SCD phenotype onset, there was no difference in spot urine osmolality between HbSS-floxBMT and HbSS-VEETKOBMT mice (3244 ± 268 vs. 3096 ± 165 mOsm/kg, $p>0.05$). Following SCD phenotype onset, mortality in the HbSS-floxBMT group left only a single mouse for the assessment 24-hour urine osmolality, and this mouse showed a low urine osmolality (930 mOsm/kg). However, when compared to HbSS mice, HbSS-VEETKOBMT mice demonstrated preserved urine-concentrating ability as indicated by significantly higher 24-hour urine osmolality (584 ± 11 vs. 2512 ± 361 mOsm/kg, $p=0.006$). These data indicate that endothelial-derived ET-1 is a major mediator of SCD pathophysiology and that lack of endothelial ET-1 production is sufficient to prevent renal dysfunction and mortality in SCD mice.

French, Hunter Michael

Project Length: Short

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Namasivayam Ambalavanan

Co-Authors: Ammar Saadoon, Maria S Johnson

Title: 3D Model Printing of Mouse Airway Development

Prior Research Experience: Yes

Abstract Approved: Yes

The lung's development of terminal airways, saccules, and alveoli is still incompletely understood. Impairment of lung development leads to several different infant and newborn pulmonary diseases which are associated with morbidity and mortality which includes bronchopulmonary dysplasia, congenital pulmonary airway malformations, and lung hypoplasia that has been associated with congenital diaphragmatic hernia. Gaining a better understanding in the process of lung development could lead help efforts in tissue regeneration or inhibiting lung injury during development, and may help develop fluid dynamics models for aerosol delivery. The production of a 3D model and ultimately mathematical models of the developing airways which describe the gas exchange area of newborn mice over the first two postnatal weeks would allow for further progress to be made in the field of pulmonary development. To produce the image files, tracheobronchial casts of mice lungs were first created with Karnovsky's fixative followed by a silicone mixture with acetic acid. The lung cast was scanned using the Scanco micro-CT40 desktop cone-beam micro-CT scanner. The cast was placed vertically in a 20mm diameter scanning holder and scanned at a 10 micrometer resolution, and the individual slices were then converted to a DICOM file format. Currently we are attempting to convert the DICOM image files into STL files while preserving the original resolution. Further work will involve creating a 3D model which preserves the original DICOM image files' resolutions capable of resolving pertinent pulmonary structures for producing meaningful 3D models.

Gans, Asaf Daniel

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Santiago Borasino

Abstract Approved: Yes

Co-Authors: Santiago Borasino, Yuvraj Kalra, Jeffrey Alten, David Cleveland

Title: Early Ventilator Variables and Outcomes are Associated with Prolonged Mechanical Ventilation in Infants after Cardiac Surgery with Cardiopulmonary Bypass

Background- Acute lung injury (ALI) is a complication of cardiopulmonary bypass (CPB) in infants with congenital heart disease and often leads to prolonged mechanical ventilation (PMV) and other morbidities. We sought to describe the association between early ventilator parameters and PMV in infants after cardiac surgery requiring CPB.

Methods-All biventricular patients <6months who underwent CPB from December 2012-April 2015 were included for analysis while patients requiring extracorporeal membrane oxygenation were excluded. Ventilator variables, blood gases, and outcomes were collected on admission to the CVICU, at 6 hours, and at 12 hours post admission. PMV was defined as mechanical ventilation (MV) >44 hours from arrival time to the CVICU. AKI was defined as doubling of serum creatinine from baseline. Dynamic compliance of the lungs and oxygenation index (OI) were also calculated and analyzed.

Results-113 patients met inclusion criteria. Median duration of MV was 18.3 hours, with 30 patients having PMV. Patients with PMV were younger, smaller, had higher STAT categories, longer CPB and aortic cross clamp times. Patients with PMV had higher median inotrope scores at admission, 6 hours, and 12 hours; higher median lactic acid levels at admission and 6 hours; and higher median postoperative serum creatinine levels. PMV was associated with lower dynamic compliance and higher OIs at admission, 6 hours, and 12 hours. Ventilation parameters including PIP, PEEP, MAP, and FiO₂ were also statistically different between the two groups at admission, 6, and 12 hours. PMV was not associated with respiratory rate, exhaled tidal volume, minute ventilation, or blood gas variables (including pH, PaO₂, PaCO₂, SVO₂, and AVO₂ saturation difference). PMV was not associated with mortality, AKI, or fluid balance at 24 hours post-operative.

Conclusion-Dynamic lung compliance and OI calculated in the early postoperative period may be associated with PMV in infants after biventricular cardiac surgical repairs with CPB. Identification of this cohort could enable targeted management and studies/quality improvement efforts aimed at ameliorating the morbidity of ALI after CPB.

Gragg, Stephen Douglas

Project Length: Short

Source of Funding: NIH MSTP

Faculty Advisor: Tika Benveniste

Co-Authors: Rajbhandari R, Benveniste EN, and Nozell SE

Title: CDC42, ID2, and SIRT2 are promising targets for regulation by microRNA-31

Prior Research Experience: Yes

Abstract Approved: Yes

Glioblastoma (or grade IV astrocytoma) is the most common and uniformly fatal primary tumor of the central nervous system, and can also originate from lower-grade gliomas. The mechanisms of pathogenesis vary between glioblastoma tumors, but often involve a diverse collection of copy number variations in genes related to a smaller number of common pathways. One of the most frequently deleted chromosomal loci in glioblastoma is 9p21.3. While this loci contains CDKN2A/B, loss of CDKN2A/B alone is not sufficient to drive gliomagenesis. Interestingly, >72% of glioblastomas contain a deletion of MIR31HG, which encodes microRNA-31 (miR-31), a small non-coding tumor suppressor also found at the 9p21.3 site. Previously, we have shown that miR-31 is required for astrocyte development from neural precursor cells, that miR-31 is required to maintain astrocyte identity, and that loss of miR-31 expression enhances tumor growth and reduces survival. For this reason, we believe miR-31 to be critical as both a regulator of astrocyte differentiation and a tumor suppressor. In this pilot study, we sought to provide initial verification of putative miR-31 targets which were previously identified in RNAseq experiments. Here, we have shown that CDC42, ID2, and SIRT2 are promising candidate genes and warrant further investigation.

Griswold, Branum Gage

Project Length: Short

Source of Funding: T35

Faculty Advisor: Nicole K Behnke, MD

Co-Authors:

Title: Frequency of skeletal surveillance in primary carcinomas at high risk for metastasis to bone

Prior Research Experience: No

Abstract Approved: Yes

Introduction: It is estimated that over 2.5 million people in the United States are living with breast cancer, with more than 200,000 of new cases annually. With improvements in detection and treatment, survival rates are increasing, thus metastatic disease prevalence is rising. The skeleton is a common site of breast cancer metastasis, with an estimated risk of 20-75% over a patient's lifetime. Current surveillance guidelines for skeletal metastatic disease are nebulous; adherence to these guidelines is generally unknown. Our aim was to examine a large population of patients with breast cancer, estimate the frequency of skeletal metastatic disease and examine the frequency of skeletal surveillance imaging.

Materials and Methods: This retrospective chart review identified patients with an ICD-9 documented diagnosis of breast cancer seen at UAB in 2014. Patients without a documented oncologic history were excluded. The National Cancer Center Network breast cancer screening guidelines were used to determine risk factors prompting dedicated skeletal imaging.

Results: We identified 850 patients with a diagnosis of breast cancer that met inclusion criteria. 40 patients had skeletal metastatic disease and 62 patients had metastatic disease at other sites. 392 (45.9%) patients had one or more risk factors that met criteria for skeletal imaging. Of these, 243 (59.7%) had dedicated skeletal imaging: 63 (16.1%) had a PET scan, 128 (32.7%) had a nuclear medicine whole body bone scan, and 122 (31.1%) had a plain radiograph.

Conclusions: In this breast cancer population at a tertiary medical center, overall skeletal metastatic rates were lower than expected. Although nearly half of this patient population had risk factors for bony metastasis that should prompt dedicated skeletal imaging, the low number of at-risk patients who underwent imaging studies leaves room for improvements in surveillance.

Guzman Karlsson, Mikael Carl Gustav

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Dr. J. David Sweatt

Abstract Approved: Yes

Co-Authors: Jordan A. Brown, Fatumata Sesay, Andrew J. Kennedy, Jeremy J. Day, Erik D.

Roberson, and J. David Sweatt

Title: Genome-wide transcription profiling in an APP mouse model of Alzheimer's disease.

Neuronal plasticity and long-term memory rely on dynamic, bidirectional regulation of transcription. Recent evidence suggests that dysregulated transcription and epigenetic mechanisms may contribute to neuronal dysfunction and cognitive impairment in Alzheimer's disease (AD). Previous research in human patients and AD mouse models have utilized gene-candidate and microarray-based methods to reveal aberrant hippocampal expression of genes involved in cell signaling, inflammation, and neurotransmission. However, a systematic characterization of genome-wide alterations in transcription is lacking. To address this we utilized RNA sequencing to identify differentially expressed genes in the dentate gyrus of naïve hAPPJ20 mice, an amyloid-beta (A β) over-expressing mouse model of AD. Bioinformatic analysis revealed widespread bidirectional alterations in gene expression with upregulated genes involved in steroid biosynthesis and extracellular matrix restructuring and downregulated transcripts implicated in ion channel activity, transcriptional regulation, and calcium signaling. Additionally, comparison with other sequencing data revealed a high degree of overlap between the hAPPJ20-transcriptome and that of mice trained in contextual fear conditioning as well as mice treated with histone deacetylase (HDAC) inhibitors, a promising therapeutic option that ameliorates cognitive impairments in hAPPJ20 mice as well as other AD mouse models. The similarity between A β - and learning-induced transcriptional changes suggests the existence of robust plasticity-promoting compensatory mechanisms in hAPPJ20 mice and/or the presence of an overall hyperexcitable network. In contrast, the resemblance to changes induced by HDAC inhibition suggests that the beneficial effects of HDAC inhibition may involve the potentiation of already existing compensatory mechanisms. These observations encourage the use of such integrative analyses to identify novel therapeutic, plasticity-promoting targets that may ameliorate AD-related cognitive impairment.

Hackney, Andrew Cleveland

Project Length: Short

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Neway

Co-Authors:

Title: MAP Management and Acute Spinal Cord Injuries

Prior Research Experience: No

Abstract Approved: Yes

The main goal of this project is to look at the current guidelines for treatment of acute spinal cord injury (SCI) patients, which is maintaining a mean arterial pressure (MAP) of greater than 85 mmHg for 7 days; and define any correlation between the sustained systemic hypertension and adverse medical events. Vasopressors are used to achieve the target elevated MAP. The project will also look at different types of vasopressors used and any correlation between vasopressor use and adverse events.

If correlation is established between the sustained systemic hypertension and adverse events this will provide more information on the benefits and risks of elevating blood pressure. If the risk of elevating the blood pressure to a certain point outweighs the benefit of perfusion to the spinal cord this could suggest altering the level of increase in MAP or the amount of time the MAP is increased after acute SCI. Further research would be needed to investigate the optimal level of mean arterial pressure for greatest improvement of neurological function with minimal adverse events. This information could change how doctors sustain mean atrial pressure and as a result could decrease patient care costs via limiting potentially preventable adverse events and decreasing length of hospital stay.

Currently there is limited knowledge of the effect of maintaining a mean arterial pressure above 85 mmHg has on the patient. Establishing correlation between sustained hypertension and adverse events during treatment of acute spinal cord injuries will allow physicians to improve quality of care and result in better outcomes. A proved correlation between sustained hypertension and adverse events could suggest the need for changes in the current suggested maintenance of MAP which could include changes in vasopressor type, level of MAP elevation, or duration of MAP elevation. This information will better allow analysis of the benefits versus risk factors of sustaining an elevated mean arterial pressure for 7 days post injury.

At this point in the project there has not been enough data collected to report results or major conclusions.

Hardigan, Andrew Alexander

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Dr. Richard Myers

Abstract Approved: Yes

Co-Authors: Brian S. Roberts, Marie K. Kirby, Meredith B. Fitz-Gerald, C. Mel Wilcox, Robert P.

Kimberly and Richard M. Myers

Title: Blocking of targeted microRNAs from next-generation sequencing libraries

The discovery of stable miRNA species in blood and other easily accessible human biological fluids has led to their investigation as potential biomarkers for a variety of diseases such as cancer, neurodegenerative disease, and cardiovascular disease. Next-generation sequencing (NGS) of small RNAs in these fluids is a powerful method for comprehensive identification and quantification of miRNAs species. However, due to methodological challenges related to the small size of miRNA species and their relatively low abundance in human plasma, the identification of reproducible and specific miRNA biomarkers has been difficult. Relatively high abundant microRNAs in small RNA sequencing libraries represent an obstacle to the efficient measurement of more lowly expressed species. We present a new method that allows for the selective blocking of targeted miRNAs from representation in sequencing libraries. This method is specific, has limited and predictable off-target effects, and maintains library reproducibility of non-blocked miRNA species. Hsa-mir-16-5p is highly abundant in human plasma as a result of erythrocyte hemolysis, and its removal from sequencing libraries yields improved detection of lowly expressed miRNAs and more precise measurement of differential expression overall. Additionally, we establish the ability to target other miRNA species and multiplex the blocking of multiple miRNAs simultaneously. In summary, this technique for small RNA sequencing is comparable to existing methods to remove ribosomal or globin proteins during messenger RNA sequencing.

Harper, Jordan

Project Length: Short

Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Carlos Estrada

Abstract Approved: Yes

Co-Authors: F. Stanford Massie, MD, Carlos Estrada, MD, MS.

Title: Knowledge and Attitudes in an Open-Access Online Cultural Competency Training

Introduction: Evidence suggests that cultural competency training improves knowledge, attitudes, and skills of health professionals. We designed an open-access case-based online education, Cultural Competence Online for Medical Practice (CCOMP; www.c-comp.org), to examine knowledge and attitudes relevant to the care of patients of diverse backgrounds. In this report, we examined knowledge and attitudinal differences between medical students, physicians, and other professionals in the open-access case-based online education.

Methods: Design: cross-sectional study (2011-2015). Setting: Internet. Participants: medical students, physicians, others. Online education: two interactive cases with dynamic feedback aimed at exploring stereotype and bias in the setting of African American patients with hypertension. Inclusion: unique users who registered. Measures: 11 multiple choice questions (7 knowledge; 4 attitudes). Analysis: for questions using a Likert scale (often, sometimes, rarely, never), 'often' (percent) was compared with all other responses. Similarly, positive responses (yes, maybe) were compared with negative responses (no, don't know). We used the Chi-square test to compare responses between groups (p value <0.05).

Results: Of the 1,745 users, 17% were physicians, 38% medical students, and 45% other health care professionals. We observed differences in responses to the knowledge questions between the groups, stereotype definition ($p=0.01$), beliefs impact treatment ($p<0.001$), and bias definition ($p<0.001$). We also observed differences in two attitudes questions for a case presented, non-adherence as the cause of uncontrolled hypertension ($p<0.001$), MD had enough information to decide the patient was not taking the medication ($p=0.01$).

Discussion: All groups can identify stereotype and bias in clinical encounters, and recognizing stereotype and bias is not the most difficult obstacle for providers. The challenge for health care providers lies in not acting on stereotypes and bias when treating actual patients. Areas for future research include studying if online cultural competency courses change the actions of providers with patients in real clinical encounters.

Harris, David Marshall

Project Length: Intermediate

Source of Funding: CaRES Program

Faculty Advisor: John Fiveash

Co-Authors: Andrew McDonald, John Fiveash

Title: The Importance and Risks of CBCT Alignment for Prostate Cancer Radiotherapy

Prior Research Experience: Yes

Abstract Approved: Yes

Cone beam computed tomography (CBCT) enables visualization of the pelvic organs, allowing for radiotherapy alignment to the prostate itself and for correction of organ filling if necessary. The objective is to determine how often CBCT is needed to identify and correct variations in pelvic anatomy (particularly bladder filling) prior to radiotherapy and furthermore to determine the effect of CBCT alignment compared to fiducial alignment on irradiation of the bladder and rectum. All prostate radiotherapy fractions conducted over a one year period (2013-2014) with three linacs at a single institution were included in the analysis (2455 fractions in total from 80 different patients). The percentage of all fractions prior to which CBCT scans were repeated at least once was calculated for each patient. CBCT was repeated if the therapist qualitatively judged the organ filling to be significantly different from simulation. 27 fraction images were then selected from 18 patients who received both implanted fiducials and CBCT imaging. These fractions were each realigned to the prostate (traditional CBCT alignment) and then to the fiducials. For each alignment, the treatment plan was run to calculate the dose delivered to the bladder and rectum. The median percentage of fractions prior to which CBCT was repeated was 7.14% (interquartile range: 3.49% - 13.71%) for the 80 patients. The median volume of the bladder receiving 100% of the prescribed dose was 7.46 cm³ for CBCT alignment and 7.14 cm³ for fiducial alignment ($p = 0.728$). The median volume of the rectum receiving this dose was 3.40 cm³ for CBCT alignment and 1.92 cm³ for fiducial alignment ($p = 0.047$). In conclusion, multiple CBCT scans per fraction are frequently performed, highlighting the need for visualizing pelvic organs with CBCT. Alignment using CBCT instead of fiducials increased rectum irradiation, indicating that fiducial alignment has less inter-observer variability.

Headrick, Andrew Todd

Project Length: Intermediate

Source of Funding: Other

Faculty Advisor: Martin Rodriguez

Co-Authors: Carlos McFarlane Pecol, Elsa González Lagos, Martin Rodriguez, Cesar Quevedo Peñaloza

Prior Research Experience: Yes

Abstract Approved: Yes

Title: Individual and Family Perception of Living with Chronic Disability Secondary to Human T-lymphotropic Virus 1 (HTLV-1) Infection in Peru

Human T cell Leukemia/Lymphotropic Virus (HTLV) infection has been associated with a variety of conditions, including two severe disorders, Adult T Cell Leukemia/Lymphoma (ATL) and HTLV-Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP). The former is an aggressive, typically adult-onset, blood cancer while the latter is a currently incurable, progressively debilitating, paralytic process.

In the sentiment of HAM/TSP, chronic health problems are many times not simple predicaments of individuals but rather challenges experienced by the entire family unit. Such has been well documented for severe and/or long-standing conditions, such as cancer, Down syndrome, intellectual disability, and HIV/AIDS. Links between the health condition of an individual family member and the interactions and relationships within the family, known as family functioning, can be complex and comprise a field ripe for new research.

Previous studies have focused on the socioeconomic and psychosocial challenges faced by HTLV-1 seropositive individuals. This study serves to elaborate upon these same issues as they affect the family unit. Findings herein were produced via a mixed methods study using interviews and participants' basic data. The study was conducted in Lima, Peru at the Alexander von Humbolt Institute for Tropical Medicine. Data was gathered working specifically with HTLV-1 seropositive patients, with varying degrees of physical impairment, as well as their close family members and caregivers.

Within this data, three major themes have been uncovered: families facing chronic disabilities confront significant additional challenges when traversing the medical system, society and culture poorly educate and prepare able-bodied persons to understand the challenges and needs of persons with disabilities, and health care workers similarly lack training and experience in this field serving to perpetuate these problems. The study is still ongoing as further interviews are being conducted until it has been determined that the aforementioned themes are saturated.

Hess, Matthew Charles

Project Length: Short

Source of Funding: T35

Faculty Advisor: Dr. Jason A. Lowe

Co-Authors: Justin Woods

Title: The Influence of Tranexamic Acid on Blood Loss During Acetabulum Fixation

Prior Research Experience: Yes

Abstract Approved: Yes

Introduction: Surgical site infections (SSI) following open reduction and internal fixation (ORIF) of the acetabulum can occur in up to 22% of patients, and intra-operative blood loss has been linked to increased incidence of SSI. Tranexamic acid (TXA) has been shown to reduce intra-operative blood loss in elective total hip/knee arthroplasty as well as orthopaedic trauma surgery. No studies to date have examined the effect of TXA on intraoperative blood loss during acetabular fixation. The authors hypothesize that pre-operative intravenous TXA will reduce intra-operative estimated blood loss (EBL), intra-operative transfusions, and post-operative transfusions without increasing the incidence of venothrombotic events (VTE).

Methods: A retrospective review of a prospective trauma registry was performed in which all acetabular fractures fixed with ORIF were evaluated. Fractures were grouped into a control Group 1 (no TXA) vs Group 2 (pre-operative IV TXA).

Results: 155 patients were evaluated with an average age of 44. Base line demographics between Groups 1 and 2 were statistically similar in all regards. Average EBL was 833cc and 811cc for Groups 1 and 2 respectively where $p=0.43$. Similarly the difference between intra-operative and post-operative transfusions was not statistically significant with $p=0.45$ and $p=0.49$. The VTE incidence was 2.3% in Group 2 and 13% in Group 1, which was statistically significant. While there was a statistically significant difference in VTE rates between groups, TXA was not linked to increased incidence of VTE as it was the control group that presented with a greater incidence of VTE.

Discussion/Conclusion: Pre-operative administration of 1 gram IV TXA does not reduce EBL or intra-op/post-op transfusions in ORIF of acetabular fractures. However this dosing regimen does not increase incidence of VTE. In the current study only one dosing regimen was tested, so an alternative accepted, dosing regimens should be evaluated in a prospective randomized controlled trial.

Hoepfner, Lauren Danee'

Project Length: Intermediate

Source of Funding: Other

Faculty Advisor: Jeffrey Kerby MD, PhD

Co-Authors: Russell Griffin PhD, Thomas Swain

Title: Validity of the Braden Scale in Grading Pressure Ulcers in Trauma and Burn Patients

Prior Research Experience: Yes

Abstract Approved: Yes

Background: Pressure ulcers are a costly hospital-acquired condition in terms of clinical outcome and expense. The Braden Scale was developed in 1987 as a risk scoring method for pressure ulcers, and uses six different risk factors: sensory perception, moisture, activity, mobility, nutrition and friction and shear. A score of 18 or lower is considered high risk. To date, research on the utility of the Braden Scale has focused on general medicine and non-trauma/burn surgery patients. We hypothesize that the Braden Scale does not accurately discriminate who will get a pressure ulcer among trauma and burn patients.

Methods: We collected from medical records data regarding documented Braden scores and presence of pressure ulcers regardless of staging. Patients with ulcers present on admission were excluded from analysis. For each patient, the lowest Braden score documented prior to the occurrence of the pressure ulcer was determined. Sensitivity, specificity, and positive predictive value (PPV) were calculated for trauma and burn patients separately, and ROC analysis was used to estimate the area under the curve (AUC) for the continuous Braden measurement.

Results: The AUC for trauma patients was 0.69, and for burn patients was 0.72. The best discrimination for trauma patients was at a Braden score threshold of 14 or lower for trauma patients, and 16 or lower for burn patients. The PPV using the above thresholds was approximately 2.5% for both trauma and burn patients.

Conclusion: The Braden scale has mediocre discriminatory ability among the trauma/burn population. In addition, the extremely low PPV suggests that the Braden scale may not be a useful clinical tool as it may result in unnecessary expenditure of time and personnel resources in preventing pressure ulcer formation.

Hoffman, Kyle Jon

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Do-Yeon Cho

Abstract Approved: Yes

Co-Authors: Dainel Skinner, B.S.; Shaoyan Zhang, Ph.D.; Steven M. Rowe, M.D.; Bradford A. Woodworth, M.D.

Title: Protective Properties of Nanodisk-Amphotericin B (ND-AMB) over commercially available Amphotericin B in Human Nasal Epithelia

Background:

Amphotericin B (AMB), a potent antifungal agent, has been employed as topical and systemic therapy for sinonasal fungal infections. A novel formulation of nanodisc (ND) containing super aggregated AMB (ND-AMB) for the treatment of fungal infections has been recently developed to provide greater protection from AMB toxicity than current, clinically approved lipid-based formulations. The objective of the current study was to evaluate the safety of ND-AMB for sinonasal delivery using an in vitro model.

Methods:

Human sinonasal tissue was harvested during endoscopic sinus surgery and grown at air-liquid interface until well-differentiated. Cultures were exposed to ND-AMB vs AMB and changes in K⁺ permeability and resistance were measured and recorded via Ussing chamber assay. To quantify the release of lactate dehydrogenase (a marker of cell toxicity), cell culture media was collected after exposure (18hrs) to AMB and ND-AMB. Ciliary beat frequency (CBF) was analyzed in parallel as well as cytotoxic assay.

