UASOM

DALE J. BENOS MEDICAL STUDENT RESEARCH DAY

10:00 am – 12:00 pm: Oral Presentations
1:00 pm - 3:00 pm: Judging of Posters

Tuesday, October 28th, 2014
Volker Hall, 1st Floor

MSRD 2014
JUDGES

Dr. Farrukh Afaq
Dept. of Dermatology

Dr. Marilyn Crain
Dept. of Infectious Diseases

Dr. John Fiveash
Dept. of Radiation Oncology

Dr. Catherine Fuller
Dept. of Cell, Developmental and Integrative Biology

Dr. Fadi Hage
Dept. of Medicine

Dr. John Hartman
Dept. of Genetics

Dr. Rojymon Jacob
Dept. of Radiation Oncology

Dr. Silvio Litovsky
Dept. of Pathology

Dr. Peter Mannon
Dept. of Medicine

Dr. William Neway
Dept. of Surgery

Dr. Robert Oster
Dept. of Medicine

Dr. Laura Timares
Dept. of Dermatology

Dr. Henry Wang
Dept. of Emergency Medicine

Dr. John Waterbor
Dept. of Epidemiology

Dr. Teresa Wilborn
Dept. of Pharmacology and Toxicology

Dr. Nabiha Yusuf
Dept. of Dermatology

Dr. David Cleveland
Dept. of Surgery

Dr. Derek Dubay
Dept. of Surgery

Dr. Gregory Friedman
Dept. of Pediatrics

Dr. James George
Dept. of Surgery

Dr. Lorie Harper
Dept. of Ob/GYN

Dr. Patricia L. Jackson
Dept. of Medicine

Dr. Amy Knight
Dept. of Physical Medicine & Rehabilitation

Dr. Colin Martin
Dept. of Surgery

Dr. Carmel McNicholas
Dept. of Cell, Developmental and Integrative Biology

Dr. Susan Nozell
Dept. of Radiation Oncology

Dr. Brent Ponce
Dept. of Surgery

Dr. Peter Smith
Dept. of Cell, Developmental and Integrative Biology

Dr. Lizhong Wang
Dept. of Genetics

Dr. Roger White
Dept. of Medicine

Dr. Bradford Woodworth
Dept. of Surgery

Dale J. Benos Medical Student Research Day

Oral Presentations

Tuesday, October 28, 2014

Lecture Room E

Short Term Research

10:00 – 10:15 am **Matthew S. Carle, MS2**
Assessing the relationship of education level and medication adherence with patients' perception of autonomous support by health-care provides in a sample of low incomes African Americans with diabetes
Mentor: Dr. Andrea Cherrington

10:15 – 10:30 am **Joy M. DeShazo, MS2**
Physical health and wellbeing of persons with Spina Bifida
Mentor: Dr. Danielle Powell

10:30 – 10:45 am **Jennifer L. Jackson, MS2**
Associations of 25-hydroxyvitamin D with markers of inflammation, insulin resistance, and obesity in adults
Mentor: Dr. Orlando Gutierrez

10:45 – 11:00 am **James Thompson McMurtrie, MS3**
Hematocrit, blood transfusion, and outcomes in patients with coronary stents and cardiac risk factors undergoing surgery
Mentor: Dr. Mary Hawn

11:00 – 11:15 am **Landon R. Mueller, MS2**
National characteristics of EMS care in frontier and remote areas
Mentor: Dr. Henry Wang

11:15 – 11:30 am **Jaclyn P. Souder, MSTP (MS1)**
Creating an inducible CRISPR-Cas9 system for spatiotemporal genome editing
Mentor: Dr. Daniel Gorelick

11:30 – 11:45 am **Courtney L. Culbreath, MS3**
Environmental mediated intestinal homeostasis in neonatal mice
Mentor: Dr. Colin Martin

Dale J. Benos Medical Student Research Day
Oral Presentations
Tuesday, October 28, 2014
Lecture Room E

Intermediate Term Research

10:00 - 10:15 am **Yun Ju (Janis) Cho, MS4**
Racial differences in mitochondrial dysfunction and social determinants of obesity
Mentor: Dr. Amanda Willig

10:15 – 10:30 am **Justin C. Chuang, MS4**
In situ simulation of precipitous labor in a pediatric emergency department
Mentor: Dr. Marjorie-Lee White and Dr. John Woods

10:30 – 10:45 am **Frederick A. Kebbel, MS4**
Replacing conventional unenhanced with dual-energy virtual unenhanced series: radiation and reimbursement implication
Mentor: Dr. Desiree Morgan

Long Term Research

10:45 – 11:00 am **Alexander W. Bray, MSTP (GS3)**
Mitochondrial genetic background influences susceptibility to atherosclerosis
Mentor: Dr. Scott Ballinger

11:00 – 11:15 am **William H. Ennis, MS4**
Irradiation of the stem cell niche in glioblastoma
Mentor: Dr. John Fiveash

11:15 – 11:30 am **Travis D. Hull, MSTP (GS4)**
Heme-oxygenase-1 expression regulates trafficking of myeloid cells in acute kidney injury
Mentors: Dr. James George and Dr. Anupam Agarwal

11:30 – 11:45 am **Jennifer A. Stanley, MSTP (GS4)**
Novel interaction between EGFR and PARP1 may modulate DNA repair in human triple negative breast cancer
Mentor: Dr. Eddy Yang

Group A

A-1 Anwer, Tooba (MS2)
Understanding the role of autophagy in chemotherapy resistant ovarian cancer by targeting the Sphigosine-1-phosphate pathway
Mentor: Dr. Charles Landen

A-2 Chang, Michelle (MS2)
Toll-like receptor-4 deficiency enhances repair of ultraviolet light radiation induced DNA damage in skin and prevents skin cancer
Mentor: Dr. Nabiha Yusuf

A-3 Diamond, Ariana (MS2)
Fisetin potentiates the anti-proliferative and anti-EMT effects of Sorafenib in malignant melanoma
Mentor: Dr. Farrukh Afaq

A-4 Ellis, Ashley (MS4) (Not Presenting)
Primary cilia in ovarian neoplasms: immunofluorescence detection
Mentor: Dr. Andra Frost

A-5 Fletcher, Jacob (MS2)
Fluorescence-based methodology for measuring drug accumulation in tissue
Mentor: Dr. Eben Rosenthal

A-6 Hu, Muhan (MSTP-MS2)
Hedgehog signaling in breast cancer: Role in adaptation to hypoxia
Mentor: Dr. Lalita Sheved-Samant

A-7 LeGrand, Jason (MSTP-GS4)
Identification of cytogenetically normal human $CD34^{+}CD38^{-}$ hematopoietic stem/progenitor cells from $inv(16)^{+}$ leukemic bone marrow
Mentor: Dr. Christopher Klug

A-8 McAtee, Christopher (MS2)
Evolution of 5-Fluorouracil resistance in Saccharomyces cerevisiae
Mentor: Dr. John Hartman

A-9 McCaw, Tyler (MSTP-MS2)
Solid tumor targeting with T cells, linker proteins and precise gene editing
Mentors: Dr. Tim Townes and Dr. Troy Randall

A-10 Ramaker, Ryne (MSTP-GS1)
Metabolomic analysis of serum and urine from pancreatic ductal adenocarcinoma patients
Mentors: Dr. Sara Cooper and Dr. Richard Myers

A-11 Roberson, Johnny (MS3)
Factors associated with increased incidence of toxicities following administration of yttrium-90 resin microspheres
Mentor: Dr. Omer Burnett, III

A-12 Weaver, Alice (MSTP-GS3)
Defects in repair of DNA double strand breaks and sensitivity to PARP inhibition in HPV-positive oropharyngeal squamous cell carcinoma
Mentor: Dr. Eddy Yang

Group B

B-1 **Evers, Caroline (MS2) & Kennemer, Caroline (MS2)**
Racial disparities in treatment outcomes of epithelial ovarian cancer
Mentor: Dr. Charles Leath, III and Dr. Warner Huh

B-2 **Gardner, Meg (MS2)**
EKG abnormalities in asymptomatic childhood cancer survivors attending a long-term follow-up clinic
Mentor: Dr. Kimberly Whelan

B-3 **Harris, David (MS2)**
Toxicity effects of alignment using fiducials versus computerized tomography (CT) imaging for the radiation treatment of prostate cancer
Mentor: Dr. John Fiveash

B-4 **Haywood, Nathan (MS2)**
The modified response evaluation criteria in solid tumors (mRECIST) predicts survival following transarterial chemoembolization (TACE) for hepatocellular carcinoma
Mentor: Dr. Derek DuBay

B-5 **Hyndman, LaKeshia (MS3)**
Exercise timing and sleep quality response to an exercise intervention in breast cancer survivors
Mentor: Dr. Laura Rogers

B-6 **Machemehl, Hannah (MS3)**
Is observation reasonable in older patients with early stage uterine papillary serous carcinoma and clear cell carcinoma?
Mentor: J. Michael Straughn

B-7 **Mulpur, Bhagee (MS2)**
Complementary therapy and survival in glioblastoma mutliforme (GBM)
Mentor: Dr. Burt Nabors

B-8 **Seeley, Ashlyn (MS4)**
Neoadjuvant Vemurafenib followed by aggressive local therapy for surgically unresectable stage III melanoma
Mentor: D. Jennifer De Los Santos

B-9 **Whitaker, Jessica (MS2)**
Efficacy of treatment options for metastatic neuroendocrine tumors
Mentor: Dr. Rojymon Jacob

Group C

C-1 Allon, Steven (MS2)
The differential vasoprotective effects of estrogen in pre- and post-menopausal women
Mentors: Dr. Suzanne Oparil and Dr. Fadi Hage

C-2 Antipenko, Sergey (MSTP-GS2)
Inflammation alters the phenotype of cardiac mesenchymal stem cells
Mentor: Dr. Tim Townes

C-3 Berry, Ryan (MSTP-GS2)
Circadian clock knockout in heart leads to altered growth hormone signaling
Mentor: Dr. Stuart Frank

C-4 Carlisle, Matthew (MS2)
Bromine exposure induces fetal growth restriction during pregnancy
Mentor: Dr. Sadis Matalon

C-5 Colon, Chad (MS3)
Estrogen-induced vasoprotection is preserved after prolonged estrogen deprivation
Mentor: Dr. Suzanne Oparil

C-6 Fox, Brandon (MSTP-MS1)
Humanized sickle cell disease mice display an increased sensitivity to alpha-1 mediated vasoconstriction
Mentor: Dr. Jennifer S. Pollock

C-7 Lever, Jeremie (MSTP-MS2)
Alpha-mannosidase activity and N-glycans in atherosclerosis
Mentor: Dr. Rakesh Patel

C-8 Liu, Mingchun (MS2)
Short Term
High prevalence of type 2 diabetes mellitus exists in resistant hypertensive patients with primary aldosteronism
Mentor: Dr. Suzanne Oparil

C-9 Locy, Morgan (MSTP-GS1)
Platelet mitochondrial metabolism is disrupted by 4-hydorxynonenal: Implications for thrombus formation in atherosclerosis
Mentor: Dr. Victor Darley-Usmar

C-10 Wang, Tim (MS4) (Not Presenting)
Prevalence of metabolic syndrome in patients with and without primary aldosteronism
Mentors: Dr. Tanja Dudenbostel and Dr. Suzanne Oparil

Group D

D-1 Hong, Winston (MS2)
Impact of screening for gestational diabetes
Mentor: Dr. Lorie Harper

D-2 Luker, Austin (MS4)
The role of visceral obesity induced systemic inflammation in depression
Mentor: Dr. Richard Shelton

D-3 Lyons, Jake (MS2)
The clinical and biochemical characterization of pancreatic diabetes
Mentor: Dr. Fernando Ovalle

D-4 Ma, Elizabeth (MSTP-GS2)
Role of microRNAs -150 and -33 in human insulin resistance
Mentor: Dr. Tim Garvey

D-5 Nichols, Nona (MS2)
Pro-inflammatory markers: A link between obesity and depression?
Mentor: Dr. Richard Shelton

D-6 Pelham, Heath (MS2)
Analysis of dyslipidemia in children with type 2 diabetes mellitus
Mentor: Dr. Ambika Ashraf

D-7 Sherrer, Nathan (MS2)
Targeted disruption of the skeletal myocyte circadian clock markedly impacts skeletal muscle insulin sensitivity and metabolism
Mentor: Dr. Marin Young

Group E

E-1 Akers, Zeb (MS1)
The efficacy of Peer-lead weight loss interventions: A systematic review
Mentor:

E-2 Ahmed, Bilal (MS2)
Link between depression and weight loss in overweight African American women
Mentor: Dr. Monika Baskin

E-3 Cotter, Alex (MS4)
Designing MyDiabetsConnect.com: development and implementation of an interactive community resource website for diabetes
Mentor: Dr. Andrea Cherrington

E-4 Dowla, Shima (MSTP-GS1)
Primary care provides, peer advisor, and patient reported barriers to improvement of cardiovascular health for individuals living in the Alabama black belt
Mentor: Dr. Monika Safford

E-5 McFarland, Alex (MS3)
A novel primary care program for homeless veterans: descriptive analysis of the Homeless Patient-Aligned Care Team (HPACT) in Birmingham
Mentor: Dr. Stefan Kertesz

E-6 Owens, Sarah (MS2)
Attitudes and beliefs about diabetes medications and illness acceptance in the rural black belt
Mentor: Dr. Monika Safford

E-7 Sheth, Roshni (MS2)
Examining the relationship between socioeconomic status (SES), stress, and dietary intake of women in the deep south.
Mentor: Dr. Tiffany Carson

E-8 Thai, Ynhi (MS2)
Social determinants of obesity: Recruitment methods, strategies, and challenges for a health survey among Latino and non-Latino individuals in Albertville, Al
Mentor: Dr. Andrea Cherrington

E-9 Urazakova, Elina (MS3)
Resiliency: Factors that contribute to recovery in community-dwelling older adults
Mentor: Dr. Cynthia Brown

E-10 Wesson, Emily (MS2)
Qualities of diabetes patients with medication adherence in rural Alabama
Mentor: Dr. Monika Safford

Group F

F-1 Boyle, Shannon (MS2)
Changes in medical students' attitudes on abortion and other reproductive health topics
Mentor: Dr. Nathaniel Robin

F-2 Ehlinger, Megan (MS4)
Survey of Cardiologists' and electrophysiologists' hopes to gain new information on genetic services offered to Long QTsyndrome patients
Mentor: Dr. Nathaniel Robin

F-3 Elliott, Carter (MS2)
Shift-to-shift handoff evaluation and feedback tools: A systematic review of the literature
Mentor: Dr. Lee Ann Riesenberg

F-4 Harper, Jeff (MS4)
Knowledge of anaphylaxis and epinephrine autoinjectors among pediatric fellows and residents
Mentor: Dr. Nancy Tofil

F-5 Jacobs, Adam (MS2)
The evolution of physician attitudes: Trisomy 18
Mentor: Dr. Nathaniel Robin

F-6 Johnston, Lucy (MS3)
Self-reported OB/GYN resident experiences with difficult consultations: A platform for curriculum development
Mentor: Dr. John Woods

F-7 Kennell, Tim (MS2)
This is your brain on informatics: A total-immersion data sciences course for the next generation of informaticists
Mentor: Dr. Seung Park

F-8 Lander, Jessica (MS4)
Creating a safe sleep environment on the mother-baby unit: More than just infant sleeping position
Mentor: Dr. DeeAnee Jackson

F-9 Mascia, Katherine (MS2)
Attitudes of deaf individuals towards genetic testing of genes known to cause deafness
Mentor: Dr. Nathaniel Robin

F-10 Venkatesh, Raam (MS2)
Methods for longitudinally tracking graduates of a short-term cancer research training program
Mentor: Dr. John Waterbor

F-11 Wooten, Melanie (MS4)
The art of empathy: Does exposure to a humanities-based extracurricular activity affect empathy changes in third-year medical students?
Mentor: Dr. Melanie Tucker

Group G

G-1 Anderson, Jennifer (MS2) and Koplon, Joshua (MS2)
Correlation between HCV and mental illness in the ED
Mentor: Dr. James Galbraith

G-2 Davison, Peter (MS2)
Ketamine as an analgesic in the emergency department
Mentor: Dr. Matthew DeLaney

G-3 Ference, Edward (MS2)
Contribution of demographics and psychological risk factors to the expression of acute stress reactivity in the inpatient setting following acute medical trauma
Mentor: Dr. Amy Knight

G-4 Herrera, Nicholas (MS2)
National characteristics of EMS responses of older adults in the United States
Mentor: Dr. Henry Wang

G-5 Morris, James (MS3)
Pediatric emergency department asthma pathway effect on length of stay
Mentor: Dr. Valerie Davis

G-6 Pearce, Robertson (MS2)
Emergency department-based palliative care needs assessment of adults with heart failure
Mentor: Dr. Alexander Lo

G-7 Powell, T. Clark (MS4)
Characteristics of patients with acute kidney injury (AKI): Resolving community acquired AKI (CA-AKI) compared to hospital acquired AKI (HA-AKI)
Mentors: Dr. Henry Wang and Dr. David Warnock

G-8 Staggers, Rucker (MS2)
Civilian gunshot injuries to the spine: Application to current spinal injury classification systems that were designed for blunt force trauma
Mentor: Dr. William Neway

G-9 Stiff, Robyn (MS2)
Observing and comparing the effects of dilaudid, morphine, and low dose ketamine in severe pain patients
Mentor: Dr. Matthew Delany

G-10 Vaughan, Laurel (MS4)
Penetrating limb injuries: a 5 year retrospective analysis from a Level 1 Trauma Facility
Mentor: Dr. Duraid Younan

Group H

H-1 Boppana, Sushma (MSTP-M1)
Heterogeneity in ficolin-2 recognition of serotype 31 Streptococcus pneumoniae clinical isolates
Mentor: Dr. Moon Nahm

H-2 Gragg, Stephen (MSTP-MS2)
CX3CL1 in Aspergillus-associated fungal asthma
Mentor: Dr. Chad Steele

H-3 Hewitt, Ben (MS2)
Variability in HSV-2 index values over time
Mentor: Dr. Nicholas Van Wagoner

H-4 Kraus, Alex (MS2)
The creation of lldD1/lldD2 knockouts: Insight into Mycobacterium tuberculosis' utilization of alternate metabolic pathways
Mentor: Dr. Adrie Stein

H-5 Theiss, Lauren (MS2)
Proteomic atlas of the human tuberculous lung
Mentor: Dr. Adrie Steyn

H-6 Olson, Kristin (MS2)
Correlation of Nugent score with vaginal symptomatology among sexual risk behavior groups of women
Mentor: Dr. Christina Muzny

H-7 Stone, Sara (MSTP-G3)
T-bet and IFNγR signaling regulate germinal center responses and long-lived plasma cell development in an influenza model
Mentor: Dr. Frances Lund

H-8 Wallace, Suzanne (MS2)
Pregnancy outcomes in Alabama women with HIV1 infection
Mentors: Dr. Marilyn Crain and Dr. Michelle Khan

Group I

I-1 **Azerf, Saji (MS4)**
Rituximab treatment for chronic Henoch-Schonlein Purpura
Mentor: Dr. Randy Cron

I-2 **Chen, Edward (MS2)**
Investigation of the role of CD11b in the contact hypersensitivity model
Mentor: Dr. Xu Hui

I-3 **Dennis, Evida (MSTP-GS1)**
The pro-inflammatory effect of Cytomegalovirus on primary intestinal macrophages
Mentor: Dr. Phillip Smith

I-4 **Moseley, Carson (MSTP-GS4)**
Transcriptional regulation of Interleukin 10 in autoimmunity
Mentor: Dr. Casey Weaver

I-5 **Murphy, Austin (MS2)**
Environmental mediated intestinal restitution
Mentor: Dr. Colin Martin

I-6 **Sethi, Jaskirat (MS2)**
Identifying cell source of IL-13 production in ulcerative colitis
Mentor: Dr. Peter Mannon

I-7 **Singer, Jeff (MSTP-GS3)**
Rorgt positive innate lymphoid cells are important for neonatal intestinal barrier development
Mentor: Dr. Casey Weaver

Group J

J-1 **Al Sadek, Camli (MS2**)
The effect of UV radiation on the skin microbiome
Mentor: Dr. Nabiha Yusuf

J-2 **Carey, Christopher (MS2)**
Genetic analysis of chronological aging in yeast
Mentor: Dr. John Hartman

J-3 **Dussaq, Alex (MSTP-GS3)**
Kinomic dashboard: a webApp ecosystem for the analysis of kinase activity data
Mentor: Dr. Jonas Almieda

J-4 **Fernandez, Timothy (MS2)**
A novel method for quantifying chaperone protein activity using isothermal titration calorimetry
Mentor: Dr. James Bardwell

J-5 **Hardigan, Andrew (MSTP-GS3)**
Creating a high throughput RNA-seq analysis pipeline
Mentor: Dr. Richard Myers

J-6 **Hubbard, Meredith (MS3)**
Amelioration of telomere-mediated DNA damage responses and reactive oxygen species by antioxidants
Mentor: Dr. Frederick Goldman

J-7 **Hyde, Andrew (MS2)**
A strategy to identify natural genetic variation affecting longevity in S. cerevisiae
Mentor: Dr. John Hartman

J-8 **Laufer, Vincent (MSTP-GS2)**
The genetics of rheumatoid arthritis in persons of African-American ancestry
Mentor: Dr. Lou Bridges

J-9 **Patel, Jit (MS2)**
Quantitative high throughput cell array phenotyping of Bortezomib in Saccharomyces cereveisiae
Mentor: Dr. John Hartman

J-10 **Pepin, Mark (MSTP-MS2)**
A systems biology approach to understanding the metabolic origin of diabetic cardiomyopathy
Mentor: Dr. Adam Wende

Group K

K-1 Allen, Heather (MSTP-GS5)
Role of C3 in the AAV-SYN model of Parkinson disease
Mentor: Dr. David Standaert

K-2 Eustace, Nicholas (MSTP-GS1)
MARCKS has a critical role in growth and proliferation of glioblastoma multiforme
Mentor: Dr. Chris Willey

K-3 Figge, David (MSTP-GS3)
Genetic susceptibility in Levodopa induced dyskinesia
Mentor: Dr. David Standaert

K-4 Guzman Karlsson, Mikael (MSTP-GS4)
The effect of soluble β-amyloid oligomers on memory associated transcription and DNA methylation
Mentor: Dr. David Sweatt

K-5 Meadows, Jarrod (MSTP- GS4)
Epigenetic regulation of homeostatic synaptic scaling via DNA methylation
Mentor: Dr. John Hablitz

K-6 Mulhern, Cherie (MS2) and Taylor Pickens (MS2)
The consequences of MicroRNA -31 deletions in GBM
Mentor: Dr. Susan Nozell

K-7 Patterson, Kelsey (MSTP-GS1) (Not Presenting)
Altered astrocyte function in a mouse model of Rett Syndrome
Mentor: Dr. Michele Olsen

K-8 Robert, Stephanie (MSTP-GS4)
Gliomas upset the excitatory/inhibitory balance in the brain, creating tumor-associated excitotoxicity and seizures
Mentor: Dr. Harald Sontheimer

K-9 Stoyka, Lindsay (MSTP-MS2)
The impact of the LRRK2G2019S mutation on alpha-synuclein aggregation
Mentor: Dr. David Standaert and Dr. Laura Volpicelli-Daley

K-10 Webb, William (MSTP-GS2)
Histone ubiquitination is a critical epigenetic regulator of memory formation
Mentor: Dr. Farah Lubin

Group L

L-1 Cohen, Joshua (MSTP-GS2)
Maternal style shapes limbic brain development and emotional behavior in rats genetically prone to high anxiety
Mentor: Dr. Sarah Clinton

L-2 Ference, Edward (MS2)
Barriers to recruitment of patients with acute traumatic injury for neuroimaging studies
Mentor: Dr. Amy Knight

L-3 Lysek, Michael (MS2)
Oxidative stress in a porcine model of spinal cord injury
Mentor: Dr. Candace Floyd

L-4 Newsome, Courtney (MS2)
Predictors of outcome and mortality following traumatic brain injury in children
Mentor: Dr. James Johnston

L-5 Singh, Lovepreet (MS2)
Subanesthetic ketamine as model for psychosis- A preliminary analysis
Mentors: Dr. Nina Kraguljac and Dr. Michael Froelich

L-6 Vande Lune, Patrick (MS2)
A new therapeutic approach to managing the aftermath of traumatic brain injury: Manipulation of O-GlcNAcylation via Thiamet-G
Mentor: Dr. Candace Floyd

L-7 Zipplerly, Morgan (MSTP-MS1)
Individual differences in novelty-seeking and emotional reactivity: noradrenergic activation in the brainstem following forced-swim stress

Group M

M-1 Bliss, Kody (MS2)
PE+ exosomes as a novel proteolytic pathway of inflammation
Mentor: Dr. J. Edwin Blalock

M-2 Dunlap, Quinn (MS4)
Chlorogenic acid- a potential activator of dysfunctional mucus transport in chronic rhinosinusitis
Mentor: Dr. Brad Woodworth

M-3 Englert, Daniel (MS2)
Ion transport phenotype of upper airway epithelium in the CFTR -/- rat
Mentor: Dr. Brad Woodworth

M-4 Lam, Adam (MS2)
The role of heme in bromine induced lung injury
Mentor: Dr. Sadis Matalon

M-5 Lin, Erica (MS4)
Association between early coagulopathy and ventilator-associated pneumonia in spinal cord injury patients
Mentor: Dr. Duraid Younan

M-6 Lockhart, Jon (MSTP-GS3)
Cure of humanized mouse model of Cooley's anemia by non-cytoreductive bone marrow transplantation from a MHC-mismatched donor.
Mentor: Dr. Thomas Ryan

M-7 Tisher, Neal (MS2)
Heme-oxygenase-1 expression prevents doxorubicin-induced cardiac toxicity
Mentor: Dr. Anupam Agarwal

Group N

N-1 Epps, Nathan (MS4)
A multidisciplinary, longitudinal simulation to teach pediatric residents and nurses how to diagnose, treat, and manage pediatric patients with diabetic ketoacidosis
Mentor: Dr. Marjorie Lee White

N-2 Jaleel, Ayesha (MS4)
Intensive care unit interprofessional education simulation
Mentor: Dr. Marjorie Lee White

N-3 McDonald, Matt (MS4) (Not Presenting)
Rapid cycle deliberate practice: Implementing a new approach to team building and education in neonatal resuscitation team training
Mentor: Dr. Lindy Winter

N-4 Starling Klebbel, Kayla (MS4)
Pilot of Masters of Science in Health Administration student participation in simulation-based education
Mentor: Dr. Marjorie Lee White

N-5 Trenina, Anastasia (MS4)
First five minutes of the code
Mentor: Dr. Marjorie Lee White

Group O

O-1 **Broadwater, Devin Reese (MS2)**
Intracranial EEG Resection Planning and Long-Term Postoperative Outcomes Following Epilepsy Surgery
Mentor: Dr. Matthew Davis

0-2 **Craig, Eric**
Flexor tenon repair with a knotless, bidirectional barbed suture: An in vivo biomechanical analysis
Mentor: Dr. Grady Maddox

O-3 **Douglass, Kendall**
Hypoalbuminemia in neonatal patients during the post-operative period from cardiac surgery with cardiopulmonary bypass
Mentor: Dr. Jeffrey Allen

O-4 **Hingoranai, Neha (Not Presenting)**
Quality of life in Fontan survivors: A comparison with heart transplant recipients without Fontan and general US population without heart disease
Mentors: Dr. David Cleveland and Dr. Manisha Kukreja

O-5 **Madhav, Jaya (MS**
Sonographic predictors of outcomes in prenatally-diagnosed gastroschisis
Mentor: Dr. Joseph Biggio

O-6 **Massey, Julia (MS2)**
Outcomes of cardiac surgery in adult renal transplant recipients
Mentor: Dr. William Holman

O-7 **May, Matthew**
Clinical practice trends of vena cava filter utilization at a single tertiary care center over a 12 year period
Mentors: Dr. William Jordan and Dr. Marc Passman

O-8 **Merriman, John & Watson, Andrew (MS2)**
Early and late outcomes after surgical correction of anomalous left coronary artery from the pulmonary artery: a 41 year experience
Mentor: Dr. David Cleveland

O-9 **Pavnica, Jozef (MS2)**
A forty-three year experience with surgical correction of transposition of the great arteries with ventricular septal defect and left ventricular outflow tract obstruction
Mentor: Dr. James George

O-10 **Taylor, Malcolm (MS2)**
Risk factors for pediatric surgical readmissions: An analysis of the Pediatric NSQIP database
Mentor: Dr. Robert Russell

O-11 **Young, Brad (MS2)**
Risk factors for pulmonary embolism following shoulder arthroplasty
Mentor: Dr. Brent Ponce

Ahmed, Malik Bilal (Bilal) MBAHMED@uab.edu

Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Monica Baskin Abstract Approved By Advisor: Yes

Co-Authors:

Title: Link Between Depression and Weight Loss in Overweight African American Women

It is well-established in the literature that African American women experience a disproportionate level of obesity relative to the general population. An overwhelming 78% of African American women can be characterized as “overweight” or “obese”, while 50% fit the definition of “obese” (Flegal et. al., 2010). Furthermore, With this in mind, the Journey to Better Health project aimed to introduce evidence-based individual weight loss programs along with evidence-based community intervention in order to achieve maximal weight loss among overweight or obese African American women living in rural Alabama and Mississippi. As preparation for participation in the project, participants were given multiple questionnaires, two of which were the Center for Epidemiological Studies Depression Scale, measuring depressive symptoms using ten questions, and the Hassles Scale, measuring recent stress levels using fourteen questions. These required subjects to self-report feelings of stress and depression on standardized scales that have been used in past assessments.

A characterization of depression among individuals attempting to lose weight promises better clinical outcomes, as much of the population is currently overweight and often, individuals attempting to lose weight fail or relapse (source). If depression plays a large role in failure, attempts can be made to identify depressed individuals before their depression leads them back to weight gain. With proper counseling and access to appropriate healthcare measures, healthcare providers stand a better chance of successfully combating weight gain and obesity, perhaps leading to a healthier overall population.

A cursory search of the literature yields precious few studies investigating links between depression and weight loss, and as such, the data collected from the participants of Journey to Better Health could help bridge a gap in understanding regarding links between weight loss and psychosocial factors. While this study focused on a specific population, the outcomes from this study may help guide future studies.

Akers, Saier W. (Zeb) zebakers@uab.edu

Project Length: Prior Research Experience:

Source of Funding:

Faculty Advisor: Abstract Approved By Advisor:

Co-Authors:

Title: The Efficacy of Peer-Led Weight Loss Interventions: A Systematic Review

Given the rising cost of healthcare and the high prevalence of obesity, there is urgent need for cost-effective weight loss interventions. Though medical professionals are in a unique position to treat obesity, utilizing them as weight loss interventionists is relatively expensive, and they often lack the time and skills necessary to effectively do so. Thus, alternative interventionists may be needed. The aim of this systematic review was to assess the efficacy of weight loss programs delivered by peer-interventionists. A review of PubMed was conducted to identify randomized controlled trials reporting the effects of peer-delivered weight loss interventions with adults. For the purposes of this review, peers were defined as lay members of the community from which participants were recruited. The following combinations of search terms were utilized: 1) 'obesity', 'overweight', or 'weight loss'; AND 2) 'intervention' or 'treatment'; AND 3) 'peer', 'coach', 'community health worker', 'CHW', or 'promotora'. Eight studies met inclusion criteria and were included for review. Five of the eight trials compared peer-led to professionally-led weight loss interventions, four implemented intensive weight loss interventions ($\geq$14 treatment contacts), four focused on ethnic minorities, three focused on patients with specific chronic conditions, and two reported extended outcomes (assessed $\geq$6 months following baseline). Reported mean outcomes of peer-led weight loss interventions ranged from a loss of -5.57 kg to a gain of +0.2 kg. Five studies reported significant weight loss in their peer-led treatment arms, four of which utilized intensive interventions ($\geq$14 contacts). Three studies found peer-led interventions to be significantly more effective than professionally-led interventions. In conclusion, peer-led weight loss interventions appear to be an effective short-term option for treating obesity, contingent upon a sufficient 'dose' of treatment contacts. Further research is needed to determine the long-term effects and cost-effectiveness of peer-led weight loss interventions.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Nabiha Yusuf Abstract Approved By Advisor: Yes

Co-Authors:

Title: The effect of UV radiation on the skin microbiome

With skin cancer being one of the most commonly diagnosed cancers in the world, research is needed to determine factors that may cause individuals to be more susceptible to developing skin cancer. One such target for research is the skin microbiome, the ecosystem of living biological components that live in balance with the host. Factors that disrupt the natural microbiome balance could explain how certain populations have a higher incidence of skin cancer. It is known that skin is exposed to external stressors like UV radiation, a potent carcinogen and mutagen, on a daily basis. In addition, UVR is a known microbicidal and can disrupt the skin microbiome balance with the host. This research hypothesizes that UV radiation alters the skin microbiome causing the skin to be more susceptible to skin cancer due to Toll-like receptors that may be increasingly activated with an altered skin microbiome. To test this hypothesis, patient skin samples exposed to UVB radiation at different time points are swabbed to collect it's microbiome. The DNA of the micro biome was isolated and then analyzed using PCR and compared to non-irradiated samples to determine differences in the populations of the skin microbiomes.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Nabiha Yusuf Abstract Approved By Advisor: Yes

Co-Authors: Erin Burns, Thompson Foy, Mohammad Abdelgawwad, Sumeira Huda, Abdullah Shaheen, Prescilia N. Isedeh, Ranjit, Kumar, Travis Ptacek, Henry Lim, Casey M. Morrow, Craig A. Elmets, Nabiha Yusuf

Title: The effect of UV radiation on the skin microbiome

Skin is continuously exposed to external environmental stressors, such as ultraviolet (UV) radiation that may modulate colonization by the skin microbiota. There is no information on the effect of UV on the skin microbiome, despite the fact that UV radiation is one of the major environmental factors to which people are exposed, has a number of biological effects that may be influenced by the microbiota. There is no information on the relation of skin microbiome with susceptibility to UV radiation and the adverse and beneficial health effects of this form of radiant energy. We hypothesize that cutaneous microbiome will change following exposure to ultraviolet radiation. To examine the effect of UV on skin microbiome, participants were exposed to different doses of UVA or UVB in the Dermatology clinic of Henry Ford Foundation (Detroit, MI). The skin of the participants was swabbed before UV exposure, immediately after UV exposure, and 24h after UV exposure. DNA was isolated from the swabs, and then subjected to PCR and NextGen sequencing to identify the microbial populations in the samples. The irradiated samples were compared to the non-irradiated samples to determine differences in the skin microbiome. The sequencing data is currently being analyzed. The results from this study will provide new information about the resistance of certain microbial strains to UV and their re-colonization after UV exposure.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES

ProgramFaculty Advisor: Dr. Nabiha Yusuf Abstract Approved By Advisor: Yes

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Nabiha Yusuf Abstract Approved By Advisor: Yes

Co-Authors: Erin Burns, Thompson Foy, Mohammad Abdelgawwad, Sumeira Huda, Abdullah Shaheen, Prescilia N. Isedeh, Ranjit, Kumar, Travis Ptacek, Henry Lim, Casey M. Morrow, Craig A. Elmets, Nabiha Yusuf

Title: The effect of UV radiation on the skin microbiome

Skin is continuously exposed to external environmental stressors, such as ultraviolet (UV) radiation that may modulate colonization by the skin microbiota. There is no information on the effect of UV on the skin microbiome, despite the fact that UV radiation is one of the major environmental factors to which people are exposed, has a number of biological effects that may be influenced by the microbiota. There is no information on the relation of skin microbiome with susceptibility to UV radiation and the adverse and beneficial health effects of this form of radiant energy. We hypothesize that cutaneous microbiome will change following exposure to ultraviolet radiation. To examine the effect of UV on skin microbiome, participants were exposed to different doses of UVA or UVB in the Dermatology clinic of Henry Ford Foundation (Detroit, MI). The skin of the participants was swabbed before UV exposure, immediately after UV exposure, and 24h after UV exposure. DNA was isolated from the swabs, and then subjected to PCR and NextGen sequencing to identify the microbial populations in the samples. The irradiated samples were compared to the non-irradiated samples to determine differences in the skin microbiome. The sequencing data is currently being analyzed. The results from this study will provide new information about the resistance of certain microbial strains to UV and their re-colonization after UV exposure.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: David G Standaert Abstract Approved By Advisor: Yes

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

Title: Role of C3 in the AAV-SYN model of Parkinson disease

Parkinson disease (PD) is a neurodegenerative disorder characterized by loss of dopaminergic neurons in the substantia nigra (SN) and intraneuronal aggregates of alpha-synuclein (a-syn). In human PD, there is evidence of chronic neuroinflammation, an important contributor to neuron loss; however, the mechanism by which a-syn-induced neuroinflammatory changes lead to neurotoxic effects are unclear. This study investigates a role for the complement component 3 (C3) in an a-syn-based model of PD.

To model PD, we injected an adeno-associated virus overexpressing a-syn (AAV-SYN) into the SN. To determine whether a-syn induces C3 upregulation *in vivo* and *in vitro*, we assessed C3 mRNA production 4 weeks post-injection of AAV-SYN; we also assessed C3 protein production in primary microglia treated with aggregated a-syn for 4 hours. At 4 weeks post-AAV-SYN-injection, we observed induction of C3 mRNA 4.5 fold over control-injected mice ($p<0.05$). In primary microglia treated with aggregated a-syn for 4 hours, we observed a 2 fold upregulation of C3 protein over vehicle ($p<0.01$). These results suggest that a-syn induces C3 expression.

To determine whether neuroinflammation in AAV-SYN mice was C3-dependent, we assessed microglial activation and IgG deposition by immunohistochemistry and blinded rating in C3-/- mice 4 weeks post-AAV-SYN-injection. We observed microgliosis and IgG deposition in both wildtype and C3-/- AAV-SYN mice, suggesting that neuroinflammation occurred in a C3-independent manner. To determine whether complement activation occurred independent of C3, we assessed C9 deposition in both wildtype and C3-/- mice 4 weeks post-injection with AAV-SYN; we did not see C9 deposition in either wildtype or C3-/- mice.

These experiments show a-syn-induced expression of C3 both *in vivo* and *in vitro*. Although knocking out C3 does not protect mice from neuroinflammation in the AAV-SYN model of PD, it will be interesting to determine whether C3-/- AAV-SYN mice are protected from dopaminergic neurodegeneration 6 months post-injection.

PD

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Suzanne Oparil and Fadi Hage Abstract Approved By Advisor: Yes

Co-Authors: Samantha Giordano, Daisy Xing, Yuan-Yuan Gao, Fadi Hage, Suzanne Oparil

Title: The Differential Vasoprotective Effects of Estrogen in Pre- and Post-Menopausal Women

Motivation: Cardiovascular disease (CVD) is the leading cause of mortality of in women, accounting for 25% of all deaths. The onset of disease typically occurs later in women than men, and it is thought that this delay is due in part to the anti-inflammatory effects of estrogen (17B-estradiol, or E2) on the vasculature. This anti-inflammatory property is in part mediated by attenuating the expression of inflammatory molecules by activated monocytes, or macrophages. This mechanism is well-established in young women, but its effect on the vasculature in post-menopausal women – who no longer produce estrogen – is unclear.

Objective: We hypothesized that E2's effects on macrophages will be age and hormone status dependent. We expected that E2 would attenuate expression of inflammatory mediators in macrophages in both pre-menopausal women and post-menopausal women who have taken exogenous E2 (i.e. hormone replacement therapy, or HRT) since menopause; in post-menopausal women who do not take HRT, however, we expected that E2 would not attenuate inflammatory mediator expression.

Approach and Results: Peripheral monocytes were isolated and grown from three groups of women: (1) pre-menopausal, (2) post-menopausal women taking HRT since menopause, and (3) post-menopausal women not taking HRT. Nine women were recruited in the study: five women in group 1, one in group 2 and 3 in group 3. Cells were pretreated with E2 or vehicle, then treated with C-reactive protein (a pro-inflammatory mediator) or vehicle. Results are presently pending, with analysis of expression of mRNA of inflammatory mediators (IL-1, TNF-a, etc.) to be evaluated with RT-PCR.

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Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: James Galbraith Abstract Approved By Advisor: Yes

Co-Authors: Joshua Koplon, James Galbraith, Joel Rodgers

Title: CORRELATION BETWEEN HCV AND MENTAL ILLNESS IN THE ED

Intro
To address the estimated 3.3% nationwide prevalence of HCV among the “baby boomer” birth cohort, emergency departments (ED) have been identified as potentially high-yield settings for HCV screening and linkage-to-care. Barriers to successfully linking HCV-positive cases to treatment primarily include lack of health coverage, limited access to primary care services, and mental health co-morbidities. To better understand mental health related burdens, we compared mental health co-morbidities among UAB-ED “baby boomers” that screened HCV antibody (Ab) positive and HCV Ab-negative.

Methods
We conducted a retrospective chart review of UAB-ED “baby boomer” patients screened for HCV between September 2013 and May 2014. Medical record data were abstracted using mental health-related ICD9 codes 290-319. Individuals screened for HCV during this period were randomized. A total of 707 cases were included in the final data analysis, including 377 Ab-positive and 330 Ab-negative cases. Data were examined using standard frequency and descriptive statistics.

Results
Compared to HCV negative controls (n=330), HCV Ab-positive cases (n=377) were disproportionately affected by higher prevalence of Drug Psychosis (ICD9 292), Alcoholic Dependence Syndrome (ICD9 303), Drug Dependence (ICD9 304), and Non-dependent Abuse of Drugs And Tobacco (ICD9 305). Following are comparative results listed by ICD9 codes: 292: (6.63%) vs (2.42%) p = 0.008; 303: (14.59%) vs (7.27%) p=0.002; 304: (9.81%) vs (3.64%) p=0.001; 305: (27.06%) vs (21.21%) p= 0.071

Conclusions
Mental health co-morbidities are greater among HCV Ab-positive “baby boomers” compared to similar Ab-negative cases. Efforts to link HCV Ab-positive “baby boomers” should include strategies to mitigate barriers attributable to mental health co-morbidities.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Tim Townes Abstract Approved By Advisor: Yes

Co-Authors: Sumanth Prabhu, Tim Townes

Title: Inflammation Alters the Phenotype of Cardiac Mesenchymal Stem Cells

Background: Cardiovascular diseases are the most prominent cause of mortality in the US with ischemic heart disease as the predominant cause resulting in 1 million myocardial infarctions occurring every year in the US. Additionally, 5 million Americans live with chronic heart failure. Early intervention, in the form of thrombolytic therapy or primary percutaneous coronary intervention, has helped to reduce mortality due to acute causes, but treatment for chronic dysfunction is limited. Dysfunction occurs because the healing process is reparative and not regenerative. We hypothesize that inflammation pushes mesenchymal stem cells to differentiate into myofibroblasts resulting in pathologic fibrosis.

Methods: Cardiac mesenchymal stem cells were co-cultured with polarized macrophages for 5 days. These cells were mixed with collagen gel, which was allowed to polymerize. Contraction of the gel was evaluated after 48 hours.

Results: Cardiac mesenchymal stem cells looked phenotypically more like myofibroblasts. These cells had similar contraction of the collagen gel as compared to control myofibroblasts.

Conclusion: Inflammation does appear to alter the phenotype of cardiac mesenchymal stem cells. Whether that is the cause of pathologic fibrosis in vivo still needs to be determined.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Charles N. Landen, Jr Abstract Approved By Advisor: Yes

Co-Authors: Kelly Kreitzburg

Title: Understanding the role of autophagy in chemotherapy resistant ovarian cancer by targeting the Sphingosine-1-phosphate pathway

Ovarian cancer is the 5th leading cause of cancer death in women. Treatment typically consists of a combination of chemotherapy and surgery; however, many patients relapse within 2 years of initial treatment. Identifying the molecular pathways responsible for drug resistance will enable the development of more efficacious therapies. High-throughput analysis indicates that the Sphingosine-1-phosphate pathway is upregulated in ovarian cancer tumors treated with chemotherapy. This pathway can be inhibited by FTY-720, an oral agent used to treat multiple myeloma. Thus, the purpose of this project was to determine if treating chemotherapy-resistant ovarian cancer cells in combination with FTY-720 would overcome resistance, leading to greater tumor cell death. We performed cell viability assays on chemotherapy sensitive and resistant ovarian cancer cells treated with FTY-720 and various combinations of Carboplatin and Paclitaxel. However, we found that adding FTY-720 to chemotherapy increased tumor cell resistance. A hypothesis to explain the increase in resistance was that the cancer cells undergo cytoprotective autophagy when exposed to FTY-720. To test this, we looked at levels of autophagy proteins such as LC3-II in treated cells via immunoblot analysis. Elevated LC3-II levels indicated an increased level of autophagy occurring in treated cells. We also treated cells with Hydroxychloroquine, an inhibitor of autophagic flux, to further confirm the role of autophagy. We found that blocking autophagy in the treated cancer cells lead to an accumulation of autophagic proteins. These findings indicate that the antagonistic effect of FTY-720 is ascribable to its induction of autophagy. Future directions of the study will focus on further investigating the role of autophagy in chemotherapy resistance and developing therapy that inhibits autophagy.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Randy Cron Abstract Approved By Advisor: Yes

Co-Authors: Saji P. Azerf, Peter Weiser, Timothy Beukelman, Matthew L. Stoll, Daniel I. Feig, and Randy Quentin Cron

Title: Rituximab Treatment for Chronic Henoch-Schonlein Purpura

Objective. Evaluate the benefit of rituximab (RTX) in treating chronic corticosteroid (CS) dependent and CS sparing immunomodulatory treatment refractory Henoch-Schonlein purpura (HSP).
Methods. Children diagnosed with HSP treated with RTX during the years 2006-2013 at a single institution were identified). Clinical, laboratory, and therapeutic data were abstracted.
Results. Seven children, not previously reported, treated with RTX for chronic CS dependent HSP were identified. RTX was effective in achieving clinical remission, eliminating CS and other immunomodulatory treatment, and decreasing hospitalizations. No serious adverse events were noted.
Conclusion. RTX appears safe and effective for chronic CS dependent and immunomodulatory refractory childhood HSP.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Stuart J. Frank Abstract Approved By Advisor: Yes

Co-Authors: Dr. Martin E. Young

Title: Circadian Clock Knockout in Heart leads to altered Growth Hormone Signaling

The circadian clock is the body's way of keeping its trillions of cells and the countless signals and processes that occur inside each one all on the same page much like the director of an orchestra keeps time so the musicians know when to play their instruments. Likewise, when things are not in sync you have either clashing notes making terrible music that is painful to listen to or clashes in signaling that often lead to sickness and disease. Specific knockout of the circadian clock protein Bmal1 in the heart of C57 B6 mice (Cardiomyocyte-specific Bmal 1 Knockout, CBK) leads aberrant cell signaling and age onset cardiomyopathy. One signaling pathway that appears to be altered is the Growth hormone (GH)/Insulin-like growth factor 1 (IGF-1) axis as evidenced by increased IGF-1 gene expression throughout the day. Interestingly, this is achieved without altering the mRNA expression for the GH receptor (GHR); therefore the cause of increased signaling in this pathway must be post GHR translation. Our primary target is the ubiquitin ligase Suppressor of cytokine signaling 2 (SOCS2), a known suppressor of GH signaling, whose expression is decreased by 30% according to microarray analysis. This work is important in elucidating novel roles of the circadian clock in mammalian physiology and pathology.