Results:

Ussing chamber studies revealed K⁺ currents that increased rapidly within 30 seconds of adding AMB (10µg/mL) to the apical side, indicating apical membranes had become permeable to K⁺ ions. In contrast, negligible induction of K⁺ current was obtained following addition of ND-AMB [AMB = $107.7 \pm 15.9 \mu\text{A}/\text{cm}^2$ AMB vs ND-AMB = $2.3 \pm 0.66 \mu\text{A}/\text{cm}^2$ ND-AMB; $p = 0.005$]. ND-AMB also protected nasal epithelial cells from cytotoxicity of AMB as determined by almost 85% reduction in lactate dehydrogenase (LDH) levels ($p < 0.05$). There was no difference in ciliary beat frequency between the two groups ($p = 0.96$).

Conclusions:

Data from the present study suggests ND-AMB protects human nasal epithelia membranes from AMB toxicity by protecting against apical cell K⁺ permeability and could provide a novel topical therapy for fungal disease.

Hu, Muhan

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH MSTP

Faculty Advisor: Michael Miller

Abstract Approved: Yes

Co-Authors:

Title: Mechanisms of TGF β signaling critical for *C. elegans* fertilization

Fertilization is essential for sexual reproduction and is fundamental to genetic diversity. This critical event requires that sperm navigate the female reproductive tract to locate the oocyte. Prostaglandins are lipid signaling molecules derived from dietary polyunsaturated fatty acids (PUFAs). Mutations in *C. elegans* that decrease PUFA synthesis or transport to oocytes cause non-autonomous defects in sperm velocity and directional velocity. These defects can be rescued by microinjecting F-series prostaglandins (PGFs) into the mutant worms. These studies, together with mass spectrometry studies, support the model that multiple PGF isomers act as sperm guidance cues. *C. elegans* lack the classical cyclooxygenase (Cox) enzymes, and oocytes synthesize specific PGF isomers via a novel, unidentified mechanism. Similar F-series prostaglandins have been found in Cox knockout mice and human fallopian fluid, suggesting related mechanisms exist in mammals. DAF-7 TGF β is a neuroendocrine factor that couples environmental cues, such as pheromones to oocyte PGF synthesis. In this study, we aim to investigate the mechanism by which TGF β promotes PGF synthesis. *daf-1* type I TGF β receptor loss causes strong sperm guidance defects that are suppressed by *daf-3* co-SMAD loss. These data suggest that SMADs regulate the transcription of genes critical for oocyte PGF metabolism. To test this hypothesis, we are developing an RNAi screening method to identify DAF-3 target genes essential for sperm guidance. At the same time, we are conducting RNAseq and lipidomics studies to identify DAF-3-dependent target genes and abnormalities in PGF metabolism. I will present our current efforts to further understand how TGF β signaling impacts fertilization.

Iannuzzi, Luke Antony

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Cunningham Fellowship

Faculty Advisor: Dr. William Tom Harris

Abstract Approved: Yes

Co-Authors: Dr. William Tom Harris, Lacrechia K Thomas

Title: The impact of caregiver well-being on infant pulmonary function in Cystic Fibrosis

Background: Cystic Fibrosis (CF) is a heterogeneous disease, even among patients sharing the same genotype. We have previously observed that some of this variance in infants (who are completely dependent on CF caregivers) is secondary to socioeconomic factors such as household income or paternal education. The mechanisms behind these disease associations remain uncertain.

Hypothesis: Low socioeconomic status impairs caregiver support in pediatric CF.

Methods: Caregivers of CF infants were provided a validated written questionnaire to analyze socioeconomic factors, support, and 5 categories of well-being (composite, financial, family/social, personal strain, and mastery). These factors were compared to infant pulmonary function and a 5-item composite clinical score (nutrition, microbiology, cough, pulmonary exacerbations, hospitalizations). T-tests analyzed continuous data and Fisher's exact test analyzed categorical data. Significance was assigned at $p \leq 0.05$.

Results: Lead caregivers of 34 CF infants participated. Socioeconomic status and education were not predictive of overall caregiving well-being (average score 75.1/96). Most caregivers reported being well supported (average score 8.4/10). However, perceived support was significantly decreased in lower income (<\$50,000/year) families (Lower income: 5.92 ± 1.29 ; Higher income: 9.38 ± 0.35 , $p=0.02$). Perceived support was also lessened in association with lower paternal education (\leq High School: 6.12 ± 1.22 ; College 9.20 ± 0.39 , $p=0.03$). Children of caregivers who report lower support manifest diminished clinical scores (Low support: 5.80 ± 0.57 , High support: 7.33 ± 0.41 , $p=0.04$). Conversely, children with high clinical scores have caregivers who report excellent support (High clinical score: 9.74 ± 0.17 ; Low clinical score: 5.733 ± 1.12 , $p<0.005$). Fisher's exact confirmed that low support impacts clinical score (Likelihood ratio = 4.5, positive predictive value = 0.80, specificity = 0.89, $p=0.02$).

Conclusion: CF caregivers generally report adequate support and general well-being. However, infants of less supported caregivers are at risk for developing increased disease. Assessing caregiver's perceived support may enable targeted interventions to enhance the care environment during infancy and optimize CF outcomes.

Ives, Christopher Winthrop, JR

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Suzanne Oparil

Abstract Approved: Yes

Co-Authors: Samantha S Giordano, Yuanyuan Guo, Yiu-Fai Chen, Dongqi Xing, Suzanne Oparil, Fadi G Hage

Title: Estrogen reduces inflammation in postmenopausal women through modulation of macrophage phenotype

Introduction: The increased cardiovascular disease (CVD) risk in postmenopausal compared to premenopausal women has been partially attributed to decreased levels of estrogen (E2) with menopause. Inflammatory cells, particularly macrophages, are intimately involved in the development of CVD. Classically activated (M1) macrophages are pro-inflammatory, while alternatively activated (M2) macrophages are anti-inflammatory. We tested the hypothesis that menopausal status will alter macrophage activation such that postmenopausal women will have a pro-inflammatory macrophage state and that menopausal hormone therapy (MHT) will attenuate this effect.

Methods and Results: Mononuclear cells isolated from peripheral blood phlebotomy samples were differentiated into macrophages from 3 groups of women: 1) premenopausal women aged 20-40 with regular menstrual cycles, 2) postmenopausal women aged >55 years with no menses >12 months, and 3) postmenopausal women aged >55 years who have received MHT since menopause. Macrophages derived from postmenopausal women were skewed towards an M1 phenotype (using CCL5 as M1 marker and CD163, IL-10, and PPAR γ as M2 markers) compared to premenopausal women. MHT restored M1/M2 ratio to premenopausal levels.

Conclusions: Menopausal status alters macrophage polarization by favoring the pro-inflammatory classically activated M1 phenotype. This pro-inflammatory state is reduced by MHT. These data reveal a novel mechanism of the vasoprotective effects of E2.

Jani, Aditi Hirenkumar

Project Length: Short

Source of Funding: Other

Faculty Advisor: Stefan Kertesz

Co-Authors: Alex McFarland, Stefan Kertesz

Title: For Homeless Veterans Entering Care, does Co-Existent Addiction and Chronic Pain Influence Housing Outcomes?

Prior Research Experience: Yes

Abstract Approved: Yes

Introduction

The Department of Veterans Affairs has implemented a combination of housing and social services in an effort to end homelessness among veterans. Some research has suggested that coexistent addiction and chronic pain identifies a uniquely challenging veteran subgroup. Whether this combination affects housing success is unstudied. New specialized VA primary care clinics (Homeless Patient-Aligned Care Teams, HPACTs) capture information regarding chronic pain and addiction at care entry. This quality evaluation pilot study examined whether chronic pain and addiction were associated with worse housing outcomes at 6 months after entering HPACT care.

Methods

We used structured chart review for all HPACT entrants (n=115), focusing on those for whom housing status at 6 months' follow-up was known (n=92, 80%). Individuals were classified as having (a) addiction & chronic pain, (b) addiction no chronic pain, (c) no addiction (regardless of chronic pain). Descriptive analyses compared the attainment of 2 potentially favorable housing outcomes: (a) permanent housing (PH) and (b) a broader category of PH or residing with family/friends (PH+F).

Results

Among 92 veterans, 31 (34%) had addiction & pain at baseline; 27 (29%) had addiction & no pain; 34 (37%) had no addiction. Attainment of PH was less likely among persons with addiction & pain (16%), compared to addiction & no pain (30%), or no addiction (32%), which did not attain significance ($p=0.29$). PH + F was attained by 52%, 52%, and 59% of these three groups, respectively ($p>0.5$).

Conclusions

These preliminary data suggest that coexistent addiction and pain may indicate greater risk of an unfavorable housing outcome. Low subject numbers limited statistical power, but future analyses will collate data with parallel reviews in two other VA Medical Centers.

Jariwala, Ravi Hasmukh

Project Length: Short

Source of Funding: T35\

Faculty Advisor: Ricardo Franco, MD

Co-Authors: Ashutosh Tamhane, MD, PhD

Title: Concordance between SAFE Biopsy and Transient Elastography: Assessing Clinic Utility of Non-Invasive Liver Disease Staging in Patients with HCV and HIV/HCV Co-infection.

Prior Research Experience: Yes

Abstract Approved: Yes

Chronic hepatitis C is a public health priority and a leading cause of liver disease and cirrhosis. The evaluation and management of chronic hepatitis C rely on accurate assessment of liver fibrosis stage. Patients with significant fibrosis (METAVIR score ≥ 2) are in need of treatment to avoid further liver fibrosis progression. Patients with cirrhosis (METAVIR score F4) are in need of treatment and surveillance for cirrhosis complications (ascites, encephalopathy, gastrointestinal bleeding and hepatocellular carcinoma). Liver biopsy is considered to be the gold standard for liver fibrosis staging, but has limited accuracy and it is invasive. Therefore, several non-invasive modalities of liver fibrosis staging have been developed. These include the Sequential Algorithm for Fibrosis Evaluation (SAFE) Biopsy as well as transient elastography (FibroScan). SAFE Biopsy utilizes common serum markers to estimate fibrosis staging and has undergone validation in hepatitis C mono-infection. However, the clinical utility of SAFE Biopsy in decreasing the need for liver biopsy among patients with HIV/HCV co-infection is unclear. In this project, we conduct a retrospective chart review on 390 patients who were either HCV mono-infected or HCV/HIV co-infected and extracted FibroScan and/or SAFE Biopsy data. We hypothesize that SAFE Biopsy is a useful tool in reducing the number of liver biopsies in both HCV mono-infected as well as HCV/HIV co-infected patients. Our also hypothesize was that there will be a high concordance between FibroScan and SAFE Biopsy staging scores in both populations, providing evidence that accurate staging is feasible even when liver biopsy is not performed or available. Data analysis is ongoing. The results of this pilot study will guide large scale multi-site studies within CNICS (CFAR Network of Integrated Clinical Systems).

Jiang, Qiuchen

Project Length: Short

Source of Funding: T35

Faculty Advisor: Chad Steele

Co-Authors:

Prior Research Experience: Yes

Abstract Approved: Yes

Title: Immunopathogenic mechanisms associated with fungal colonization and sensitization in individuals with cystic fibrosis and asthmatics

Fungal colonization in the lungs of cystic fibrosis (CF) and asthmatic patients is a known exacerbating factor of the underlying disease states and is heavily associated with poor outcomes in both patient populations. In fact, sensitization alone has been shown to be associated with decreased lung function in CF patients and increased hospitalizations from asthma-related symptoms in asthmatics. Despite the clinical significance of fungal colonization and sensitization, the nature of the immunologic pathways leading to the observed pro-inflammatory response in colonized and atopic patients is still unclear. The Steele laboratory is attempting to identify key biomarkers linked with fungal sensitization in asthmatics and colonization in CF patients. This preliminary project collected bronchial alveolar lavage samples from both CF and asthmatic patients for multiplex analysis of 64 different analytes. In the asthmatic samples, those that were fungal atopic demonstrated statistically significant elevations in the pro-inflammatory cytokines eotaxin, IL-5, and ENA-78. For the CF samples, IP-10 was significantly increased in fungal colonized samples. This data provides the groundwork for future projects to explore each identified cytokine in more detail in order to explicate their role in fungal immunologic response.

Joshi, Madhura Bhalchandra

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Tiffany L. Carson

Abstract Approved: Yes

Co-Authors: Justin B. Simms, Tiffany L. Carson

Title: Exploring stress as a contributor to racial and gender disparities

The differences in stress among gender groups are not well understood. Previous studies that have measured traumatic lifetime events show mixed results with men reporting more traumatic experiences (Breslau et al., 1991) in contrast to women reporting higher scores on stressful life events (Bieliauskas et al., 1995). Some studies have found that there are no gender differences in mean number of lifetime events that were stressful or considered of “high magnitude” (Costello et al., 2002). It is important to measure gender differences related to stress due to chronic stress leading to increased risk of several morbidities. The goal of this summer project was to look at the differences in perceived stress between males and females by comparing responses from five stress surveys and measurements of stress biomarkers using cortisol and gut microbiota with male and female participants being paired based on race and placed in groups based on age and household income. Data for the male participants was collected over the duration of this project. Currently, results are not conclusive because male samples have not been processed for biomarker and gut microbiota analysis.

Junkin, Elizabeth Ann

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Lea G. Yerby, PhD

Abstract Approved: Yes

Co-Authors: Lea G. Yerby, PhD

Title: Moving Pickens County Primary Care towards Patient-Centered Medical Home Qualifications through a Diabetes Self-Management Education Program

Background: Pickens County Primary Care is located in Reform, AL, and it is home to 1 of the 7 primary care physicians in the county. In Pickens County, 13.9% of the population over 20 years old has been told by a physician that they have diabetes. To better serve this high percentage of diabetic patients, Pickens County Primary Care would like to create a Diabetes Self-Management Education program that is recognized by the American Diabetes Association (ADA). Diabetes Self-Management Education (DSME) is very important in the successful control of blood glucose in a diabetic patient, and is one of the key tools in the prevention of diabetic-related health complications. Also, ADA recognition is crucial in order to receive reimbursement for education services through Medicaid and Medicare. In addition, this DSME Program will help the clinic move towards Patient-Centered Medical Home (PCMH) qualifications. PCMH is a model being used to reshape healthcare using standards that focus on patient-centered care, physician-led healthcare teams, increased access, and higher quality of care.

Methods: This project will assess the needs and feasibility of a DSME program at the clinic through three parts. Part 1 will consist of a review of the clinic's Electronic Health Records (EHR) to assess the number and characteristics of the diabetic patients in the clinic. Part 2 will consist of a diabetic patient survey that will include demographics, health status, education/advice received, understanding of diabetes care, and social support. Part 3 will consist of a clinic staff survey to assess the resources and willingness of the staff to help with the development and implementation of a DSME program.

Results/Impact: This project will provide valuable information to the clinic about the interest of its diabetic patients and clinic staff. This information will be used to choose the best curriculum for their DSME Program, and will result in a preliminary plan of implementation.

Kamal, Salmaan Zaki

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Department of Medicine Fellowship

Faculty Advisor: Stefan G. Kertesz

Abstract Approved: Yes

Co-Authors: David E. Pollio, Erika L. Austin

Title: Understanding the Primary Care Experience for Vulnerable Patients in a Student-Run Free Clinic

Purpose. Over 100 student-run free clinics (SRFCs) operate in the US, typically serving underserved populations. To date, there has been no effort to compare the patient-reported primary care experience in SRFCs to those of mainstream primary care (PC) clinics serving similarly vulnerable individuals. In this study, we surveyed clients at Equal Access Birmingham (EAB), an SRFC, and compared our results to those from two PC clinics serving homeless-experienced clientele.

Methods. We surveyed 60 EAB patients with the “Primary Care Quality-Homeless” (PCQ-H) survey, a validated instrument developed to capture primary care aspirations important to homeless patients. It generates an overall score and 4 subscales pertaining to clinician-patient Relationship, perceived inter-provider Cooperation, Accessibility/Coordination, and Homeless-Specific Needs. We compared EAB patient responses to those published for homeless-experienced patients in a Veterans Affairs (VA) mainstream PC clinic and a homeless-tailored non-VA Health Care for the Homeless (HCH) program.

Results. EAB’s overall and subscale ratings were similar to those of the mainstream VA clinic ($p>0.4$). However, EAB scored lower than the homeless-tailored non-VA HCH program ($p<0.003$ for Relationship and Cooperation subscales). EAB patients most often praised the staff’s interpersonal skills. Items on which $>25\%$ of respondents gave a negative rating concerned wait times (29%), coordination of care (65%) and perceptions of provider skill (43%).

Conclusions. In spite of highly constrained monetary and human resources, an SRFC was able to score comparably to a mainstream VA PC setting in Alabama. However, its scores fell short of those of a tailored non-VA HCH program in Massachusetts. In states that have declined to expand Medicaid, SRFCs will play a continuing role in care of uninsured individuals. While these data suggest SRFC patient experiences are mostly favorable, additional resources and training may be required to deliver the level of patient experience available through clinics tailored for homeless persons.

Kasanagottu, Koushik

Project Length: Intermediate

Source of Funding: Department of Medicine Fellowship

Faculty Advisor: Dr. Monika Safford

Co-Authors:

Title: Development and Assessment of a Video Health Education Program

Prior Research Experience: Yes

Abstract Approved: Yes

The prevalence for diabetes and heart disease in our community is one of the highest in the country. We consistently rank in the top 5 states for chronic diseases every year. One of the major reasons for this prevalence in our state is the lack of access to quality, engaging health education information to the underserved populations. Health Education is an extremely crucial component of chronic disease management. Only a small portion (about ~15%) of individuals diagnosed with chronic diseases attend a health education session. This promotes unhealthy management of these disorders and leads to serious complications.

This study aims to understand the factors behind low participation in health education sessions and create an interactive, video health education program. Furthermore, we will test the effectiveness of this novel program in underserved communities versus standard health education. We hypothesize that individuals will respond better to a video, electronic program with an increase in information retention and program participation. Data will be collected from individuals who attend Equal Access Birmingham and M-Power Free Clinics as part of their routine visit. Participants will be presented with a tablet that has educational videos. They will also take a pre/post test and a survey that will be analyzed for this study. Preliminary qualitative surveys of the videos to nutritionist and health care providers show overall positive reviews.

Keeley, Jordan Michelle

Project Length: Short

Source of Funding: T35

Faculty Advisor: Charitharth Vivek Lal, MD

Co-Authors: Rakesh Patel, PhD; Namasivayam Ambalavanan, MD; Charitharth Vivek Lal, MD

Title: Nitrites as a Biomarker of Bronchopulmonary Dysplasia (BPD) Disease in Extremely Preterm Infants

Prior Research Experience: No

Abstract Approved: Yes

BACKGROUND: BPD is the most common complication of prematurity and is marked by chronic oxygen requirement in infants who are born premature. BPD is marked by significant mortality and morbidity, but biomarkers for disease progression and diagnosis have not yet been established. Nitrites have been implicated in pathways associated with lung diseases.

OBJECTIVE: We hypothesized that nitrite levels would be altered in the airways of premature infants diagnosed with BPD and could serve as a disease biomarker.

METHODS: We conducted a prospective cohort study of extremely low birth infants (<28 week gestation) at the University of Alabama Regional Neonatal Intensive Care Unit. We collected tracheal aspirates (TAs) from infants who were intubated and ventilated, and compared the nitrite levels in TAs from infants with established BPD with that of gestation matched full term (FT) controls. We also measured nitrite levels in day 1 TAs samples of infants who either went on to develop BPD in the future (BPD-Prone) vs infants who did not develop BPD in the future (BPD-Resistant).

RESULTS: Infants with BPD were found to have significantly elevated nitrite levels in their tracheal aspirates compared to gestation matched FT controls ($p < 0.05$). There was no difference in nitrite levels in day 1 TAs of infants who were 'BPD-Prone' vs infants who were 'BPD-Resistant'.

CONCLUSIONS: Nitrite levels are significantly increased in airways of infants with established BPD and could be potentially used as a biomarker of the disease diagnosis and progression. Nitrite levels soon after birth are not predictive of future development of BPD and are not a good predictive biomarker of BPD. In the future, we plan to conduct mechanistic studies to further understand the nitrite surge associated with diseased preterm lungs.

Kennell, Timothy Irving, Jr.

Project Length: Intermediate

Source of Funding: NIH MSTP

Faculty Advisor: James J. Cimino

Co-Authors: Robert D. Johnson, Don Dempsey

Title: An OpenInfoButton and I2B2 Merger: Bringing Info Buttons to the translational research tool I2B2

Prior Research Experience: Yes

Abstract Approved: Yes

Introduction: In today's modern medical era, the information needs of physician's are enormous. Info buttons, which are integrated into electronic health records (EHRs) through OpenInfoButton, an external info button manager, fill these needs by providing context-specific information. Many translational researchers have similar needs, which could be filled by placing info buttons into I2B2, an application designed to find study patient sets for translational research. Integrating OpenInfoButton and I2B2 will allow researchers to more easily request valuable information regarding study patients found through querying this system.

Methods: Info buttons were integrated into I2B2 through design of an I2B2 plugin. The design of the plugin takes advantage of the RESTful (REpresentational State Transfer) APIs (Application Program Interfaces) utilized by both OpenInfoButton and I2B2. First, I2B2 transfers data to OpenInfoButton through URL GET verbs, allowing OpenInfoButton to query appropriate resources based on prior setup in LITE (Librarian Infobutton Tailoring Environment). The resources respond with URLs pointing to patient-specific information, which OpenInfoButton processes and displays in a browser window.

Results: Using a plugin for integration of OpenInfoButton into I2B2 provides an easy mechanism for institutions to integrate info buttons into currently installed I2B2 instances. Currently, the plugin allows a user to send both a pre-selected medical concept (such as a disease) and the demographic information associated with each patient in a patient set to OpenInfoButton. By utilizing LITE to inform OpenInfoButton of the appropriate resources to use for a given request, it is able to provide I2B2 a response consisting of patient-specific information regarding the requested concept.

Conclusions: While the current structure only allows users to request patient-specific information regarding a chosen medical concept, future implementations will list a patient's diseases or medications in order to allow selection of medical concepts directly related to patients.

Kim, Sanghun

Project Length: Short

Source of Funding: T35

Faculty Advisor: Ahmed M. Kamel Abdel Aal

Co-Authors:

Title: Sarcopenia as predictor TIPS procedure outcomes

Prior Research Experience: Yes

Abstract Approved: Yes

Outcomes of transjugular intrahepatic portosystemic shunt (TIPS) procedure is variable due to several factors including extent of cirrhosis, prior transplantation, causes of cirrhosis that led to complications of portal hypertension, and cancer. Currently, outcome is determined by MELD score, presence of fluid retention, recurrent variceal bleeding, right heart failure, stenosis of the shunt requiring revision procedure, and mortality. However, the patient's nutritional status has not been taken into account when determining the outcome of the procedure. We hypothesize that it is important to determine the nutritional status of the patient before TIPS placement because it is one of the most common factors that negatively impacts survival. The nutritional status of the patient can be reliably determined by measuring the muscle density. Prior studies have shown that TIPS procedure improved the patient's nutritional status by measuring muscle densities pre and post-operatively. However, the effect of low muscle density (sarcopenia) measured before the TIPS procedure has not been correlated with the outcomes. To find the correlation between patient's nutritional status before the procedure and the outcomes of TIPS procedure, patients who underwent TIPS procedure in UAB in the past 10 years were identified. Demographics, presence of decompensation, lab values pre and post TIPS, and TIPS procedure values itself along with postoperative outcomes were identified. Using preoperative non-contrast CT images, region of interest were drawn over the psoas muscle in the L4-5 level, and the density was recorded. Using muscle density data and corresponding outcomes in these patients, we will be able to determine whether or not sarcopenia adversely affects the survival outcomes in patients undergoing TIPS procedure.