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: J Edwin Blalock Abstract Approved By Advisor: Yes

Co-Authors:

Title: PE+ exosomes as a novel proteolytic pathway of inflammation

In the past our lab has redefined the “classic” mode of inflammation associated with IL-8. Specifically, IL-8 initiates neutrophilic influx, they in turn release Matrix metalloproteases (MMP), and Prolyl Endopeptidase (PE). The MMPs and PE then sequentially fragment collagen ultimately releasing Proline-Glycine-Proline (PGP) sequences. PGP, via structural similarity with IL-8 and consequent action on the IL-8 receptor CXCR2, propagates PMN influx and inflammation even after IL-8 levels have subsided.

Principal Findings:

1. After two weeks of treatment intratracheally (IT) with PE^+ exosomes, exosome-treated mice showed marked increases in their alveolar and right ventricular size as compared to the control group.
2. PMN influx and alveolar enlargement is negated by inhibition of PE activity. Mice were treated for two weeks with PE^+ exosomes, which included either 10µg ZPP or diluent. A separate control group was treated similarly with mesenchymal stem cell derived exosomes.
3. There is a time-dependent progressive increase in both alveolar enlargement and RVH. We treated mice with PE^+ exosomes three times per week IT, and sacrificed them at intervals of 2, 4, and 8 weeks. The difference in alveolar size between the controls and mice treated with PE^+ exosomes increased steadily over time.
4. Exosome counts are elevated in airways of cigarette smoke (CS) exposed mice. Mice were exposed to either room air or CS for 6 weeks. Exosomes were then isolated from BAL fluids, and analyzed.
5. Exosomal PE activity was enriched in exosomes obtained from COPD patients as compared to a control group.

These results demonstrate a novel pathway of inflammation in which the tripeptide PGP regulates the release of PE^+ exosomes. Considering that PE is the pivotal and nonredundant protease in the generation of PGP, it would seem an ideal therapeutic target to interrupt the PGP pathway and potentially ameliorate COPD.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Moon H. Nahm Abstract Approved By Advisor: Yes

Co-Authors: K. Aaron Geno

Title: Heterogeneity in ficolin-2 recognition of serotype 31 Streptococcus pneumoniae clinical isolates

Streptococcus pneumoniae (pneumococcus) is the leading cause of bacterial pneumonia and meningitis and is a major cause of otitis media. Its hallmark virulence factor is a polysaccharide capsule that protects the organism from opsonophagocytic killing. Over 90 capsular types (serotypes) have been identified, and each serotype differs in its capacity to cause disease and its interactions with host immunity. Serotype 31 (ST31) pneumococcus has a low prevalence in the general population but a higher-than-average mortality rate in patients older than five years with pneumococcal bacteremia or meningitis. Ficolin-2 is an innate lectin capable of supporting complement activation through the lectin pathway and was recently shown to bind to pneumococcal serotypes acetylated by the O-acetyltransferase WcjE, including ST31. In other serogroups, *wcjE* can be variably inactivated, yielding a spectrum of ficolin-2 binding; this is proposed to allow immune avoidance for serotypes normally acetylated by WcjE. Because ST31 encodes *wcjE*, we hypothesized that it may harbor similarly variable subtypes and examined nine ST31 isolates. Ficolin-2 binding was heterogeneous among our ST31 isolates but clustered in three distinct groups containing no, intermediate, or high ficolin-2 binding. However, sequencing of *wcjE* in all nine isolates showed that the gene was identical. To test whether the variability in ficolin-2 binding was due to the genetic background of the isolates or an unsequenced region within the capsular biosynthetic genes, we transformed these genes from the highest- and lowest-binding strains into a common genetic background. The resulting transformants belonged to the lowest ficolin-2-binding group, suggesting that the genetic background of ST31 strains may influence ficolin-2 binding and therefore influence the immune response to this serotype. These studies suggest that ficolin-2 binding (and perhaps the extent of O-acetylation on the capsule) in ST31 may be affected through mechanisms distinct from those of other serotypes.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Genetics Fellowship

Faculty Advisor: Nathaniel Robin, MD Abstract Approved By Advisor: Yes

Co-Authors: Nathaniel Robin, MD

Title: Changes in Medical Students' Attitudes on Abortion and Other Reproductive Health Topics

Introduction: Reproductive health care can be a controversial matter, especially when discussing options such as abortion. While the topic is highly debated, patients have the right to choose their treatment. Therefore, it is important that future physicians are properly educated on these topics. Espey's 2005 and Steinauer's 2009 studies together demonstrated how education on reproductive health topics varies greatly for medical students, and is especially limited for topics like abortion. Another set of studies, Shotorboni et al's 2004 and Rosenbalt et al's 1999, demonstrated that in general, the majority of preclinical medical students at one university believed most reproductive options should be allowed under at least some circumstances and were willing to have certain aspects available in their future practice. Our study aims to expand on these studies and investigate whether the opinions of medical students changes form the early preclinical to late clinical years and whether the curriculum plays a role in these changes.

Methods: A computer-based questionnaire will be distributed to 1st year and 4th year medical students at participating medical schools to survey their opinions on various reproductive care measures and how these opinions correlate to different demographics. We will then look to see if there is a change in students' opinions between the 1st and 4th year of medical school and whether change is correlated to emphasis of reproductive education and exposure.

Results: The questionnaire is in the end stages of revision and will be distributed to participating universities during the 2014 fall semester

Conclusion: Our study plans to expand on previous studies and potentially make a stronger case for the importance of appropriate reproductive health education for medical students. We anticipate that with more extensive education we will see the opinions of medical students shift in favor of allowing and administering these procedures and treatments.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Scott Ballinger Abstract Approved By Advisor: 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 causes are due to atherosclerosis. Despite the widespread prevalence of this disorder, the contribution of inherited genetics to CVD susceptibility remains poorly understood. Furthermore, the cellular mechanisms through which defined CVD risk factors such as age, ethnicity, family history, hypercholesterolemia, and tobacco smoke converge to stimulate atherogenesis have yet to be clearly articulated. Mitochondria are multifunctional organelles that sustain oxidant-mediated damage following chronic exposure to these CVD risk factors. In addition, mitochondria possess their own maternally inherited genome that reflects maternal geographic origins and contains polymorphisms capable of influencing mitochondrial and cellular function. In the following study, we directly assessed the causal role mitochondrial genetics and function play in the pathogenesis of atherosclerosis. Utilizing novel Mitochondrial-Nuclear eXchange (MNX) mouse technology developed in the our laboratory, apoE$^{-/-}$ WT (apoE$^{-/-}$ C57^{n}:C57^{mt}) and MNX (apoE$^{-/-}$ C57^{n}:C3H^{mt}) mice were generated in order to test the hypothesis that altering a mouse's mitochondrial genetic background would influence atherogenesis in this setting of genetically driven hypercholesterolemia. Our data has supported this hypothesis by demonstrating that apoE$^{-/-}$ C57^{n}:C3H^{mt} mice develop atherosclerotic lesions at a significantly lower degree than their apoE$^{-/-}$ C57^{n}:C57^{mt} counterparts. Moreover, studies in non-hypercholesterolemic C57 WT (C57^{n}:C57^{mt}) and C57 MNX (C57^{n}:C3H^{mt}) mice have demonstrated that the C3H mtDNA is also associated with altered vascular bioenergetics *ex vivo* and increased endothelial dependent vessel relaxation capacity, parameters that are closely linked to development of vascular dysfunction and pathology. Future experiments will build on these results by determining whether differences vascular oxidant production, mtDNA damage and inflammatory signaling exist between apoE$^{-/-}$ C57^{n}:C57^{mt} and apoE$^{-/-}$ C57^{n}:C3H^{mt} mice.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding:

Faculty Advisor: Matthew Davis Abstract Approved By Advisor: Yes

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Title: Intracranial EEG Resection Planning and Long-Term Postoperative Outcomes Following Epilepsy Surgery

Object: Intracranial EEG (ICEEG) recordings are used to plan resection boundaries for epilepsy surgery. Precise definition of the epileptogenic zone based on ICEEG can be complex, and standards for evaluating ictal and interictal ICEEG findings are lacking.

Methods: Patients with ICEEG electrodes and subsequent surgical resection with mean 22 month follow-up were identified. The first 15 seconds of ictal activity, divided into five 3-second epochs, was considered. A logistic regression model predicted whether cortex under a given electrode was included in the resection. Long-term outcomes were assessed through chart review.

Results: 19 included patients had 37 unique seizures. Rhythmic low-voltage fast activity in Epoch 1, rhythmic spikes in Epoch 1, low-voltage fast activity in Epoch 2, interictal paroxysmal fast activity, and “continuous” or “very frequent” interictal spikes associated with inclusion in the resection map. 58% of patients were Engle Class 1 more than 1 year postoperatively. Temporal lobectomy was not associated with either incidence of residual intra-operative spikes (χ_2, $p=0.2585$) or rate of seizure freedom (χ_2, $p=0.2937$) relative to neocortical resection. Presence of residual spikes was not associated with postoperative seizure freedom (χ_2, $p=0.622$).

Conclusions: Standardized methods for creating a resection map are essential for assessing the effectiveness of epilepsy surgery. In this practice, ictal early low voltage fast activity, ictal rhythmic spikes, and interictal paroxysmal fast activity were strongly associated with ultimate cortical resection. No covariates showed any association with long-term outcomes. Further studies may determine which resection map creation strategy results in the greatest rate of postoperative seizure freedom.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: John Hartman Abstract Approved By Advisor: Yes

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Title: Genetic analysis of chronological aging in yeast

Aging is a phenomenon common to all cellular organisms, about which the genetic basis is poorly understood. To investigate the genetics of aging we utilize the genomic knock out library of Saccharomyces cerevisiae. We apply a high through put growth curve technology (quantitative high throughput cell array phenotyping, Q-HTCP) to screen for genes that impact the percentage of cells surviving in stationary phase, a phenotype called chronological lifespan (CLS). Multiple genome-wide screens have been performed with limited reproducibility between them. To address this problem, we selected long-lived strains from the different screens and tested them in a new media designed to improve reproducibility and correct for the know effect of CLS-shortening due to acidity by buffering the media. Preliminary analysis of the screen revealed long-lived phenotypes due to knockout of genes associated with a variety of cellular functions, including mitochondrial (MAE1, FCM1, YDR379C-A, MRPL24, MBA1), nucleotide synthesis (ADE1, ADE5,7), and proteins linked to the TOR pathway (NNK1, MSD3). Short-lived phenotypes were also associated with knockout of genes encoding mitochondrial proteins (COQ4, ATP5, ATP17, ATP7, COQ3). Some of these phenotype have also been demonstrated across different media types. The results from this work support the idea that cellular respiration as well as other aspects of mitochondrial function play important roles in chronological lifespan, and provides a starting point toward a more unified understanding of the genetically complex process of CLS.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Andrea Cherrington Abstract Approved By Advisor: Yes

Co-Authors: Robert Oster, PhD; April Agne, MPH; Andrea Cherrington, MD MPH

Title: Assessing the Relationship of Education Level and Medication Adherence with Patients' Perception of Autonomous Support by Health-Care Providers in a Sample of Low Income African Americans with Diabetes.

Objective: Studies suggest that when health behaviors are autonomously motivated individuals are more likely maintain those behaviors over the long-term. We sought to assess the association between the degree to which patients' perceive their health care team as autonomy supportive (vs. controlling) and measures of diabetes self-care and glycemic control in a low income, African American population with type 2 diabetes.

Methods: Patients were recruited from a safety-net clinic in Jefferson County, AL for a 6-month diabetes management intervention. Patients were included if they indentified as African American, were ≥19 years, not pregnant, had no history of end-stage medical conditions, and had poorly controlled type 2 diabetes (HbA1c >7.5%). Face to face questionnaires assessed medication adherence (modified 8-item Morisky scale) diabetes self-care (Toobert) and perceived health care provider support via a 6-item Health Care Climate Questionnaire (HCCQ) modified for diabetes management. Demographic information was collected along with physiologic measures.

Results: Participants (n=119) had a mean age of 55yo (SD 8.4) as well as a mean HbA1c of 10.0% (SD 1.8). Out of all participants, 67% were female, and 81% had a HS degree, GED, or more. The HCCQ mean was 5.7 (SD 1.4). The Morisky medication adherence score was 6.0 (SD 1.9) suggesting moderate adherence on average. An association was found between autonomy-supportive care (HCCQ) and medication adherence ($r = 0.273$, $p = 0.007$) for general diet ($r=0.212$, $p=0.02$) and for exercise ($r=0.217$, $p=0.02$). There was no significant association between HCCQ and glycemic control (HgbA1c).

Conclusion: In this sample of low income African American with diabetes, medication adherence, dietary behaviors and physical activity were positively associated with the degree to which patients' perceive their health care team as autonomy supportive. These findings are consistent with previous studies demonstrating that autonomous support correlates with better patient self-care outcomes.

Keywords: type 2 diabetes, education level, HCCQ, Morisky
Word count: 298

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Sadis Matalon Abstract Approved By Advisor: Yes

Co-Authors: Alexandria Krasny, Adam Lam, Saurabh Aggarwal, Tamas Jilling, Sadis Matalon

Title: Bromine exposure induces fetal growth restriction during pregnancy

Halogen gases are used in a variety of industrial applications, and exposure can result in respiratory failure. Currently, there are no specific treatments available after halogen exposure. Much interest in Br_2 exposure research is directed at vulnerable populations, such as pregnant females and children. Halogen-induced pulmonary injury and elevated pulmonary vascular resistance have been shown to be partially ameliorated by endothelin-1 (ET-1) antagonism. Halogen exposure also results in an inhibition of endothelial nitric oxide synthase (eNOS) with compensatory up-regulation of inducible nitric oxide synthase (iNOS). Previously, it was demonstrated in animal models of fetal growth restriction and preeclampsia that increased ET-1, and decreased nitric oxide (NO) production leads to the vasoconstriction of maternal blood flow to the developing fetus, resulting in fetal growth restriction and preeclampsia. Based on this research, we hypothesized that Br_2 exposure would increase the risk of preeclampsia and intrauterine fetal growth restriction. Pregnant mice (15 days gestation) were exposed to Br_2 gas (400ppm or 600ppm) for 30 minutes. We found that there was a higher drop in oxygen saturation, increased weight loss, and higher mortality in pregnant mice post Br_2 exposure, as compared to non-pregnant counterparts. Pregnant mice post exposure had fetuses with profound fetal growth restriction. At higher Br_2 concentrations (600ppm, 30min), 100% maternal mortality was observed in all pregnant animals prior to the expected delivery date along with severe growth restriction of the non-viable fetuses. These results correlated with an increase in the levels of the preeclampsia markers, soluble fms-like tyrosine kinase-1 (sFlt1) and ET-1, in the placenta and maternal lung tissue of the Br_2 exposed pregnant mice. In conclusion, our data indicates that pregnancy renders the mother and fetuses vulnerable to Br_2. Our preliminary understanding of the mechanisms suggest that Br_2-exposure induces preeclampsia/eclampsia syndrome that may be the reason for pregnancy-specific increased vulnerability.

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Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Nabiha Yusuf Abstract Approved By Advisor: Yes

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Title: Toll-Like Receptor-4 deficiency enhances repair of ultraviolet radiation induced DNA damage in skin and prevents skin cancer

UV (ultraviolet) B-induced DNA damage in the form of cyclobutane pyrimidine dimers (CPD) plays a critical role in skin carcinogenesis. XPA (Xeroderma pigmentosum complementation group A) is a repair enzyme that gets activated upon UVB-induced DNA damage. Toll-like receptors (TLR), one component of innate immunity, are intricately associated with host immunity. The purpose of this study was to determine whether repair of UVB-induced DNA repair responses is regulated by toll-like receptor-4 (TLR4). TLR4-deficient and wild type (WT) mice were subjected to 90 mJ/cm^2 UVB radiation. WT mice exhibited significant (p<0.05) DNA damage in the form of CPD, whereas TLR4-deficient mice developed significantly fewer cutaneous CPD (p<0.05). The expression of XPA mRNA and protein was significantly less (p<0.05) in skin from WT mice than TLR4-deficient mice after UVB exposure. This was followed by a concomitant decrease in *XPA* expression. When mice were exposed to multiple doses of UVB radiation (200 mJ/cm^2) for 40 weeks, cutaneous carcinogenesis was retarded in terms of tumor incidence and latency in TLR4-deficient mice compared to TLR4-competent mice, whereas significantly greater (p<0.05) numbers of tumors developed in TLR4-competent mice. There was significant (p<0.05) up-regulation of cutaneous inflammatory markers in TLR4-competent mice compared to TLR4-deficient mice. To study whether TLR4-mediated DNA damage, inflammation, and tumor development is due to this repair mechanism, we generated TLR4-/-/XPA-/- mice by crossing TLR4-/- and XPA-/- mice. After two weeks of exposure to UVB (25 mJ/cm^2), severe sunburn was observed in the skin of all XPA-/- mice, whereas only 50% of TLR4-/-/XPA-/- mice developed sunburn. There was minimal sunburn observed in WT mice and TLR4-/- mice remained free of sunburn. Future studies will examine inflammatory markers in these mice. Thus, strategies to inhibit TLR4 may allow us to develop preventive and therapeutic approaches for management of UVB-induced cutaneous DNA damage and skin cancer.

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Project Length: Short

Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Xu Hui

Abstract Approved By Advisor: Yes

Co-Authors: Anna Hui Li, Xu Hui

Title: Investigation of the Role of CD11b in the Contact Hypersensitivity Model

CD11b is a member of beta2 integrin molecules, which is expressed on granulocytes, monocytes, and macrophages. Together with CD18, it forms an integrin molecule which serves as a receptor for many ligands. CD11b mediates inflammatory responses by regulating leukocyte adhesion, migration and function.

Previous research has indicated that the function of CD11b is context dependent. In this study, we investigate the role of CD11b in cutaneous immune responses using the contact hypersensitivity model and hypothesize that CD11b deficiency alters immune response in the skin. The cutaneous immune response has vital roles in the development of skin tumors.

To examine whether CD11b has an effect on the activation of macrophages, we isolated bone marrow cells from wild type and $CD11b^{-/-}$ mice and generated macrophages in cultures with M-CSF. We then stimulated the macrophages and examined levels of signal molecules using Western blot. We also took skin tissues from wild type and $CD11b^{-/-}$ mice with cutaneous inflammation in the CHS model and stained tissue sections with fluorescent antibodies to compare infiltration of immune cells through microscopy. Additionally, lymphocytes from lymph nodes of immunized wild type and $CD11b^{-/-}$ mice were harvested and stimulated with anti-CD3 antibodies, and we measured cytokine levels in the culture supernatants.

The results from our experiments showed that with $CD11b^{-/-}$ mice, there was a decreased overall immune cell infiltration compared to wild type skin tissues, while Western blot experiments had varied outcomes not readily generalized. Moreover, there was a decreased production of the cytokines of interest by lymphocytes of $CD11b^{-/-}$ mice.

In conclusion, we believe that though some original predictions were not confirmed concerning CD11b, there is evidence that suggests that CD11b has an immunologic role in the skin. We will continue to investigate CD11b and hope to shed more light into immune responses and tumorigenesis in the skin.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Amanda Willig Abstract Approved By Advisor: Yes

Co-Authors: Janis Cho, Philip A Kramer, Balu K Chack, Ashutosh Tamhane, E. Turner Overton, Victor M Darley-Usmar, Sonya L Heath, Amanda L Willig.

Title: Racial Differences in Mitochondrial Dysfunction and Social Determinants of Obesity.

Introduction: Infection with human immunodeficiency virus (HIV) has become a chronic, manageable disease, yet HIV also may impact risk for metabolic disease through impaired mitochondrial function. Racial disparities in chronic disease risk have been observed, and differences in mitochondrial function may explain a portion of this variance. Our objective was to compare mitochondrial function between HIV infected black and white women.
Method: Virologically suppressed HIV-infected women on antiretroviral therapy for at least 1 year at the University of Alabama – Birmingham 1917 HIV/AIDS Clinic were included. Body Mass Index (BMI) was categorized as normal weight (20 – 25) and obese (≥30). The XF24 analyzer was used for a novel real-time cellular energetics platform to assess basal mitochondrial respiration, mitochondrial efficiency through proton (ATP-linked) leak, maximal oxygen respiration, reserve capacity, and non-mitochondrial respiration. A composite Bioenergetic Health Index (BHI) was computed for each cell type as ([reserve capacity x ATP-linked] / [non-mitochondrial x proton leak])[1].
Results: Among 35 participants, 28 were black with mean BMI 33 ± 5.76 compared to 7 white women with BMI 28 ± 7.56 ($P<0.01$). There were no significant racial differences in BHI for lymphocytes or monocytes. However, a trend for lower monocyte ATP-linked function was observed in black (35.48 ± 2.32) compared to white (50.35 ± 4.93) women ($P = 0.09$). Lymphocyte function also differed by race, with a trend for lower ATP-linked function in black (16.12 ± 0.88) versus white (19.00 ± 1.85) women ($P = 0.10$), and a lower maximal respiration was noted (24.53±1.30 black; 32.07±3.08 white; $P = 0.05$).
Conclusion: As expected, black women had higher mean BMI. The overall trend in monocyte ATP-linked, lymphocyte ATP-linked, and lymphocyte maximal respiration shows increased mitochondrial dysfunction in black compared to white women. Ongoing analysis will further enhance understanding of the relationship between HIV and mitochondrial health.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Marjorie Lee White Abstract Approved By Advisor: Yes

Co-Authors: Youngblood A, Peterson DT, Davis V, Zinkan L and Woods

Title: IN-SITU SIMULATION OF PRECIPITOUS LABOR IN A PEDIATRIC EMERGENCY DEPARTMENT

Background:
Precipitous labor is a possibility for which all emergency departments must be prepared. At times, there may be contraindications for patient transfer necessitating immediate delivery in an area where staff is unprepared and specialized equipment is difficult to locate. In these cases, the medical team must be prepared for possible maternal and fetal complications.
Hypothesis:
In-situ simulation in a pediatric emergency department where emergent delivery is a rare event will increase provider comfort and familiarity with managing precipitous labor and delivery.
Methods:
A simulated patient encounter was initiated in an emergency department treatment room with a standardized patient and a false hemi-pelvis. The patient with abdominal pain was managed by available emergency department staff. The scenario proceeded through delivery and neonatal resuscitation. Afterwards, a debriefing occurred with a content expert in OB/GYN to review team and system performance and discuss potential complications.
Results:
Participants achieved goals of initiating proper transfer protocols, managing the delivery of the baby, and performing neonatal resuscitation. Equipment deficits and organizational issues were also identified. Of participants (N=26), 84.6% reported an increase in confidence and 76.9% reported an increase in familiarity with equipment following simulation.
Conclusion:
Results indicated that provider comfort with management of precipitous labor and delivery in the emergency department increased subsequent to the in-situ simulation. Additionally, systemic deficits in personnel management and the availability of necessary equipment were identified. These results suggest that primary benefits of in-situ simulation involve instruction on necessary equipment and implementation of correct protocols. These results are limited by a lack of a control group that received only lecture-based instruction. Additional studies will be required to demonstrate the long-term effectiveness of this intervention.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Sarah Clinton Abstract Approved By Advisor: Yes

Co-Authors: Matthew E. Glover, Phyllis C. Pugh, Andrew D. Fant, Rebecca K. Simmons, Huda Akil, Sarah M. Clinton

Title: Maternal style shapes limbic brain development and emotional behavior in rats genetically-prone to high anxiety

Early-life environmental factors critically influence brain development and later psychological health. To elucidate neural and environmental elements that shape brain development and emotional behavior, we developed a rat model of individual differences in temperament and environmental reactivity. We selectively bred rats for high vs. low behavioral response to novelty and found that high reactive (bHR) rats display greater risk-taking, impulsivity, and aggression relative to low reactive (bLR) rats, which show high levels of anxiety/depression-like behavior and stress vulnerability. The bHR/bLR traits are heritable but prior work revealed bHR/bLR maternal style differences, with bLR dams showing more maternal care than bHRs. The present study implemented a cross-fostering paradigm to examine the contribution of maternal behavior on bLR offspring's brain development and emotional behavior. bLR offspring were reared by biological bLR mothers or fostered to a bLR or bHR mother and then evaluated to determine effects on *1)* developmental gene expression in the hippocampus and amygdala; and *2)* anxiety/depression-like behavior. Genome-wide expression profiling showed that cross-fostering bLR rats to bHR mothers shifted developmental gene expression in the amygdala (but not hippocampus) and reduced multiple measures of adult anxiety. Although the bHR/bLR traits are strongly heritable, our current findings demonstrate how environmental factors influence the bLR phenotype. Moreover, while earlier studies highlighted hippocampal differences contributing to the bHR/bLR phenotypes, our results point to a role of the amygdala as well. Future work will pursue genetic and cellular mechanisms within the amygdala that contribute to bHR/bLR behavior either at baseline or following environmental manipulations.

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Project Length: Intermediate Prior Research Experience: Yes

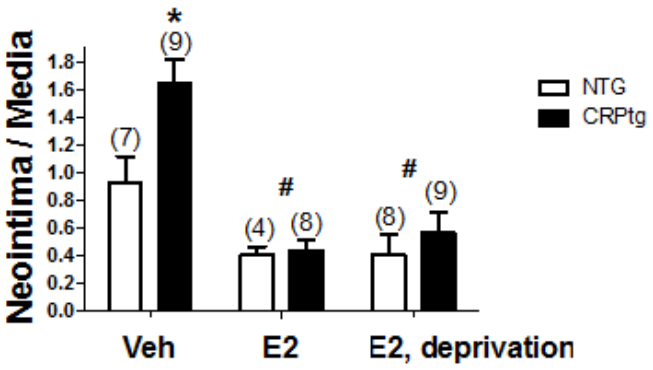
Source of Funding:

Faculty Advisor: Dr. Suzanne Oparil Abstract Approved By Advisor: Yes

Co-Authors: Dongqi Xing, Yuanyuan Guo, Alexander J Szalai, Yiu-Fai Chen, Suzanne Oparil, Fadi G. Hage

Title: Estrogen-Induced Vasoprotection is Preserved After Prolonged Estrogen Deprivation

Introduction: 17β-Estradiol (E2) offers cardiovascular protection in young female animals and peri-menopausal women. Clinical trials carried out in older women deprived of E2 for many years have shown harm or no cardiovascular benefit. We have recently demonstrated that E2 attenuates C-reactive protein (CRP)-driven inflammatory response in vascular smooth muscle cells and macrophages derived from young but not aged mice and reduces neointima formation in injured carotid arteries of young but not aged CRP transgenic mice (CRPtg).
Hypothesis: After prolonged E2 deprivation, E2 will not attenuate neointimal response to vascular injury.
Methods and Results: C57BL/6 non-transgenic (NTG) and CRPtg (10 wk old) mice underwent ovariectomy and then received vehicle (veh), uninterrupted E2 for 97 days (E2), or veh for 90 days followed by E2 for 7 days (E2, deprivation) delivered using subcutaneous pellets. Mice were then subjected to right common carotid artery ligation. At 28 days after injury, the carotid arteries were harvested, fixed, sectioned, stained, and subjected to computer-assisted morphometric analysis to assess the extent of the injury response. In veh treated mice, neointima formation was exaggerated in CRPtg compared to NTG (Figure). E2 treatment, whether continuous or after prolonged deprivation, was associated with greatly diminished neointima formation in both genotypes (2-way ANOVA interaction not significant). Importantly, the extent of neointima formation was not different between the two E2-treated groups (E2 vs. E2, deprivation).
Conclusions: In mice, E2-induced vasoprotection abolishes CRP-mediated vascular injury and this effect is preserved even after prolonged E2 deprivation. In combination with our previous finding that the vasoprotective effects of E2 are age-dependent, the current data suggest that the lack of benefit associated with E2 seen in clinical trials is associated with advanced age rather than prolonged E2 deprivation.



* p< 0.05 vs. NTG
# p< 0.05 vs. Veh

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Andrea Cherrington Abstract Approved By Advisor: Yes

Co-Authors: April Agne, Alfredo Guzman, Andrea Cherrington

Title: Designing MyDiabetesConnect.com: development and implementation of an interactive community resource website for diabetes

Introduction: Type 2 Diabetes prevalence continues to grow in the U.S. The internet can facilitate patients' disease management. This paper describes the development, implementation, and use of an interactive community resource website for individuals affected by diabetes.
Methods: The study was performed in two phases. Phase I used a grassroots approach, including 7 qualitative interviews to identify existing resources related to lifestyle modification, barriers to accessing resources, and gaps in resources. Phase II involved a retrospective mixed methods evaluation of MyDiabetesConnect.com after 18 months of active use, including follow up interviews with key informants, and analysis of the analytic data gathered on website use.
Results:
Phase I: Themes identified from semi-structured interviews included: need for ongoing user engagement and current information, need for low cost resources, and gaps in resources, especially low cost/free diabetes education and some supplies (test strips). MyDiabetesConnect.com, was developed based on this gathered information.
Phase II: MyDiabetesConnect.com has more than 28000 page views and 472 active local resources. MyDiabetesConnect.com saw a new visitor rate of 73.47%, with 26.53% of users returning to the website. Average new session duration was 5:49 minutes with returning visitors having an average time of 7:42 minutes. The majority of sessions (77.2%) occurred on desktop computers, and 14.6% of user sessions occurred on internet enabled telephones. Users were from the greater Birmingham area as well as throughout the state. Areas of improvement noted by key Interviewees included: resource submission, interest in a social media presence, and a need for a list of local physicians accepting new patients.
Discussion:
Communities often have existing resources related to lifestyle modification but are unable to connect them with individuals. We developed an interactive website to provide comprehensive, accurate information on community resources. Future research should include examination of user demographics and resource utilization.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Grady Maddox Abstract Approved By Advisor: Yes

Co-Authors: Grady E. Maddox, MD, Jonathan Ludwig, MD, David Woods, BS, Aaron Joiner, BA, Nilesh Chaudhari, MD, Gene P. Siegal MD, PhD, Alan Eberhardt, PhD, Brent Ponce, MD

Title: Flexor Tendon Repair with a Knotless, Bidirectional Barbed Suture: An In Vivo Biomechanical Analysis

Purpose
To compare and analyze biomechanical properties and histological characteristics of flexor tendons repaired either by a traditional 4-strand modified Kessler technique or using barbed suture with a knotless repair technique utilizing an in vivo animal model.
Methods
Twenty-five chickens underwent surgical transection of the flexor digitorum profundus tendon followed by either a traditional 4-strand modified Kessler repair or a knotless repair with barbed suture. Chickens were randomly assigned to one of three groups that varied in postoperative time to euthanasia. Harvested tendons were then sent to either the biomechanics testing lab or the pathology lab for further analysis.
Results
Review of the harvested tendons revealed failures in 25% (8/32) knotless repairs and 8% (2/24) traditional repairs. Biomechanical testing revealed no statistically significant difference in tensile strength between traditional and barbed repairs. However, there was a trend for improved early strength in the barbed repairs and a gradual decrease in strength over time, while the opposite trend was noticed for the traditional repairs. Method of failures during testing was different between repair types, with barbed tendon repairs tending to have suture breakage as opposed to traditional repairs with sutures pulling through the tendon. Histological analysis identified no difference in the degree of inflammation or fibrosis, however there was no foreign body reaction to barbed repairs whereas the traditional repair did elicit this response.
Discussion
In this in vivo model, both repair types demonstrated similar tensile strength with differing modes of failures and histologic reaction. This study demonstrates the need for further investigations to assess outcomes of repair when using barbed suture vs. the traditional repair.
Clinical relevance
Barbed suture may be of clinical use in repairing flexor tendon injuries.

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Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Colin Martin Abstract Approved By Advisor: Yes

Co-Authors: c. Culbreath, S. Tanner, T. Berryhill, R. G. Lorenz, C. A. Martin

Title: Environmental Mediated Intestinal Homeostasis In Neonatal Mice

Introduction: Maintenance of intestinal homeostasis by protection against pathogenic bacteria and dietary antigens is critical for intestinal homeostasis. Immunoglobulins, specifically IgA, play a key role in coating luminal antigens and preventing translocation of harmful bacteria. The aryl hydrocarbon receptor (AhR) is a basic-helix-loop transcription factor, that when stimulated by exogenous pollutants, microbial products, and dietary components, activates factors important for barrier function and intestinal homeostasis. To date, the function of AhR has not been studied in the developing innate immune system. Furthermore it is not clear how the extrauterine environmental influences the establishment of host/microbial mutualism. We hypothesize that AhR signaling is critical for establishment of intestinal homeostasis in neonates.

Methods: Three groups of mice were used. C57BL/6 (B6) $AhR^{+/+}$ (WT), B6.$AhR^{-/-}$ (KO) , and B6.$AhR^{+/+}$ raised on an AhR Ligand Free diet (AhR LF). AhR LF is defined as mice whose parents and the subsequent pups were maintained on a nutritionally balanced diet as well as cage bedding that was free of all exogenous AhR ligands. Enzyme-linked immunosorbent assay (ELISA) was used to measure fecal IgA levels in these groups of mice at 2 and 8 weeks of age. To determine the contribution of IgA from breast milk the gastric contents of 2 week old pups were harvested from the 3 groups of mice. Intestinal homeostasis was measured by culturing the mesenteric lymph nodes (MLN) under aerobic conditions to determine the number of bacterial colony forming units (CFU) after 72 hours. Results were analyzed by the Student's unpaired T-test and expressed as the mean ± standard error of the mean.

Results: Two week old KO mice had significantly less fecal IgA (37 ± 37 µg/ml) compared to WT (2519 ± 807 µg/ml) and AhR LF (3043 ± 764 µg/ml), p value = 0.0393. The amount of IgA from the gastric contents of 2 week old mice was not significant, WT (40 ± 14 µg/ml), KO (40 ± 18 µg/ml), AhR LF (24 ± 5 µg/ml), p value = 0.322. At 8 weeks of age AhR LF mice (1769 ± 369 µg/ml) had significantly less fecal IgA than WT (17,574 ± 4916 µg/ml) and KO (12,553 ± 2666 µg/ml), p value = 0.0077. At 2 weeks, KO mice had significantly higher levels of bacterial translocation (158 ± 37 CFU) compared to WT (2 ± 1 CFU) and AhR LF (9 ± 5 CFU), p value = 0 .0132. At 8 weeks AhR LF had significantly higher levels of bacterial translocation (119 ± 57 CFU) compared to WT (15 ± 7) and KO (11 ± 10) , p value = 0.019

Conclusion: In neonatal mice, the lack of AhR signaling is associated with loss of intestinal homeostasis, evidenced by decreased levels of IgA and increased bacterial translocation. In adult mice, exogenous AhR ligand and not receptor signaling is necessary for maintenance of intestinal integrity.

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Project Length: Short Prior Research Experience: No

Source of Funding:

Faculty Advisor: Matthew DeLaney Abstract Approved By Advisor: Yes

Co-Authors: Matthew DeLaney

Title: Ketamine as an Analgesic in the Emergency Department

The purpose of this study is to analyze the effectiveness of low dose ketamine as an analgesic in the Emergency Department (ED) to treat acute pain. Currently, IV opioids are the cornerstone of analgesia in the ED to treat severe pain, however despite the prevalence of various opioid agents in the ED, pain is still not effectively managed for many patients. While historically used for sedation, ketamine is also a potent analgesic. To date there are no large studies that evaluate the role that ketamine can play as a single agent analgesic. In higher doses, ketamine has powerful sedative properties, but for this study we will use a lower weight based dosing, known as a “sub-dissociative” dose, which provides analgesia without causing significant sedation.

The study evaluated pain scores in three groups of patients who present to the ED with acute pain. Patients were divided into three groups. Each group received Ketamine, Morphine, or Dilaudid. The goal is to analyze how effective Ketamine is compared to these commonly used opioids. The patients were asked their pain level before and after receiving pain medications. The data collection is nearing completion after which the data will be analyzed to see how effective Ketamine was.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Phillip D. Smith Abstract Approved By Advisor: Yes

Co-Authors: Lesley E. Smythies

Title: The Pro-Inflammatory effect of Cytomegalovirus on Primary Intestinal Macrophages

HCMV (Human Cytomegalovirus) is an opportunistic infection associated with exacerbated inflammatory states and dysregulated immune function, especially in immunocompromised hosts, infants and chronic disease states. Monocytes are the primary source of latent HCMV infection and are an important mediator of viral persistence and when immunosuppression occurs, dissemination throughout the body. In patients with inflammatory bowel disease, HCMV may induce relapse, exacerbation, and/or steroid refractions. Despite advances in elucidating the molecular biology of HCMV, the pathogenicity of HCMV in the gastrointestinal mucosa remains unclear. In normal conditions, the gastrointestinal mucosa contains resident lamina propria macrophages (LPMs) that are inflammation anergic thereby contributing to intestinal homeostasis. This unique feature stands in sharp contrast to blood monocytes, which rapidly respond to pro-inflammatory stimuli. We hypothesize that blood monocytes are a vehicle for transmission of HCMV into the intestinal mucosa and that HCMV-infected LPMs may mediate aberrant intestinal inflammation. Our aim was to characterize the mechanism of HCMV infection in LPMs using blood monocytes and LPMs isolated from intestinal tissue of healthy donors. We utilized a co-culture system where fluorescently tagged HCMV-infected monocytes were cultured with primary LPMs. We isolated and sorted both cells populations and quantified HCMV DNA to assess the transfer of virus from blood monocytes to LPMs from day 4 -10. We measured levels of pro-inflammatory cytokine IL-6, which is known to mediate inflammation in HCMV infection. Our results indicate that LPMs can take up virus via cell transfer and that LPMs co-cultured with HCMV-infected blood monocytes have heightened IL-6 production compared with both HCMV-infected LPMs and HCMV-infected monocytes alone. We conclude that blood monocytes infected with HCMV may transfer HCMV into LPMs in the intestinal mucosa, thereby enhancing inflammation in gastrointestinal disease.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Physical Medicine and Rehabilitation Fellowship

Faculty Advisor: Danielle Powell, MD Abstract Approved By Advisor: Yes

Co-Authors:

Title: Physical Health and Wellbeing of Persons with Spina Bifida

Background: The life expectancy for individuals with Spina Bifida (SB) has increased due to advancements in technology and healthcare, which has placed them at risk for developing the same conditions as the general aging population. Evaluating the physical and mental health of adults with SB will identify certain conditions that this group is at risk for developing, leading to future health promotion and disease prevention.
Objective: To assess common secondary conditions and quality of life among adults with Spina Bifida
Design: Cross-sectional study
Setting: A university hospital rehabilitation medicine clinic
Participants: 78 persons with SB age 19 years and older
Methods: A telephone survey about common secondary conditions was administered to 78 adults with SB attending an outpatient clinic. The questions were adapted from the Behavior Risk Factor Surveillance Survey (BRFSS), an on-going telephone health survey system sponsored by the Centers for Disease Control.
Main Outcomes: Measures for general health, exercise frequency, emotional support, satisfaction with life, history of cardiovascular disease, stroke, or diabetes, and tobacco and alcohol usage were compared between individuals with SB and the able-bodied population.
Results: Those with SB reported lower measures of general health (p=0.0012), life satisfaction (p=0.0001), and exercise frequency (p=0.0001) than the able-bodied population. Lower rates of diabetes (p=0.001) and tobacco usage (p=0.0001) were also observed among those with SB. Measures for emotional support and history of cardiovascular disease and stroke did not have a statistically significant difference between the two groups.
Conclusion: Individuals with SB tend to have a lower level of exercise and lower perception of satisfaction with life and general health compared to the general population. Future research needs to explore the factors associated with general health, satisfaction with life, and exercise practices among adults with SB in order to improve the physical and mental health of this population.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Farrukh Afaq Abstract Approved By Advisor: Yes

Co-Authors: Harish Pal Ph.D., Farrukh Afaq Ph.D.

Title: Fisetin Potentiates the Anti-proliferative and Anti-EMT Effects of Sorafenib in Malignant Melanoma

Despite only accounting for 5% of all skin cancer cases, malignant melanoma is responsible for 75% of all skin cancer related deaths due to its propensity to metastasize. BRAF, a serine/threonine kinase, is mutated in ~60% of melanoma cases. The BRAF-MEK-ERK (MAPK) signaling pathway plays an important role in regulating melanoma cell proliferation, invasion, epithelial to mesenchymal transition (EMT), and metastasis. The NFκB signaling pathway also regulates these processes and is constitutively activated in BRAF mutated melanoma. Treatment with BRAF inhibitors has improved survival of melanoma patients with BRAF mutations, but unfortunately, they have shown limited efficacy as monotherapies due to the development of resistance to these agents. Fisetin is a phytochemical found in several fruits and vegetables and has been shown to possess anti-oxidant, anti-inflammatory, and anti-proliferative properties against various cancers, including melanoma. Recently, our lab has shown that fisetin inhibits melanoma cell invasion and EMT by targeting MAPK and NFκB signaling. The aim of this study was to investigate whether fisetin in combination with sorafenib, a BRAF kinase inhibitor, further reduces proliferation and EMT of BRAF mutated melanoma cells. Results indicate that sorafenib in combination with fisetin inhibited cell proliferation and colony formation of melanoma cells more effectively than the individual agents. Furthermore, the combination treatment more effectively inhibited the progression of EMT, as observed by the reduction in mesenchymal marker proteins (N-cadherin, vimetin, snail, and fibronectin) and the increase in epithelial marker protein (E-cadherin). In addition, combination treatment inhibited NFκB signaling by reducing the expression of IKKα/β, phosphorylation and degradation of IκBα, and nuclear translocation of NFκBp65. These data suggest that fisetin enhances the efficacy of sorafenib as a treatment for melanoma and can be used in combination with BRAF inhibitors to improve patient outcomes.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Jeffrey Alten Abstract Approved By Advisor: Yes

Co-Authors:

Title: Hypoalbuminemia in Neonatal Patients during the Post-Operative Period from Cardiac Surgery with Cardiopulmonary Bypass

Objective: Low serum albumin results from a systemic inflammatory response to cardiopulmonary bypass. Previous research in adults has shown the nadir of serum albumin correlates better with outcomes than pre-operative risk assessment scores. Similar studies in pediatric populations have demonstrated conflicting results. We conducted a multicenter, retrospective cohort study to characterize the incidence and associated outcomes of post-operative hypoalbuminemia in neonatal patients undergoing cardiac surgery.

Methods: Serum albumin concentrations within the 24 hour post-operative period were retrospectively collected on 126 consecutive neonatal (0-28 days) patients undergoing cardiac surgery with cardiopulmonary bypass at three different academic centers. Patients were divided into a low albumin cohort (<3.0 mg/dL) and a normal albumin cohort (>3.0mg/dL). Subsequent outcomes were assessed by t-test and Fischer exact test.

Results: Mean ICU length of stay was significantly longer in the low albumin group (36 days vs 17 days, $p = 0.0010$). Mean hospital length of stay was longer, though not significantly (42 days vs 32 days, $p = 0.077$). Mean post-operative vent time was longer, though not significantly (240 hours vs 170 hours, $p = 0.29$). Mean post-operative chest tube drainage was significantly longer (223 hours vs 136 hours, $p = 0.018$). Hospital mortality ($p = 0.54$) and rate of chylothorax ($p = 0.21$) were not significantly correlated.

Conclusions: Hypoalbuminemia was correlated significantly with a longer ICU length of stay and duration of chest tube drainage. It was not significantly associated with increased rate of chylothorax, mortality, time to extubation, or hospital length of stay.

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Project Length: Short Prior Research Experience: No

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Monika Safford Abstract Approved By Advisor: Yes

Co-Authors: Kelly Kenzik, Monika Safford

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

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

Chlorogenic acid – a potential activator of dysfunctional mucus transport in chronic rhinosinusits

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

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Co-Authors: Elisa Illing, M.D., Shaoyan Zhang, Ph.D., Daniel F. Skinner, B.S., Quinn A. Dunlap, B.S., Eric J. Sorscher, M.D., Bradford A. Woodworth, M.D., F.A.C.S.

Title: Chlorogenic acid – a potential activator of dysfunctional mucus transport in chronic rhinosinusits

Introduction: Salubrious effects of the green coffee bean are purportedly secondary to high concentrations of chlorogenic acid (CA). CA has a molecular structure similar to bioflavonoid polyphenols known to activate transepithelial Cl^- transport in sinonasal epithelia. In contrast to flavonoids, chlorogenic acid is freely soluble in water. The objective of this study is to evaluate the Cl^- secretory capability of CA and its potential as a therapeutic activator of mucus clearance in sinus disease.
Methods: CA was tested on primary murine nasal septal epithelial(MNSE)[$CFTR^{+/+}$ and transgenic $CFTR^{-/-}$] and human sinonasal epithelial(HSNE)[$CFTR^{+/+}$ and F508del/F508del] cultures under pharmacologic conditions in Ussing chambers to evaluate effects on transepithelial Cl^- transport. Cellular cAMP (ELISA) and subsequent CFTR regulatory domain (R-D) phosphorylation (gel-shift assay) were also measured. Effects on CFTR mRNA transcription were evaluated with quantitative RT-PCR
Results: CA stimulated transepithelial Cl^- secretion [(change in short-circuit current(ΔI_{SC})] in MNSE(13.11+/-0.9 vs. 0.1+/-0.1, $p<0.05$) and HSNE(34.3+/-0.9 vs. 0.0+/-0.1, $p<0.05$). The drug had a slow onset with peak effect at 15 minutes after application. Administration of the CFTR blocker INH-172 significantly reduced I_{SC}(MNSE -16.4+/-0.9 vs. -9+/-1.1 and HSNE(-44.6+/-1.0 vs. 34.1+/-0.3,$p<0.05$) indicating effects of the drug are likely mediated through CFTR. CA-mediated Cl^- secretion was absent in $CFTR^{-/-}$ MNSE and F508del/F508del HSNE confirming CFTR dependency. No elevation in cellular cAMP or phosphorylation of the CFTR R-D was detected. The compound did not alter CFTR mRNA levels when analyzed by quantitative RT-PCR.
Conclusion: CA is a water soluble agent that promotes CFTR-mediated Cl- transport in sinonasal epithelium. Further *in vivo* evaluation as a therapeutic activator of mucus clearance is planned.