Laskay, Nicholas Michael Berry (Nicholas)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Jason Lowe, MD

Abstract Approved: Yes

Co-Authors: Hiatt, L., Laskay, NM

Title: The Perioperative Outcomes of Spinopelvic Fixation following Unstable Sacral Fractures with Spinopelvic Dissociation

Background: Unstable sacral injuries require operative fixation in order to achieve anatomic stability and maintain patient functionality. Spinopelvic fixation has been proposed to be superior to other biomechanical techniques such as percutaneous screw fixation to manage these fractures. However, open surgery of this magnitude can be followed by complications.

Objective: To report the perioperative outcomes of spinopelvic fixation in patients with highly unstable transverse sacral fractures resulting in spinopelvic dissociation.

Hypothesis: The team hypothesizes that when compared to other techniques, spinopelvic fixation allows for immediate weight bearing post operatively without loss of reduction, increase incidence of hardware failure, DVT, or difference in union rates. In addition, we propose that spinopelvic fixation has a higher incidence of secondary procedures post-operatively.

Methods: Retrospective clinical study done at a level one trauma center. Twenty seven patients with U, H, lambda, and comminuted Denis zone III sacral fracture patterns resulting in spinopelvic dissociation were identified in the patient database using ICD-9 and CPT codes between 2010-2015. SF-36 Health Surveys were sent to all of the identified patients to assess quality of life post-operatively. However, there was only a 26% response rate among these patients.

***Results: The following results reported are based upon empirical observation.** Following an immediate weight-bearing status postoperatively, patients in this study showed no increase in incidence for loss of reduction, hardware failure, infection, DVT, hospital length of stay, or neurologic deficit. However, there was an increased rate in secondary procedures to remove hardware used in the initial operation.

***Conclusion: The following conclusions reported are based upon empirical observation.** Spinopelvic fixation provides reliable fracture stability and allows for consistent fracture union without an increase in incidence of relative complications postoperatively. The advantage of immediate weightbearing but disadvantage of increased secondary procedures postoperatively demonstrates that spinopelvic fixation should be seen as a trade off technique.

***Notable:** Because the outcome results of the data for this study are currently under calculation, significant results and conclusions cannot be accurately reported at this time. However, general observational results and conclusions can be drawn.

Laufer, Vincent Albert (Vincent)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: S Louis Bridges

Abstract Approved: Yes

Co-Authors: Hemant K Tiwari, Richard J Reynolds, Donna K Arnett, Robert P Kimberly, S Louis Bridges

Title: Genetic Influences on Rheumatoid Arthritis and its Severity in African Americans
Rheumatoid arthritis (RA) is an autoimmune inflammatory disease that targets the synovial lining of joints and affects 0.5-1% of populations worldwide. To test the hypothesis that genotyping data can help elucidate the genetic basis of RA, we sought to identify genetic variants associated with susceptibility to RA in African-Americans.

After relatedness checks, SNP, and individual-level quality control procedures, and PCA, we conducted genome wide association testing using logistic regression on anti-citrullinated peptide antibody (ACPA)-positive RA patients (n=535) and unaffected African-American controls (n=1,505).

We confirm the association of several validated risk loci from other populations (Europeans, Asians) with RA in African-Americans, including the *HLA-DRB1* locus (lead SNP rs116713910, $p=3.92 \times 10^{-16}$). We provide evidence for confirmation of a previously identified risk locus, *PRKCCQ* (rs73617902, $p=1.09 \times 10^{-6}$) and report a novel association of a SNP on 5p15.31 near the *MTRR* locus, with RA in African-Americans ($p=4.87 \times 10^{-8}$, dominant model). We found significant enrichment of Probabilistically Identified Causal SNPs (PICS) reported by others to be associated with 21 autoimmune diseases in our dataset ($p = 1.55 \times 10^{-11}$, exact binomial test).

These findings suggest a degree of genetic overlap across autoimmune diseases that span multiple races/ethnicities. Our study highlights similarities and differences in the genetic architecture of RA among different ethnic populations and will help to inform future association, fine-mapping, and functional genomic analyses.

LeGrand, Jason Nathaniel (Jason)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Christopher Klug

Abstract Approved: Yes

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

Title: Identification of Cytogenetically Normal Human CD34⁺CD38⁻ Hematopoietic Stem/Progenitor Cells from inv(16)⁺ Leukemic Bone Marrow

For many subtypes of AML including cases with the inv(16), mutations that give rise to the leukemic phenotype occur, at least in part, in the hematopoietic stem/progenitor (HSPC) cell subset, as suggested by studies showing that primitive CD34⁺ CD38⁻ bone marrow cells can function as leukemia-initiating cells (LIC) when transferred into immunodeficient mice. A significant challenge has been that LIC share many of the same cell-surface markers as their normal HSPC counterparts, thus making it difficult to purify and functionally characterize either subset from the bulk bone marrow of leukemia patients. Here we report the FACS analysis of several previously reported human LIC markers on bone marrow samples from inv(16) AML patients and show that a combination of TIM3, CLL1, and CD33 can significantly enrich for a rare population of CD34⁺ CD38⁻ cells that lack the inv(16) fusion mRNA when tested by nested RT-PCR and FISH. Heterogeneous expression of these markers among different patient samples often causes incomplete elimination of the fusion mRNA when FACS-sorting the CD34⁺ CD38⁻ population as single TIM3⁻, CLL1⁻, or CD33⁻ subsets. The combination of TIM3 with CLL1 and/or CD33 leads to a more consistent elimination of the fusion mRNA from the FACS-sorted CD34⁺ CD38⁻ subsets. Results from colony-forming assays showed that the TIM3⁻ CLL1⁻ CD33⁻ subset of CD34⁺CD38⁻ cells was significantly enriched for progenitor activity and could form multiple colony types that were negative for the inv(16) fusion mRNA by RT-PCR. In contrast, colonies derived from bulk bone marrow were positive for the inv(16) fusion mRNA. Unfortunately, transplants of the TIM3⁻ CLL1⁻ CD33⁻ subset into immunodeficient NSG mice were unsuccessful. These results have important implications for the therapeutic targeting of leukemic stem cells in patients with inv(16) AML and for the purification of normal HSPC from leukemic bone marrow samples.

Lever, Jeremie Matthew (Jeremie)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Anupam Agarwal & James George

Abstract Approved: Yes

Co-Authors: Bo Chen, Ravindra Boddu, Travis D. Hull

Title: Characterization of renal inflammation in a model of ischemic Acute Kidney Injury leading to Chronic Kidney Disease

Ischemic acute kidney injury (AKI) increases risk of morbidity and mortality and is highly prevalent in hospitalized patients, those with hemodynamic instability and the elderly. AKI has been associated with increased risk of chronic kidney disease (CKD). Our laboratory has previously demonstrated a pivotal role for myeloid cells and heme oxygenase-1 in modulating damage from ischemic AKI. We sought to determine the role of renal mononuclear cells in the development of fibrosis, which occurs late after AKI, using a recently developed murine model in which injury is induced by 30 minutes ischemia in the left kidney, while leaving the right kidney intact. This procedure is known to induce fibrosis by 3 weeks post-AKI in the ischemic kidney. The changes in inflammatory resident mononuclear phagocytic and infiltrating cells in terms of function and phenotype are unknown in this model.

C57BL/6 mice will be subjected to 30 minutes of ischemia followed by reperfusion. Tissues will be harvested at 1 week and 3 weeks post-ischemia and will be compared to sham controls. Flow cytometry will be used to characterize the immune phenotype of myeloid and lymphoid infiltration following AKI. Histologic analysis using H&E, picrosirius red (collagen deposition), periodic acid-Schiff (tubule injury and cast formation) and western blot analysis (markers of fibrosis) will be performed. Serum creatinine and BUN will be measured to assess kidney function.

These studies will elucidate the role of inflammation in modulating the progression of AKI to CKD and provide avenues for therapeutic intervention.

Lewis, Justin Walton (Justin) JUSTINWL@uab.edu Last Updated on: 9/2/2015 12:32:09
PMProject Length: Short Prior Research Experience: Yes Source of Funding: T35Faculty
Advisor: Dr. Monika Safford Abstract Approved: YesCo-Authors: Title: Living Well with
Diabetes

Hypothesis: An intervention designed within the Corbin and Strauss framework can improve adherence and health outcomes compared to usual care. *Aim 1:* With our community partners, using qualitative research methods, build on already developed culturally tailored education material to develop the medication adherence intervention. The intervention will consist of educational DVDs with integrated storytelling about how community members accepted their disease and overcame barriers to medication adherence, plus one-on-one telephonic peer coaching. Activities include conducting focus groups with patients; creating the DVDs and the coaching intervention protocol; training peer coaches; and pilot testing. *Aim 2:* Conduct a randomized controlled trial with 500 individuals with type 2 diabetes and medication nonadherence. The trial will compare the effect of usual care and the intervention on medication adherence and physiologic risk factors including A1c, blood pressure and low density lipoprotein cholesterol (primary outcomes), and quality of life and self-efficacy (secondary outcomes). I completed my training DVD which will be incorporated into the overall study. I look forward to the testing phase to determine if the approach of the study has an impact in improving patients' understanding of how to manage their diabetes and their compliance with following through with treatment plans.

Locy, Morgan Lee (Morgan)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Victor J. Thannickal

Abstract Approved: Yes

Co-Authors: Subramaniam Pennathur, Anuradha Vivekanandan-Giri, Tejaswini Kulkarni, Degui Zhi, Jaeman Byun, Joao A. de Andrade, and Victor J. Thannickal

Title: Modifications of Tyrosine are Increased in Plasma of Human Subjects with Interstitial Lung Disease

OBJECTIVE: Interstitial lung disease (ILD) is a variably progressive lung disorder that results in impaired gas exchange with high mortality and morbidity. Oxidative stress mediated through reactive oxygen and nitrogen species have been shown to play a role in the impaired repair mechanisms of ILD. Tyrosine oxidative modifications are stable interactions allowing them to be observed in human plasma. Therefore, this study tested the hypothesis that tyrosine modification by reactive oxygen and nitrogen species is increased in the plasma of human ILD patients.

METHODS: Three tyrosine modifications, *o,o'*-dityrosine, 3-chlorotyrosine, and 3-nitrotyrosine, were quantified by tandem mass-spectrometry in plasma from age and sex matched healthy control (n=20) and ILD patients (n=20). The study was approved by the University of Alabama at Birmingham and the University of Michigan Institutional Review Board. Data were analyzed by Welch's ANOVA (Mean \pm SD, $p < 0.05$).

RESULTS: ILD patients demonstrated an increase in protein tyrosine modification content in plasma when compared to healthy controls. Plasma protein *o,o'*-dityrosine concentration was most significantly increased by 24.1 fold (7.42 ± 1.38 vs. 0.31 ± 0.02) in ILD patients when compared to healthy controls. Both 3-chlorotyrosine and 3-nitrotyrosine were also increased in ILD patient plasma 3.0 fold (9.03 ± 1.2 vs. 3.06 ± 0.91), and 3.2 fold (128.96 ± 20.84 vs. 40.00 ± 6.2), respectively, when compared to healthy controls.

CONCLUSIONS: These data support the idea that oxidants play a central role in ILD pathophysiology, and that plasma tyrosine modifications is a novel, potential biomarker for ILD. These findings have the potential to aide in the identification of new treatment regimens for ILD patients.

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T32 GM008361

Love, Ashley Barnett (Ashley)
Prior Research Experience: Yes
Source of Funding: Other

Project Length: Short

Faculty Advisor: Nancy Tofil

Abstract Approved: Yes

Co-Authors: Leslie Rhodes, MD, Ashley Love MSIV, Chrystal Rutledge, MD, Nancy Tofil, MD, MEd

Title: Pediatric Cardiology Simulation: When to Give Fluids and Oxygen and When Not

Background/Objectives: The assessment and management of pediatric patients with a cardiac condition can be challenging. The patients encountered frequently have complex cardiac lesions which completely alter their physiology and response to supportive therapies such as oxygen, fluids, and intubation. Many residents have few encounters caring for a cardiac patient, as these patients are often cared for by cardiac intensivists. In effort to change this, a new cardiac simulation module was developed. The hypothesis is that participation in the simulation will increase the resident's understanding of initial care of cardiac patients.

Setting & Participants: The cardiac simulation module is offered monthly, and consists of four cases, with each case presenting to the emergency department with an acute problem. The participants include second or third year pediatrics residents currently on their pediatric cardiology rotation and any medical students on cardiology or simulation rotations.

Description/Methods: Between each case, there is a group debriefing with time devoted to review of underlying physiology. Emphasis is placed on understanding appropriate use of common therapeutic interventions, and how the physiology affects response to them.

Evaluation/Results: 24 learners have participated in the cardiac simulation module. Evaluations completed by the residents show that 100% (24 of 24) of learners rated the simulation 5/5 ("strongly agree") as a valuable learning experience, as well as 100% of learners rating the debriefing 5/5 ("strongly agree") as a valuable learning experience. In addition, 22/24 learners (92%) reported 5/5 for the experience improving performance in actual clinical setting.

Discussion/Reflection: The results from the evaluations are extremely positive, with almost all residents commenting on how beneficial the simulation courses were and appreciating the reviews of physiology. The simulation module should continue to be offered. Future studies will evaluate the residents' knowledge of cardiac physiology and management of cardiac lesions, both before and after the course.

Ma, Elizabeth Yean (Elizabeth)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: W. Timothy Garvey, MD

Abstract Approved: Yes

Co-Authors: Katherine H. Ingram, PhD

Title: Urinary F2-Isoprostanes Do Not Reflect Oxidative Stress Operative in Human Insulin Resistance, but are Correlated with Lean Mass and Serum Lipids

Background: F2-isoprostanes (F2-IsoPs), generated through lipid peroxidation, are biomarkers for oxidative stress in humans. Some studies show that F2-IsoPs are positively correlated with BMI and %body fat, and are elevated in patients with cardiovascular disease or diabetes. We have previously shown that muscle lipid peroxidation, assessed by hydroxynonenal adducts, was increased in insulin resistance. In this context, F2-IsoPs are widely interpreted to reflect oxidative stress contributing to the pathogenesis of insulin resistance; however, this has not been rigorously examined.

Methods: 57 patients recruited for metabolic characterization on a research ward were measured for insulin sensitivity via hyperinsulinemic-euglycemic clamp, substrate oxidation rates by indirect calorimetry, urinary F2-IsoP's and metabolites by gas chromatography-mass spectrometry, and body composition by DXA. We assessed whether urinary F2-IsoPs were predictive of insulin sensitivity or related to other metabolic parameters.

Results: No correlations were found between urinary F2-IsoP's or their metabolites with either glucose disposal rates ($r=0.121$, $p=0.380$; $r=0.134$, $p=0.330$) or lipid oxidation rates ($p=NS$). However, both were significantly negatively associated with lean body mass ($r=-0.495$, $p<.0001$; $r=-0.360$, $p=0.006$). In addition, urinary F2-IsoPs were positively correlated with serum triglycerides ($r=0.283$, $p=0.032$), total cholesterol ($r=0.340$, $p=0.009$), and LDL cholesterol ($r=0.261$, $p=0.048$).

Conclusions: 1) Urinary F2-IsoPs and metabolites are not associated with insulin sensitivity. 2) The lipid oxidation process that produces F2-IsoPs does not reflect oxidative stress reactions operative in insulin resistance. 3) Urinary F2-IsoP's are negatively correlated with lean body mass and positively correlated with TG and cholesterol, suggesting that they reflect processes regulating muscle mass and lipid metabolism. Thus, the significance of F2-IsoPs in cardiometabolic disease should be scrutinized pending further study.

Mahalingam, Mythreyi (Mythreyi)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Dr. Henry Wang

Abstract Approved: Yes

Co-Authors: Justin X. Moore, MPH, John P. Donnelly, MSPH, Monika M. Stafford, MD, Henry E. Wang, MD, MS

Title: Frailty and Risk of Sepsis: A prospective analysis of the Reasons for Geographic And Racial Differences in Stroke (REGARDS) cohort

INTRODUCTION: Sepsis is a major public health problem. Frailty refers to increased vulnerability from aging-associated decline in physiologic reserve and function. While associated with increased morbidity and mortality, no studies have assessed frailty as a risk factor for sepsis. We examined the association between frailty and sepsis incidence and case fatality in a large cohort of community-dwelling adults.

METHODS: We performed a prospective cohort analysis using 30,239 participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort. We determined frailty from participant reports of physical status. We defined frailty as the presence at least two of the following components: 1) weakness, 2) self-reported exhaustion, 3) low physical activity. We defined sepsis events as hospital admission for a serious infection with presence of at least two Systemic Inflammatory Response Syndrome criteria. We identified sepsis events during a 10-year observation period (2003-2012). Using Cox regression, we determined associations between frailty and first-sepsis events, adjusting for sociodemographics, health behaviors, and chronic medical conditions. We assessed adjusted association between frailty and 30-day case fatality after a sepsis event.

RESULTS: Among eligible REGARDS participants, there were 5,921 (20.6%) frail and 22,807 (79.4%) non-frail individuals. During the 10-year observation period, there were 1,476 first-sepsis hospitalizations. Frailty was associated with increased rates of first-sepsis events (adjusted HR 1.56; 1.36 – 1.78). Among first-sepsis events, frailty was associated with increased rates of case-fatality (adjusted HR 1.94; 95% CI: 1.21-3.11). Among frailty components, weakness was most strongly associated with rates of sepsis (adjusted HR 1.54; 95% CI 1.37-1.73). Rates of sepsis were associated with number of frailty components (1 – HR: 1.26; 2 – HR: 1.69; 3 – HR: 2.02; p-trend <0.001). The association between frailty and sepsis persisted for whites but not blacks.

CONCLUSION: In community-dwelling adults, frailty is associated with increased rates of sepsis incidence and case fatality.

McCaw, Tyler Robert (Tyler)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Troy Randall; Tim Townes

Abstract Approved: Yes

Co-Authors:

Title: Solid Tumor Targeting with T cells, Linker Proteins, and Precise Gene Editing

Therapeutic transformation of many impressive advances in cancer vaccines are too often stymied by recurrence and metastasis of the primary tumor, typically a negative prognostic factor. Here, malignant cells downregulate surface antigens or upregulate alternative intracellular pathways, thereby rendering first-line therapies ineffective. If, however, multiple surface antigens were targeted simultaneously, rather than individually, the likelihood of tumor escape may be dramatically reduced. Furthermore, such a strategy can target profiles of antigen expression, allowing for markedly enhanced selectivity. Chimeric antigen receptors (CARs), fusion proteins comprised of antibody specificity and intracellular T-cell signaling domains, are a promising mode of immunotherapy, as they can redirect T-cells to virtually any tumor associated antigen (TAA). Despite their putative wealth of potential, CARs have only proven clinically successful thus far in the context of CD19⁺ hematologic malignancies. Additionally, current methods of transduction to introduce CAR gene constructs to T-cells are liable to insertional mutagenesis and emergence of a secondary leukemia. We addressed these issues in two steps. First, highly activated T-cells expressing CD19 specific CARs (Ta19s), putatively as a result of interactions with CD19⁺ B-cells in lymph tissues, can then be redirected to any other TAA via specific linker peptides. These peptides contain a CD19 extracellular domain, able to interact with the CD19⁺ CAR, linked to an antibody fragment of tailorable specificity, able to interact with any TAA or profiles thereof. Second, dedifferentiating patient cells into induced pluripotent stem cells (iPSCs) and introducing the CAR construct with site-specific CRISPR/Cas technology will minimize the risk of secondary malignancies. Here, we have shown that Ta19s are substantially more activated than similar CARs with other specificities and, moreover, that these T-cells can be redirected to various TAAs through appropriate linker peptides. Future studies will determine the ability of CRISPR/Cas gene engineering to circumvent secondary leukemias.

McClanahan, Stephen Taylor (Taylor)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Arianna Shirk, Pediatrics - Emergency Medicine

Abstract Approved: Yes

Co-Authors: Arianna Shirk, MD; Robert Mugo, MD; Ruth Hennebery, MS-2; Samuel Kraus

Title: Creation of an Antibiogram for Kijabe Hospital in Kijabe, Kenya

The aim of this project was to create an antibiogram for Kijabe Hospital in Kijabe, Kenya that would allow local physicians to better understand their patterns of bacterial growth and resistance, establish evidence-based guidelines for empiric treatment, and ultimately, better serve the patients in their mission hospital. An antibiogram is an ongoing publication of the institutional pattern of antimicrobial susceptibilities of local bacterial isolates. The utilization of an antibiogram is a fundamental aspect of institutional patient care because it allows clinicians to monitor patterns of antimicrobial resistance and appropriately select evidence-based empiric antimicrobial therapy. The construction of an antibiogram at Kijabe Hospital would be one of the first antibiograms to be constructed at a mission hospital in sub-Saharan Africa. An antibiogram is needed at Kijabe Hospital to challenge the current clinical practice guidelines, allowing for either confirmation or changes in empiric antibiotic therapy, which would be vital for all clinicians, especially for visiting clinicians at the mission hospital. This project involved extracting culture and sensitivity data from culture results at Kijabe Hospital from June 1, 2014 to May 31, 2015, and then analyzing this data to create an antibiogram. Data was extracted from 1,552 microbiology laboratory culture results and placed into a MS Excel spreadsheet that was uploaded to WHO NET5.5 database software, which was used to analyze the data for creation of the antibiogram according to Clinical and Laboratory Standards Institute (CLSI) standards. This project was completed in July 2015 and resulted in the successful construction of an antibiogram for Kijabe Hospital. This data is currently being used at the bedside in Kijabe, Kenya. Findings are included on the printed antibiogram. Further study will involve investigation into the 39% Vancomycin-resistant *Staphylococcus aureus* to determine if the resistance is legitimate or laboratory error.

McMonigle, Ryan James (Ryan)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Scott Ballinger

Abstract Approved: Yes

Co-Authors: Ryan McMonigle, Kimberly J Dunham-Snary, Michael W Sandel

Title: Mitochondrial Influence on Gene Expression

Mitochondrial DNA encodes key oxidative phosphorylation enzyme subunits that are utilized in the production of cellular energy. Small variation in mitochondrial DNA has been proposed to impact disease susceptibility through multiple mechanisms including oxidative stress and cellular bioenergetics. The goal of this study was determine if differences in mitochondrial DNA can influence nuclear gene expression. Mitochondrial Nuclear eXchange mice were generated by removing the nucleus from the embryo of a C57BL6/J mice and replacing it with a C3H/HeN nucleus. The C3H/HeN nucleus paired with the C57BL6/J mitochondria (C3Hⁿ: C57^{mt}) embryo was then placed into a surrogate CD-1 surrogate mouse. The C3Hⁿ: C57^{mt} offspring were followed for 12 weeks and interestingly had increased weight gain (5 grams, 19.6%) and an increased ratio of fat/lean body composition compared to the C3H/HeN wild type. At 12 weeks of age, C3Hⁿ: C57^{mt} mice and control C3H/HeN mice were euthanized and the epididymal adipose tissue was harvested for RNA sequencing analysis using Illumina HiSeq2000 sequencing technology. The C3Hⁿ: C57^{mt} adipose tissue had 39 increased and 30 decreased differentially expressed mRNA transcripts compared to C3H:HeN wild type control mice. Of particular interest was the 2 fold decreased expression of beta-adrenergic receptor 3, which is involved in the activation of lipolysis in adipose tissue. These results implicate mitochondrial DNA in the regulation of genomic DNA expression and may shed light on differences in individual susceptibility to certain diseases such as obesity.

Moseley, Carson Edward (Carson)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Casey T. Weaver

Abstract Approved: Yes

Co-Authors: Carson E. Moseley, Craig L. Maynard, Stacey N. Harbour, Duy Pham, Henrietta Turner, Trenton R. Schoeb, Theresa N. Ramos, Scott R. Barnum, Laura Timares, Robin D. Hatton, and Casey T. Weaver

Title: A transcriptional regulatory mechanism governing Th17-driven autoimmunity

Altered transcription of genes involved in T cell activation and function is a key mediator of predisposition to numerous autoimmune disorders, including Multiple Sclerosis (MS) and Inflammatory Bowel Disease (IBD). However, we have an inadequate understanding of how the transcriptional circuits controlling these genes are dysregulated in disease.