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Project Length: Long Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Jonas Almieda Abstract Approved By Advisor: Yes

Co-Authors: Joshua Anderson PhD, Christopher Willey MD PhD

Title: Kinomic dashboard: a webApp ecosystem for the analysis of kinase activity data.

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. The PamGene PamChip system records and compares the phosphorylation of 144 tyrosine or serine/threonine peptides as they respond to cellular kinases. This gives the researcher an evolving view of cellular kinase activity and the kinome. The data produced then requires use of the manufacturers' proprietary software for analysis. Unfortunately this software does not allow web-based data sharing, which has created powerful queryable data repositories such as The Cancer Genome Atlas (TCGA). To allow for this we created an interactive, web based, 'Kinomics Dashboard'. This dashboard stands on a computational environment in the user's own browser where private and public data can be integrated in the same analysis without compromising local data or private cloud resources. Accordingly, bioinformatic analyses can be done using algorithms that have been built into the application, as well as those that have been made available by other users. We were able to achieve this high level of analytical flexibility with a novel two-backend system for data storage. One relies on a more traditional server based mechanism that complies to HIPAA regulations. The other uses an encrypted social media based backend that allows for cloud based storage and data transfer. Social computing is emerging as the natural middle layer for the third generation of Web Technologies (Web 3.0, semantic web) and kinomics is quickly moving towards clinical trials for cancer therapeutic decision making. Therefore, applying Web 3.0 technologies to kinomics was identified as a particularly effective route towards collaborative science in personalized medicine.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Nathaniel Robin Abstract Approved By Advisor: Yes

Co-Authors:

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

Long QT syndrome (LQTS) is an inherited cardiac channelopathy that predisposes individuals to syncope, seizures, torsades de pointes, and sudden cardiac death. This condition may be treated either medically or with an implanted cardioverter-defibrillator, but diagnosis is essential for proper management[1]. There are over six loci currently identified with mutations leading to LQTS, and there is evidence that there is a strong correlation between genotype and phenotype[2]. Although genetic testing has been available for years, its cost-effectiveness among different populations, including definitive and inconclusive index cases and potentially affected family members, has been debated and genetic testing is not routinely performed in clinical settings[1]. Although gene specific stratification of LQTS has been shown to be of use in clinical management of LQTS[2], guidelines for testing individuals have not been established and little is known about the genetic services currently offered by heart rhythm specialists treating LQTS patients. The goal of this study was to learn more about genetic services offered to definitive and inconclusive LQTS patients and potentially affected family members, which we achieved by distributing a survey among cardiologists and electrophysiologists in southeastern United States with 29 responses. Responses revealed that 58% of respondents had limited genetic training. Results also revealed that clinicians have many varying approaches to using genetic testing for both LQTS patients and their family members, and that the largest perceived barrier to genetic testing is cost. Utilizing these results can help standardize the use of genetic testing for LQTS in the future.

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: Dr. Lee Ann Riesenberg Abstract Approved By Advisor: Yes

Co-Authors: Lee Ann Riesenberg, PhD, RN; Joshua Davis, MS2; Matthew Mardis, BS; Leila Jarhomi MD, MS; Charvla King

Title: Shift-to-Shift Handoff Evaluation and Feedback Tools: A Systematic Review of the Literature

Background: Residency hour restrictions have led to an increase in the frequency of shift-to-shift handoffs, which present opportunities for inefficiency, medical errors, and poorer patient outcomes. Recently, there has been growing interest in the ineffective transfer of patient information during shift-to-shift handoffs. Our research team conducted a systematic review of the literature on physician shift-to-shift handoffs with a focus on research articles containing feedback or evaluation tools.
Methods: The research team developed a systematic review of the literature protocol for article inclusion and exclusion. “Feedback” and “Evaluation” were clearly defined in the protocol. We conducted a comprehensive search of the literature on shift-to-shift handoffs articles published between January 1, 2008 and December 31, 2013 .
Results: The search yielded 8,649 unique articles. Articles were reviewed by pairs of trained research assistants for possible inclusion. The first review yielded 1,234 articles focused on shift-to-shift handoffs, which were obtained and included in a database. These articles were then reviewed by pairs of trained research assistants for articles that included either a feedback or evaluation tool. Eighteen articles were deemed relevant: 9 feedback articles and 9 evaluation articles. All articles were independently abstracted by 2 trained research assistants into summary tables. Feedback articles included results on improved handoff content or process, simulations with feedback, or some form of faculty-to-learner feedback. Evaluation articles included evaluation tool validation, evaluation of learner handoff ability including process or content, and general evaluation of other aspects of handoffs.
Conclusion: Our systematic review of the literature identified only 18 published articles on physician shift-to-shift handoff feedback and/or evaluation tools used in medical education. We conclude that there is a paucity of research providing medical educators with evidence supporting specific feedback and evaluation tools or methods.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Andra Frost Abstract Approved By Advisor: Yes

Co-Authors: Yuan, K. Frost, A

Title: Primary Cilia in Ovarian Neoplasms: Immunofluorescence Detection

Introduction: Ovarian cancer carries a more dismal prognosis than most cancers because it often presents at an advanced stage. Primary cilia (PC) are microtubule-based sensory organelles that are present on many benign and malignant tissues. The presence of PC has been found to correlate with prognosis in pancreatic cancer; however, a similar analysis in ovarian cancer has not been performed. PC can be visualized microscopically by immunofluorescence staining for acetylated alpha tubulin (AAT) or detyrosinated tubulin (DT). However, cancer cells have a particularly high level of cytoplasmic tubulin, which interferes with the accurate identification of PC. In this investigation, we compare immunofluorescence staining (IF) for PC using an antibody to AAT alone or in combination with an antibody to DT in ovarian neoplasms.
Methods: Formalin fixed paraffin embedded ovarian tissue was obtain from UAB Surgical Pathology after IRB approval. 5 micron thick sections were prepared from granulosa cell tumors and papillary serous carcinomas. Sections underwent antigen retrieval followed by IF with anti-AAT, with or without co-staining with anti-DT, at several concentrations (1:200, 1:500, 1:1000) for each antibody. The percentage of cells with PC was determined for each neoplasm.
Results: PC were best visualized with concentrations of 1:200 for anti-AAT and 1:1000 for anti-DT. The mean percentage of cells with PC in granulosa cell tumors (n=4) was 10.0% using anti-ATT alone and 9.9% with the combination of anti-ATT and anti-DT. The mean percentage of cells with PC in papillary serous carcinomas (n=5) was 1.8% with anti-ATT only and 1.9% with the combination of antibodies. IF of additional ovarian neoplasms is underway.
Conclusions: In the cases examined thus far, the number of PC detected was similar when using anti-ATT or the combination of anti-ATT and anti-DT. PC were more frequent in granulosa cell tumors than papillary serous carcinomas of the ovary.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Bradford Woodworth Abstract Approved By Advisor: Yes

Co-Authors: Daniel Skinner, BS; Shaoyan Zhang, PhD; Quinn Dunlap, BS; Eric J. Sorscher, MD; Katherine L. Tuggle, PhD; Bradford A. Woodworth, MD

Title: Ion Transport Phenotype of Upper Airway Epithelium in the CFTR-/- Rat

Background
Transgenic cystic fibrosis (CF) murine models have greatly facilitated studies of CF pathogenesis by enabling the analysis of pharmaceutical and other interventions, but murine nasal airways do not recapitulate many of the most important characteristics of human upper airway pathophysiology. Porcine and ferret CF models demonstrate a respiratory phenotype resembling that observed in humans, but time to sexual maturation, expense, and specialized care requirements have significantly limited their widespread use. The newly developed transgenic CF rat may confer advantages for studying cystic fibrosis sinus disease, particularly since rat sinuses are much larger than mice and mature more rapidly than in pigs or ferrets. The objectives of the current experiments were to develop and characterize primary rat nasal epithelial (RNE) cultures and evaluate their usefulness as a model of sinonasal transepithelial transport and CFTR function.

Methods
RNE derived from the septum of WT and $CFTR^{-/-}$ rats were cultured at an air-liquid interface to confluence and full differentiation. Ciliary beating and degree of ciliation were evaluated by the Sisson-Ammons Video Analysis system and scanning electron microscopy. Monolayers were mounted in Ussing chambers for pharmacologic manipulation of ion transport. Histologic analyses of nasal septa and cultured RNE monolayers were performed and ASL depth measured using confocal laser scanning microscopy.
Results
Forskolin-stimulated anion transport (ΔIsc in $\mu A/cm^2$) was significantly greater in epithelia derived from the WT when compared to $CFTR^{-/-}$ animals (108.9+/-2.1 vs. 10.5+/-0.9, $p<0.0001$). Amiloride-sensitive I_{SC} was equivalent (-47.9+/-1.0 vs. -46.1+/-2.3). No inhibition of CFTR-mediated Cl^- secretion was exhibited in $CFTR^{-/-}$ epithelia with the addition of the specific CFTR inhibitor INH-172. However, calcium-activated Cl^- secretion (UTP) was significantly increased in $CFTR^{-/-}$ RNE (WT - 21.5+/-0.9 vs. $CFTR^{-/-}$ - 106.8+/-1.6; $p<0.001$). Robust ciliary beating with 80 to 90% ciliation was identified in all cultures. Tissue samples of nasal septum and RNE monolayers indicate the CF rat exhibits a pronounced mucus clearance defect, with histopathologic changes that include airway epithelial cells with accumulation of intraepithelial mucus and inspissated secretions overlying the epithelium, as well as decreased airway surface liquid.

Discussion
The successful development of the $CFTR^{-/-}$ rat will enable improved evaluation of CF sinus disease based on a robust clinical phenotype, and characteristic abnormalities of ion transport. Cultured RNE provide a useful model for studying other CF genotypes, testing pharmacotherapeutics, and correlating to rat nasal potential difference measurements *in vivo*.

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Project Length: Long Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: John Fiveash Abstract Approved By Advisor: Yes

Co-Authors: John B. Fiveash, M.D., Markus Bredel, M.D.,Ph.D., Richard A. Popple, Ph.D., Louis B. Nabors, M.D., James Markert, M.D.,M.P.H., and Brian J. Gebhardt, M.D.

Title: Irradiation of the Stem Cell Niche in Glioblastoma

Background: The glioma stem cell hypothesis attempts to explain many of the characteristics of glioblastoma including its heterogeneity along with its abilities to present or recur multi-focally, to fail both locally and distally, and its poor response to treatments. Cancer stem cells are thought to retain properties similar to neuronal stem cells and may be associated with the neural stem cell niche. We hypothesize that high radiation doses incidentally administered to the neural stem cell niche would be associated with better progression free survival in patients with glioblastoma.
Methods: This was a retrospective study of 75 patients that were treated at UAB Department of Radiation Oncology from the years 2000-2011 for newly diagnosed glioblastoma. Eligible patients had available dosimetry and MRI demonstrating disease progression after receiving treatment. All patients were treated with surgical resection followed by radiation with concurrent temozolomide. Stem cell niches including ipsilateral, contralateral, and bilateral subventricular zone (SVZ), and ipsilateral hippocampus were contoured on treatment plans and dosimetry was retrospectively calculated.
Results: Analysis of progression free survival for all 75 patients receiving $\geq$ 40 Gy mean dose to ipsilateral, contralateral, or bilateral SVZ was found to be insignificant. When the patients were divided into subsets based on surgical resection, a trend of improved progression free survival was found in the GTR subgroup of patients who received a mean dose $\geq$ 40 Gy to the ipsilateral SVZ with estimated mean time to progression of 16.1 months vs 10.8 months ($p = .138$).
Conclusion: The trend in the GTR subgroup might illustrate possible benefits of treating the ipsilateral SVZ in the setting of good local tumor control. It is also possible that the trend is due to chance or confounding variables. There are current plans to increase the power of study and limit confounding effects.

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Project Length: Long Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. Marjorie Lee White, Dr. Larson-Williams

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Marjorie Lee White, Amber Youngblood, Dr. Dawn Peterson, Lynn Zinkan, Dr. Larson-Williams, and Dr. Nancy Tofil

Title: A multidisciplinary, longitudinal simulation to teach pediatric residents and nurses how to diagnose, treat, and manage pediatric patients with Diabetic Ketoacidosis

Background: Diabetic ketoacidosis (DKA) is a complication of diabetes mellitus (DM) that is associated with an increased risk of morbidity and mortality. It is important residents and nurses receive training on DKA management, as it continues to become an increasing cause for hospital admissions. Medical education literature suggests that simulation based learning is an effective education tool. We hypothesize that a better understanding of the management of DKA could be obtained using a simulation.
Setting and Participants: Sixteen residents took a DKA management questionnaire during their last month of residency and serve as the controls for our study. Nine residents participated in a multistep simulation in the Pediatric Simulation Center at Children's of Alabama. Nine nurses participated as well.
Methods: A knowledge questionnaire was given to graduating residents during the last month of their training. These graduating residents were instructed in a traditional manner regarding DKA. A new set of residents complete the same assessment as the control group prior to the simulation. For the simulation, residents are given the clinical presentation and laboratory evidence consistent with DKA. Based on the initial management and clinical course, the participants are presented with different complications of treatment. After the simulation, a participant centered debriefing occurs and the same assessment is taken again. We analyzed residents' performance on the same assessment from both the control group and simulation group.
Results: The control group's assessment (N=16) demonstrated an average score of 77$\pm$9%. The average pre-test score for residents participating in the simulation was 79$\pm$13%. The results from the simulation (N=9) demonstrate an improved post-simulation test score of 86$\pm$11%.
Discussion: The improvement in questionnaire scores between the control group and those participating in the simulation suggest that traditional education on DKA could be enhanced with simulation based education. Furthermore, medical residents can enhance their knowledge without risk to patients. The major limitation of this study is the number of participants.
References: Rosenbloom, A. The Management of Diabetic Ketoacidosis in Children. *Diabetes Ther* (2010) 1(2): 103-120.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Chris WIlley Abstract Approved By Advisor: Yes

Co-Authors: Timothy Rohnbach, Brent Jones, John Jarboe, Stephen Alexander

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

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)-bisphosphate (PIP2) into Phosphatidylinositol 3-kinase (PI3K) allowing for AKT activation. PIP3 recruits AKT to the plasma membrane where it phosphorylated 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].

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

Methods: MARCKS mutants were created using a GBM cell lines with low native MARCKS expression (U87) using a tetracycline inducible lentiviral vector. We created cell lines that will express 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). Cells were plated and subsequently treated with doxycycline and TMZ. ATP-light assay assessed cell viability after one week.

Results: Increasing MARCKS expression in combination with TMZ therapy 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.

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: Amy J. Knight, Ph.D. Abstract Approved By Advisor: Yes

Co-Authors: Nathan Harnett, BS, James Bishop, MS, Martin Setliff, MD, Sherry Melton, MD David Knight, PhD

Title: Contribution of demographics and psychological risk factors to the expression of acute stress reactivity in the inpatient setting following acute medical trauma

Introduction: This prospective study examined the relationship of the stress reaction to emotional, cognitive, and demographic variables following acute medical trauma. The goal of this research is to identify factors that mediate pathological and healthy emotion regulation, and translate this work into therapeutic strategies to provide targets for early intervention efforts. This goal will be accomplished by comparing self-reported trauma measures of affect, emotional reactivity, and attention between trauma-exposed individuals. The central hypothesis of this research is that trauma exposure will be associated with elevated self-reported psychological symptoms and decreased performance on attention, and will potentially be modulated by demographic factors.

Methods: 21 participants were recruited from the Acute Trauma Unit at UAB Hospital and completed a Posttraumatic Stress Diagnostic Scale (PDS), Psychosocial Risk Factor Survey (PRFS), and Connors' Continuous Performance Test II (CPT II). Correlational analysis was conducted on variables of interest, including demographic factors of gender, race, education, and estimated IQ.

Results: Endorsement of PTSD symptoms was correlated with depression, anxiety, and social isolation. African Americans had higher guardedness scores (an individual's willingness to divulge personal information) than Caucasians ($p=.044$), suggesting potential bias in oral survey administration. Guardedness was not found to influence a willingness to disclose PTSD symptoms, while it lowered the severity of other mood symptoms endorsed. IQ scores correlated with social isolation. Mood and PTSD scores were not consistently correlated with attention measures.

Conclusion: Results suggest that risk factors for emotional reactivity (depression, anxiety, social isolation) were related to the expression of acute stress (PDS) in the first 30 days following injury. Importantly, while we did find differences in ethnicity for emotional guardedness, this factor was not related to admission of an acute stress response. Contrary to our hypothesis, sustained attention was not reliably affected by the extent of symptoms reported.

(FUNDING: UAB Medical Student Summer Research Program; UAB Faculty Development Grant Program; UAB Functional Neuro-Recovery Award Program)

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: Amy J. Knight, Ph.D. Abstract Approved By Advisor: Yes

Co-Authors: Nathan Harnett, BS, James Bishop, MS, Martin Setliff, MD, Sherry Melton, MD David Knight, PhD

Title: Barriers to recruitment of patients with acute traumatic injury for neuroimaging studies

Introduction: The neural activity preceding the development of Posttraumatic Stress Disorder (PTSD) after acute trauma is largely unknown. In an ongoing study at UAB, functional magnetic resonance imaging (fMRI) is being used to investigate mechanisms that mediate the stress response in humans within 30 days of acute medical trauma. Exclusionary criteria for the neuroimaging study includes prior head injury, substance abuse, significant psychiatric illness, claustrophobia, weight limit restrictions, embedded metal, or other medical history precluding functional neuroimaging. The purpose of this research is to examine the eligibility of the patient population through the UAB Hospital Trauma and Burn Unit to participate in neuroimaging research. This epidemiology information will guide future fMRI projects with trauma exposed individuals.

Methods: Over a 9 week period, the trauma intake history of present illness (HPI) for every new patient in the Acute Trauma and Burn Unit at UAB Hospital was screened for study eligibility, including demographic information and prior comorbidity. A secondary in-person screen was conducted on the unit. Eligible participants were either recruited in person or by follow-up phone call.

Results: Of the 315 screened patients that came through UAB's trauma bay, 61 were MRI eligible after a primary screen of their HPI (19%), while only 22 patients remained MRI-eligible following secondary screen (7%). The primary disqualifiers were loss of consciousness, neurological disorder, and hypertension. A total of 2 patients were recruited and completed participation in the fMRI study during the review, with 6 other individuals still in the recruiting phase.

Conclusion: Results from this study will be used to direct current and future fMRI studies conducted at UAB. Significant restrictions on MRI eligibility and less than 1% completing participation with the 9 week time period highlights the need for special attention to recruitment in the acute trauma setting for neuroimaging projects.

(FUNDING: UAB Medical Student Summer Research Program; UAB Faculty Development Grant Program; UAB Functional Neuro-Recovery Award Program)

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. James Bardwell Abstract Approved By Advisor: Yes

Co-Authors: Scott Horowitz

Title: A Novel Method for Quantifying Chaperone Protein Activity using Isothermal Titration Calorimetry

To prevent folding defects, cells have evolved co-factors, called molecular chaperones, to properly fold proteins in the crowded cellular environment. They not only help in de-novo protein synthesis, but also counteract stress-induced misfolding and protein aggregation, and some chaperones even assist in the disassembly of already formed aggregates. While most chaperones exhibit protective effects, it has been shown that some chaperones maintain mutated or abnormal disease-causing protein aggregates in diseases such as Alzheimer's disease, Parkinson's disease, and Type-II diabetes. Therefore, understanding the mechanism of action of chaperones is essential in the fight against these illnesses. Traditionally, dynamic light scattering (DLS) has been used to measure the activity of chaperone proteins through measurement of the size of aggregates, but it is limited by both its reproducibility and quantification. Thus, I sought to create a more quantifiable assay to measure chaperone activity. Here I have developed a novel, highly reproducible, and highly sensitive aggregation assay that is based on the energy of aggregation using isothermal titration calorimetry (ITC). Conventionally, this technique is used to study the thermodynamic parameters of molecular interactions, most notably in the design and discovery of new therapeutic agents. However, using ITC, I have uniquely measured the heat of aggregation of several substrates, such as malate dehydrogenase (MDH), and have demonstrated the loss of this heat of aggregation with the addition of chaperones with far greater sensitivity than is possible with DLS. This new method potentially allows for the determination of the dissociation constant (Kd) between a chaperone and an aggregating substrate, which has never been calculated before. These results indicate that ITC is a promising approach for comprehensively studying the thermodynamics and bioenergetics of chaperone proteins action upon their substrates, and ultimately, this method will play a prominent role in the molecular design of new drugs for protein-folding diseases.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: David Standaert Abstract Approved By Advisor: Yes

Co-Authors: Lieb L, Guthrie SL, Bowling K, Lasseigne BN, Myers RM, Limdi NA, Standaert DG

Title: Genetic Susceptibility in Levodopa Induced Dyskinesia

Levodopa (L-DOPA) induced dyskinesia (LID) is the primary factor which limits the utility of L-DOPA, the most effective treatment for Parkinson's disease (PD). However, patients treated with L-DOPA are known to have significant inter-individual variability, as large doses of L-DOPA for long periods of time can be tolerated in some patients (L-DOPA Tolerance, LDT) while short duration low dose treatment can quickly induce dyskinetic behaviors in others (L-DOPA Susceptible, LDS). Although dose and duration of L-DOPA therapy are known risk factors, the significant inter-individual variability in LID remains largely unexplained. Recent evidence has implicated genetic modulation of vulnerability in LID, but these studies have been limited in their conclusion and have only looked at specific targeted genes. The application of unbiased sequencing to identify novel genetic variants predictive for LID could have important and immediate effects on personalized treatment decisions: aggressively using L-DOPA for its anti-PD effects in L-DOPA tolerant patients (LTS), while providing L-DOPA sparing therapies for L-DOPA sensitive (LDS) patients. Using an "extreme discordant" study design, we selected patients representing the extreme outliers in responsiveness (LDS/LDT), allowing us to enrich for genetic variants influencing LID sensitivity that would not be easily seen in the general patient population. Previous studies addressing genetic variants associated with LID may have been limited by the lack of prospective case collection and small sample size relative to the variation in LID phenotype. By using the extreme discordant phenotypes seen in LID, we can analyze a smaller sample size while still utilizing the power of whole exome sequencing to identify genetic variants that directly impact amino acid sequence and are associated with LID. In the modern era of personalized medicine, the pharmacogenetic data gathered in this study could be used in the future to design patient specific treatment plans and provide further insight into the pathophysiology of LID.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Eben Rosenthal Abstract Approved By Advisor: Yes

Co-Authors: Jason M. Warram, Ph.D. Yolanda Hartman BSc, Esther de Boer BSc, Eben L. Rosenthal, M.D.

Title: Fluorescence-based Methodology for Measuring Drug Accumulation in Tissue

Fluorescent-based techniques are being introduced to guide surgical excision of cancer. Antibodies can be covalently conjugated to near-infrared (NIR) dyes to permit real-time, optical localization of cancer in the surgical setting. Successful antibody-dye combinations are not identified by total tumor accumulation, but by the greatest difference between tumor and normal tissue. While this strategy has the potential to achieve complete resection, the accurate characterization of study drugs is essential to understanding binding kinetics of antibody-NIR dye candidates for this technique. Using tissues obtained from a dose-escalation clinical trial assessing the safety of cetuximab conjugated to a NIR dye (cetuximab-IRDYe800) in patients with head and neck cancer, a novel methodology was explored to normalize for optical-based attenuation to accurately quantify drug uptake within tissues. Tumor and muscle (n=4) specimens were systematically homogenized and a SDS-PAGE assay was performed on cell lysate (40ug) from each sample. In addition, a serial dilution (0.02ug-0.1ng) of cetuximab-IRDye800 was run on a separate gel to serve as a standard. Using a specialized NIR fluorescent scanner designed to image IRDye800 (Odyssey, LICOR, Lincoln, NE), the gels were imaged and mean fluorescent intensity (MFI) from cetuximab-IRDye800 (150kd) bands were quantified in tumor and patient-matched muscle. MFI were compared to the standard curve to determine percentage of cetuximab-IRDye800 injected dose per gram of tissue (%ID/g). In the lowest cetuximab-IRDye800 dose group, average %ID/g for tumor ($2.8x10^{-6}$ MFI) was found to be 8-fold greater than %ID/g for muscle ($3.5x10^{-7}$ MFI). In the higher dose group (2.5-fold dose increase), average %ID/g for tumor ($3.2x10^{-6}$ MFI) was found to be 3-fold greater than %ID/g for muscle ($1.0x10^{-6}$ MFI). Using this technique, the lower cetuximab-IRDye800 dose was shown to be optimal to provide the greatest difference between tumor and muscle tissue.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Jennifer S. Pollock Abstract Approved By Advisor: Yes

Co-Authors:

Title: Humanized sickle cell disease mice display an increased sensitivity to alpha1-mediated vasoconstriction

Sickle cell disease (SCD) is the most common inherited blood disorder in the United States, and SCD patients suffer significant morbidity and early mortality. Vascular dysfunction is now known to be a common pathway contributing to the diverse pathologies seen in SCD. However, the mechanisms underlying this vascular dysfunction are not fully understood. In order to study vascular dysfunction in SCD, we utilized a humanized SCD mouse model, expressing exclusively human hemoglobin. Mice expressing two copies of mutant human beta globin (β_S/β_S) display many of the pathophysiological complications seen in SCD patients, and mice heterozygous for mutant beta globin (β_A/β_S) have a phenotype similar to wild type mice and were used as controls. We hypothesized that the thoracic aorta of SCD mice would have endothelial dysfunction and increased sensitivity to α_1-mediated vasoconstriction. Vascular reactivity of the thoracic aorta was examined *in vitro* using wire myographs, and cumulative concentration-response curves were generated for acetylcholine (ACh), sodium nitroprusside (SNP), phenylephrine (PE), and potassium chloride (KCl). %maximum constriction to PE was significantly increased in SCD mice compared to controls, yet there was no change in EC50 between groups. No differences in %maximum constriction/dilation or EC50 were observed between SCD and control mice for ACh, SNP, and KCl. Thus, the thoracic aorta of SCD mice display exaggerated α_1-mediated vasoconstriction, despite the lack of difference in endothelial function evidenced by similar endothelial-dependent vasodilation. This suggests that SCD selectively impairs vascular smooth muscle function in conduit vessels, which may contribute to organ dysfunction seen in SCD.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Cunningham Fellowship

Faculty Advisor: Kimberly Whelan, M.D. Abstract Approved By Advisor: Yes

Co-Authors: Sherri L. Davidson

Title: EKG Abnormalities in Asymptomatic Childhood Cancer Survivors Attending a Long-term Follow-up Clinic

Background: Over the past 50 years, the probability of surviving childhood cancer has improved dramatically due in part to intensive therapeutic protocols. However, these may result in long-term adverse effects, including cardiopulmonary disease. Treatment with anthracycline chemotherapy and/or radiotherapy has been shown to increase the risk for cardiotoxicity. The purpose of this study is to review EKG abnormalities in asymptomatic childhood cancer survivors who are at risk for cardiac complications.

Methods: In this retrospective chart review of all survivors from the Taking on Life after Cancer database (n=503), EKG and echocardiogram findings were reviewed for survivors who were treated with radiation affecting the heart (n= 94) and/or anthracycline chemotherapy (n=324).

Results: For patients who received both anthracycline agents and radiation, the calculated adherence to the Children's Oncology Group screening guidelines is 95.7% for ECHO and 88.3% for EKG. The overall rate of abnormal ECHOs is 16.7% with a significant difference between groups that received higher anthracycline dose and groups that received lower dose. Also, a significant trend is observed correlating a higher rate of abnormal ECHOs with increasing radiation exposure. The overall rate of abnormal EKGs is 20.5% with no significant dose response observed. Among patients who received anthracyclines without radiation, the overall rate of abnormal ECHOs and EKGs are 7.4% and 16.8% respectively. A significant trend is observed showing an increasing rate of abnormal EKGs with increasing anthracycline dose.

Conclusions: The relatively high rate of abnormal EKGs in asymptomatic survivors suggests that EKG is a valuable screening tool for cardiac late effects in childhood cancer survivors. A larger sample size may provide more specific dose-dependent information.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Chad Steele Abstract Approved By Advisor: Yes

Co-Authors: Jaleesa Garth and Kristin Reeder

Title: CX3CL1 in Aspergillus-associated fungal asthma

Asthma represents an enormous public health burden with 300 million individuals affected globally, and contributing to 3,447 deaths per year and $56 billion dollars in spending within the United States. Of patients suffering from severe asthma, 25-70% are sensitive to fungal antigens, particularly those of *Aspergillus fumigatus*. In fact, *Aspergillus*-hypersensitivity among asthmatics is estimated to have a prevalence of 40%, with 12% found to be susceptible to a more severe manifestation of the illness known as allergic bronchopulmonary aspergillosis (ABPA). This data clearly demonstrates the utility of studying the mechanisms which drive *Aspergillus*-related asthma exacerbations. Previously, we demonstrated by multiplex analysis that concentrations of the cytokine CX3CL1 (also known as fractalkine) were higher in sputum and bronchoalveolar lavage fluid (BAL) of fungal antigen (*Alternaria, Cladosporium* or *Aspergillus*) skin test + asthmatics versus that of skin test – asthmatics. In this latest study, we have found that intratracheal administration of anti-CX3CL1 neutralizing antibody to a chronic exposure *Aspergillus*-asthma model in mice had little effect on the levels of pro-inflammatory cytokines CCL17, CCL22 and IL-33 as compared to isotype-administered controls. Furthermore, the levels of the immunopathogenic cytokine IL-22 seemed to paradoxically be significantly decreased in mice treated with anti-CX3CL1 antibody. These results complicate the potential role of CX3CL1 in fungal asthmatic response and inflammation if such a relationship exists.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: J. David Sweatt Abstract Approved By Advisor: Yes

Co-Authors: Fatmata Seay

Title: The effect of soluble β-amyloid oligomers on memory-associated transcription and DNA methylation

Alzheimer's disease (AD) is an age-related neurodegenerative disorder, characterized by memory loss and the accumulation of amyloid-beta (Aβ). Soluble β-amyloid (sAβ) oligomers, rather than their fibrillar aggregates, contribute to the pathogenesis of AD by affecting synaptic plasticity and inhibiting long-term potentiation. Additionally, several lines of evidence suggest that dysregulated transcriptional and epigenetic mechanisms, including DNA methylation, contribute to the neuronal dysfunction and cognitive impairment in AD. However, how sAβ oligomers alters nuclear function remains unknown. Our overarching hypothesis is that sAβ oligomers modify the expression of DNA methylation/demethylation enzymes that in turn leads to aberrant methylation and transcription of plasticity-associated genes. To examine this, primary hippocampal murine cultures were treated with 100μM of sAβ monomers or oligomers for 24 hours, after which RNA and DNA were collected. Preliminary data indicates that exposure to sAβ oligomers resulted in reduced transcription of well-characterized memory activating genes including *Arc*, *Fos*, *Egr1*, and *Gria1*. Interestingly, sAβ oligomers also reduced the expression of ten-eleven translocation (TET) enzymes without altering the expression of DNA methyltransferase (DNMT) enzymes. These findings suggest that sAβ oligomers trigger changes in memory-associated transcription, potentially via altered DNA demethylation.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Richard Myers Abstract Approved By Advisor: Yes

Co-Authors: Ryne Ramaker, Marie Kirby, Kevin Bowling, Richard Myers

Title: Creating a High Throughput RNA-seq Analysis Pipeline

Next-Generation, massively parallel sequencing methods are a vital tool in understanding complex pathologies resulting from interaction between genetic, epigenetic and environmental factors. Specifically, RNA-sequencing (RNA-seq) allows for the identification and quantification of genome-wide RNA expression in a sample as one tool for understanding phenotypic differences. The primary goal of this project was to develop a high-throughput data analysis pipeline for RNA-seq count data that would identify differentially expressed genes for hypothesis generation and consequent functional studies.

In order to analyze RNA-seq data and determine statistically significant genes, our lab utilizes an R-based pipeline consisting of the BioConductor package DESeq2 in addition to subsequent clustering algorithms and graphical representation. This is performed with a series of scripts that increase the ease of application for these specific packages with RNA-seq analysis. Nevertheless, this workflow still requires a large amount of user data manipulation that can become time-consuming and yield more inconsistent output for downstream analysis. To alleviate this bottleneck and improve RNA-seq analysis quality and consistency, we wrote a new R-pipeline combining the previous pipeline's functionality while improving the user experience and enhancing downstream analysis. This workflow is fully automated, allows for customization of multiple analysis parameters such as false discovery rate and included covariates, and specifically labels and organizes all output files using an explicit and consistent format.

Future work will focus on further pipeline quality control, followed by applying this new analysis workflow to a wide variety of projects. This will provide a foundation for next-generation RNA-sequencing based hypothesis generation for subsequent targeted functional validation experiments.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Nancy Tofil Abstract Approved By Advisor: Yes

Co-Authors: Jeff Harper, Nancy Tofil

Title: Knowledge of Anaphylaxis and Epinephrine Autoinjectors among Pediatric Fellows and Residents

Background/Objectives: Anaphylaxis is a rapid, serious allergic or hypersensitivity reaction that has the potential to progress to life-threatening cardiovascular and respiratory complications within minutes to hours of exposure to an inciting agent. The treatment primarily consists of epinephrine and supportive care (supplemental oxygen, fluid resuscitation). Epinephrine is the drug of choice because it prevents or reverses cardiovascular collapse, prevents or reverses airway obstruction, and reduces mast-cell mediator release. Multiple concentrations and routes of administration are available, leading to confusion and potentially medication errors. Epinephrine auto-injectors are commonly prescribed for patients with a history of anaphylaxis, however their use within hospitals varies between institutions. We hypothesize that many physicians in training are not comfortable with the appropriate usage of epinephrine during treatment of anaphylaxis or with epinephrine auto-injectors.
Setting and Participants: A survey was taken by PGY1-3 pediatric residents, medicine-pediatric residents on pediatric rotations, and PGY4-7 pediatric critical care and emergency medicine fellows during spring of 2014.
Description/Methods: A knowledge assessment questionnaire was given to pediatric residents, medicine-pediatric residents, and pediatric critical care and emergency medicine fellows. The assessment consisted of 30 multiple-choice questions designed to assess experience and training with epinephrine auto-injectors, knowledge of how anaphylaxis is handled in different areas of the hospital, with 8 questions specifically to test knowledge of epinephrine and auto-injector use in treatment of anaphylaxis. Statistics were done with SPSS version 11.5 (SPSS Inc, Chicago, IL). Data is presented as mean ± standard deviation. T-test was done when comparing means of 2 groups and ANOVA was done when comparing means of more than 2 groups.
Evaluation/Results: For all participating residents and fellows (N=86), the mean knowledge score was 53 ± 22%. . Fellows scored significantly higher than residents (71.3± 21.1% vs 41.5± 19.9%, p <0.0001) Fellows also had a significantly greater knowledge of epinephrine auto-injector concentration (p=0.007, p=0.019 from two separate questions) and dose (p=0.028) when compared with residents. Commonly missed questions included ‘concentration of epi in anaphylaxis not requiring cardiopulmonary resuscitation (CPR)’ (Residents: 40.6% correct, Fellows: 70.6% correct), ‘dose for cpr anaphylaxis’ (Residents: 39.1% correct, Fellows: 70.6% correct), ‘concentration of epi in cpr anaphylaxis’ (Residents: 43.5% correct, Fellows: 47.1% correct), ‘auto-injector concentration’ (Residents: 24.6% correct, Fellows: 47.1% correct), and ‘auto-injector dose’ (Residents: 33.3% correct, Fellows: 76.5% correct). Knowledge of route of administration was not significantly different between groups (p=0.474). ANOVA was used to compare all residents and fellows by post-graduate year (PGY1-7), and significant differences were found between groups for questions pertaining to auto-injector dose for junior and regular (F=4.080, p = 0.001), and overall percent correct (F=5.323, p = <0.001). Upon comparing knowledge among PGY levels, the only statistical difference was PGY1 (interns) compared to upper level residents and fellows.

Discussion: The results demonstrate that knowledge gaps exist in the use of epinephrine and auto-injectors in anaphylaxis amongst pediatric residents and pediatric critical care and emergency medicine fellows, as seen with the mean score of 53%. Certain questions addressing dose and concentration were commonly missed, making these obvious areas for clarification and reinforcement. While the overall mean score was 53%, the difference between fellows and residents was significant (71% vs 48%, p<0.0001). Primarily, this difference was between PGY1 interns and other levels of training. This suggests that a large learning curve for this topic during the first year of post-graduate training, however the improvement plateaus and does not continue to improve as level of training increases. The difference seen between residents and fellows may largely be due to the effects of PGY1 on the resident group, since both PGY2 and PGY3 residents are not statistically different from fellows.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: John Fiveash Abstract Approved By Advisor: Yes

Co-Authors: Andrew McDonald and John Fiveash

Title: Toxicity Effects of Alignment Using Fiducials versus Computed Tomography (CT) Imaging for the Radiation Treatment of Prostate Cancer

The purpose of this study is to compare the rates of acute and late gastrointestinal (GI) and genitourinary (GU) toxicity associated with daily radiotherapy alignment to implanted fiducials versus alignment to the prostate via computed tomography (CT) based imaging. CT-based alignment methods are distinguished from the use of implanted fiducials because CT-based alignment does not require an implantation procedure and CT allows for the daily visualization of the surrounding organs at risk (the bladder and the rectum). Two-hundred twelve patients with clinically localized prostate cancer treated with hypofractionated prostate radiotherapy (RT) between 2005 and 2011 were included in this analysis to compare the toxicities associated with the two alignment techniques. All patients were prescribed 70 Gy to the prostate in 28 fractions and 103 patients were simultaneously prescribed 50.4 Gy to the pelvic lymph nodes. Daily image-guided alignment was performed using implanted prostate fiducial markers or using CT-based alignment to the prostate with emphasis on the prostate-rectum interface. This CT-based imaging was either cone beam computed tomography (CBCT) or tomotherapy. Acute and late GI and GU toxicities were retrospectively scored by the CTCAE 4.0 scale and statistical analysis was performed using IBM SPSS version 22 software. An analysis of the data revealed that acute GU and GI toxicities were similar in patients receiving fiducials or CT-based alignment. For patients receiving prostate-only radiotherapy, the rate of late GI toxicity was increased for patients with implanted fiducials (14.6% rate of toxicity at 2 years for patients with fiducials versus 2.9% for patients with CT-based alignment, $p = 0.020$). Late GU toxicity was not increased for patients receiving fiducials despite the inability to evaluate daily bladder filling in this group. The study indicates that using CT-based alignment instead of implanted fiducials could lower the risk of late GI toxicity; however, further study with a larger sample size is needed to draw a definitive conclusion.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Derek DuBay Abstract Approved By Advisor: Yes

Co-Authors: Kyle Gennaro, Jessica Zarzour, J Kevin Smith, David Bolus, David T Redden, Souheil Saddekni, Ahmed Kamel Abdel Aal, Stephen Gray, Jared White, Devin E Eckhoff, and Derek A DuBay

Title: THE MODIFIED RESPONSE EVALUATION CRITERIA IN SOLID TUMORS (mRECIST) PREDICTS SURVIVAL FOLLOWING TRANSARTERIAL CHEMOEMBOLIZATION (TACE) FOR HEPATOCELLULAR CARCINOMA

Transarterial chemoembolization (TACE) is the recommended oncologic treatment for non-transplantable, non-resectable, non-ablatable hepatocellular carcinoma (HCC). TACE is indicated in 50-70% of all new HCC diagnoses. The impact of TACE-induced HCC tumor necrosis, as measured by the Modified Response Evaluation Criteria in Solid Tumors (mRECIST), on patient survival, is poorly defined. We hypothesize that survival will be superior in patients with increased TACE-induced tumor necrosis. All first TACE interventions for HCC performed at a single institution from 2008 – 2013 were retrospectively reviewed (n=344). HCC tumor response to TACE was quantified via the mRECIST criteria. Differences in survival were compared using the log-rank test. Patients were censored if they received a liver transplant. The median survival following TACE treatment for HCC varied according to the mRECIST response, with the longest survival observed in patients with a complete response and shortest survival in patients with progressive disease. Patients with a complete response had the lowest frequency of repeat TACE, and highest probability of receiving a liver transplant. The mRECIST response was not associated with receiving post-TACE radiation therapy or tumor ablation. The mRECIST response to TACE in patients with HCC was predictive of survival, the need for repeat TACE, and the probability of receiving a liver transplant. However, the absolute differences in median survival were not as large as predicted, perhaps because patients with the best mRECIST response(s) were also the most likely to undergo liver transplant (and be censored in the survival analysis).

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Henry E Wang Abstract Approved By Advisor: Yes

Co-Authors: John Donnelly, Karen E. Jacobson, N. Clay Mann, Jestin Carlson, Alexander Lo

Title: National Characteristics of EMS Responses for Older Adults in the United States

OBJECTIVE: While frequently requiring emergency care, only limited national data describe the EMS care of older adults. We sought to determine the characteristics of EMS responses for the older adults (>65 years) in the United States.

METHODS: We used 2012 data from the National Emergency Medical Services Information System (NEMSIS), encompassing EMS response data from 42 States. We defined older adults as age >65 years, and younger adults as 18-65 years. We excluded children <18 years, interfacility transports, intercepts, non-emergency medical transports and standby responses. Using logistic regression and Mann-Whitney rank sum test, we compared patient demographics (age, sex, race, ethnicity, primary payer), response characteristics (dispatch time, location type, time intervals, use of lights and sirens) and clinical course (clinical impression, injury, procedures) between older and young adult responses.

RESULTS: During the study period there were 12,626,141 adult EMS responses, including 5,208,755 (41.1%) older and 7,417,386 (58.75%) younger adults. Older adult responses were more likely at a residential institution (9.0% vs 2.6%; OR 3.02 [95% CI: 3.00-3.04]). Older adult responses were more likely to involve critical illness; respiratory distress/arrest (16.2% vs. 7.9%, OR 2.54 [95% CI: 2.53-2.55]), or cardiac rhythm disturbance (3.9% vs. 1.7%; 2.85 [2.82-2.87]), stroke (4.2% vs. 1.3%; 3.96 [3.92-4.01]) While less likely to involve injury (25% vs 18%; OR 0.666 [95% CI: 0.664-0.668]), older adult responses were more likely to be due to a fall (83% vs 28%; OR 2.42 [95% CI: 2.41-2.43]). Older adult responses were more likely to involve airway management (7.0% vs. 4.7%; OR 1.54 [95% CI: 1.53-1.55]) or other life-saving procedures (26.3% vs 23.8%; OR 1.14 [95% CI: 1.14-1.14]).

CONCLUSION: Almost half of all EMS events in the US involve older adults. EMS responses involving older adults are more likely to involve critical illness and to require life-saving interventions.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Henry E Wang Abstract Approved By Advisor: Yes

Co-Authors: John Donnelly, Karen E. Jacobson, N. Clay Mann, Jestin Carlson, Alexander Lo

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CONCLUSION: Almost half of all EMS events in the US involve older adults. EMS responses involving older adults are more likely to involve critical illness and to require life-saving interventions.

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Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Nicholas Van Wagoner, MD, PHD

Abstract Approved By Advisor: Yes

Co-Authors: Nicholas Van Wagoner, MD, PHD

Title: Variability in HSV-2 Index Values Over Time

Herpes Simplex Virus Type 2 (HSV-2) is common in HIV-infected persons. Because asymptomatic HSV-2 is the norm, when HSV-2 diagnosis is needed, serologic assays are used. Among persons with HIV, HSV-2 serologic tests require nuanced interpretation that include higher index value cutoffs for positive results. In addition, there is concern for the stability of HSV-2 serologic results over time among HIV-infected persons. The purpose of this study was to assess the stability of serologic results among HIV-infected persons over time. Serum from HIV-infected persons receiving care at a University HIV clinic and participating in the CFAR Network of Integrated Clinical Systems (CNICS) were assayed for HSV-2 using HerpeSelect 2. HerpeSelect 2 was performed on consecutive sera from participants with negative, low positive, and high positive serological results. A total of 4 samples from each participant covering a median of 24 months were evaluated. Samples were run in duplicate to determine both within and between sample variability. Samples from each patient were run in the same assay to reduce any differences attributable to different runs of the HerpeSelect. Sample variability was least for negative samples and greatest from sera of participants with high positives results. However, interpretation of the assay results did not change for these two groups. Sera from individuals with initial low positive index values showed intermediate variability. However, this variability crossed the cutoffs for interpretation of negative and positive results over time.
In conclusion, low positive HerpeSelect 2 test results remain difficult to interpret. In patients with low positive test results, repeating assays may not help in confirming whether the patient is positive or negative. Low positive test results should be interpreted with caution in persons will HIV.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Drs. David Cleveland and Manisha Kukreja Abstract Approved By Advisor: Yes

Co-Authors:

Title: Quality of life in Fontan survivors: A comparison with heart transplant recipients without fontan and general US population without heart disease

Background: As advances in therapies for children with single ventricle congenital anomalies offer improved outcomes for operative and long-term survival, attention is shifting towards assessing quality of life (QOL) in these patients. Several studies have assessed QOL in children and adolescents after undergoing reconstructive procedures (Fontan circulation), but limited attention has been given to adult Fontan survivors. Since understanding QOL is important to optimize health care outcomes, this study determines the perceived health of long-term Fontan survivors by assessing physical, mental, and social aspects of their QOL and comparing the results to that reported by the normal, healthy US population as well as by those who received heart transplants as children.
Methods: Using the SF-36, we assessed QOL of 50 adult Fontan patients (i.e. >19 years age) as well as 13 adult patients who received a heart transplant as children. Results of each of the 3 facets of QOL (physical, mental, social) for both groups were translated into numerical scores out of 100 and subsequently compared to each other as well as to an age and gender matched healthy general population.
Results: Fontan patients perceived their overall physical, emotional, and social health to be comparable to the general population and heart transplant recipients; however, their level of pain (Mean +/- SD= 88.3 +/- 17.8) is higher than both [(75.6+/-25.8) and (84.2 +/-25.4), respectively]. Furthermore, Fontan patients' general health perception (60.3 +/- 21.6) is significantly lower than the general US population (70 +/- 20.3).
Conclusion: Fontan patients have statistically significant impairment of pain and general health perception when compared to the general healthy US population. However, when Fontan patients are compared to heart transplant recipients of similar age, the QOL is not significantly different.