Interleukin-10 (IL-10) is cytokine with potent anti-inflammatory activity that is critical for restraining immune-mediated pathology to self-tissues. Notably, patients with nullifying mutations in *IL10* develop a severe IBD in the first years of life, and variants in *IL10* are associated with several inflammatory disorders. 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 potent 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 *in vitro*, and mice deficient in *Gfi1* in the T cell compartment are highly resistant to mouse models of MS and IBD. This reduced disease is dependent upon increased T cell expression of IL-10 *in vivo*. Molecular studies of Gfi1 function at the *IL10* locus have identified a transcriptional regulatory mechanism critical in Th17-driven inflammation. These studies have generated new insights into T cell biology, and have identified a genetic circuit that may be of prognostic or therapeutic value in the future.

Mosher, Zachary Andrew (Zachary)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Santiago Borasino

Abstract Approved: Yes

Co-Authors: Dr. Santiago Borasino, Dr. Jeffrey Alten, Dr. David C. Cleveland

Title: Renal function during and after prophylactic peritoneal dialysis after cardiopulmonary bypass surgery in infants

Background: Peritoneal dialysis (PD) has been shown to decrease need for fluid resuscitation after CPB. Our aim is to describe patients who received PD emphasizing renal function and acute kidney injury (AKI).

Methods: Infants who underwent CPB surgery and PD were included. Admission to the CVICU was defined as time 0 for length of mechanical ventilation, hospital length of stay, and duration of PD. AKI was defined as doubling of baseline serum creatinine (SCr) and/or urine output (UOP) $<0.5\text{ml/kg/hr}$ in 24 hours over the first 7 days post-operative.

Results: 84 patients were identified. Median CPB time was 132 minutes. Median length of PD was 58 hours. A ScR decrease ($p<0.05$) was observed when comparing levels 1 day prior to PD discontinuation, the day of discontinuation, and one day after [0.6mg/dL vs. 0.5 mg/dL vs. 0.4 , $p<0.01$]; UOP increased ($p<0.05$) [1.2ml/kg/hr vs. 2.3ml/kg/hr vs. 3.9ml/kg/hr , $p<0.01$]; potassium remained unchanged. 43.7% of patients had AKI. Peak median SCr occurred on day 1. CPB time was longer in those with AKI, 123 minutes vs. 150 minutes, $p<0.01$. There was no difference in inotrope score or maximum lactate level. Patients with AKI had lower UOP on day 1 and 2 [1.1ml/kg/hr vs. 2ml/kg/hr , $p<0.01$; 1ml/kg/hr vs. 2.2ml/kg/hr , $p<0.01$]. They also had higher UOP one day prior to discontinuing PD [1.1ml/kg/hr vs. 1.6ml/kg/hr , $p=0.02$] and higher potassium one day after (4mEq/dL vs. 3.6mEq/dL , $p=0.03$). Mortality, length of hospital stay and time to first successful extubation were not different for AKI vs. non AKI.

Conclusions: Patients receiving PD maintained a normal UOP while on PD. SCr decreased after discontinuation and UOP increased. Despite an important incidence of AKI with a lower UOP during the first 2 postoperative days, patients had similar fluid balances and there was no significant difference in clinical outcomes.

Nadendla, Kavita Devi (Kavita
Prior Research Experience: Yes
Source of Funding: Other

Project Length: Intermediate

Faculty Advisor: Dr. Colin Martin

Abstract Approved: Yes

Co-Authors: Michelle Shroyer, Linda Wilkinson, Dr. David Galloway, Dr. Reed Dimmitt, Dr. Colin Martin

Title: Predictors of Central Venous Line Infection Salvage in Patients with Intestinal Failure

Introduction

Life threatening central venous line (CVL) sepsis is a primary cause of mortality in patients with intestinal failure (IF). Current Infectious Diseases Society of America (IDSA) guidelines recommend CVL removal for bacteremia. However, many IF patients have limited venous access prompting initial attempts to salvage the line (non-removal of the CVL and antibiotic treatment). Here we describe predictors of line salvage at our institution.

Methods

The database for the Georgeson Center for Advanced Intestinal Rehabilitation (GCAIR) at the University of Alabama at Birmingham was queried from 2010-2015 to identify all patients with IF that were admitted for a CVL infection. Demographics and clinical parameters were compared among patients who underwent line removal to patients where the line was salvaged. Results were compared by a student's unpaired T test.

Results

Forty patients were identified with 125 admissions for CVL infections. Line removal occurred in 71 (56.8%) and 54 (43.8%) successfully had their lines salvaged. Episodes of fungemia were significantly less frequent among the salvaged group ($p < 0.0001$). Twelve patients were identified with 16 admissions for *E. coli* CVL infections. Line removal occurred in 11 (68.8%) and 5 (31.2%) successfully had their lines salvaged ($p < 0.05$). Ten patients were identified with 13 admissions for *Enterobacter* CVL infections. Line removal occurred in 10 (76.9%) and 3 (23.1%) successfully had their lines salvaged ($p < 0.05$). There was no difference in the number of salvaged or removed CVLs in patients with *Staph aureus* or *Pseudomonas* line infections.

Conclusion:

With the exception of cases of fungemia, line salvage of infected CVLs should be attempted in patients with IF when clinically possible. In our cohort, cases of *E. coli* and *Enterobacter* were less likely to be salvaged. General pediatric CVL infection guidelines should be modified for patients with IF with limited venous access to address line salvaging methods.

Neu, Matthew Benjamin (Matthew)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Greg Cooper

Abstract Approved: Yes

Co-Authors: Greg Cooper

Title: De novo variant analysis in whole genomes

Background/Introduction: *De novo* mutations are variations that occur in an individual's genome that are not inherited from either parent. In humans, they are a significant cause of genetic disease, and may be difficult to find in a patient without using an unbiased genomic approach. This difficulty is further compounded by sequencing error causing many false positive variants to appear *de novo*. This project seeks to study *de novo* variants in the context of Combined Annotation Depletion Dependent (CADD) scores, a recently developed algorithm that estimates relative pathogenicity using a combination metrics such as conservation and predicted protein effect.

Methods: Human whole genomes were sequenced from mother-father-child trios, and annotated using HudsonAlpha's genome annotation pipeline to determine *de novo* variants as well as all variations from the hg19 reference assembly. Python scripts were written to parse the resulting VCF (Variant Call Format) files for CADD score and variant type, and resulting plots and statistics were calculated using R in R Studio.

Results: Heterozygous *de novo* variants had a distribution skewed towards lower CADD scores when compared to all heterozygous variants in the same individual, and this was not fully corrected when variants found in repetitive regions were excluded. This is an unexpected result considering that most variants in a genome would be considered common and thus would correspond to a lower CADD score. More studies into the cause of this discrepancy may yield insight into the identification of *de novo* variants in whole genome sequences.

Olson, Kristin Marie (Kristin)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Christina Muzny

Abstract Approved: Yes

Co-Authors: Louis Boohaker; Erika L. Austin, PhD; Jane R. Schwebke, MD; Christina A. Muzny, MD

Title: Comparisons of Vaginal Flora Patterns among Sexual Risk Behaviors Groups of Women – Implications for the Pathogenesis of Bacterial Vaginosis

OBJECTIVE:

The pathogenesis of bacterial vaginosis (BV), the most common vaginal infection, remains controversial. Our primary objective was to compare the distribution of Nugent scores among African-American women who have sex with women (WSW) and women who have sex with women and men (WSWM) to an age/race-matched group of women who have sex with men (WSM). We hypothesized that there would be a significant difference in the number of women with BV based on Nugent score between sexual risk behavior groups, perhaps due to behavioral differences. Our secondary objective was to correlate low (7-8) vs. high (9-10) BV Nugent scores with vaginal symptomology among women with BV. We hypothesized that women with higher BV Nugent scores (9-10) may be more likely to have vaginal symptoms due to a larger proportion of strict anaerobes.

METHODS:

We performed a secondary analysis of clinical and laboratory data collected from African-American WSW (n=73) and WSWM (n=68) participating in a Women's Sexual Health Project at the Jefferson County Department of Health STD Clinic and a 3:1 age-matched group of African American WSM participating in a study of vaginal flora at the same clinic (n=423) using SAS, v9.2.

RESULTS:

WSW and WSWM were significantly more likely than WSM to have a diagnosis of BV based on Nugent score ($p < 0.001$). However, there was no significant difference in the distribution of BV Nugent scores among groups. In addition, there was no difference in vaginal symptomatology among women with low BV Nugent scores vs. those with high BV Nugent scores.

CONCLUSION:

Further analysis of sexual behavior data among sexual risk behavior groups of women is warranted to determine the impact of differing sexual behaviors on rates of BV. The finding of no significant difference in vaginal symptomatology among women with low vs. high BV Nugent scores requires further study.

Pacl, Hayden Thomas (Hayden)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Erik D. Roberson

Abstract Approved: Yes

Co-Authors: J. Nick Cochran, Ph.D., Erik D. Roberson, MD, Ph.D.

Title: Effects of the Alzheimer's Disease Risk Factor BIN1 on Amyloid Plaque Deposition in a Mouse Model of Alzheimer's Disease

Introduction: Bridging Integrator 1 (*BIN1*) is a newly-identified risk factor for Alzheimer's disease that is second only to *APOE* in significance. *BIN1* has been studied mostly in the heart, where it regulates calcium channels and excitability. However, its role in the brain has yet to be established.

Purpose: We hypothesized that *BIN1* plays a similar role in regulating excitability in the brain. As part of addressing this hypothesis, we asked if *BIN1* affected amyloid plaque deposition.

Methods: Using a Cre-loxP system, we created a conditional knockout of *BIN1* targeting excitatory neurons in mice. The brains were sectioned and stained using immunohistochemical techniques. Sections containing dorsal hippocampus were imaged at 10x magnification. The percentage of plaque area within the hippocampus was quantified in ImageJ.

Results: Amyloid plaque burden did not differ between Cre-positive mice [$n = 6$; $M \pm SEM = 0.96\% \pm 0.41\%$] and Cre-negative mice [$n = 6$; $M \pm SEM = 0.24\% \pm 0.07\%$; $t = 1.75$; $p > 0.10$]. Additionally, three mice in the Cre-negative group were two or more months older than the oldest mouse in the Cre positive group and had substantially greater plaque burden [$M \pm SEM = 1.71\% \pm 0.52\%$]. When these unmatched mice were excluded from the analysis, the average plaque burden of the Cre-negative mice [$n = 3$; $M \pm SEM = 0.22\% \pm 0.03\%$] suggested an even smaller difference ($t = 0.29$; $p > 0.75$).

Conclusion: This study found no overt differences between age-matched groups, and while preliminary, these results do not suggest a major effect of *BIN1* on amyloid plaque deposition. If confirmed in a larger dataset with older mice, this suggests that the role for *BIN1* in humans is not related to amyloid pathology, but perhaps to a disease mechanism that acts downstream.

Parker, Cameron Jamal (Cameron)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Sherry Collawn

Abstract Approved: Yes

Co-Authors: Dr. Sherry Collawn

Title: Effect of Conditioned Media on Adipose-Derived Stromal Cells in Wound Healing using 3-Dimensional Skin Organotypic Cultures

Wound healing involves an abundant number of factors that results in the production of a “closed” wound. Studies have shown an acceleration of wound healing in 3-dimensional and animal models with the addition of adipose-derived stromal cells (ADSC). The positive effect these cells have on wound healing has been through an unknown mechanism in 3-D cultures, but the use of conditioned media has shed some preliminary information on a possible mode of action. Prior research from my lab has shown an acceleration of re-epithelialization in their 3-D cultures of primary keratinocytes on a dermal equivalent containing fibroblasts and ADSC. We now can demonstrate that conditioned media from ADSC cultures produces a similar rate of healing without the addition of ADSC. With the use of mass spectrometry we have identified specific proteins that are involved in the healing process. Of note, a large amount of extracellular matrix proteins such as the collagens alpha-1(I, IV-VI) chains and fibronectin are produced. This information provides support for ADSC paracrine signaling as a major contributor for accelerated re-epithelialization in 3-D cultures. These paracrine signaling molecules have the potential to be used in a clinical setting for faster wound healing after medical procedures.

Patel, Bhavika Nitin (Bhavika)
Prior Research Experience: Yes
Source of Funding: T35
Faculty Advisor: MiYoung Kwon
Co-Authors: Rong Liu, MiYoung Kwon
Title: Assessing binocular function in glaucoma

Project Length: Short

Abstract Approved: Yes

Glaucoma is a leading cause of world blindness, characterized by progressive neurodegeneration of retinal ganglion cells and associated visual field defects.

While glaucoma often causes asymmetric visual impairment in each eye, little is known about binocular function in patients with glaucoma and its relationships with visual field impairment and daily visual function. In this study, we asked the following three questions: 1) whether there is binocular imbalance in patients with glaucoma; 2) whether the degree of binocular imbalance is associated with the degree of asymmetry in visual field loss between the two eyes; and 3) whether glaucomatous visual field affects reading performance, one of the most common daily visual activities.

To address these questions, various aspects of binocular function such as interocular acuity difference, stereoacuity, dichoptic letter chart (which quantifies interocular suppression), and interocular difference in visual field index (obtained from the Humphrey visual field analyzer) and reading speed were measured in 17 glaucoma patients and 10 age-matched normally-sighted individuals. We found that a majority of glaucoma patients showed poor stereoacuity and greater binocular imbalance, indicating poor binocular function compared to normal cohorts. More importantly, our results showed that poor binocular function was significantly associated with the degree of asymmetry in visual field loss between the two eyes ($r = 0.7$, $p = 0.002$). We also found reading speed in glaucoma patients was associated with severity of visual field impairment.

Our findings showed that despite normal visual acuity in glaucoma patients, binocular function in these patients is considerably impaired. Asymmetric glaucomatous visual field loss appears to play a key role in the observed abnormal binocular interactions. Our findings suggest the importance of characterizing binocular function in glaucoma patients for improving the management of glaucomatous vision.

Patel, Dhruv Prakash (Dhruv)
Prior Research Experience: Yes
Source of Funding: T35

Project Length: Short

Faculty Advisor: Christopher Pruitt

Abstract Approved: Yes

Co-Authors: John Thomas, Christopher Pruitt, Johanna Hall

Title: Child Life Services Lessens the Emotional Response of Children During Laceration Repair in the Emergency Department.

Background: In the past few decades, the utilization of Child Life Specialists (CLS) has steadily increased in many arenas of pediatric medicine. By using age-appropriate education, preparation, and supportive activities, CLS help children cope with potentially stressful clinical situations.

Objectives: The goal of the study was to evaluate the impact of CLS on the emotional response of children undergoing laceration repair in the emergency department.

Methods: Patients 4-12 years of age who required suture laceration repair were prospectively enrolled (via convenience sampling) in the Children's of Alabama Emergency Department. CLS availability is varied in our center, allowing for *a priori* categorization of subjects into 2 comparison groups – those with and those without CLS involvement during the procedure. The Children's Emotional Manifestation Scale (CEMS), a previously validated, Likert-like tool, was used to quantify the patients' emotional responses; a higher score reflects a more anxious child. Scales were completed (just prior to placement of the first suture) by trained, unblinded observers. Subjects were excluded if they required sedation or restraint with a board ("papoose"). Age, gender, ethnicity, type of anesthetic or pain control, and length and location of laceration were recorded. Data are presented as medians and interquartile ranges. CEMS scores were compared with a 2-tailed Mann-Whitney U test, with a $P < 0.05$ considered statistically significant.

Results: To date there are 140 patients enrolled in the study. One patient was excluded for being outside the predefined age range. There were 75 children with CLS during laceration repair and 64 without CLS. These groups did not differ in regards to age, gender, or ethnicity. Median CEMS score for patients with CLS present was 7 (6-9) versus 10 (8-13.5) for those without CLS ($P < 0.0005$).

Conclusions: CLS help lower a child's emotional response just prior to laceration repair in the emergency department

Patel, Fenil (Fenil)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Melanie Morris

Abstract Approved: Yes

Co-Authors: Allison Gullick MSPH, Aerin DeRussy MPH, Daniel I. Chu MD, Jayleen Grams MD, Melanie S. Morris MD

Title: Post-Operative Outcomes Following Elective Colorectal Surgery in the Obese Population

Background: Obesity remains a growing epidemic in the United States. Studies have suggested that obesity may worsen post-operative outcomes such as surgical site infection (SSI), but many of these studies categorized patients only as obese or non-obese. By further stratifying the obese population, we aim to investigate the role of obesity classes in determining post-operative outcomes for patients undergoing elective colorectal surgery.

Methods: Patients who underwent elective colorectal surgery were queried from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) 2011-2013 cohort and stratified by body mass index category into underweight ($<18.5 \text{ kg/m}^2$), normal weight ($18.5\text{-}24.9 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$), and class I ($30\text{-}34.9 \text{ kg/m}^2$), II ($35\text{-}39.9 \text{ kg/m}^2$), and III ($>40 \text{ kg/m}^2$) obesity. Univariate and bivariate comparisons were made with Chi-square and Wilcoxon Rank Sums tests to determine differences among categorical and continuous variables, respectively. Logistic regression analyses identified risk factors for 30-day mortality, 30-day readmission, and wound infection (SSI – defined as superficial SSI, deep incisional SSI, and wound disruption, but does not include organ space infection).

Results: Of 74,891 patients who underwent elective colorectal surgery, 3,265 (4.4%) were underweight, 21,685 (29%) normal weight, 24,705 (33%) overweight, 14,797 (19.8%) class I obesity, 6,324 (8.4%) class II obesity, and 4,115 (5.5%) class III obesity. Comorbidities included non-insulin-dependent diabetes (10%), smoking (17.5%), and hypertension (49.2%). Surgical site infection (SSI) rates in the overall cohort were 8.7% and ranged from the highest in class III obesity to the lowest in normal weight patients (15% vs. 6.5%, $p<0.001$). Fully adjusted modelling showed an increased risk of post-operative SSI with increased obesity class: Overweight (OR 1.34, CI 1.24-1.44), Class I (OR 1.68, CI 1.55-1.82), Class II (OR 2.32 CI 2.10-2.55), and Class III (OR 2.56 CI 2.20-2.74). Underweight patients were at increased risk of 30-day mortality (OR 1.34 CI 1.01-1.79), but obesity did not predict mortality. No weight categories were associated with an increased risk of readmission.

Conclusions: Obesity has a dose dependent association with SSI following elective colorectal surgery, but is not associated with readmission or 30-day mortality. BMI may account for some of the variation in post-operative outcomes such as SSI. In order to improve post-operative outcomes, pre-habilitation including supervised weight loss may play an important role prior to elective surgery.

Patel, Fenil (Fenil)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Daniel Chu

Abstract Approved: Yes

Co-Authors: Matthew D. Giglia MD, Allison Gullick MSPH, Melanie S. Morris MD, Benjamin J. Pearce MD, Daniel I. Chu MD

Title: Racial Disparities in Length of Stay Among Patients Undergoing Lower Extremity Revascularization

Background: Racial disparities in surgical outcomes, such as readmissions, have been demonstrated in minority populations. Few studies have examined disparities in length-of-stay (LOS) for vascular procedures. We aim to investigate the role of race in determining LOS for patients undergoing lower extremity revascularization (LER) using a national, surgical outcomes registry.

Methods: We queried the 2012-2013 American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) to identify all patients who underwent elective LER and stratified patients by approach (open versus endovascular) and race. Patients were excluded if they had any in-hospital, post-operative complications during their index admission or a 30-day mortality. Chi-square and Wilcoxon Rank Sums tests were used to determine the differences among categorical and continuous variables, respectively. The primary model outcome was total post-operative LOS. Predictors of LOS were identified with multivariate regression using a negative binomial model.

Results: Of 6,843 patients who underwent lower extremity revascularization, 76.2% and 23.8% of patients underwent an open or endovascular approach, respectively. Black patients represented 16.3% of the overall cohort, with women representing 47.5% and 34.3% of black and white patients, respectively. Black and white patients were similar with respect to BMI (27.4 vs. 27.3), ASA class distribution, and functional health. Compared to white patients, black patients were younger (65 vs. 74 years, $p < 0.05$) and had significantly higher rates of smoking, hypertension, dialysis, insulin-dependent diabetes, and steroid use ($p < 0.05$). On adjusted comparison, black patients who underwent an open LER experienced a longer post-operative LOS (4 vs. 3 days, $p < 0.001$) compared to white patients. With an endovascular approach, no significant difference in LOS existed between races (1 vs. 1 day, $p > 0.05$).

Conclusions: Black patients undergoing open LER have a significantly longer LOS in comparison to white patients even with no in-hospital complications. No racial disparities in LOS were observed for patients undergoing LER by endovascular approach. Further investigations will need to examine non-NSQIP elements such as psychosocial, behavioral, and educational factors that may explain disparities in open LER.

Patterson, Kelsey Claire (Kelsey)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Michelle Olsen

Abstract Approved: Yes

Co-Authors: Kara Arps, Michelle Olsen

Title: Motor and Behavioral Pheotypes in a Novel Rat Model of Rett Syndrome

Background: Rett Syndrome is an x-linked neurodevelopmental disorder caused by mutations in the transcriptional regulator MeCP2, affecting approximately 1/10,000 girls annually. Historically, researchers have utilized transgenic mouse models in the study of this disease. Recently, Sage® Labs made available a functional knockout rat model of Rett Syndrome that contains a 74 base pair deletion in exon 4 of the MECP2 gene. Here, we developmentally track changes in growth as well as motor and behavioral deficits of male and female rats in order to address the utility of this novel model in the study of Rett Syndrome.

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

Results: When compared to wildtype controls, MeCP2 heterozygous females display differences in brain weight, locomotor activity, and motor coordination as early as postnatal day (DPN) 21, and increases in body weight are observable by 6 months. MeCP2 null males demonstrate decreased brain weight by DPN 14 and are noticeably symptomatic as early as DPN 21, displaying lethargy, hindlimb claspings, an unkempt appearance, locomotor and motor coordination deficits, and breathing abnormalities. Malocclusion develops in the majority of MeCP2 null males by ~DPN 35, and body weights do not differ between MeCP2 null and wildtype males after the 4th postnatal week when animals affected by malocclusion are excluded from analysis.

Conclusions: This Sage® Labs knockout rat model recapitulates many hallmark features observed in existing mouse models of, as well as human patients with, Rett Syndrome, and offers a novel and valuable addition to the arsenal of resources available for the study of this disease.

Paulsen, Jesseca Alexandra (Alex)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Laura Q. Rogers, M.D., M.P.H.

Abstract Approved: Yes

Co-Authors: Travis Ptacek, Ph.D., Ranjit Kumar, Ph.D., Elliot J. Lefkowitz, Ph.D., Nianjun Liu, Ph.D., LaKeshia Hyndman, B.S., Casey Morrow, Ph.D., Laura Q. Rogers, M.D., M.P.H.

Title: Associations between changes in gut microbiota composition and psychosocial outcomes in breast cancer survivors participating in a randomized controlled physical activity trial

Breast cancer survivors (BCS) are often plagued by anxiety, fatigue, and/or sleep disturbances years after completing treatment. Physical activity has been shown to improve these psychosocial outcomes, but the mechanisms underlying these improvements remain unclear. One possible and understudied mechanism involves changes in the gut microbiome composition. Exercise has been associated with alterations in the composition of the gut microbiota, and the microbiota composition has been tentatively linked with anxiety and stress response behaviors in animals and humans. However, these effects have not been studied in BCS. The present pilot study sought to investigate associations between changes in the composition of the gut microbiota and improvements in anxiety, fatigue, and sleep quality in 12 BCS participating in a three-month randomized controlled physical activity trial. Fecal samples were collected at baseline (Month 0) and immediately following the intervention (Month 3). Fecal DNA was isolated and the V4 region of the 16S rRNA gene was amplified using PCR and analyzed using Illumina MiSeq DNA sequencing. QIIME software was used for statistical analysis of microbiome sequencing results. Principal Coordinate Analysis (PCoA) revealed statistically significant associations between the gut microbiome and the quartile of magnitude change in anxiety ($p = 0.017$), fatigue ($p = 0.01$), and cardiorespiratory fitness ($p = 0.023$). Additionally, a trend was noted between the association of the gut microbiota and changes in global sleep dysfunction (PSQI) ($p = 0.056$). These promising results suggest a possible connection between physical activity-induced changes in the composition of the gut microbiota and improvements in anxiety, fatigue, and cardiorespiratory fitness in BCS. Additional studies on a larger scale are indicated to investigate whether direct modification of the gut microbiota can be used to improve psychosocial outcomes in BCS.