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Project Length: Short Prior Research Experience: No

Source of Funding:

Faculty Advisor: Lorie Harper, MD Abstract Approved By Advisor: Yes

Co-Authors: Joseph Biggio MD, Alan Tita MD PhD, Lorie Harper MD MSCI

Title: Impact of Early Screening for Gestational Diabetes

Objective: ACOG suggests screening patients at high risk for gestational diabetes (GDM) at the first visit. However, no studies have examined the benefits of early screening. We sought to examine the benefits of early GDM screening in a high risk population.
Study Design: Retrospective cohort of all singleton gestations diagnosed with GDM from 2007-2013. Indications for early screening were defined as prior pregnancy with GDM, obesity (BMI≥30 kg/m^2), and prior macrosomia (birth weight>4000g). Subjects were classified as having early (<20 weeks) or routine (≥20 weeks) screening. Maternal outcomes examined were cesarean delivery (CD), preeclampsia, A2 diabetes, and insulin use. Neonatal outcomes included birth weight, macrosomia (>4000 g), large for gestational age (LGA, >90^{th} percentile), small for gestational age (SGA, <10^{th} percentile), birth injury (shoulder dystocia, fracture, brachial plexus injury), and preterm delivery (<37 weeks). Exposure groups were compared using Student's t-test, Mann-Whitney test, or chi-squared tests. Logistic regression was used to estimate the impact of early screening on maternal and neonatal outcomes while adjusting for confounding factors.
Results: Of 594 subjects, 112 (18.9%) were screened early. Subjects screened early were more likely to have had GDM in a prior pregnancy, hypertension, higher BMI, and higher fasting glucose. Rates of preeclampsia and CD were similar in both groups, but women screened early were more likely to require insulin. Early and routine screening groups had similar incidences of macrosomia, LGA, SGA, and birth injury. Subjects in the early screening group had a higher incidence of preterm delivery.
Conclusion: Among women at high risk for GDM, we did not detect a benefit to early screening. Despite earlier diagnosis and treatment, women in the early screening group were more likely to require insulin and deliver preterm. The utility of early GDM screening requires a prospective trial.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Lalita Shevde-Samant Abstract Approved By Advisor: Yes

Co-Authors: Shamik Das; Lalita Shevde-Samant

Title: Hedgehog signaling in breast cancer: Role in adaptation to hypoxia

Breast cancer is the second most common cause of cancer related death in women. This high mortality rate is largely due to the aggressive nature of breast cancer metastases. Numerous studies have implicated hypoxia, a microenvironment commonly found in solid tumors, in increasing tumor aggression and metastatic potential. Canonical Hedgehog (Hh) signaling is largely active during embryogenesis to guide growth and patterning. However, aberrant activation of the Hedgehog pathway has been causally associated with multiple malignancies, including breast cancer. GLI1 is the predominant transcription factor of Hh signaling; increased GLI1 transcriptional activity results in increased expression of proliferative factors and decreased expression of apoptotic genes. Hedgehog pathway inhibitors have been exploited as therapeutics with many inhibitors being in clinical trials in several cancer types.

The objective of this research is to elucidate the mechanism(s) by which Hh signaling impacts the ability of breast cancer cells to adapt to hypoxia. We studied the SUM1315 breast cancer cell system cultured under normoxic and hypoxic conditions. We used three inhibitors of Hh signaling viz. KAAD-cyclopamine, the BMS compound, and GANT61. We evaluated the effect of these culture conditions on the ability of these inhibitors to impact Hh signaling. We monitored the transcriptional activity of GLI using a luciferase reporter assay, queried the status of target gene read-outs of Hh signaling by quantitative real time RT-PCR, and monitored the expression of these target read-outs by immunoblotting.

We find that overall the activity of Hh signaling is enhanced under hypoxic conditions; the BMS compound was effective in inhibiting Hh activity under normoxic and hypoxic conditions. We also determined that KAAD-cyclopamine and GANT61 blunted cellular response to hypoxia as evidenced by the decreased HIF-1α expression, clearly suggestive of Hh signaling in adaptation to hypoxia. Future investigations will aim to characterize the impacts on breast cancer metabolism.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Fredrick Goldman Abstract Approved By Advisor: Yes

Co-Authors: Larisa Pereboeva and Erik Westin

Title: Amelioration of Telomere-Mediated DNA Damage Responses and Reactive Oxygen Species by Antioxidants

Introduction/ Background: Dyskeratosis congenita (DC) is a rare, multisystem, genetic disorder that presents with a characteristic triad of nail dystrophy, leukoplakia, and abnormal skin pigmentation along with progressive bone marrow failure and premature aging. Clinically, DC patients have variable presentations, yet exhibit correlations between phenotype and genotype and disease anticipation. Genetically, causative mutations have been identified in nine genes (*TERT, TERC, TINF2, DKC1, NOP10, NHP2, TCAB1, CTC1, C16orf57*), all of which affect the maintenance of telomeres or telomerase activity. Despite the variation in genetic background and disease presentation, all DC patients have critically shortened telomeres in common. These shortened telomeres are suggested to be the mediator of increased reactive oxygen species (ROS) and the activation of DNA damage response (DDR) elements within DC cells.
Hypothesis: Telomere attrition within DC lymphocytes will lead to increased ROS/DDR and application of antioxidants will ameliorate this DDR activity by reducing ROS.
Methods: DDR was measured in steady-state or irradiated T lymphocytes from DC subjects with *TERC* and *TERT* mutations and age-matched controls by western blotting with antibodies targeting total p53, its activated form (phosphorylated serine-15; p53S15), phosphorylated H2AX (yH2AX), and Actin. Western blots were quantified utilizing ImageJ software (total band density of DDR normalized to Actin) and graphed for comparison.
Results: DDR were consistently up-regulated in *TERT* and *TERC* DC patients' cells, likely in part due to increased ROS. We also found antioxidants, such as a low oxygen environment or other antioxidant drug therapies, have an ameliorative effect on ROS and DDR.
Conclusion: Our findings indicate an increase in both steady-state and irradiation-induced p53 and ROS levels in DC lymphocytes. This evidence suggests shortened telomeres or telomerase deficiency have a role in regulating ROS and DDR. Reduction of these responses in antioxidant-treated cells highlights one potential pharmacological therapy to alleviate symptoms in DC patients.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: American Heart Association Fellowship

Faculty Advisor: James George and Anupam Agarwal Abstract Approved By Advisor: Yes

Co-Authors: Ahmed I. Kamal, Ravindra Boddu, Subhashini Bolisetty, Cornelia C. Tisher, James F. George and Anupam Agarwal

Title: Heme Oxygenase-1 Expression Regulates Trafficking of Myeloid Cells in Acute Kidney Injury

Ischemia reperfusion injury (IRI) is a common cause of acute kidney injury (AKI). Its pathogenesis is mediated by a complex cascade of immunological events secondary to oxidative injury to renal epithelial cells. Heme oxygenase-1 (HO-1) induction is a protective response to IRI. Because of its emerging role in immunoregulation and transplantation, we hypothesized that HO-1 expression plays a critical role in the response to renal IRI by modulating the trafficking of myeloid cells into the kidney as well as controlling emigration of intra-renal resident dendritic cells to the primary lymphoid organs. Age-matched male wild-type ($HO\text{-}1^{+/+}$), HO-1 knockout ($HO\text{-}1^{-/-}$), and $HO\text{-}1^{-/-}$ mice overexpressing the human HO-1 gene (HBAC) underwent bilateral renal ischemia. IRI resulted in significantly more structure and functional kidney injury and mortality in $HO\text{-}1^{-/-}$ mice. There was an increase in macrophages ($CD45^{+}$ $CD11b^{hi}$ $F4/80^{lo}$) and neutrophils ($CD45^{+}$ $Gr\text{-}1^{hi}$ $CD11b^{hi}$ $MHCII^{-}$) in $HO\text{-}1^{-/-}$ kidneys subjected to IRI compared to sham and $HO\text{-}1^{+/+}$ controls. However, IRI resulted in a significant decrease in the intra-renal resident dendritic cell population, which is characterized as $CD45^{+}$ $MHCII^{+}$ $CD11b^{lo}$ $F4/80^{hi}$. Syngeneic kidney transplant experiments utilizing GFP^{+} $HO\text{-}1^{+/+}$ or GFP^{+} $HO\text{-}1^{-/-}$ donor kidneys and $HO\text{-}1^{+/+}$ GFP^{-} recipients confirmed increased migration of the intra-renal resident DC population from $HO\text{-}1^{-/-}$ donor kidneys to the primary lymphoid organs, which included the renal and mesenteric lymph nodes as well as the spleen. Increased renal DC emigration was corroborated in myeloid-specific HO-1 deficient mice ($HO\text{-}1^{LysM\text{-}/\text{-}}$), which lack HO-1 expression in neutrophils, macrophages, and tissue-resident dendritic cells. Pro-inflammatory ($Ly6C^{+}$) macrophage infiltration was also significantly increased in $HO\text{-}1^{LysM\text{-}/\text{-}}$ mice compared to wild-type controls. However no appreciable difference was evident in the extent of IRI-induced structural or functional kidney injury in $HO\text{-}1^{LysM\text{-}/\text{-}}$ mice compared to controls, suggesting that myeloid-specific HO-1 expression plays a key role in regulating the innate immune response to AKI.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: John L. Hartman IV, MD Abstract Approved By Advisor: Yes

Co-Authors: Haley Albright, John L. Hartman IV

Title: A strategy to identify natural genetic variation affecting longevity in S. cerevisiae

This project aims to survey genetically diverse strains of *Saccharomyces cerevisiae* to discover natural genetic variation influencing aging as measured by chronological lifespan. Genetically variant strains from the National Collection of Yeast Cultures (NCYC) were obtained from different geographic regions of the world that have been characterized by the Saccharomyces Genome Resequencing Project (SGRP). We screened this collection to identify three long-lived and three short-lived strains. In order to identify functional genetic variants that influence lifespan, we are knocking out HIS3 in these strains so that recombinogenic progeny can be recovered after crossing with the strains against the background of the yeast knockout and knockdown (YKO/KD) library by the Synthetic Genetic Array (SGA) method. The genetically recombinogenic haploid progeny will be screened for longevity phenotypes using quantitative high throughput cell array phenotyping (Q-HTCP). Informative progeny (those with lifespan phenotypes) will be further analyzed by RNAseq to determine differential gene expression and map crossovers for quantitative trait locus (QTL) and expression-QTL (eQTL) analysis to discover genetic variants contributing to longevity phenotype. Of the twelve strains selected (both mating types, a and alpha, for three long-lived and three-short lived strains), three were successfully transformed, knocking out HIS3 with the nourseothricin resistance gene. We are troubleshooting the transformation of the other strains and clarifying some unexpected mating phenotypes.

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Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. Laura Rogers Abstract Approved By Advisor: Yes

Co-Authors: Courtney Blair, MA2 ; Karen Gamble1, Laura Q. Rogers, MD, MPH2

Title: Exercise Timing and Sleep Quality Response to an Exercise Intervention in Breast Cancer Survivors

Sleep disturbances are common in breast cancer survivors with an estimated prevalence of 65-90%. Cancer survivors are encouraged to exercise to improve health, reduce risk of recurrence, and improve psychosocial outcomes such as sleep quality. Because the effects of exercise on sleep quality in breast cancer survivors are understudied and inconsistent, our primary aim was to determine if exercise timing could potentially explain the varying effects of exercise on sleep quality in breast cancer survivors. A post hoc analysis of breast cancer survivors participating in a randomized controlled trial comparing a 3-month exercise intervention with control group was done. The intervention group was asked to participate in aerobic walking and strength training with resistance bands while the control group was asked to avoid changing current exercise habits. Accelerometer measured physical activity during the day (worn on waist) and sleep (worn on wrist; participant recorded time in and out of bed) at baseline and 3 months. Perceived sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI) global score (higher score = greater sleep disturbance). Of the 46 breast cancer survivors enrolled, two were dropped due to cancer recurrence and five did not have complete data. The participants had a mean age of 56±8 years and education of 14±2 years; 95.5% were Caucasian. Breast cancer stage was DCIS (18%), stage I (48%), or stage II (34%). Among all participants at 3 months (intervention and control; n=39), physical activity counts 2 and 3 hours before bed were significantly associated with more accelerometer mean minutes awake (r=.35, p=.027 for both) and reduced accelerometer efficiency (r=-.37, p=.019 and r=-.39, p=.013, respectively). For the 17 participants receiving the intervention, accelerometer sleep outcomes and PSQI global were dichotomized as decrease versus no change/increase from baseline to 3 months. A decrease in PSQI global indicates improved sleep quality while the beneficial direction with accelerometer sleep outcomes may differ (e.g., it is beneficial to decrease latency and increase efficiency). Using an independent groups t-test, a greater mean increase in activity counts 3 hours before bedtime occurred for participants with no change or increase in accelerometer minutes awake when compared with those with a decrease (or improvement) in minutes awake (21,950±24,510 versus 2,272±17,013, trend only, p = .069). Intervention participants with a decrease in the PSQI global (i.e., intervention responder) had a significantly higher mean change in physical activity counts 1 hour before bed from baseline to 3 months when compared with intervention participants reporting no change or increase in PSQI global score (4,126±8,328 versus -5,849±5,144, p = .026). Although higher activity counts before bed were associated with greater minutes awake and lower efficiency (i.e., detrimental changes in sleep quality), participants with improvements in perceived sleep quality during the intervention had an increase in activity counts prior to bedtime. Exercise timing may cause detrimental changes in accelerometer sleep measures but not the general perception of better sleep quality. Further study to more fully understand how exercise timing may influence sleep response to an exercise intervention for breast cancer survivors is warranted.

Jackson, Jennifer Leigh (Jennifer) JLEIGH02@uab.edu

Project Length: Short Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Orlando Gutierrez Abstract Approved By Advisor: Yes

Co-Authors:

Title: Associations of 25-hydroxyvitamin D with markers of inflammation, insulin resistance, and obesity in adults

Vitamin D is a fat-soluble vitamin classically known for its role in calcium absorption and bone health. Vitamin D deficiency has traditionally been associated with rickets and osteomalacia. However, growing evidence indicates that vitamin D may be of even greater importance in metabolic health. Vitamin D deficiency has been associated with such conditions as inflammation, insulin resistance, and obesity. To further understand the relationship between vitamin D and metabolic health, associations of vitamin D levels with markers of inflammation (IL-6, IL-10, hsCRP), insulin utilization (adiponectin, resistin, HOMA-IR), and obesity were examined in participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, a large national cohort of community-dwelling adults. We found that lower levels of 25(OH)D were associated with lower levels of adiponectin and higher levels of interleukin-6, homeostatic model of insulin resistance, body mass index, and waist circumference when adjusted for age, sex, race, geographic region of residence, and other sociodemographic, clinical, lifestyle, and laboratory variables ($P < 0.05$ for all). We conclude that low vitamin D levels are associated with disturbances in specific markers of inflammation, insulin resistance, and obesity. These results suggest that correcting vitamin D deficiency in certain metabolic disturbances could offer a beneficial therapy and additional disease prevention with important implications for the escalation of metabolic syndrome in the general population.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Nathaniel Robin, MD Abstract Approved By Advisor: Yes

Co-Authors: Akila Subramaniam, MD, Joseph Philips, MD

Title: The Evolution of Physician Attitudes: Trisomy 18

Introduction:
While infants diagnosed with Trisomy 18 have a 13% chance of survival beyond 12 months of age without intervention, this figure increases to 25% with full clinical intervention with the exception of cardiac surgery. This has led to Trisomy 18 being grouped into the category of "lethal anomalies" based on the severe neurological compromise and structural/functional disabilities the genetic defect presents with. Great debate has risen in the past several years as to the amount of aggressive therapy that needs to be offered to parents in the treatment of their affected neonate. Also, if aggressive therapy is not pursued, what palliative care measures are appropriate? To explore this ethically centric issue, I developed a survey, with cooperation from MFM, Neonatology, and Medical Genetics department faculty, which is directed at practicing neonatologists from across the nation asking them what specific aggressive therapy they would offer versus what palliative measures they would offer, and a series of demographic questions.

Methods:
Through a multilateral effort, a 25 question survey was created using SurveyMonkey that is currently being sent to a national network of neonatologists. The survey first asks a series of demographic questions about topics such as religious/political affiliations and views on abortion. The latter part of the survey gives a series of clinical vignettes about a female pregnant with a fetus diagnosed with full Trisomy 18. The vignettes are followed by a series of questions asking the neonatologist about the extent of aggressive therapy versus the extent of palliative care they are willing to offer the parents of the affected neonate after birth.

Results and Conclusion:
After the allotted time for survey completion has elapsed, statistical analysis will be performed on the responses to attempt to draw any correlations between the physicians' demographic data and their subsequent responses to the vignette-based, clinical care questions.

Jaleel, Ayesha (Ayesha) AJ701@uab.edu

Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Marjorie Lee White Abstract Approved By Advisor: Yes

Co-Authors: Peterson, DT, Watts, PI, Jaleel, A, White, ML, Chad, E, Leon, K,

Title: INTENSIVE CARE UNIT INTERPROFESSIONAL EDUCATION SIMULATION

Background/Objectives:
Health care currently has shifted from only physician-based care to team-based care. Professional team skills are highly integrated and interdependent. The purpose of interdisciplinary simulation is to foster collaborative relationships, teamwork and proper communication to improve the overall patient care. There are many factors that play into this overall care such as situational awareness, decision-making, communication, leadership and role identification. The simulations are used as an education strategy to inspire students from various fields to work with different interprofessionals.

Setting and Participants:
Six ICU interprofessional simulations have been conducted at UAB Medical Simulation Center in a two-day span with three sessions per day. Students and residents from seven different interprofessional fields participated in the simulations. These fields include: Physical Therapy, Respiratory Therapy, Laboratory, Nuclear Medicine, Nursing, Physician Assistant, and Medicine.

Description/Methods:
ICU Simulations: Six ICU Simulations are carried on simultaneously for one hour during each session. Simulations include Blood reaction, GI bleed, Pulseless Electrical Alternans, COPD, Disseminated Intravascular Coagulopathy and Stroke. Faculty and staff aided in running the cases and manipulation of the simulators. Participants came in as groups during the three, two hour sessions per day from 12 pm to 6 pm. Before participants entered, they were pre-briefed and told that they were in an ICU setting. They were not told about the details of the cases. The cases ran for about forty-five minutes and once forty-five minutes have elapsed, there was an in room debriefing for fifteen minutes for the participants. The participants are then moved to group room for a forty-five minute debriefing session with all the participants of that session and then a fifteen-minute session with their own professional faculty. After the sessions, the participants are asked to fill out evaluations on the session and their perspectives.

Evaluation/Results:
Overall, there were a total of 193 students from seven different professional fields participating during the two days. There were 98 students during day 1 and 95 on day 2. There were a total of 22 lab students, 12 medical students and residents, 14 nuclear medicine students, 5 physician assistant students, 47 physical therapy students, 64 nursing students, and 29 respiratory therapy students. 93.8% of the group believed that this experience with improve that care of their patients. 92.7% of the participants believed that this was a valuable experience. 90.70% of students said they would recommend the simulation to others. Participants also commented on what they learned most from the session. 66% stated communication is important, 16% indicated the importance of communication, 11% learned some clinical skills/knowledge, 5% indicated the importance of multitasking, and 2% of the participants had no comments.
Comparing day 1 to day 2, during day 1, 70% of participants emphasized communication compared to 63 % of day 2. The shift was noted with the nursing students, 88% of the students on day 1 wrote down the importance of communication compared 69% of RNs during day 2. Role Identification was 11% on day 1 compared to 21 % on day 2. Importance of multitasking shifted from 3% to 5% on day 2.

Discussion:
Overall the ICU simulations have properly delivered our two goals, which are finding the importance of proper communication within different professionals and proper professional clinical behavior. The majority of the participants valued the power of communication and identification of roles amongst each other. These are the top two responses and comprised of about 82% of the responses. Pertaining to the evaluation comments, the physical therapy students were more neutral and had no responses. This occurrence could be due to the cases being ICU emergency cases that the physical therapists were not used to dealing with. The importance

of multitasking is a negative response in our study, since our goal was to enforce assigned tasks and only to focus on them. This response increased 3% to 7% the second day. This response was higher with the lab students. This could be due to the fact that these students may have felt overwhelmed with the amount of work presented. This aspect will be furthered studied. Overall we believe that these simulations have really helped students appreciate different interprofessional teams and the power of effective communication.
IRB approval of this project is pending.
Category: Research and Innovation in Medical Education (RIME), Simulation **Publish Online:** Yes
References: Dillion, PM, KA Noble, and L. Kaplan. "Simulation as a Means to Foster Collaborative Interdisciplinary Education." Nursing Education Perspect 30.2 (2009): 87-90. Print

Johnston, Lucy Baldwin (Lucy) JOHNSTLB@uab.edu

Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: John Woods, MD Abstract Approved By Advisor: Yes

Co-Authors: Kerri Bevis, MD

Title: Self-Reported OB/GYN Resident Experience with Difficult Consultations: A Platform for Curriculum Development

Background: No formal curriculum exists to educate UAB OB/GYN residents to deliver bad news or navigate difficult conversations with patients. Our goal was to assess the self reported needs of OB/GYN residents regarding their education in communication skills. The data collected will be used to develop a curriculum to improve communication training and increase self-confidence among trainees during difficult conversations.

Methods: We developed a needs assessment tool based on previously published studies evaluating educational experience with difficult conversations among medical trainees and their reported self-efficacy with those skills. The instrument was piloted on six recent graduates of OB/GYN residency and then administered to current residents in the OB/GYN department.

Results: All OB/GYN residents completed the assessment. 100% of surveyed residents reported skills in difficult conversations are valuable to practice. 52% felt adequately trained in communication skills. Residents identified “observation of others” as most valuable in learning these skills. 8% of respondents observe conversations (>10 times) involving infertility issues. 68% personally deliver bad news less than 5 times a month. Intrauterine fetal demise and discussion of code status were the two situations specifically identified as difficult for trainees. 80% of residents reported formalized communication training during medical school. 77% agree that formal graduate medical education training on “breaking bad news” would be beneficial.