- Source of funding = The following are acknowledged for their support of the Microbiome Resource at the University of Alabama at Birmingham: School of Medicine, Comprehensive Cancer Center (P30AR050948), Center for AIDS Research (5P30AI027767), Center for Clinical Translational Science (UL1TR000165) and Heflin Center.
- We also acknowledge the following funding sources: R25CA76023 (CaRES) & R01CA136859 & U01CA136859-05S1.

Payne, Alaina Mobley (Alaina)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Nileshkumar Chaudhari, MD

Abstract Approved: Yes

Co-Authors: Erin Fynan, MD

Title: Patient outcomes after a protocol of preliminary external fixation and staged conversion in distal radius fractures

Purpose: Distal radius fractures are among the most common types of fractures. Standard of care includes several types of treatment based upon patient and fracture characteristics, including splinting, external fixation, and open reduction internal fixation. In some settings, particularly with open fractures where the bone has been exposed through the skin, the patient is placed in a temporary external fixator for a few days or up to several weeks before conversion to open reduction internal fixation. This practice may have increased risk of post-operative stiffness and of infection as compared to primary open reduction internal fixation. This protocol proposes a retrospective cohort study to evaluate rates of infection and post-operative outcomes of distal radius fractures treated with various protocols.

Background: Distal radius fractures are common fractures. At a Level I Trauma Center, the care of these patients often involves multiple surgeons, particularly when open fractures dictate immediate intervention. An external fixator is sometimes used as a temporizing measure to maintain length and alignment until definitive open reduction internal fixation can be performed. However, several instances of infection have been noted at this institution in patients who underwent preliminary external fixation prior to open reduction internal fixation.

Few prior studies have examined the practice of preliminary external fixation. Glueck et al (2009) used this protocol in 6 of their 42 patients with open distal radius fractures and reported no infections. Kurylo et al (2011) used this protocol in 5 of their 32 patients with open distal radius fractures and noted no infections but an increased rate of other complications requiring secondary surgical procedures. An observation of an increased rate of infection with this protocol would be a novel contribution to the literature and would guide future treatment of distal radius fractures.

Screening and Selection: We anticipate finding records of approximately 600 patients who were treated for distal radius fractures at UAB during the selected time period.

Payne, Alaina Mobley (Alaina)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: William Coleman, MD

Abstract Approved: Yes

Co-Authors: none

Title: An analytical study of the Alabama Rural Physicians Tax Credit Law

The purpose of this study is to take an analytical look at the criteria, geographical area, hospitals, and recipients of the Alabama Rural Physicians Tax Credit Law. We will obtain information from the Alabama Department of Revenue, National Center for Educational Statistics, the U.S. Census Bureau, the Office of Management and Budget, and the Economic Research Service of the U.S. Department of Agriculture, as well as other resources. We aim to revise the tax credit law in order to better serve the rural populations of Alabama and provide more satisfactory credits to rural primary care physicians in order to serve the health needs of rural Alabama.

Pearlman, Ross Lane (Ross)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Farrukh Afaq

Abstract Approved: Yes

Co-Authors: Harish Chandra Pal, Farrukh Afaq

Title: Plumbagin Reduces Proliferation and Induces Apoptosis in Melanoma Cells by Inhibiting PI3K/AKT Signaling

Background: Melanoma is the deadliest form of skin cancer due to its tendency to aggressively metastasize. Despite advances in therapy options, the five-year survival rate for metastatic melanoma has not significantly improved. Exploration of novel therapeutic agents remains critical to the fight against melanoma progression. Recently, interest in phytochemicals as potential adjuvant or chemoprotective agents has risen. Plumbagin is a phytochemical found in flowers and roots of the family *Plumbaginaceae* that has been shown to exhibit anti-proliferative and anti-tumorigenic properties but has not been studied extensively in melanoma. In this study, we aimed to determine the effect of plumbagin on melanoma cell proliferation and apoptosis in cells from different genetic backgrounds.

Methods: The effects of plumbagin on melanoma cell proliferation were determined using MTT and colony assays, and effects on cell morphology were evaluated using phase contrast microscopy. Melanoma cell apoptosis, cell cycle, and mitochondrial membrane potential were analyzed after treatment using flow cytometry. Western blotting was used to evaluate PI3K/AKT signaling.

Results: Treatment of BRAF-mutated (A375, SK-MEL-28, WM35, RPMI-7951), NRAS-mutated (SK-MEL-119), and BRAF/NRAS wild type (Hs294T) melanoma cells with plumbagin resulted in dose-dependent (i) reduction of cell proliferation, (ii) repression of motile morphology, and (iii) induction of apoptosis. Furthermore, treatment of melanoma cells with plumbagin decreased the proportion of cells in G1 phase, indicating cell death at G2/M phase. Plumbagin treatment reduced cell mitochondrial membrane potential, and addition of N-acetyl-L-cysteine inhibited the apoptotic effects of plumbagin. Expression of PI3K and phosphorylation of AKT were decreased by plumbagin treatment.

Conclusions: We conclude that plumbagin reduces proliferation, induces apoptosis, and inhibits PI3K/AKT signaling in melanoma. Our data suggest that plumbagin is a good candidate for in-depth future studies as a potential adjuvant melanoma therapy and further studies are being conducted to elucidate its mechanism of action.

Pelham, James Heath (Heath)
Prior Research Experience: Yes
Source of Funding: Cunningham Fellowship
Faculty Advisor: Ambika Ashraf
Co-Authors: Lynae J Hanks, Ambika P Ashraf
Title: Analysis of Dyslipidemia in Children with Type 2 Diabetes Mellitus

Project Length: Intermediate

Abstract Approved: Yes

Background: Patients with Type 2 Diabetes Mellitus (T2DM) are at high risk for cardiovascular disease (CVD) and CV mortality. Dyslipidemia is commonly noted in T2DM patients, which is associated with increased risk of atherosclerosis. Low-density lipoprotein (LDL) is commonly assessed to identify patients at-risk for CVD. Although LDL is a therapeutic target risk marker, other non-high-density (Non-HDL), apolipoprotein B100 (apoB)-containing lipoproteins play a role in the progression of atherogenic dyslipidemia common with T2DM. Predicting CV risk, particularly in the pediatric population, is of great importance for early identification and intervention.

Objective: The primary objective of this study was to analyze the type and nature of lipoprotein abnormalities prevalent in children with T2DM and to identify determinants of adverse lipoprotein profiles. We also evaluated whether LDL was comparable to Non-HDL as a risk marker in children with T2DM.

Methods: This is a cross sectional retrospective chart review of children with T2DM who underwent standard (n=121) and/or vertical autoprofile (VAP)-derived lipid profile analysis (n=93) within the last 10 years. Statistical analysis was conducted controlling for BMI, A1C and duration of T2DM, as well as stratifying by A1C.

Results: The participants (mean age 14 ± 3 y) were 31% male, 77% African American (AA) and 23% European American (EA). AA were heavier than EA (97.7kg vs. 88.3kg, $P=0.03$) and had higher HDL (44.7 vs. 36.6mg/dL, $P<0.0001$). Males were heavier (102.1 vs. 92.7kg, $P=0.02$), had higher systolic blood pressure (128.0 vs. 121.5mm Hg, $P=0.01$), and lower HDL (40.5 vs. 43.9 mg/dl, $P=0.06$). ApoB100 was positively ($r=0.21$, $P=0.04$) and HDL-2 and HDL-3 were negatively (each $r=-0.3$, $P<0.05$) associated with BMI, even after adjusting for A1C and duration of diabetes. A1C was significantly associated with apoB100 ($r=0.4$, $P<0.0001$), non-HDL ($r=0.4$, $P<0.0001$) and LDL pattern B ($r=0.5$, $P<0.0001$). Patients with an HbA1C $>7\%$ had a higher total cholesterol (4.0 vs. 4.7mg/dL, $P=0.002$), LDL (97.3 vs. 115.3mg/dL, $P=0.001$), apoB100 (80.7 vs. 96.4mg/dL, $P=0.005$), non-HDL (119.9 vs. 142.8, $P=0.0001$), and frequency of LDL pattern B (23 vs. 16, $P=0.01$). When LDL was >130 mg/dl, non-HDL was >160 mg/dl in 96% of the participants.

Discussion: Assessment of elevated LDL was sufficient to detect dyslipidemia in most of the participants and may be a good indicator for assessing T2DM adolescents at-risk for CV morbidity and mortality. HbA1C and BMI were associated with adverse lipoprotein outcomes. Elevated HbA1C indicates adverse lipid profiles, representing a need for strict glycemic control in CV risk reduction.

Pepin, Mark Emile (Mark)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Adam Wende

Abstract Approved: Yes

Co-Authors:

Title: The Diabetic Heart: GABA signaling and Heart Failure.

Diabetes Mellitus has become a subject of increasing interest as its worldwide prevalence continues to grow. Of critical importance is the effect of chronically elevated plasma glucose and fatty acid concentrations on the substrate utilization flexibility of various organ tissues, particularly in cardiac muscle. Hyperglycemia has been shown to increase glycosylation, specifically through β -GlcNAcylation, of several key mitochondrial enzymes involved in glucose oxidative phosphorylation, thereby decreasing their activity (Hu 2009). In the current study, an inducible cardiac-specific GLUT4 overexpression mouse model is used to identify glucose-regulated pathways with and without the presence of diabetes. We are using systems-biologic approaches to demonstrate cellular regulation at both the level of altered gene expression associated with DNA of genes for key enzymes involved in glucose metabolism and the functional sequelae of these epigenetic alternations. Of future interest is determining whether these changes confer protection to cardiac myocytes, or whether these changes in gene expression are a maladaptive extension of the hyperglycemic disease.

Phillips, Caroline Evers (Caroline)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Mark Tafazoli

Abstract Approved: Yes

Co-Authors: Mark Tafazoli

Title: CT-determined Airway Size and Severity of Obstructive Sleep Apnea

Objective: Male gender, obesity, advancing age, and upper airway soft tissue abnormalities have been shown to be the most significant risk factors of obstructive sleep apnea (OSA). Clinical suspicion suggests airway size also affects OSA severity. The objective of this study was to determine the relationship between minimum airway size, as determined by CT scan, and OSA severity.

Methods: Approximately 90 patients undergoing OSA workup were identified in our patient database. Criteria for selection included a clinical suspicion of OSA, completion of polysomnographic study, completion of continuous positive airway pressure (CPAP) titration, and an upper airway CT evaluation. The patient population was limited by the low number of patients who completed an upper airway CT evaluation. Demographics, airway size, apnea severity, and required treatment regimen were collected on each patient.

Anticipated Results: Based on clinical suspicion, we predict that a smaller airway size will increase OSA severity. However, the significance of the airway size in OSA severity is unknown: other risk factors may mask the significance of airway size. Additionally, airway size could be more or less clinically significant depending on the level of OSA severity.

Anticipated Conclusions: Pending results.

Pope, Brandon Jay (Brandon)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. ETTY Benveniste

Abstract Approved: Yes

Co-Authors: Gibson, S., Qin, H.

Title: The Role of Protein Kinase CK2 in the Function of Th17 Cell Polarization and EAE.

Protein kinase CK2 regulates the activity of multiple pathways within a variety of cell types, having been studied for its role in solid and hematologic cancers. It is a serine/threonine kinase that is composed of a combination of CK2 α , CK2 α' , and CK2 β . CK2 α and CK2 α' are the catalytic subunits within the fully functioning tetrameric protein, whereas CK2 β plays a distinct regulatory role. As a regulator of JAK/STAT, NF- κ B, and PI3K/Akt/mTOR activity, CK2 promotes cell growth and apoptosis signals based upon its context, localization, and cell type.

CD4⁺ T cells are immune cells that are derived from lymphoid cells that come from the hematopoietic lineage. Th17 CD4⁺ T cells are pathogenic in many autoimmune disorders, whereas T regulatory CD4⁺ cells are suppressors of inflammation in disease. T cells require activation via their T cell receptor (TCR) and from antigen presenting cells (APCs) to facilitate an immune response. When activated, CD4⁺ T cells upregulate gene programs that lead to immune cell proliferation and differentiation, based upon the signals they receive. CD4⁺ T cells use CK2 sensitive JAK/STAT, NF- κ B, and PI3K/Akt/mTOR pathways to upregulate many of the aforementioned gene programs.

Our goal is to understand how CK2 functions in T cells and how the absence of CK2 can potentially impact T-cell driven autoimmune disease. Our hypothesis is that CK2 is active in CD4⁺ T cells and that it functions to promote inflammatory CD4⁺ T cell responses, therefore it can be a useful target in context of multiple sclerosis. Multiple sclerosis is a disease where various activated immune cells cause inflammation and damage to myelin within the brain. Using a pharmacological inhibitor of CK2, CX-4945, we hope to better elucidate the mechanisms by which CK2 homeostasis becomes perturbed and the consequences that this plays in the context of autoreactive CD4⁺ T cells in multiple sclerosis.

Prince, Andrew Carvel (Andrew)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Jason Warram

Abstract Approved: Yes

Co-Authors: Moore LS, Kasten BB, Tushar R, Walsh EM, Rosenthal EL, Warram JM

Title: Dual-Modality Approach to Improving Surgical Intervention in Head and Neck Cancer Using ^{89}Zr and IRDye800 Labeled Panitumumab

The incidence of post-operative positive margins in head and neck squamous cell carcinoma (HNSCC) approaches 40%. To improve this, we hypothesize that a multi-modality approach to surgical treatment using both radionuclide and fluorescently labeled Panitumumab (Pan) can improve rates of complete resection. In a murine flank model of HNSCC (n=10), 100 μCi of Pan- ^{89}Zr was injected. Over 5d, daily static microPET/CT imaging identified EGFR+ tumor cells in all mice at each time point. On day5, an *ex vivo* whole-body biodistribution was performed (20 tissues/mouse). Tissue counts confirmed specific Pan tumor localization (13.9% injection dose per gram, ID/g) compared to liver 11.1%ID/g and blood 5.9%ID/g. In a second bioluminescence (BLI) tumor model, Pan- ^{89}Zr (100 μCi) and Pan-IRDye800 were injected simultaneously. Five days post injection, microPET imaging was used to localize tumor (n=10). Tumors were then resected using fluorescence imaging (FLI), open-field (LUNA) and closed-field (Pearl). Using bioluminescence as the gold standard for tumor localization, FLI successfully correlated with BLI. Quantitative analysis of FLI images revealed tumor to background ratios (TBR) of, 4.7 (LUNA) and 4.3 (Pearl). Using FLI-guidance, complete resection was accomplished in all tumors as determined by BLI. Using a partial resection technique, residual disease was mimicked by placing a resected tumor fragment in the post-resection, closed wound bed. Forty-eight hours post, mice were reimaged with microPET and as little as 2.5mg of tumor fragment was identified with a TBR of 2.9 (LUNA), demonstrating the post-operative utility of Pan- ^{89}Zr to evaluate resection success. Lastly, in an orthotopic mouse model of HNSCC (n=10), microPET and FLI imaging of Pan- ^{89}Zr and Pan-IRDye800 were successfully used to identify cervical neck metastases, confirmed by BLI, with a TBR of 4.1 (LUNA). These results demonstrate the synergy of multiple image modalities in improving surgical outcomes.

Pritchett, Marshall Cleveland, III (Marshall)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Andrea Cherrington

Abstract Approved: Yes

Co-Authors: Robert Oster, PhD; Monika M. Safford, MD; April A. Agne, MPH; Andrea L. Cherrington, MD MPH

Title: Is Social Support Associated with Diabetes Distress and Glycemic Control in African Americans with Type 2 Diabetes?

Intro

African Americans suffer disproportionately from type 2 diabetes (T2D) and its complications. Stress associated with the burden of diabetes (diabetes distress) has been associated with worse diabetes control. We examined the relationship between diabetes distress, social support, and glycemic control in a sample of low-income African Americans with T2D in the context of a pilot randomized trial of education with and without a community health worker.

Methods

A 120 low-income African American adults (age \geq 19) with T2D living in a southern county were enrolled in the trial. Participants were recruited from a local safety-net health system and were included if they had poor glycemic control (HbA1c \geq 7.5%), no history of end-stage medical conditions, and were not pregnant. HbA1c was assessed at baseline and at 6 months. Diabetes distress and perceived support from the health care team and from family and friends were assessed at baseline and at 6 months using validated instruments. Follow-up data were available for 97 participants (81%). The paired t-test was used to assess the change from baseline to 6 months. Linear regression analyses tested for bivariate associations between the change in diabetes distress, glycemic control, support from health care providers (HCP), and support from family and friends. Linear regression analysis also tested whether perceived support mediated the relationship between diabetes distress and glycemic control.

Results

The study sample had a mean age 55years (SD=8.3, range 31-74), the mean HbA1c was 10% (SD=1.7%, range=7.5-13), and 57 (59%) were insulin users. At 6 months, HbA1c was reduced by 0.6 (p=0.003), diabetes distress was reduced by 0.4 (p<0.001), perceived support from HCP increased by 0.2 (p=0.065), satisfaction with support from HCP increased by 0.4 (p=0.004), and support from friends and family increased by 0.3 (p=0.004). Change in HbA1c was positively associated with change in diabetes distress (p=0.009), which was inversely associated with social support from family/friends (p=0.051), but was not associated with perceived support from HCP (p=0.55) or satisfaction with support from HCP (p=0.92). Neither support from HCP nor support from friends and family were significantly associated with change in HbA1c. In the final mediation model, perceived support did not significantly mediate the relationship between diabetes distress and change in glycemic control.

Conclusion

While we observed no mediation of social support on the relationship between diabetes distress and glycemic control in this small study, we observed that social support from family/friends was associated with less diabetes distress. These relationships should be examined in a larger sample and in randomized studies of interventions designed to improve social support.

Pynes, Malissa Lynne (Malissa)
Prior Research Experience: Yes
Source of Funding: T35

Project Length: Short

Faculty Advisor: Jessica Merlin MD MBA

Abstract Approved: Yes

Co-Authors: Jessica S. Merlin MD MBA, Courtney P. Williams MPH, Catherine McCarty, Christine Ritchie MD MSPH, Judith Paice PhD, Elizabeth Kvale MD

Title: Chronic pain in the ambulatory palliative care setting: a distinct entity from acute pain?

Original Research Background: Acute pain is common in ambulatory palliative care (APC) and includes pain related to the progression of serious illnesses and at the end-of-life. Chronic pain is defined as pain lasting > 3 months--beyond the period of normal tissue healing. It has a unique pathophysiology and negatively impacts health outcomes. Acute pain management typically involves opioids, whereas treatment of chronic pain often limits opioids and focuses on physical therapy, treatment of comorbid mood disorders, and pain self-management/coping. Distinguishing these groups is important clinically. Objective: To characterize individuals with acute and chronic pain in APC. Methods: Clinical surveillance data from 165 consecutive consenting APC patients between 7/18/2012-5/22/2015 was examined. Chronic pain was defined as average pain on the Brief Pain Inventory (BPI) $\geq 4/10$ at least twice > 3 months apart, acute pain as average pain $\geq 4/10$ only once, and depressive symptoms as PHQ-9 ≥ 10 . Multiple regression was used to investigate the cross-sectional relationship between pain category and outcomes (BPI pain interference and depressive symptoms). Results: Among 165 participants, mean age was 52 and 75% were female. Mean number of visits was 2.5. 35% had chronic pain and 51% had acute pain. Compared to individuals with no pain and after adjusting for age and sex, pain interference was 0.55 points higher on average for individuals with acute pain on a 0 to 10 scale, and 1.0 points higher for individuals with chronic pain ($p=0.03$ and 0.0003 respectively). Odds of depression were 3.7 times higher in acute pain and 4.0 times higher in chronic pain than in individuals without pain. Conclusion: Acute and chronic pain were common and associated with worse outcomes; chronic pain was more strongly associated with higher levels of pain interference and depression. Additional research is needed to understand differences between acute and chronic pain in this setting.

Ramaker, Ryne (Ryne)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Sara Cooper, Rick Myers

Abstract Approved: Yes

Co-Authors: Kevin M. Bowling, Brittany N. Lasseigne, Pritzker Neuropsychiatric Research

Consortium, Sara J. Cooper and Richard M. Myers

Title: Comparative transcriptomic and metabolomic profiling of psychiatric disorders across three brain regions

Neuropsychiatric disorders comprise 13% of the global burden of disease and account for a staggering 184 million disability-adjusted life years (DALYs) worldwide. Schizophrenia (SZ), bipolar disorder (BPD), and major depression disorder (MDD) are multigenic diseases with complex etiology that combine to account for over 50% of these mental health related DALYs. Furthermore, current therapies for these psychiatric disorders are not effective in many patients and may treat only a subset of an individual patient's symptoms. Approaches targeting the underlying molecular pathologies within and across these disorders are necessary to address the enormous psychiatric component of global disease burden. We performed gene expression profiling by RNA sequencing on dissected post-mortem tissues from the anterior cingulate cortex (AnCg), dorsolateral prefrontal cortex (DLPFC), and nucleus accumbens (nAcc) from four well-documented cohorts of 24 patients each with SZ, BPD, MDD and 24 matched controls (CTL). We also conducted untargeted metabolomic profiling via two-dimensional gas chromatography with mass spectrometry (2D-GCMS) in AnCg tissue from the same subjects across each disorder. The most significant gene expression signals were brain region-specific with the most robust disease differences seen in the AnCg of SZs compared to CTLs although more subtle changes were observed in the DLPFC and nACC. Our identification of overlapping RNA expression profiles between BPD and SZ suggest that a subset of patients with these disorders share a common molecular signature. Combined transcriptomic and metabolomic analyses provide evidence to further previous work demonstrating that dysregulated γ -aminobutyric acid (GABA) and glutamate metabolism are major drivers in a subset of SZ and BPD patients. Examination of transcripts previously associated with individual neuronal cell types indicates different cell populations are present between brain regions and disease groups. This study highlights the power of pairing transcriptomic and metabolomic profiling to better understand complex psychiatric disorders.

Raman, Fabio Suraj (Fabio) FABIOR@uab.edu

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Hassan Fathallah-Shaykh

Abstract Approved: Yes

Co-Authors: Elizabeth Scribner

Title: Unraveling Mechanisms and Treatment Options of Glioblastoma Multiforme Progression Patterns: A Computational Analysis

Background: Glioblastoma multiforme (GBM) is a highly invasive brain tumor with a median survival less than 15 months. Hypoxia-driven motility (HM) and concentration-driven motility (CM) are two mechanisms of GBM invasion in the brain. The use of anti-angiogenic drugs has uncovered new progression patterns of GBM associated with significant differences in overall survival times. We have recently reported a concise mathematical model that encompasses replication rates, the motility phenotypes, and angiogenesis. The purpose of this study is to elucidate the mechanisms behind the patterns of progression of GBM patients treated by anti-angiogenesis and to study the effects of rate- and motility-reducing agents on overall survival times.

Materials and Methods: We apply our model of GBM and design in silico clinical trials by varying the tumor size and necrosis at the start of treatment and death. The numerical methods use finite element schemes written in PETSc; the code was run on 200 processors of a supercomputer (Alabama Supercomputer Authority, Huntsville, AL). Matlab (Mathworks, v.R2015a, Natick, MA) was used for data analysis. Log-rank $p < 0.05$ is the cutoff for statistical significance.

Results: The findings link highly-dispersive tumors (high CM), moderately-dispersive tumors (moderate CM), and hypoxia-driven tumors (high HM and low CM) to the clinical phenotypes observed in GBM treated by anti-angiogenesis; these phenotypes generate progression by Expanding FLAIR, Expanding FLAIR + Necrosis, and Expanding Necrosis, respectively. Furthermore, rate-reducing strategies (e.g. cytotoxic agents and TTF fields) appear to be effective in highly-dispersive and moderately-dispersive tumors but not in hypoxia-driven tumors. The latter respond to motility-reducing agents. A population based clinical trial, including all three phenotypes, reveals a relationship between the efficacy of the rate-reducing agent and the prolongation of overall survival times.

Conclusion: Our results suggest hypotheses on GBM phenotypes and treatment options and highlight the potential of in silico clinical trials.

Ramesh, Tushar (Tushar)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Jason Warram

Abstract Approved: Yes

Co-Authors: L. Moore, S. Bevans, M. Limdi¹, E. Rosenthal, J. Warram

Title: Evaluation of optical imaging agents in a fluorescence-guided surgical model of head and neck cancer

Background

Tumor growth and metastasis often activates physiologic processes that lead to the pathologic upregulation of certain epithelial and vascular receptors. These receptors can effectively be targeted for applications in fluorescence-guided surgery. Here we demonstrate the use of three non-peptide smart probes in flank xenograft, orthotopic tongue, and lymph node metastatic disease models of head and neck cancer. A dose-escalation study was performed at three doses each of IntegriSense750, ProSense750EX, and ProSense750FAST in mice bearing luciferase positive SCC1 flank xenografts (n=5). Mice bearing orthotopic tongue (n=3) and lymph node (n=3) models received 2nmol of IntegriSense750.

Methods

Fluorescence imaging was performed twice daily following infusion using commercially available open-field (LUNA, Novadaq, Canada) and closed-field Near-infrared (NIR) systems (PEARL, LICOR, Lincoln, NE). NIR renderings of resected specimens were compared to bioluminescence images to confirm localization of probe to tumor. Progressively smaller tumor fragments were re-introduced into the wound bed to determine the smallest cancerous mass detectable. Exploratory surgeries were performed to demonstrate agent localization to orthotopic tumors and lymph node metastases with IntegriSense 750. Biodistribution studies were performed.

Results

Intraoperative imaging differentiated tumor from normal tissue with mean tumor-to-background ratios (TBRs) of 3.73, 5.35, and 9.62 on day 4 for the 1, 2, and 4nmol doses, respectively, of IntegriSense750. TBRs of ProSense750EX mice were 3.13, 2.38, and 3.65 for the 1, 2, and 4nmol doses respectively. TBRs of ProSense750FAST mice were 4.88, 3.94, and 3.00 for the 2, 4, and 6nmol doses, respectively. The smallest tumor fragment detectable ranged from 0.5mg to 5mg across optimal doses of each drug. All diseased lymph nodes (3/3) were fluorescently visible *in situ* in mice during exploratory surgeries. The 4nmol doses of IntegriSense750 and ProSense750EX and 2nmol dose of ProSense750FAST were determined to be the optimal doses.

Conclusion

All three agents appeared to be effective for applications in fluorescence-guided surgery.

Rana, Amaad Bashir (Amaad)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: James Willig, MD, MSPH

Abstract Approved: Yes

Co-Authors: Nicholas Van Wagoner, MD, MPH

Title: Kaizen-UME: Utilization patterns and educational outcomes of a software application to improve medical knowledge among medical students

Introduction:

While much effort has been directed toward improving learning methods for the preclinical years of medical school, the literature regarding improvement of medical student education in the clinical years is lacking. Given the recent resident work hour restrictions, the time spent in training hospitals has decreased, and as a consequence, so has the time for traditional medical student clerkship education. Also, the millennial generation of learners favor more active and self-directed learning approaches. Therefore, there is a need to explore novel strategies to supplement traditional medical education during the clinical years.

Objectives:

To determine the most commonly utilized learning tools and methods by medical students during their clinical clerkships; to characterize historical performance on IM shelf exams by UASOM students and identify opportunities for improvement; and to assess use and acceptance of a gamification based learning software among medical students as well as retention of medical knowledge by users of this software.

Methods:

We developed a survey for medical students at the University of Alabama School of Medicine (UASOM) who have completed their third-year clerkships to assess learning methods and tools utilized. We also designed and developed software using the principles of gamification to launch an online medical knowledge competition among medical students at the four branch campuses of UASOM. Students will participate both individually and on teams, and they will be accessing questions daily and tracking the online leaderboard from any internet-enabled device.

Results:

Currently collecting data.

Conclusions:

Ray, Christopher Austin (Christopher)

Project Length: Short

Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Jayme Locke, MD, MPH

Abstract Approved: Yes

Co-Authors: Rhiannon Reed, MPH; Brittany Shelton, MPH; Paul MacLennan, PhD

Title: Impact of Deceased Donor Allocation Changes on Outcomes among Pediatric Kidney Transplant Recipients

Introduction: In September 2005, the United Network for Organ Sharing (UNOS) modified the allocation criteria for deceased donor (DD) kidneys, prioritizing kidneys from donors younger than 35 years to pediatric waitlist candidates with the stated goals of reducing waiting times and improving outcomes among pediatric transplant recipients. To date, no study has examined the impact of this policy change.

Methods: We studied associations between pre and post policy change eras (2000-2005 vs. 2005- 2010) and outcomes in 4039 pediatric (<18 years) DD kidney transplant recipients using national registry data from the Scientific Registry of Transplant Recipients. Time on waitlist and time on pre-transplant dialysis were compared across eras using Wilcoxon tests. Risk of graft loss (death-censored) and patient death were examined using Cox proportional hazards modeling.

Results: There were significant decreases in both waiting time (median 142.4 days vs. 233.6 days, $p < .0001$) and dialysis time (median 372.3 vs. 456.3, $p < .0001$) during the post-change era compared to the pre-change era. There was no significant difference in risk of graft loss by era (aHR; 95%CI; $p = .88$), while the risk of death was significantly lower in the post-change era (aHR; 95%CI; $p = .0001$).

Discussion: This study suggests that shifts in donation patterns following the 2005 UNOS kidney allocation change did result in shorter waiting times and shorter duration of pre-transplant dialysis for pediatric recipients of DD kidneys. Moreover, and perhaps most importantly, the policy change was associated with improvements in patient survival.

Read, Connor Ray (Connor)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Glenn S. Fleisig, PhD

Abstract Approved: Yes

Co-Authors: Kyle T. Aune, MPH, Glenn S. Fleisig, PhD

Title: Outcomes Following Anterior Cruciate Ligament Reconstruction to Defensive Players in the National Football League

Anterior cruciate ligament (ACL) injuries to national football league (NFL) athletes occur frequently with maneuvers such as cutting, pivoting, jumping, collisions, changes in acceleration, player contact, and even celebrations. More often than not, ACL injuries result in season-ending ligament tears requiring ACL reconstruction (ACLR) followed by months of strenuous rehabilitation. The daunting road to recovery creates anxiety over patient health and performance, offering no guarantee of return to play and significant time away from sport. Career impact of ACLR to NFL defensive players has not been well studied. The purpose of this study was to quantify NFL defensive player performance before ACL injury and after ACLR. NFL defensive players having undergone ACLR from 2006-2012 were recorded. Demographic data for each player were recorded, as well as performance statistics for two years of play prior to injury, the injury year, and three years following injury. The defensive players with a history of ACLR were compared to a matched cohort of defensive control players based on position and similar years of NFL experience prior to injury. Overall, 31 of 40 defensive players (78%) returned to play at least one game. Tackles per game were reduced by 40% ($p=0.001$), with the largest decrease in defensive linemen (61%, $p=0.006$) and smallest decrease in linebackers (37%, $p=0.03$). Further, defensive backs were found to have a significant decrease in interceptions (64%, $p=0.004$) and passes defended (39%, $p=0.025$). This is the first study to quantify career impact data of ACLR to NFL defensive players. Briefly, more than three fourths of NFL defensive players returned to play, however, player performance was diminished by over one third.

Real, Kelsey Caitlin (Kelsey)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Department of Medicine Fellowship

Faculty Advisor: Kellie Flood

Abstract Approved: Yes

Co-Authors: E Simmons, A Viles, K Booth, M Robinson, W Gray, K Flood

Title: Implementing Virtual ACE on Two Orthopedic Surgery Units: A Feasibility Study

Background: Under-recognition of geriatric syndromes such as functional and cognitive impairment in hospitalized elders is common and contributes to adverse outcomes. The UAB Acute Care for Elders (ACE) Unit utilizes an interdisciplinary team to deliver geriatric care. This is only 1 of > 50 hospital units, compelling an intervention to scale ACE care to all units. We term this care delivery redesign the "Virtual ACE" Intervention.

Objectives: To assess the feasibility of implementing Virtual ACE care on non-ACE units

Methods: Prospective, quasi-experimental study on 2 orthopedic surgery units

Setting: 1,152 bed tertiary care academic hospital

Intervention: Four 1-hour in-person training modules were delivered to 1) hardwire the screening of hospitalized elders for performance of activities of daily living (ADLs) with the Katz Index and delirium using the Nursing Delirium Screening Scale (NUDESC), and 2) implement nurse-driven care protocols for safe mobility, pain management, and delirium

Main outcomes: 1) staff performance of Katz Index and NUDESC, 2) patient mobility, and 3) prevalence of delirium.

Results: In a random sample of chart audits, staff completion of screening both baseline and current ADLs improved post-training (42% to 58%; $p < .05$) The NUDESC was a new skill taught; staff completion was 0% pre-training, but 72% post-training ($p < .001$). In convenience sample of patients independent in ADLs at baseline, significantly more patients got out of bed to a chair (38% vs 67%, $p < .01$) and walked in the hall (14% vs 35%, $p = .04$) in the audited 24 hour period with Virtual ACE care. Delirium prevalence amongst all elders was significantly reduced (17% vs 5%, $p = .02$).

Conclusions: The Virtual ACE Intervention that includes hardwiring geriatric screens and protocols on non-ACE units is feasible and may improve patient mobility and reduce delirium prevalence. Further study is needed regarding impact on incident delirium.

Reddy, Alexander Terry (Alex)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Martin Young

Abstract Approved: Yes

Co-Authors: Lan He, David Sams, Martin Young

Title: Biotinylation: Novel Mechanism Linking the Cardiomyocyte Circadian Clock to Cardiac Metabolism

Recent studies suggest a role for the intrinsic cardiomyocyte circadian clock as a primary mediator of daily oscillations in cardiac metabolism. However, the mechanistic links between the cardiomyocyte clock and metabolism remain unknown. The goal of this project was to test the hypothesis that biotinylation serves as this mechanistic link.

At the center of the circadian clock mechanism are two critical transcription factors, named CLOCK and BMAL1. In an attempt to identify novel mechanistic links, an unbiased microarray approach was taken and revealed that the biotin transporter SMVT was decreased in both cardiomyocyte-specific CLOCK mutant (CCM) and cardiomyocyte-specific BMAL1 knockout (CBK) hearts. Biotin is an obligate cofactor for five mammalian carboxylases, including acetyl-CoA carboxylase β (ACC β) and methylcrotonyl CoA carboxylase (MCC). Importantly, biotinylation of all these carboxylases was found to be decreased in both CCM and CBK hearts.

ACC β and MCC play key roles in the fatty acid and leucine oxidation, respectively. In order to investigate whether decreased biotinylation of these carboxylases observed in CBK hearts impacts metabolic fluxes, hearts were isolated and perfused ex vivo (in the presence of radiolabeled tracers) from four groups of mice: 1) wildtypes fed control diet; 2) wildtypes fed biotin-supplemented diet; 3) CBKs fed control diet; and 4) CBKs fed biotin-supplemented diet.

Consistent with decreased ACC β and MCC biotinylation, CBK hearts exhibited increased fatty acid oxidation and decreased leucine oxidation, respectively. Importantly, biotin supplementation normalized both fatty acid and leucine oxidation in CBK hearts (without effect in wildtype hearts). Interestingly, these studies revealed increased protein synthesis in CBK hearts, which was again normalized by biotin supplementation.

In summary, these results are consistent with the original hypothesis and highlight the possibility biotin supplementation as a future therapeutic strategy for normalization of cardiac metabolism during periods of circadian clock disruption (e.g., shift work, jet lag).

Riley, William Logan (William)

Project Length: Short

Prior Research Experience: No

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Todd Peterson, MD

Abstract Approved: Yes

Co-Authors: Charles Khoury, MD; Walter Smith

Title: Medical Students as Diabetes Intervention Educators in the Emergency Department Setting

Intro –In recent decades, the international “health promoting hospitals movement” successfully integrated health education and health promotion into its health care culture. Although several medical disciplines have adopted a health promotion philosophy, U.S. Emergency Departments (ED) have been slower to incorporate these services. A large proportion of U.S. citizens visit EDs seeking routine health care, and it is accepted that many of these individuals lack adequate knowledge about diagnoses involving chronic disease conditions, such as diabetes. “Teaching hospitals” have the luxury of utilizing students to deliver health education services to under informed patients. In an effort to expand its health education services, the UAB-ED has developed a plan to train UAB medical students to perform brief health education interventions targeting patients with a diagnosis of diabetes.

Hypothesis – The majority of study participants lack adequate knowledge about their disease condition, including actions and behaviors to improve disease management and will achieve significant knowledge gains attributable to the brief educational intervention.

Methods – The methods involved included in-person pre- and post-tests with a brief educational intervention separating them. Eligible participants were identified by monitoring the UAB-ED’s patient tracking system for patients presenting with a previous diagnosis of diabetes. Pre- and post-test data was collected and test averages were analyzed to quantify improvement.

Results – Throughout the study period, 64 patients were enrolled. Patients, on average, increased their post-test score by 17.4%.

Conclusions – Through a brief educational intervention, patients showed significant knowledge gains, quantifiable by an increase in pre- to post-test averages. Patients were very eager to learn more about their diabetes and often had questions and concerns that had not been previously addressed by any medical professionals.

Rogers, Anna Joy Graves (Anna Joy)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Janet M. Turan

Abstract Approved: Yes

Co-Authors: Elly Weke, Zachary Kwena, Elizabeth A. Bukusi, Patrick Oyaró, Craig R. Cohen, and Janet M. Turan

Title: Barriers and enablers to repeat HIV testing during pregnancy in Kenya: A qualitative study

Background: Repeat HIV testing in late pregnancy has the potential to decrease rates of mother-to-child transmission of HIV by identifying mothers who seroconvert after having tested negative for HIV in early pregnancy. Despite being national policy in Kenya, the available data suggest that implementation rates are low.

Methods: We conducted 20 in-depth semi-structured interviews with healthcare providers and managers to explore barriers and enablers to implementation of repeat HIV testing guidelines for pregnant women. Participants were from the Nyanza region of Kenya and were purposively selected to provide variation in socio-demographics and job characteristics. Interview transcripts were coded and analyzed in Dedoose software using a thematic analysis approach. Four themes were identified a priori using Ferlie and Shortell's Framework for Change and additional themes were allowed to emerge from the data.

Results: Participants identified barriers and enablers at the client, provider, facility, and health system levels. Key barriers at the client level from the perspective of providers included late initial presentation to antenatal care and low proportions of women completing the recommended four antenatal visits. Barriers to offering repeat HIV testing for providers included heavy workloads, time limitations, and failing to remember to check for retest eligibility. At the facility level, inconsistent volume of clients and lack of space required for confidential HIV retesting were cited as barriers. Finally, at the health system level, there were challenges relating to the HIV test kit supply chain and the design of nationally standardized antenatal patient registers. Enablers to improving the implementation of repeat HIV testing included client dissemination of the benefits of antenatal care through word-of-mouth, provider cooperation and task shifting, and it was suggested that use of an electronic health record system could provide automatic reminders for retest eligibility.

Conclusions: This study highlights some important barriers to improving HIV retesting rates among pregnant women who attend antenatal clinics in the Nyanza region of Kenya at the client, provider, facility, and health system levels. To successfully implement Kenya's national repeat HIV testing guidelines during pregnancy, it is essential that these barriers be addressed and enablers capitalized on through a multi-faceted intervention program.

Sheets, Ryan Oliver (Ryan)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Winter Williams

Abstract Approved: Yes

Co-Authors: Dr. Winter Williams Title: Getting on the Bandwagon Improving Inpatient Code Status Identification

Getting on the Band-wagon – Improving Inpatient Code Status Identification

Ryan Sheets: rosheets@uab.edu, MS4, School of Medicine

Winter Williams: winterlw@uab.edu, Assistant Professor, Department of Medicine

Abstract:

There has been an increasing focus at the state and national level on improving and standardizing code status identification during inpatient stays. Several cases identified in local Morbidity and Mortality conferences and subsequent chart reviews at the Birmingham VA Medical Center highlighted flaws in the code status identification process, resulting in unnecessary resuscitation of “Do Not Resuscitate” (DNR) patients. We set out to better understand the local VA process of code status identification and use quality improvement principles to standardize and error-proof the process. A multi-pronged approach was pursued using numerous quality improvement methodologies to better understand the extent of the problem and inform solutions, including a review of local Systems Redesign data using all inpatient codes within the prior fiscal year, “Gemba walks” to discuss the DNR identification process, literature review, and serial spot checks of all inpatient records to evaluate for discordance between DNR orders, notes, and nursing unit identification of code status. Our initial data review confirmed the extent of the problem with several cases within the prior fiscal year of inpatient codes despite a pre-existing advanced directive or DNR order. Additionally, serial spot checks revealed discordance rates as high as 62% between orders, notes, and nursing documentation. Other lessons learned include that there is no use of on-patient code status identifiers as well as a high degree of variability between nursing unit processes. Based on the findings of this project, the VA leadership has approved a change to the local EMR to improve code status order visibility by creating a separate code status tab as well as routine application of standardized DNR wristbands to all patients identified as DNR. Both of these institution-wide changes are currently being implemented with plans for ongoing nurse and provider education on the process change.

Sherrod, Brandon Alan (Brandon)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Shawn R. Gilbert, MD

Abstract Approved: Yes

Co-Authors: Dustin K. Baker, BS and Shawn R. Gilbert, MD

Title: Incidence, Risk Factors, and Associated Complications of Blood Transfusion in Surgical Treatment of Developmental Dysplasia of the Hip

Background

Developmental dysplasia of the hip (DDH) is the most prevalent pediatric hip disorder and often requires surgical treatment. One complication of DDH surgery is perioperative bleeding requiring blood transfusion, which has been shown to increase risk of postoperative complications in pediatric trauma and spine surgery. No study has reviewed incidence of, risk factors for, and post-operative adverse events associated with transfusion in pediatric DDH surgery.

Methods

The American College of Surgeons (ACS) National Quality Improvement Program (NSQIP) Pediatric database was queried for patients under the age of 18 treated by an orthopaedic surgeon from 2012 to 2013. DDH cases were selected and categorized by Current Procedural Terminology (CPT) codes. Patients with neuromuscular (NM) diagnoses were filtered from the general DDH cohort and studied in a separate analysis. Univariate and multivariate regression analyses of transfusion association with procedure type, patient demographics, comorbidities, preoperative lab values, and 30-day complications were performed.

Results

A total of 1,184 DDH cases were included. In the non-NM disorder group (n=517), 105 patients (15.7%) received at least one transfusion compared to 161 patients (31.1%) in the NM disorder group (n=667). Independent risk factors for transfusion in the non-NM disorder group included American Society of Anesthesiologists (ASA) score ≥ 3 (OR=2.05, p=0.050), longer operative time (per hour increase, OR=1.93, p<0.001), and increased age (per year increase, OR=1.17, p<0.001), whereas risk factors in the NM disorder group included anemia (OR=17.61, p=0.015), cognitive developmental delay (OR=2.30, p=0.004), pulmonary comorbidity (OR=1.74, p=0.031), and longer operative time (per hour increase, OR=1.65, p<0.001). In both groups, transfusion was associated with increased risk of any adverse event (p<0.05).

Conclusion

We identified several independent risk factors for and adverse outcomes associated with transfusion in DDH surgery. The rate of transfusion in DDH surgery and its association with adverse outcomes warrants further study of appropriate guidelines for bleeding management.

Sherrod, Brandon Alan (Brandon)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Brandon G. Rocque, MD

Abstract Approved: Yes

Co-Authors: James M. Johnston, MD and Brandon G. Rocque, MD, MS

Title: Risk factors for unplanned readmission within 30 days after pediatric neurosurgery: a nationwide analysis of 9,799 procedures from ACS-NSQIP

Background: Readmission rate is increasingly used as a quality outcome measure after surgery. The purpose of this study is to establish baseline readmission rates and risk factors after pediatric neurosurgery using a national database.

Methods: The American College of Surgeons National Surgical Quality Improvement Program – Pediatric (ACS-NSQIP-Pediatric) database was queried for pediatric patients treated by a neurosurgeon from 2012-2013. Procedures were grouped into categories by CPT code. Patient demographics, comorbidities, preoperative laboratory values, and operative variables were analyzed via univariate and multivariate logistic regression to find associations with unplanned readmission within 30 days of the primary procedure.

Results: 9,799 cases met the inclusion criteria, 1,098 (11.2%) of which had an unplanned readmission within 30 days. The four procedures with the highest unplanned readmission rate were CSF shunt revision (17.3%), repair of myelomeningocele > 5 cm diameter (15.4%), creation of CSF shunt (14.1%), and craniectomy for excision of tumor (13.9%). Readmission risk was greatest in patients experiencing postoperative organ/space surgical site infection (SSI), wound disruption, and superficial SSI ($p < 0.001$ for each). Independent patient risk factors for unplanned readmission included Native American race (OR=2.228, $p=0.028$), chronic steroid use (OR=1.574, $p < 0.001$), oxygen support (OR=1.568, $p=0.016$), history of malignancy (OR=1.567, $p=0.002$), CNS comorbidity (OR=1.510, $p=0.025$), hypoalbuminemia (OR=1.452, $p=0.046$), nutritional support requirement (OR=1.385, $p=0.008$), seizure disorder (OR=1.267, $p=0.014$), American Society of Anesthesiologists score ≥ 3 (OR=1.185, $p=0.036$), emergent/urgent triage (OR=1.184, $p=0.043$), and longer operative time (per hour increase, OR=1.064, $p=0.014$).

Conclusion: This study may aid in identifying patients and procedures at risk for unplanned readmission following pediatric neurosurgery, potentially providing evidence to minimize patient risk and lower costs for health care systems.

Sherrod, Brandon Alan (Brandon)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Alan W. Eberhardt, PhD

Abstract Approved: Yes

Co-Authors: Dustin Dew, Rebecca Rogers, James Rimmer, Alan Eberhardt

Title: Design and validation of a new low cost, high-capacity weighing device for wheelchair users and bariatrics

Purpose: To design and validate a lighter, accessible, and low cost high-capacity weighing device for people who use wheelchairs or are unable to stand to record body weight.

Method: A prototype weighing device was designed and fabricated featuring a capacity of 360 kg, a wheelchair-accessible ramp, and wireless data transmission. Forty-five participants (n=45) had their weight measured using the prototype weighing device and a calibrated weighing device. Participants were divided into three groups by mobility: 20 standing, 20 manual wheelchair users, and 5 power wheelchair users. Participants completed a survey to assess perception of each weighing device.

Results: Weight measurements between devices demonstrated a strong linear correlation ($R^2 = 0.997$ overall). Absolute values of measurement differences were $1.4 \pm 2.0\%$ of the calibrated measurements. Participants rated the prototype device more favorably in the following categories: user friendliness, ease of access, safety, comfort/privacy, and device aesthetics. Preference ratings showed no difference between devices. The prototype weighs 38% less than the next lightest commercial device and has a commercial target price range estimated at \$500-600.

Conclusion: Identifying a new lower-cost weighing device for populations that have limited access to proper medical instrumentation is a positive step toward improving accessibility to medical care. Future work is needed to determine feasibility of transition to market and to improve prototype features.

Sherrod, Brandon Alan (Brandon

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Shawn R. Gilbert, MD

Abstract Approved: Yes

Co-Authors: Dustin K. Baker, BS, Gerald McGwin, PhD, Brent A. Ponce, MD, and Shawn R. Gilbert, MD

Title: Complications and 30-day Outcomes Associated with Venous Thromboembolism in the Pediatric Orthopaedic Surgical Population

Background: Venous thromboembolism (VTE) is a serious event with well-documented adverse outcomes in adults, yet its associations with adverse postoperative events in children remains unclear. To our knowledge, no study has examined adverse outcomes associated with VTE in pediatric orthopaedic surgery. The purpose of this study was to identify incidence of, risk factors for, and associated 30-day postoperative complications with VTE using a large national database.

Methods: The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) Pediatric database was queried for patients undergoing an orthopaedic surgical procedure from 2012 to 2013. Cases were divided into categories by procedure type using Current Procedural Terminology (CPT) codes. Upper extremity operations and skin/subcutaneous operations were excluded from analysis. Associations between VTE and procedure type, patient demographics, comorbidities, pre-operative laboratory values, and adverse postoperative outcomes were evaluated.

Results: A total of 14,776 cases were included. Fifteen patients (0.10%) had a post-operative VTE event. Thirteen patients had a deep vein thrombosis (DVT) event, whereas two had a pulmonary embolic (PE) event. The procedure with the highest rate of VTE was operation for infection (1.2%). Patient factors associated with VTE included hyponatremia ($p = 0.003$), abnormal PTT ($p = 0.046$), elevated AST ($p = 0.004$), and gastrointestinal ($p = 0.011$), renal ($p = 0.016$) and hematologic disorders ($p = 0.019$). Nearly half (46.2%) of DVT events occurred post-discharge. Adverse postoperative outcomes significantly associated with VTE included prolonged hospitalization ($p < 0.001$), pneumonia ($p < 0.001$), unplanned intubation ($p = 0.003$), urinary tract infection ($p = 0.003$), and central line bloodstream infection ($p < 0.001$). The majority (66.7%) of associated complications preceded or occurred concurrent with diagnosis of VTE.

Conclusions: We have identified novel risk factors and adverse postoperative outcomes associated with VTE. The incidence of VTE of pediatric orthopaedic patients is low. In the absence of specified risk factors, thromboprophylaxis may be unnecessary for the general pediatric orthopaedic population.

Sherrod, Brandon Alan (Brandon)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Brandon G. Rocque, MD

Abstract Approved: Yes

Co-Authors: James M. Johnston, MD and Brandon G. Rocque, MD, MS

Title: Rates and risk factors for 30-day complications following pediatric neurosurgery: an analysis of 9,799 procedures

Background: Many pediatric neurosurgical procedures are considered high-risk, yet national rates and risk factors for postoperative complications remain unknown.

Methods: We queried the American College of Surgeons National Surgical Quality Improvement Program – Pediatric (ACS-NSQIP-Pediatric) database for pediatric patients treated by a neurosurgeon during the years 2012-2013. We then evaluated the incidence of post-operative complications (mortality, infection, thrombosis, stroke, nerve injury, kidney injury, etc.). Univariate and multivariate logistic regression was used to evaluate the association between complications and comorbidities, demographics, preoperative laboratory values, and operative characteristics.

Results: A total of 9,799 cases met the inclusion criteria, 716 of which (7.3%) experienced any complication within 30 days of the primary procedure. Procedures with the highest complication rates were craniotomy for craniopharyngioma excision (24.4%), myelomeningocele repair (17.9%), and laminectomy for biopsy/excision of cervical neoplasm (17.6%). Overall rate of surgical site infection (SSI) was 2.8%, making these the most common complications. Other common complications were systemic infection (2.4%), wound disruption (1.2%), and unplanned intubation (1.0%). Neurological complications included seizure (0.8%), cerebrovascular accident (0.4%), peripheral nerve injury (0.1%), and coma (0.03%). Forty-three patients (0.4%) died. Independent risk factors for postoperative complications included bleeding disorder (OR=2.655, p=0.007), preoperative nutritional support (OR=1.513, p=0.002) chronic steroid use (OR=1.426, p=0.011), CNS Tumor (OR=1.414, p=0.036), emergent/urgent triage (OR=1.246, p=0.022), female gender (OR=1.244, p=0.008), developmental delay (OR=1.224, p=0.047), longer operative time (per hour increase, OR=1.196, p<0.001), and younger age (per year decrease, OR=1.023, p=0.008).

Conclusions: These results may assist surgeons in identifying at-risk patients for complications following pediatric neurosurgery.

Shuford, Rebecca Anne (Rebecca)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Robert Y. Kim

Abstract Approved: Yes

Co-Authors: Audrey Wallace, Caleb Dulaney

Title: Racial Disparities in Sexual Function after Radiation Therapy for Gynecologic Malignancies

Radiation therapy for treatment of gynecologic cancer can cause many side effects including vaginal scarring, vaginal stenosis, loss of vaginal lubrication, sexual anxiety, and painful intercourse among others. Many of these side effects negatively impact quality of life and may persist for years after treatment. Sexual-Vaginal changes questionnaires have been collected from gynecologic cancer patients receiving or having received radiation treatment at UAB's Hazelrig-Salter Radiation Oncology Center. We are analyzing these surveys to see if there is a racial difference between baseline sexual function in these patients, or sexual function after completion of treatment. We are also analyzing differences in vaginal dilator compliance between racial and ethnic groups.

Singer, Jeffrey Robert (Jeff)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Casey Weaver

Abstract Approved: Yes

Co-Authors: Emily G. Blosser, David A. Randolph, Casey T. Weaver

Title: Postnatal Colonization Shapes the Immunologic Development of the Intestinal Barrier

The mammalian intestinal tract harbors a complex microbial ecosystem, or microbiome, with nearly 10-fold the number of cells present in the human body and nearly 100-fold the number of gene products. While germ-free and gnotobiotically reared animal models have underscored the importance of the microbiome for many aspects of health and disease, few studies have addressed how the microbiome plays a role in early life during the period of initial colonization. Understanding the relationship between microbes and newborn barrier development may shed light on the pathogenesis of Gram-negative Neonatal Late-Onset Sepsis (NLOS), a disease whereby premature infants acquire blood-borne infections from organisms typically present as part of the normal intestinal flora.

Using an engineered strain of luciferase-expressing bacteria *Klebsiella pneumoniae*, which is part of the normal flora in adults but can cause NLOS in newborns, we aimed to study how early colonization affects the *in vivo* response to infection. A 10^7 CFU intra-gastric dose of *Klebsiella pneumoniae* exhibits 50% mortality in newborns, but no mortality in adults. Interestingly, eliminating the bacteria through Germ-free or Altered Schaedler's Flora (ASF)-rearing makes both adults and pups succumb to infection. However, restricting microbial colonization with broad-spectrum antibiotics affects only newborn susceptibility to infection. Lastly, we find pharmacologic inhibition of the transcription factor *Rorgt* also increases newborn mortality and reduces the IL-17 and IL-22 cytokine production from innate lymphoid cells by flow cytometry in the small intestine and colon. This suggests a potential mechanism of protection through which early microbial colonization protects the intestinal barrier.

Singireddy, Ramya Reddy (Ramya)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Nabiha Yusuf, PhD

Abstract Approved: Yes

Co-Authors: Erin M. Burns, Pi-Ling Chang, Craig A. Elmets, Nabiha Yusuf

Title: Vitamin D receptor polymorphism status and the association with osteopontin and vitamin D receptor expression in skin tumors

cancer, with inconclusive results. Further, the expression of several factors, including osteopontin (OPN) and VDR proteins, has been shown to be altered in neoplastic skin. OPN is a glycoprotein that is believed to be involved in squamous cell carcinoma tumorigenesis, while VDR expression is essential to maintain adequate vitamin D levels, without which development of skin cancer could result. Although the effects of dysregulated OPN and VDR expression on the progression of skin cancer have been tested independently of one another, our study aims to investigate a relationship between the levels of OPN and VDR expression of each skin tumor sample, in addition to examining a correlation with VDR polymorphism status. We hypothesize that the levels of OPN and VDR expression in each tumor sample are linked, with decreased expression associated with the presence of VDR polymorphisms. In order to examine the relationship between OPN and VDR levels, we obtained 27 skin tumor samples from skin cancer patients at The Kirklin Clinic (Birmingham, AL). The tumors were fixed, paraffinized, sectioned, and immunohistochemically stained with OPN and VDR antibodies, respectively. Each sample is in the process of being scored based on frequency and intensity of the stain, and compared to its OPN or VDR counterpart in order to examine the relationship between the expression of OPN and VDR. We also obtained blood samples, isolated DNA, and sequenced the samples from each patient in order to determine VDR polymorphism status for three known polymorphisms (*Apal*, *BsmI*, and *TaqI*). The results from this study will provide new insight into the role of several key proteins in skin tumorigenesis and their association with VDR polymorphisms in the skin cancer population.

Smith, Andrew Franklin (Andrew)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Wang, Henry E

Abstract Approved: Yes

Co-Authors: James S. Booth

Title: Implementation of the National Emergency Airway Registry at UAB

OBJECTIVE: Airway management is an important intervention in the Emergency Department (ED). The National Emergency Airway Registry (NEAR) is a national multicenter registry of emergency airway management events at United States EDs. The objective of this study was to evaluate the feasibility of NEAR implementation at the UAB Hospital ED.

METHODS: NEAR uses a prospective observational design. We created a paper version of the national NEAR data form, including data on patient demographics, clinical presentation, vital signs, methods of airway management, airway course, and patient outcomes. We required ED residents and attending physicians to complete a data form for every emergency airway/endotracheal intubation event. We formulated a dissemination and collection strategy for the data forms. We developed a data form compliance strategy, using Power Insight/IMPACT queries of ED electronic health record notes to independently identify airway/intubation procedures, and using manual reconciliation to determine and prompt physicians for compliance with NEAR form completion. We defined NEAR form compliance as the proportion of electronic health record intubation events with a completed NEAR data form. We also determined basic airway management characteristics for airway encounters during the pilot study period. We analyzed the data using descriptive statistics.

RESULTS: During the pilot study period November 6th to December 17th 2014, we received completed NEAR forms on 40 patients. Based upon electronic health records indicating _____ intubation events, NEAR form compliance was 72.9%. Characteristics of patients receiving emergency airway management included (n=40): sex - 47.5% female (n=19), 50% male (n=20), 2.5% unlisted (n=1); indications – 14 different indications for intubation, “Altered Mental Status (Not Overdose)” the most common with 25% (n=10); disposition – 80% ICU (n=32), 7.5% deceased, not due to airway failure (n=3), other 12.5% (n=5).

Barriers to successful implementation included: incomplete and missing forms for airways performed at UAB ED and education of attending and resident physicians on the technicalities for completion.

CONCLUSION: We demonstrated the feasibility of implementing the National Emergency Airway Registry at UAB Hospital Emergency Department.

Smith, Burkely Payne (Burke)
Prior Research Experience: Yes
Source of Funding: Other

Project Length: Short

Faculty Advisor: Jayme Locke, MD

Abstract Approved: Yes

Co-Authors: Brittany Shelton MPH, Rhiannon Reed MPH, Darnell Momipont-Williams DNP,
Huma Fatima MD, Vineeta Kumar MD, Jayme Locke MD MPH

Title: Dosing eculizumab for antibody mediated rejection in kidney transplantation: a case report.

Background

Due to advances in immunosuppressive therapies, the number of blood type incompatible (ABOi) living donor kidney transplants (LDKT) has increased in the U.S. Severe antibody mediated rejection (AMR) of an ABOi-LDKT can lead to graft failure, and aggressive therapies are often employed to rescue the affected graft. Specifically, the administration of eculizumab (anti-complement antibody) can be crippling financially with doses costing around \$5,000/300mg vial. Identifying an eculizumab regimen that optimizes effectiveness while limiting cost is paramount to widespread adoption of this graft saving therapy. Herein we describe a limited eculizumab regimen in the setting of severe AMR that is clinically and cost effective.

Methods

Two LDKT recipients undergoing desensitization (plasmapheresis/IVIg) for ABOi who developed severe AMR within the first week of transplant were chosen. Treatment included escalation in PP/IVIg and eculizumab. Eculizumab therapy was discontinued at the first sign of clinical improvement (25% decline inSCr). All patients were maintained on prednisone, cellcept and tacrolimus.

Results

Each patient received a dose of eculizumab on the day of diagnosis of severe AMR post ABOi-LDKT (1200 mg-Patient 1, 900 mg-Patient 2). Patient #1 received 4 post-diagnosis PP/IVIg treatments and one 600mg post-pheresis dose. Patient #2 received 7 post-diagnosis PP/IVIg treatments and two 600mg post-pheresis doses. The current standard of care is to redose eculizumab after any PP treatment. Discontinuing eculizumab therapy upon observed clinical improvement saved 8 unnecessary doses at a cost of \$80,000. Both patients have more than one-year follow-up and functioning allografts.

Conclusion

The current literature suggests a wide variation in the amount and timing of eculizumab given following an AMR in an ABOi LDKT patient. Though this is a small and limited study, we suggest that a dosing regimen of eculizumab similar to that presented here may be effective in rescuing a graft following AMR while simultaneously limiting cost.

Smith, Walter Ryan (Walter)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Charles Khoury, MD

Abstract Approved: Yes

Co-Authors: William Riley and Todd Peterson, MD

Title: Using Medical Students as Hypertension Patient Educators in the Emergency Department Setting

Introduction Hypertension is one of the most common public health problems in the United States. A significant number of patients that visit the emergency department suffer from this chronic condition. It is often evident that patients have a limited understanding of basic knowledge regarding hypertension. The emergency department is often the only opportunity for these patients to receive any type of education about their disease. Therefore, taking advantage of this opportunity could be vitally important in helping patients better understand and manage their hypertension.

Hypothesis The goal or question of this study was to determine whether patient knowledge about hypertension could be improved through a short education session involving a medical student. We predicted that after our interventions, patients participating in this study would have an increased knowledge and understanding of hypertension.

Methods Patients waiting in the emergency department were screened for a previous diagnosis of hypertension and eligible patients were approached for their written consent. Once a patient agreed to participate, they were verbally administered a ten question test surveying their basic knowledge regarding hypertension. Next, a medical student guided the patient through a fifteen-minute education session using an educational pamphlet on hypertension. The patient was given a chance to ask questions after the education session. Lastly, the patient was administered a second test containing the same questions as in the original test in order to assess whether they benefited from the intervention.

Results A total of 112 patients were enrolled in this study. After the education session, patients' test scores increased an average of 11.4%.

Conclusions The initial hypothesis of this study was confirmed. Patients demonstrated an overall increase in hypertension knowledge after being educated by a medical student. Increased knowledge and understanding of the disease could potentially lead to more effective disease management and better outcomes for the patient.

Souder, Jaclyn Paige (Paige)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Michelle Olsen

Abstract Approved: Yes

Co-Authors:

Title: Expression and Function of Astrocytic Connexin-43 in a Model of Pediatric Traumatic Brain Injury

Pediatric traumatic brain injury (TBI) is an important cause of morbidity and mortality in children, contributing to 80% of trauma deaths. Toddlers show the highest injury rates, with a >50% increase in hospitalizations between 2007 and 2010. Current treatment options are limited to supportive care and surgery, based on adult TBI guidelines. Adult TBI, however, is not an adequate model of pediatric TBI considering the vast developmental changes occurring in immature brains. There is a need to develop models of pediatric TBI that will define short- and long-term injury mechanisms in an effort to discover novel therapeutic targets. Evidence suggests the astrocytic protein connexin-43 (Cx43) is involved in TBI pathophysiology. Cx43 is a transmembrane protein that comprises hemichannels, facilitating extracellular communication, and functional gap junctions, hemichannel dimers facilitating communication between astrocytes. This study aimed to elucidate the role of Cx43 in a rat model of pediatric TBI by 1) characterizing Cx43 expression in the immature brain and 2) determining changes in Cx43 expression following TBI. For developmental studies, we used cortical tissue from postnatal day 0-100 (P0-100) wild-type rats. For TBI studies, we simulated diffuse pediatric TBI via weight-drop injury of P18-22 rats. Tissues were analyzed for mRNA and protein changes, and astrocyte-specific glial fibrillary acidic protein (GFAP) was used to assess injury severity. We found that Cx43 mRNA levels remain constant throughout development, while Cx43 protein levels are low initially and begin to increase after P14. In TBI experiments, we found no significant change in Cx43 mRNA or protein expression in mildly injured animals compared to uninjured animals. These results suggest 1) post-transcriptional regulation of Cx43 during development and 2) Cx43 expression does not change following mild diffuse TBI. Future studies should study Cx43 expression and function following severe TBI.

Stone, Sara Lynn (Sara)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Fran Lund

Abstract Approved: Yes

Co-Authors: Andre Ballesteros-Tato, Fran Lund

Title: T-bet regulates memory B cell 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 IFN γ dependent manner. Therefore, we hypothesize that B cell T-bet expression will be necessary for the development of LLPC in a murine model of Influenza A (A/PR8 stain) infection. We found that T-bet expression was increased in GCB cells formed after flu infection, and was highest among CD138^{mid} GCB cells, suggesting that T-bet supports plasma cell differentiation from GCB cells. In chimeric mice in which 50% of cells are T-bet^{-/-}, plasmablasts preferentially derived from WT, rather than T-bet^{-/-} B cells and T-bet^{-/-} GCB cells expressed lower levels of Blimp1 and IRF4 than WT GCB cells. Additionally, we found reduced numbers of flu-specific antibody secreting cells and lower anti-flu titers in chimeric animals with T-bet^{-/-} B cells compared to control chimeras with WT B cells. Though we observed no impairment in Bmem formation when all B cells were T-bet^{-/-}, in chimeric mice in which 50% of cells are T-bet^{-/-}, significantly fewer T-bet^{-/-} B cells were found in the Bmem compartment compared to WT B cells. These results support a role for T-bet in determining fate of GC B cells following influenza infection.

Stoyka, Lindsay Elizabeth (Lindsay)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: David Standaert

Abstract Approved: Yes

Co-Authors: Lindsay Stoyka, Andrew West, PhD, David Standaert, MD, PhD, and Laura Volpicelli-Daley, PhD.

Title: G2019SLRRK2 May Lead to Increased Alpha-Synuclein Aggregation in Parkinson's Disease

Parkinson's Disease (PD) is a progressive central nervous system disorder characterized by bradykinesia, age-dependent progressive dopaminergic neurodegeneration, Lewy body pathology, and non-motor symptoms. Alpha-synuclein, a 140 amino acid vesicular protein, is a large component of Lewy Bodies, which are found in both idiopathic and familial forms of the disease. The G2019S mutation in leucine-rich repeat kinase 2 (LRRK2) leads to late-onset PD. Although many models have shown interactions between the effects of LRRK2 and alpha-synuclein, the exact mechanisms by which these proteins interact remains unknown. Our goal is to determine if LRRK2G2019S, the most common LRRK2 mutant, increases formation of Lewy bodies and Lewy neurites, and whether these interactions lead to increased dopaminergic cell death. Our lab uses a novel system to model alpha-synuclein aggregation by introducing fibrils of misfolded α -synuclein to "seed" endogenous protein to misfold in a manner reminiscent of the progression of PD. These pre-formed fibrils (PFFs) can cause motor impairment as well as pathologic inclusions with a phosphorylated, ubiquitinated phenotype. We show that alpha-synuclein aggregates markedly increased in LRRK2G2019S primary neurons when compared to nontransgenic neurons, and that phosphorylation of endogenous alpha-synuclein occurs upon seeding. Our early results suggest an increase in Lewy body-like aggregates in the substantia nigra of G2019S mutant rats, compared to nontransgenics. Additionally, we see a trend of increased dopaminergic cell loss in the nigra of the G2019S mutants. Future work will focus on further elucidating the changes in vivo.

Sweeney, Mary Katherine (Mary Katherine)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Carlos Estrada, MD

Abstract Approved: Yes

Co-Authors: Michael Belue, MA, William Curry, MD, Carlos Estrada, MD, MS, H. Hughes Evans, MD, PhD, B. Earl Salsler, MD, Erin Snyder, MD

Title: What Do Primary Care Physicians Offer that Others Do Not?: A Nominal Group Technique Evaluation

Objectives: The University of Alabama School of Medicine established the Dean's Primary Care Scholar's Program (DPCSP) – a merit-based scholarship – to foster leadership careers in primary care. In this report, we examined what first year medical students believe primary care physicians offer that physicians do not.

Methods: DPCSP medical students participated in May of their first year (Classes 2016-2018). We used nominal group technique (NGT), which permits equal participation and allows efficient acquisition of ranked responses. The NGT has four steps, participants: i) individually recorded responses to the question ("What do primary care physicians offer that other physicians do not?"), ii) responded in a round-robin manner without discussion, iii) clarified responses, and iv) weighed their top three responses. We categorized responses using an iterative consensus agreement process.

Results: All 20 DPCSP students generated 48 responses, and 26 received at least one vote.

The top ranked responses including "long-term relationships with their patients" were related to patient interactions (total weight, 44; percent weight, 37%).

The remaining responses were grouped into five categories: continuity of care (total weight, 29; percent weight, 24%), knowledge base (total weight, 17; percent weight, 14%), patient education and disease prevention (total weight, 17; percent weight, 14%), community impact (total weight, 7; percent weight, 6%), and lifestyle benefits (total weight, 6; percent weight, 5%).

Discussion : First year medical students committed to primary care perceive the patient-doctor relationship and continuity of care are the most important attributes that set primary care physicians apart from other specialties.

Terry, Charles Roden, III (Charles)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Michael Johnson

Abstract Approved: Yes

Co-Authors: Dr. Michael Johnson

Title: Outcomes of fixation of Calcaneus through small incisions

Background -The management of calcaneal fractures has long been a source of much debate among orthopedic surgeons due to a high risk of wound complications with surgical treatment. Currently a lateral extensile approach is commonly used but this approach is accompanied with high rate of wound complications. Surgeons are seeking an alternative treatment that restores calcaneal anatomy while minimizing the risks of wound complications. Open reduction and internal fixation of calcaneus fractures via small incisions is a potential solution to this problem. Small incision fixation of the calcaneus has been performed on a select group of patients at UAB. We review the outcomes and report the wound complications in this select group of patients

Methods – A group of 15 patients underwent surgical fixation of calcaneus fractures via the small incision technique. Post operatively, patients were followed and their outcomes were assessed using the Foot Function Index, AOFAS outcome score, Short form-36, VAS pain score. Demographic data and complications were recorded.

Results - Not Available at this time

Conclusion – Not available at this time.

Thomas, John William (John)
Prior Research Experience: Yes
Source of Funding:

Project Length: Short

Faculty Advisor: Johanna Hall
Co-Authors: Dhruv Patel, Johanna Hall

Abstract Approved: Yes

Title: Child Life Services Lessens the Emotional Response of Children During Laceration Repair in the Emergency Department.

Background: In the past few decades, the utilization of Child Life Specialists (CLS) has steadily increased in many arenas of pediatric medicine. By using age-appropriate education, preparation, and supportive activities, CLS help children cope with potentially stressful clinical situations.

Objectives: The goal of the study was to evaluate the impact of CLS on the emotional response of children undergoing laceration repair in the emergency department.

Methods: Patients 4-12 years of age who required suture laceration repair were prospectively enrolled (via convenience sampling) in the Children's of Alabama Emergency Department. CLS availability is varied in our center, allowing for a priori categorization of subjects into 2 comparison groups – those with and those without CLS involvement during the procedure. The Children's Emotional Manifestation Scale (CEMS), a previously validated, Likert-like tool, was used to quantify the patients' emotional responses; a higher score reflects a more anxious child. Scales were completed (just prior to placement of the first suture) by trained, unblinded observers. Subjects were excluded if they required sedation or restraint with a board ("papoose"). Age, gender, ethnicity, type of anesthetic or pain control, and length and location of laceration were recorded. Data are presented as medians and interquartile ranges. CEMS scores were compared with a 2-tailed Mann-Whitney U test, with a $P < 0.05$ considered statistically significant.

Results: To date there are 140 patients enrolled in the study. One patient was excluded for being outside the predefined age range. There were 75 children with CLS during laceration repair and 64 without CLS. These groups did not differ in regards to age, gender, or ethnicity. Median CEMS score for patients with CLS present was 7 (6-9) versus 10 (8-13.5) for those without CLS ($P < 0.0005$).

Conclusions: CLS help lower a child's emotional response just prior to laceration repair in the emergency department

Turner, Eric Michael (Eric)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Michelle Robbin, Jessica Zarzour

Abstract Approved: Yes

Co-Authors: Jessica Zarzour MD, Janelle West, Bradford Jackson, Michelle Robbin MD, MS, FACR, FAIUM, FSRU

Title: Validation of Bosniak Classification for Contrast Enhanced Ultrasound and Introduction of a New Classification System

Purpose: To validate the use of the Bosniak classification system in contrast enhanced ultrasound (CEUS) and to introduce a new classification system for use in CEUS.

Methods: This was an IRB approved, retrospective study to evaluate all patients who underwent CEUS from 2006-2015. We reviewed all renal lesions previously identified by computed tomography (CT) and categorized cystic renal lesions according to Bosniak classification when possible. Lesions that could not be classified definitively by CT were categorized as indeterminate (equivocal enhancement, non contrast phase only, and venous phase only). Solid enhancing masses were labeled as such. We then reviewed the subsequent CEUS and categorized similarly. The Kappa coefficient was calculated to determine inter-rater agreement between Bosniak CT classification and Bosniak CEUS classification. We then created a new CEUS classification system and lesions were categorized as A, B, C or D. Class A lesions represented simple cysts or cysts with non-enhancing, small septations (<1 mm). These lesions corresponded to combined Bosniak 1 and 2 classifications. Class B lesions represented mildly complex cystic lesions with minimally enhancing, thin septations. These lesions corresponded to Bosniak 2F classification. Class C lesions represented lesions containing thick, enhancing septations and enhancing mixed cystic-solid lesions. These lesions corresponded to combined Bosniak 3 and 4 classifications. Class D lesions corresponded to enhancing solid masses, not currently included in CT Bosniak classification. Lesions classified using this CEUS system was then compared CT-classified Bosniak lesions to examine congruency.

Results: Forty patients were female (34.5%) and 76 were male (65.5%). Patient ages ranged from 27 to 90 years (mean 59.2 ± 13.5 standard deviation). The mean lesion size was 2.9 cm (SD 1.8). The median length of time between CEUS and the CT immediately preceding it was 74.4 days (mean, 269.6 ± 472.2). Of the 134 renal lesions evaluated by CEUS, 97 lesions were previously characterized by CT. There were 11 solid enhancing masses, 12 Bosniak 1/2 lesions, 4 Bosniak 2f lesions, and 2 Bosniak 3/4 lesions. Sixty-nine renal lesions were said to be indeterminate on prior CT due to equivocal enhancement (10 to 20 HU; n = 21), presence of noncontrast scan only (n = 39), or presence of venous phase only (n = 8). Of the lesions that were indeterminate by prior CT, 79.6% were given definitive diagnoses via CEUS evaluation (95% confidence interval [CI]: 70.8%, 86.8%; p < 0.0001).

When comparing the CT bosniak classification with the CEUS bosniak classification system, the kappa coefficient was 0.68 (p<0.0001). When comparing the CT bosniak classification system with the new CEUS classification, the kappa coefficient was 0.73 (p<0.0001) and there is 80.8% agreement (kappa of 0.73), suggesting high agreement. Of the 24 lesions classified by CEUS as class C or D, 22 went on to pathologic diagnosis. 86.4 % of these lesions had a diagnosis of

malignancy (papillary renal cell carcinoma n= 11, clear cell renal cell carcinoma n=6, juxtaglomerular cell tumor n=1, chromophobe renal cell carcinoma n=1.

Conclusion: CEUS renal cyst classification using the Bosniak system as well as the newly introduced CEUS system showed good agreement. Further research with a larger patient population is necessary.

Turner, Hannah Jean (Hannah)
Prior Research Experience: Yes
Source of Funding: CaRES Program
Faculty Advisor: Dr. Pauline Jolly
Co-Authors:

Project Length: Short

Abstract Approved: Yes

Title: Screening, prevalence, and risk factors for cervical cancer/lesions in HIV positive women in Swaziland

Background

Many subtypes of the human papillomavirus are well-known causative agents of genital warts and cervical cancer. In the Kingdom of Swaziland, cervical cancer is the most common cancer affecting women between the ages of 15 and 44. In addition to the burden of HPV, the population of Swaziland also faces a significant burden of HIV, having the highest HIV prevalence in the world.

Methods

Sexually active women between the ages of 15-49 were screened at five different health clinics throughout Swaziland to see if they met all the eligibility requirements for the study. Women with confirmed negative pregnancy tests and no history of diagnosed cervical cancer or hysterectomy were assigned patient identification numbers, and informed consent was acquired. Women were interviewed with questionnaires and then seen by a nurse to obtain biological samples. Blood was collected to be screened for HIV and syphilis. The women were also screened for Chlamydia trachomatis, Neisseria gonorrhoea, and Trichomonas vaginalis. Samples were also collected for cytology screening and HPV genotyping. The women were also screened for cervical lesions using visual inspection with acetic acid. Women with cervical lesions will come back for follow-up at 6 months and 12 months to assess progression of cervical lesions and response to cryotherapy, if received.

Vachhani, Raj (Raj)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Carlos Estrada

Abstract Approved: Yes

Co-Authors: Toral Patel, MD, Carlos A. Estrada, MD, MS, Robert M. Centor, MD

Title: Rapid Antigen Group A Strep Test: Sensitivity and Specificity from Manufacturers
Background

Recent meta-analysis has shown moderate sensitivity and high specificity of the rapid antigen streptococcus tests (RAST) to diagnose group A streptococcal pharyngitis. However, only peer-reviewed publications were included. We examined the sensitivity and specificity data of RAST as provided by test manufacturers.

Methods

We performed a systematic review of RAST available on the US market listed in the Food and Drug Administration - Clinical Laboratory Improvement Amendments (FDA-CLIA) database (1993 -2015). We calculated sensitivity and specificity from package inserts or FDA documents, examined risk of bias, and used a random-effects model to calculate pooled estimates.

Results

We included 24 RAST. The overall prevalence of group A streptococcal pharyngitis was 21.1% (2,971/14,091 patients; range 8-42%). Of the 22 criteria, risk of bias was low in 16 criteria, unclear in six, and high in three (description of selection criteria, description of included patients, and exclusions explained). The pooled sensitivity was 95% (95% confidence interval [CI] 94% to 96%). The pooled specificity was 97% (95% CI 96% to 98%).

Conclusions

According to data provided by manufacturers, RAST is highly sensitive and highly specific to diagnose group A streptococcal pharyngitis.

Weaver, Alice (Alice)

Project Length: Long Prior

Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Eddy S. Yang

Abstract Approved: Yes

Co-Authors: Tiffany S. Cooper, M. Benjamin Burch, Shi Wei, Lisa Clemons, Eben L. Rosenthal, Eddy S. Yang

Title: Activation of the Notch signaling pathway is associated with poor prognosis in oral cavity squamous cell carcinoma.

Abstract Body: Head and neck squamous cell carcinoma (HNSCC) is a heterogeneous disease which typically presents at a locally advanced stage. Despite improvements in surgery and radiotherapy, relapse is still common and overall HNSCC survival rates remain below 70%. One reason for this limited progress may be the lack of reliable biomarkers for HNSCCs, especially non-oro-pharyngeal tumors. The purpose of this study was to identify molecular targets and predictive markers to improve the management of oral cavity SCC (OSCC). 19 OSCC samples were obtained from the UAB Surgical Pathology laboratory. RNA was isolated from FFPE tissue sections with >80% tumor cellularity and analyzed with the PanCancer Pathways Plus panel on the NanoString nCounter system and nSolver 2.5 software. Results were confirmed using data from the oral cavity anatomic subdivision of the Head and Neck Squamous Cell Carcinoma cancer study generated by the TCGA Research Network viewed in the cBioPortal for Cancer Genomics. NanoString PanCancer Pathway analysis identified a significant association between the Notch signaling pathway and cancer-specific mortality in OSCCs. Differential regulation of Delta-like ligands, co-repressive histone deacetylases, and Notch transcription targets suggests an overall increase in Notch pathway signaling in patients who died of their disease. Using the TCGA OSCC cohort, we identified 52/172 (30%) patients with Notch pathway activation, which was associated with a 16.69 month decrease in median overall survival (HR=1.77) that approached statistical significance ($p=0.0506$). Our results identify a subset of OSCC patients who have increased Notch pathway activity and worsened clinical outcomes. Additional studies are needed to determine biological mechanisms underlying the poor prognosis in these patients and to investigate the efficacy of therapies targeting Notch pathway signaling in OSCC.

Webb, William Mitchell (William)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Farah Lubin

Abstract Approved: Yes

Co-Authors: Farah Lubin

Title: Histone methylation and (NF- κ B) methyl-lysine signaling in the hippocampus and entorhinal cortex during memory formation.

Nuclear factor κ B (NF- κ B) is a critical mediator of learning-induced gene transcription changes involved in the process of memory formation. Furthermore, abnormal NF- κ B activation has also been implicated in the memory dysfunction experienced in Alzheimer's disease (AD). However, the signaling pathways governing NF- κ B regulation and function during memory formation are poorly understood. Outside of the brain, mono-methylation of the NF- κ B p65/RelA subunit at lysine 310 (p65K310me1) recognizes the ankyrin repeats of G9a-like protein (GLP), which it recruits to facilitate dimethylation at histone H3 lysine 9 (H3K9me2). This epigenetic modification is associated with a repressed transcriptional state in the entorhinal cortex (EC) during memory consolidation. Here, we investigated the involvement of learning-induced NF- κ B p65 methylation changes catalyzed by the SETD6 histone lysine methyltransferase during memory consolidation and in mice. We found that SETD6 co-immunoprecipitated with p65 in the mouse EC and in area CA1 of the hippocampus. Acetylation of p65 at K310 was shown to be increased in fear-conditioned animals. Furthermore, we found changes in the methylation status of p65 between fear-conditioned mice compared to controls. Collectively, these results suggest that p65 methylation plays a role in the transcriptional regulation of genes during memory consolidation and raise the possibility that dysregulation of gene transcription through methylated NF- κ B/GLP/H3K9me2 signaling may contribute to memory dysfunction.

West, Janelle Therese (Janelle)

Project Length: Intermediate

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Jessica Zarzour

Abstract Approved: Yes

Co-Authors: Jessica Zarzour MD, Eric Turner, Bradford Jackson PhD, Michelle Robbin MD

Title: The Use of Contrast-Enhanced Ultrasound in the Diagnosis of Indeterminate Small Renal Lesions

Purpose: To determine if contrast-enhanced ultrasound (CEUS) can definitively diagnose indeterminate small renal lesions.

Materials and Method: This was an IRB approved, retrospective study to evaluate all patients who underwent CEUS from 2006-2015. We reviewed renal lesions initially deemed indeterminate by computed tomography (CT), ultrasound (US), or magnetic resonance imaging (MRI). Indeterminate lesions were evaluated by CEUS; cystic lesions were categorized according to the Bosniak classification system and solid enhancing masses were labeled as such. We compared the number of lesions definitively characterized by CEUS with the indeterminate lesions by prior imaging.

Results: Of the 134 renal lesions reviewed, 108 were deemed indeterminate by prior imaging. Forty patients were female (34.5%) and 76 were male (65.5%). Participant ages ranged from 27 to 90 years (mean 59.2 ± 13.5 standard deviation). The mean lesion size was 2.9 cm (SD 1.8). Sixty-nine renal lesions were said to be indeterminate on prior CT due to equivocal enhancement (10 to 20 HU; n = 21), presence of noncontrast scan only (n = 39), or presence of venous phase only (n = 8). The median length of time between CEUS and the CT immediately preceding it was 74.4 days (mean, 269.6 ± 472.2). Six lesions were indeterminate by MRI due to lack of contrast and 36 lesions were indeterminate by US.

Of the 108 renal lesions indeterminate by prior imaging, 79.6% were given definitive diagnoses via CEUS evaluation (95% confidence interval [CI]: 70.8%, 86.8%; $p < 0.0001$). Specifically, CEUS was definitive for 83.6% of lesions deemed indeterminate by CT ($p < 0.0001$; CI: 72.5%, 91.5%), 100% of lesions deemed indeterminate by MRI ($p = 0.0143$; CI: 54.1%, 87.9%), and 73.7% of lesions deemed indeterminate by prior US ($p = 0.0035$; CI: 56.9%, 86.6%). Of those that were previously indeterminate on prior CT, 41.1% were classified as Bosniak 1 or 2, 16.1% as Bosniak 2f, 21.4% as Bosniak 3 or 4, and 21% as solid enhancing masses. Of the 24 lesions classified as Bosniak 3, Bosniak 4, or as a solid enhancing mass, 22 went on to pathologic diagnosis. 86.4% of these lesions had a diagnosis of malignancy (papillary renal cell carcinoma n= 11, clear cell renal cell carcinoma n=6, juxtaglomerular cell tumor n=1, chromophobe renal cell carcinoma n=1). Of the 26 renal lesions determinate by prior imaging, 96.1% were also determinate by CEUS.

CEUS was definitive for characterization of renal lesions in 85.0% of patients with ERSD ($p = 0.0017$; CI: 62%, 97%) and in 85.4% of patients with a GFR < 60 ($p < 0.0001$; CI: 76%, 92%).

Conclusion: CEUS may be useful for definitive characterization of small renal masses that were previously indeterminate by prior imaging; results need to be confirmed with larger studies.

Worth, Anna Christine (Anna)

Project Length: Short

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Cynthia Brown

Abstract Approved: Yes

Co-Authors:

Title: Factors influencing life-space recovery in non-surgical geriatric hospitalized patients

Background: Each year approximately 13 million older persons are hospitalized for a variety of medical and surgical problems. After hospitalization, patients experience individualized degrees of disability in activity limitation and/or participation in society. The UAB Study of Aging Life-Space Assessment (LSA) is a validated tool that describes where a person goes, the frequency that he or she goes there, and the use of equipment or help from another person to measure mobility and reflect participation in society. Identifying modifiable predictors of life-space recovery after hospitalization using the LSA will provide targets for intervention to improve community mobility and participation of older adults.

Objectives: To determine the proportion of non-surgical hospitalized older patients who recover life-space 6 months post-hospitalization; and to identify modifiable predictors of life-space recovery.

Methods: Data from 198 non-surgical patients, age ≥ 65 years who were admitted to the Birmingham VA Medical Center were analyzed. Exclusion criteria included patients on isolation, required a translator, terminally ill, or previously enrolled in the study. Patients completed baseline interviews during hospitalization and were followed with monthly telephone calls for up to 6 months after discharge to ascertain their life-space. Recovery was defined as a LSA score within 5 points or better of the pre-hospital LSA score. Baseline factors that potentially influenced recovery of life space were examined. Associations between recovery and baseline factors were examined using simple descriptive and multivariable logistic regression models.

Results: 198 participants (mean age 72 (s.d. 7.2) years, 98.5% male, 77.5% white and 22% black, 11.5% consented by proxy). The mean baseline LSA score was 57.2 (s.d. 25.1). At one month 55% of patients had recovered their LSA with a mean score of 58.6 (s.d. 26.6) while the 45% who did not recover has a mean LSA score of 44.3 (s.d. 21.6). However, in logistic regression models using baseline factors including sociodemographics, baseline life-space, nutritional factors, depression and activities of daily living, no factors were predictive of recovery of life-space after hospitalization at one month.

Conclusions: Although previous research has shown hospitalization to be associated with a loss of community mobility that was not recovered, our study demonstrated over half the patients did recover to within 5 points of their pre-hospital life-space within one month of hospital discharge. Determination of factors associated with recovery has important implications for interventions to reduce the decline associated with hospitalization. Further analysis regarding the specific modifiable factors that influence life-space is ongoing.

Young, Bradley Lane (Brad)

Project Length: Intermediate

Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Brent Ponce, MD

Abstract Approved: Yes

Co-Authors: Dustin K. Baker, Bradley L. Young, Eugene W. Brabston, William D. Jordan, Richard D. Meyer, Brent A. Ponce

Title: Risk Factors for Increased Morbidity Following Thoracic Outlet Syndrome Surgery

Despite the increase in surgical decompression for thoracic outlet syndrome (TOS) little is understood regarding associated risk factors for complications. A retrospective analysis using the American College of Surgeons National Surgical Quality Improvement Program for patients receiving surgery for TOS was performed. A total of 670 patients over a three year period were identified and had an overall 30 day any adverse event (AAE) rate of 5.7%. Readmission occurred in 6.3% of patients while 4.9% of patients required reoperation. Diabetes (OR = 6.42; P = .008) and prolonged operative time (OR 6.14; P < .001) had a higher risk of AAE. Predictors of reoperation included renal comorbidity (OR = 10.5; P = .014) and prolonged operative time (OR = 4.1; P < .001). Predictors of readmission included renal comorbidity (OR = 8.122; P = .018) and steroid use (OR = 8.122; P = .004).

Keywords: Thoracic outlet syndrome, complications, risk factors

Youngstrom, Mallory Lynn (Mallory)

Project Length: Long

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Lori Harper

Abstract Approved: Yes

Co-Authors: Dr. Lorie Harper, Dr. Tita, Dr. Anderson

Title: Outcomes in Women with a History of Chronic Hypertension but Normal Blood Pressures in Pregnancy

Objective: Due to physiologic changes of pregnancy, many women with a history of chronic hypertension (HTN) will have normal blood pressures (BP) without requiring antihypertensives (antiHTN). We sought to assess pregnancy outcomes in this group of women compared to those who require antiHTN.

Study Design: Retrospective cohort of all singletons with HTN at a tertiary care center from 2000-2014. Exclusions were fetal anomalies, major medical problems, and BP $\geq 140/90$ mmHg < 20 weeks. Outcomes were compared between those on no antiHTN < 20 weeks and those started on an antiHTN < 20 weeks. The primary outcome was preeclampsia (PE). Secondary outcomes were severe PE, cesarean delivery (CD), composite neonatal outcome (perinatal death, assisted ventilation, cord pH < 7 , 5-minute Apgar ≤ 3 , neonatal seizures), preterm birth (PTB) < 35 weeks, and small for gestational age (SGA). Groups were compared using Student's t-test and χ^2 . Logistic regression was used to adjust for confounding factors.

Results: Of 830 subjects with HTN and BP $< 140/90$ mmHg, 199 (24%) required no antiHTN. Those on antiHTN were more likely to have been on antiHTN prior to pregnancy, have baseline renal disease, be started on aspirin, and less likely to have diabetes. After adjusting for significant confounding variables, those who were not taking antiHTN were less likely to develop PE (AOR 0.5, 95% CI 0.31-0.82) or severe PE (AOR 0.5, 95% CI 0.25-0.93). Odds of CD were similar between groups (AOR 0.7, 95% CI 0.46-1.03). Odds of PTB < 35 wk (AOR 0.5, 95% CI 0.29-0.80) and SGA (AOR 0.6, 95% CI 0.33-0.99) were lower in those not on antiHTN, while odds of the composite neonatal outcome were similar (AOR 0.8, 95% CI 0.47-1.33).

Conclusion: Women with HTN who have normal BP without antiHTN are at lower risk of developing PE, severe PE, PTB < 35 weeks, or SGA compared to women who require antiHTN. Further analysis needs to be done comparing this group to women with no history of HTN.

Table 1:

Maternal and Neonatal Outcomes			
	Normal BP with Medications (n=631)	Normal BP Without Medications (n=199)	AOR (95% CI)

Maternal Outcomes			
Any Preeclampsia Diagnosis	163 (25.8%)	28 (14.1%)	0.51 (0.31-0.82)*
Severe Preeclampsia	104 (16.5%)	14 (7.0%)	0.49 (0.25-0.93)†
Cesarean Delivery	299 (47.4%)	85 (42.7%)	0.69 (0.46-1.03)‡
Neonatal Outcomes			
Composite Neonatal Outcome	90 (14.3%)	21 (10.6%)	0.79 (0.47-1.33)§
PBT<35 weeks	138 (22.5%)	21 (10.8%)	0.48 (0.29-0.80)¶
SGA	112 (17.8%)	23 (11.6%)	0.58 (0.33-0.99)**

*Adjusted for race, baseline renal disease, h/o pregnancy induced hypertension

†Adjusted for race, baseline renal disease, antihypertensives prior to pregnancy, PIH in a prior pregnancy, and BMI

‡Adjusted for age, BMI, race, tobacco use, diabetes (none, gestational, pregestational), and prior vaginal delivery

§Adjusted for tobacco use, baseline renal disease, aspirin use, and diabetes (none, gestational, pregestational)

¶Adjusted for nulliparity, prior preterm delivery, baseline renal disease, and diabetes (none, gestational, pregestational)

**Adjusted for BMI, race, tobacco, baseline renal disease, and diabetes (none, gestational, pregestational)

Zeiger, Herbert Evan, III (Herbert)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. James Markert

Abstract Approved: Yes

Co-Authors: Matthew S. Erwood, M.D., Christoph J. Griessenauer, M.D., Matthew C. Davis,

M.D., Elizabeth N. Kuhn, M.D., Winfield S. Fisher, III, M.D

Title: Subdural Hematoma in the Elderly (SHE) Study: Management and Clinical Course.

Abstract: Subdural hematoma (SDH) is an increasingly common problem among the elderly as a result of geriatric trauma and prevalent use of antiplatelet/anticoagulant agents. Whether surgical intervention for subdural hematoma in the elderly provides significant benefit with regards to mortality and functional status is unclear. The purpose of this study is to better understand and characterize the nature of SDH in the elderly along with describing the clinical course and outcomes after surgical and nonsurgical management. All adult patients with subdural hematoma who were admitted to or had neurosurgical consultation at UAB Hospital from October 25, 2005 to April 31, 2015 have been screened by the clinical investigators for inclusion in the study. The subgroup of patients ≥ 65 years old were identified from the larger cohort. A total of 1048 patients with subdural hematoma were evaluated for inclusion in the study via chart review. High speed trauma, including Motor Vehicle Collisions (MVC), were excluded. The following data was collected for each patient meeting inclusion criteria: age, gender, admission location, admission/consult, mechanism of hemorrhage, admission GCS, intubated on arrival, antiplatelet use, anticoagulant use, presence of blown pupil, SDH volume, date and type of surgical interventions (craniotomy, burr holes, SEPS), discharge disposition, date of discharge, hospital length of stay, ICU length of stay, discharge modified Rankin Scale (mRS), date of follow-up, follow-up mRS at 6 and 12 months, and date of death. Mortality was determined by querying the Social Security Death Index. The future holds performing statistical analysis to further investigate and characterize SDH in the elderly.

Zipperly, Morgan Elizabeth (Morgan)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Jeremy Day

Abstract Approved: Yes

Co-Authors: Andrew C. Brane, J.J. O'Malley

Title: Assessment of Neuronal Activity in Reward-Associated Behavioral Circuits

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

Methods: In order to assess how neuronal activity in the NAc are altered as a result of drug exposure, cell firing was recorded in vivo from electrode microarrays bilaterally implanted in the NAc of naive male Sprague Dawley rats (n=8) that have been exposed to either cocaine (10mg/kg) or saline.

Results: As predicted, acute cocaine exposure increased activity of a subpopulation of neurons in the NAc, independent of environment or context. In addition, prior cocaine exposure resulted in a significant increase in cell firing in the NAc upon subsequent exposure to saline, although this increase was to a lesser extent than that experienced when previously exposed to cocaine.

Conclusions: Considering that the majority of the neurons within the NAc are medium spiny neurons (MSNs), these cells likely have a large role in mediating the significant global increase in cell firing in the NAc following acute exposure to cocaine. By elucidating how cocaine exposure alters the activity of specific cell populations, we may identify important mechanisms underlying the etiology of addiction and novel targets for preventive and therapeutic interventions.

Zou, Chenhang (Sylvia)

Project Length: Short

Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Raymond Harris

Abstract Approved: Yes

Co-Authors: Yinqiu Wang, Aolei Niu, Bing Yao, Ming-Zhi Zhang, Raymond C. Harris

Title: Macrophage polarization in acute kidney injury: macrophage differentiation into M2 phenotype in IL-4 and IL-13 knockout mice

Macrophages play a crucial role in the inflammation and repair mechanism of kidney during an episode of acute kidney injury. Macrophages differentiate into M1 or M2 phenotypes in response to injury, mediating the inflammatory and recovery processes. The polarization of macrophages into M2 phenotype has been linked to the presence of IL-4 and IL-13. We hypothesize that by knocking out the genes coding for IL-4 and IL-13, mice will show decreased levels of M2 macrophages with impaired recovery. IL-4/13 knockout mice were bred and compared to wild type litter mates, and both groups were injected with a single dose of diphtheria toxin to mimic an episode of acute kidney injury. Western blot, immunostaining, and flow cytometry were performed on kidney tissues from both groups to assess the relative amounts of macrophages. The results showed decreased IL-4R α and arginase 1, which are markers of M2 macrophages. Furthermore, there were also increased KIM-1 and α -SMA, which are markers for kidney injury and myofibroblast formation, respectively. F4/80 immunostaining showed increased cell count. Picro-sirius red and Masson's trichrome staining both showed increased interstitial collagen deposition. Despite increased macrophage cell count, polarization toward the M2 phenotype had significantly decreased. The decreased M2 phenotype also correlated to increased injury and delayed healing, as shown by the amplified kidney fibrosis. Future efforts may include studying the pathway of M2 polarization. Since IL-4 and IL-13 activate JAK3/STAT6 receptors, examination of macrophage differentiation in JAK3/STAT6-inhibited animals may contribute to the efforts of finding effective treatment for acute kidney injury.