Conclusions: OB/GYN residents at UAB recognize the importance of effective communication skills to clinical practice and feel incorporating these skills into their graduate medical education is important. Based on the needs reported, a formal curriculum for communication is under development using intrauterine fetal demise and code status discussions as a platform for intervention.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Desiree Morgan, MD Abstract Approved By Advisor: Yes

Co-Authors: David Bolus, Lincoln Berland, Desiree Morgan

Title: Replacing conventional unenhanced with dual-energy virtual unenhanced series: radiation and reimbursement implication

Brief description
Virtual unenhanced images have been evaluated as a potential substitute for conventional unenhanced images, in efforts to improve quality by reducing radiation exposure to patients. It is also important to recognize the financial implications of this conversion to healthcare providers.
Objective
Evaluate potential reduction in radiation exposure and effects on reimbursement of using a dual-energy "virtual unenhanced" image set rather than a conventional unenhanced series for multiphasic abdominal indications.
Materials and Methods
4984 multiphasic abdominal rapid kVp-switching dual energy CT (rsDECT) scans were obtained in 3365 consecutive outpatients over 30 months. Demographics, anatomic scan coverage, radiation exposure estimates for the rsDECT arterial phase and total exam were recorded. Fiscal year 2013 payor mix percentages and published/recorded rates of reimbursement for various abdominal multiphasic CT exams were used to calculate compensation differences for potential utilization of virtual unenhanced (VU) rather than CU sequences.
Results
1712 women and 1653 men were observed for a total of 4984 studies, with an average age of 60±11years and average weight of 83±21kg. Anatomic coverage was divided with 1974 being abdomen only studies, 1633 being abdomen/pelvis, 1120 chest/abdomen/pelvis, and 257 chest/abdomen. Overall reduction in radiation exposure estimate was 6.8% for the population if unenhanced scan was omitted. A net decrease of $745,143.22, or $149.51 per exam is observed if a charge for CT abdomen "with" rather than CT abdomen "without and with" had been billed for this population.
Discussion
If there is no allowable reimbursement for substituting a "virtual unenhanced" series for a conventional unenhanced series using dual energy CT for abdominal indications, a sizable reduction in revenue may be incurred. Omitting the conventional unenhanced acquisition during abdominal multiphasic rsDECT results in a measurable reduction in radiation exposure, though modest compared to other values reported in the literature.

Kennell, Timothy Irving, Jr. (Tim) TIKENN@uab.edu

Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Seung Park, MD Abstract Approved By Advisor: Yes

Co-Authors: Vincent Laufer, BS; Robinna Lorenz, MD, PhD; Seung Park, MD

Title: This Is Your Brain On Informatics: A Total-Immersion Data Sciences Course for the Next Generation of Informaticists

Introduction: The need to train informaticists is critical, yet such training is rarely built into standard curricula, even at informatics-savvy institutions. Courses that do exist usually focusing on imparting testable knowledge rather than on building technical prowess. We have developed and implemented a one week, 40 hour long, total-immersion experience in clinical and research informatics/data sciences that enables trainees at all levels (medical students to faculty; most with zero prior exposure to informatics) to independently create and administer complex informatics systems.
Methods: On day 1, students learn the fundamentals of systems architecture and algorithmic thinking in an axiomatic fashion while they assemble a functional LEMP (Linux, nginx, MariaDB, PHP-FPM) stack from the ground up. Day 2 covers relational database design, normalization, querying and maintenance. Day 3 covers Web 2.0 user interface elements, including HTML5, PHP-FPM 5.3, CSS3, and the Twitter Bootstrap user-interface library. Days 4-5 comprise a supervised hackathon in which students form into groups, design real-world informatics projects, and begin implementation. Students continue working on their projects until completion (usually with light supervision).
Results: Over two sessions of this class thus far, 21 students have undertaken 10 major informatics projects, with a current total of 12 out of 14 abstracts accepted at national research conferences. 3 are medical education projects, all of which have been formally adopted by our institution. 4 are research-oriented analysis projects, in various stages of completion. 3 are clinical informatics projects, each of which (a) generates significant time and money savings in clinical operations and (b) has been formally adopted by our institution.
Conclusions: Engineering education-derived practices, including real-world group projects and technical skill building, reap major dividends when applied to informatics education. Future iterations of this class will see the completion and deployment of more major informatics systems.

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Evers, Caroline

Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Warner Huh Abstract Approved By Advisor: Yes

Co-Authors: Caroline Evers Phillips, Britt K. Erickson, Warner Huh, Charles A. Leath III

Title: Racial Disparities in Treatment and Outcomes of Epithelial Ovarian Cancer

Objective: Population based studies have suggested that Black women have worse progression free and overall survival compared to White women. The objective of this study was to compare survival among black versus white patients diagnosed with epithelial ovarian cancer (EOC) at a national comprehensive cancer center that serves a diverse racial and socioeconomic population. Our secondary objective is to determine other factors that may contribute to differences in survival.

Methods: Institutional IRB approval was obtained. 1,248 patients were identified using the cancer center tumor registry and billing codes from the outpatient gynecologic oncology clinic. Criteria for selection included a diagnosis of EOC between 2006-2012, treatment, and follow up at our institution. Demographics, tumor characteristics, treatment regimen, survival, comorbidities, and operative complications were collected on each patient. Progression-free survival (PFS) and overall survival (OS) were calculated with Kaplan-Meier estimates and compared with the log-rank test.

Anticipated Results: Of the 1,248 patients identified, approximately 850 will meet study criteria. Based on previously published national data and clinical experience at UAB, we predict Black women compared to White women will have shorter progression free and overall survival. There may, however, be other differences between these patient populations contributing to the survival rate differences such as comorbidities, perioperative complications, and disease stage at presentation. Through this study, we hope to establish a better understanding of this difference.

Anticipated Conclusions: Pending results.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Mary Hawn Abstract Approved By Advisor: Yes

Co-Authors: Laura A. Graham, Mary T. Hawn

Title: Colorectal Cancer Surgery and Coronary Revascularization

Background: Approximately 600,000 cardiac stents are implanted each year in the US, with 20% of patients undergoing at least one non-cardiac surgery in the two years after the stent. Guidelines recommend delaying surgery up to 12 months following stent. Colorectal cancer represents the third most commonly diagnosed cancer in the US and surgery is usually the frontline treatment. Few studies have analyzed the impact of cardiac stents on delays in cancer treatment.

Objectives: To determine whether stent characteristics and relationship to timing of colorectal cancer diagnosis impacted short-term outcomes.

Methods: We used data from a cohort of Veterans and analyzed stent, surgery, and patient characteristics. We analyzed the variation in intervals of diagnosis to surgery and stent to surgery as well as 30-day major adverse cardiac events and 1-year mortality.

Results: Overall, 196 patients had the diagnosis of colorectal cancer and had a coronary stent. If a stent was placed after diagnostic colonoscopy, it was more likely to be a bare metal stent (85.7% vs. 14.3%, $p<0.001$) and to have a non-acute coronary indication (68.6% vs. 31.4%, $p<0.001$). We did not observe a delay in time to surgical treatment by stent type nor difference in 30-day major adverse cardiac event rates. However, a history of CHF, which was correlated with placement of an intervening stent, predicted a significantly higher 1-year mortality rate (25.0% vs. 9.9%, $p=0.01$).

Conclusions: Management of cardiac risk and revascularization creates new challenges in colorectal cancer patients. We found that bare metal stents were used much more frequently after a diagnosis of colon cancer; however, we do not know the optimal timing strategy for non-acute coronary revascularization or if the presence of cancer affects stent-related outcomes in these patients.

Koplon, Joshua Samuel (Joshua) JSK769@uab.edu

Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Dr. James Galbraith

Abstract Approved By Advisor: Yes

Co-Authors: Jennifer Anderson, Joel Rodgers, James Galbraith

Title: CORRELATION BETWEEN HCV AND MENTAL ILLNESS IN THE ED

Intro
To address the estimated 3.3% nationwide prevalence of HCV among the “baby boomer” birth cohort, emergency departments (ED) have been identified as potentially high-yield settings for HCV screening and linkage-to-care. Barriers to successfully linking HCV-positive cases to treatment primarily include lack of health coverage, limited access to primary care services, and mental health co-morbidities. To better understand mental health related burdens, we compared mental health co-morbidities among UAB-ED “baby boomers” that screened HCV antibody (Ab) positive and HCV Ab-negative.

Methods
We conducted a retrospective chart review of UAB-ED “baby boomer” patients screened for HCV between September 2013 and May 2014. Medical record data were abstracted using mental health-related ICD9 codes 290-319. Individuals screened for HCV during this period were randomized. A total of 707 cases were included in the final data analysis, including 377 Ab-positive and 330 Ab-negative cases. Data were examined using standard frequency and descriptive statistics.

Results
Compared to HCV negative controls (n=330), HCV Ab-positive cases (n=377) were disproportionately affected by higher prevalence of Drug Psychosis (ICD9 292), Alcoholic Dependence Syndrome (ICD9 303), Drug Dependence (ICD9 304), and Non-dependent Abuse of Drugs And Tobacco (ICD9 305). Following are comparative results listed by ICD9 codes: 292: (6.63%) vs (2.42%) p = 0.008; 303: (14.59%) vs (7.27%) p=0.002; 304: (9.81%) vs (3.64%) p=0.001; 305: (27.06%) vs (21.21%) p= 0.071

Conclusions
Mental health co-morbidities are greater among HCV Ab-positive “baby boomers” compared to similar Ab-negative cases. Efforts to link HCV Ab-positive “baby boomers” should include strategies to mitigate barriers attributable to mental health co-morbidities.

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Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Adrie Steyn

Abstract Approved By Advisor: Yes

Co-Authors: Lauren Theiss

Title: The Creation of lldD1/lldD2 Knockouts: Insight on Mycobacterium tuberculosis' Utilization of Alternate Metabolic Pathways

Granulomatous lesions characteristic of a *Mycobacterium tuberculosis* (*Mtb*) infection oftentimes exhibit diverging metabolic profiles when compared to those of uninfected lung tissues. In addition, a significant up-regulation of lactate has been observed in the granulomas, indicating either progressive hypoxia and necrosis or The Warburg Effect. Within this context, the Steyn Lab of The Kwazulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) is questioning the influence that L-lactate dehydrogenase I (LldD1) and L-lactate dehydrogenase II (LldD2) have on not only the production and maintenance of this the metabolic variance, but also on the components of *Mtb* metabolism and virulence. This inquiry leads to the purpose of this study and its attempt to create both *lldD1* and *lldD2* knockout vectors. Initial amplification of *lldD1* and *lldD2* with polymerase chain reaction (PCR) followed by a series of digestions and ligations allowed for the insertion of *lldD1* and *lldD2* within pUC19 vectors. Inverse PCR and subsequent ligations resulted in the construction of *lldD1* and *lldD2* knockout plasmids that will ultimately be transformed into multiple aliquots of competent *Mtb* H37Rv strains. Successful transformation will allow for further investigation of *Mtb's* utilization of both alternate metabolic pathways and energy sources and their influence on the bacteria's virulence, persistence, and latency.

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Project Length: Short

Prior Research Experience: Yes

Source of Funding: Foundation for Anesthesia Education and Research

Faculty Advisor: Dr. Sadis Matalon

Abstract Approved By Advisor: Yes

Co-Authors: Saurabh Aggarwal, Subhashini Bolisetty, Amie Traylor, Matthew A Carlisle, Anupam Agarwal, and Sadis Matalon

Title: The Role of Heme in Bromine Induced Lung Injury

Bromine (Br_2) exposures pose environmental risks and have been associated with increased morbidity and mortality. While bromine inhalation is known to cause respiratory failure, the mechanisms that govern Br_2 inhalation toxicity remain poorly understood. Previously, it was shown that bromine exposure results in an upregulation of the heme oxygenase-1 (HO-1), an inducible enzyme that converts free heme to iron, biliverdin, and carbon monoxide. While heme is a strong oxidant that induces free radical damage, biliverdin is known to have anti-apoptotic, anti-oxidant, and anti-inflammatory effects. Based on this previous work, we hypothesized that Br_2-induced free heme generation is responsible for its toxicity. To test this, we exposed C57/BL6 mice to Br_2 gas (600ppm, 30min) and found heme levels were significantly elevated in plasma, bronchial alveolar lavage fluid (BALF), and whole lung lysates of mice 24 hours post-exposure. However, administration of hemopexin, a heme scavenging protein (3ug/g body weight, 30min post-Br_2 exposure), attenuated this increase in heme in the plasma, BALF, and lung lysate. Interestingly, hemopexin also attenuated increases in lung oxidation, inflammation, and resistance in Br_2 exposed mice. To further verify that heme contributes to Br_2 induced lung injury, we obtained transgenic mice with the HO-1 gene knocked-out ($HO\text{-}1^{-/-}$) and transgenic mice with the human HO-1 gene overexpressed (hHO-1). We exposed these mice to Br_2 and noted increased tissue damage and mortality in $HO\text{-}1^{-/-}$ mice and decreased tissue damage and mortality in the hHO-1 mice. To gain insight into the subcellular mechanisms of Br_2 injury, we exposed lung epithelial cells (H441) to Br_2 (200ppm, 30min), and found Br_2 increased markers of mitochondrial dysfunction and apoptosis, while hemopexin treated cells exhibited no such increases. Overall, these results suggest heme is a primary contributor in tissue injury following Br_2 exposure, and hemopexin may potentially serve a novel therapeutic for treating Br_2 exposure.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Dr. DeeAnne Jackson Abstract Approved By Advisor: Yes

Co-Authors:

Title: “Creating a Safe Sleep Environment on the Mother-Baby Unit: More than just Infant Sleeping Position”

Abstract: Sudden Infant Death Syndrome (SIDS) is the leading cause of death for children 1 month to 1 year of age in the United States. The incidence of SIDS decreased dramatically in the 1990s when the “Back to Sleep” campaign went into effect, teaching parents to place their babies in a supine position to sleep; however, progress has plateaued since the early 2000s. Sleeping position is only the tip of the iceberg, as addressed by updated guidelines published by the American Academy of Pediatrics in 2011, which address not only sleeping position, but also co-sleeping, breastfeeding, use of car seats, and crib characteristics such as absence of extra blankets, bumpers, or toys. These guidelines also stress the importance of health care providers in the immediate postpartum period in teaching and modeling good sleeping behaviors for families—especially those at risk such as low-income, African-American or Hispanic families or babies born before 37 weeks. Much of the UAB patient population is at higher risk for SIDS, making it important for staff on the Mother-Baby Unit (MBU) to be well-educated and equipped to provide good patient care and safe sleep teaching in the immediate postpartum period. This quality improvement project involved first gathering data both by surveying nurses on the MBU and by directly observing a selection of infants. The survey assessed knowledge of safe sleep principles, perceived patient responsiveness to teaching, and comfort level with correcting unsafe behaviors. Results of the data along with safe sleep education were presented to MBU staff at a mandatory education session. The same survey was again given to the nurses after completing the safe sleep education session. Results will be analyzed for impact of education on nursing practice.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Lou Bridges Abstract Approved By Advisor: Yes

Co-Authors: Richard Reynolds Maria Danila Hemant Tiwari

Title: The Genetics of Rheumatoid Arthritis in Persons of African-American Ancestry

Background/Purpose: Rheumatoid arthritis (RA) affects 0.5-1% of the population worldwide. The genetics of RA has been analyzed in large European and Asian studies, but not in RA in African-Americans (AA). Therefore, we tested the hypothesis that there are similarities and differences between AA with RA, by both validating associations trans-ethnically and ethnic-specific variants. Thus, we present genome-wide association (GWA) data on 535 AA cases (CLEAR and VARA) and 1506 AA controls (CLEAR & SLEGEN) alongside whole genome sequencing (WGS) data on a subset of the population presented in the context of publically available datasets on RA.

Methods: Genotyped was performed using Illumina Omni 1M and 1S platforms. Inclusion thresholds were: sample call rate > 98.5%, SNP call rate > 98%, HWE p-value > $1x10^{-7}$, MAF >0.05. After standard QC, associated and suggestive loci were defined empirically as linkage blocks containing a SNP with one or more SNPs having p-value of $<10^{-8}$, or $< 10^{-5}$, respectively. Next, we integrated this with analysis of copy number, structural, and rare variation (CNV, SV and RV) from WGS from CGI in the 1000 genomes project. We annotated rare variants with 27 ontologies to aid integration with published data.

Results: One associated and 40 suggestive loci were identified among AA with RA through GWAS. Two of these loci were previously associated with RA and another ten have been identified in another immune or autoimmune GWAS. Our data show both internal consistency and clear departures between GWAS and WGS evidence, meaning care is needed in constructing joint analytical designs.

Conclusions: This co-analysis of GWAS, WGS, and published data allows refinement of gene and variant-level associations. We reconfirm the importance of SV in RA, but in new loci. GBT enables confirmation and refinement of associations as well as enabling focus on RV likely to be deleterious.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Christopher Klug Abstract Approved By Advisor: Yes

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

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. 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. 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 methylcellulose assays showed that the $TIM3^{-}$ $CLL1^{-}$ $CD33^{-}$ subset of $CD34^{+}CD38^{-}$ cells could form multiple colony types, including CFU-GEMM, that were all negative for the fusion mRNA by RT-PCR. In contrast, colonies derived from bulk bone marrow were all positive for the fusion mRNA. The $TIM3^{-}$ $CLL1^{-}$ $CD33^{-}$ subset of $CD34^{+}CD38^{-}$ cells displayed greater than 600-fold enrichment for progenitor activity compared to bulk bone marrow but did not form additional colonies upon serial re-plating. These results have important implications for the therapeutic targeting of $inv(16)^{+}$ hematopoietic stem/progenitor cells in patients with relapsed and refractory disease and for purification of normal HSPC from leukemic bone marrow samples.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Rakesh P. Patel Abstract Approved By Advisor: Yes

Co-Authors:

Title: alpha-mannosidase activity and N-glycans in atherosclerosis

Atherosclerosis underlies multiple cardiovascular diseases that afflict Western societies. It is an inflammatory disease characterized by formation of hardened intravascular plaques, where interactions between immune cells and endothelial cells cause chronic inflammation and damage. Monocytes are necessary for disease. They are recruited in high numbers, differentiate to macrophages, and go on to form activated, fat-laden, foam cells. An early and ongoing step in atherosclerosis is monocyte-endothelial interactions, which is controlled by adhesion molecules. In turn, the N-glycan phenotype of cellular adhesion proteins regulates monocyte avidity to the endothelium. Previous studies have shown that a change from complex N-glycans to hybrid and high mannose N-glycans on the endothelial adhesion molecule ICAM-1 increases monocyte rolling and adhesion. This change can be elicited *in vitro* by treatment with TNF-α, modeling inflammation seen in atherosclerosis. α-mannosidases catalyze key steps that regulate conversion of high mannose and hybrid N-glycans to complex N-glycans. We hypothesized that during inflammation, α-mannosidases are inhibited and responsible for changes in cell surface N-glycans in atherosclerotic lesions. Using an aortic endothelial cell culture model, we validated an α-mannosidase activity assay using *p*-nitrophenyl-α-D-mannose as the sugar substrate. Enzymatic product formation, measured spectrophotometrically, was linear in time, and the rate of product formation was linear with respect to increasing enzyme load. TNF-α dose response had varying results, such that product formation was not directly proportional to dose. Maximal inhibition by swainsonine, a potent α-mannosidase inhibitor, was achieved at 250 μM where activity decreased by a factor of 2. In conclusion, an α-mannosidase activity assay was successfully developed and validated to study changes in N-glycan processing in endothelial cells. Further development of the assay is needed for full application to the study of glycan signaling in atherosclerosis.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

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Title: Association between Early Coagulopathy and Ventilator-Associated Pneumonia in Spinal Cord Injury Patients

Introduction: Studies report early trauma-induced coagulopathy (ETIC) may increase susceptibility to later nosocomial infections, e.g. ventilator-associated pneumonia (VAP). However, the relationship between ETIC and the later development of VAP in spinal cord injury (SCI) patients has not been evaluated.

Methods: We conducted a 5-year retrospective study of 300 SCI patients admitted to a Level 1 trauma center. Standard coagulation factors were measured upon arrival prior to fluid resuscitative efforts and at 24 hours after admission. VAP was identified utilizing the following criteria: at least 2 days of mechanical ventilation, WBC>12,000 cells/mm^3 or <4,000 cells/$mm,^3$ pulmonary opacities or infiltrates on CXR, positive bronchoalveolar lavage culture.

Results: The incidence of VAP was 54.5% (OR 4.01, 95% CI 1.76-9.15) in SCI patients with prolonged INR$\geq$1.2 upon admission, compared to the 17.5% in SCI patients with normal INR<1.2 at 0 and 24 hours after admission and the 41.1% (OR 2.3, 95% CI 0.99-5.31) in SCI patients with normal INR<1.2 upon arrival that progressed to INR$\geq$1.2 at 24 hours. The mortality rate attributed to VAP was significantly higher in SCI patients with abnormal coagulation studies at admission (17%) than in patients with normal coagulation studies at 0 and 24 hours after admission (4.8%) and in patients who developed a coagulopathy during the first 24 hours (5.5%).

Conclusion: The subset of SCI patients who were coagulopathic at admission showed a statistically significant increase in VAP incidence and mortality. This suggests an abnormal coagulation profile in SCI patients may impair the ability to fight off lung infection.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Jesse Clark, UCLA Abstract Approved By Advisor: Yes

Co-Authors: Eddy Segura, MD, MPH; José Luis Castro, MD; Carlos Anton, MD; Jesse Clark, MS, MD; Jordan Lake, MD; Robinson Cabello, MD

Title: Bringing HIV/syphilis testing to the people—Benefits of mobile unit testing in Lima, Peru 2007-2009

Background: Mobile unit (MU) HIV testing is an alternative method of providing healthcare access. We compared demographic and behavioral characteristics, HIV testing history, and HIV prevalence between participants seeking testing at a MU vs. fixed community clinic (FC) in Lima, Peru.

Methods: Our analysis included men and transwomen (TW) in Lima ≥ 18 years old seeking HIV testing at their first visit to a community-based MU or FC from Oct. 2007-Nov. 2009. HIV testing history, serostatus, and behavioral characteristics were analyzed.

Results: A large percentage of MU attendees self-identified as transgender (13%) or heterosexual (41%). MU attendees were more likely to engage in transactional sex (24% MU vs. 10% FC, $p<0.001$), use alcohol/drugs during their last sexual encounter (24% MU vs. 20% FC, $p<.01$), and/or be a first-time HIV tester (48% MU vs. 41% FC, $p<0.001$).

MU HIV prevalence was 9% overall and 5% among first-time testers (49% in TW and 11% in MSM first-time testers).

Conclusion: MU testing reached large numbers of at-risk (MSM/TW) populations engaged in unsafe sexual behaviors, making MU outreach a worthy complement to FC testing. Investigation into whether MU attendees would not otherwise access HIV testing is warranted to determine the impact of MU testing.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Dr. Suzanne Oparil Abstract Approved By Advisor: Yes

Co-Authors: Timothy Wang, Bin Zhang, Peng Li, Tanja Dudenbostel, Suzanne Oparil

Title: High Prevalence of Type 2 Diabetes Mellitus Exists in Resistant Hypertensive Patients with Primary Aldosteronism

Resistant hypertension (RHTN) is uncontrolled blood pressure (BP>140/90 mmHg) on 3 different antihypertensive drug classes. A subset of RHTN patients may have primary aldosteronism (PA), defined as aldosterone-renin ratio (ARR)>30 or 24-h urinary aldosterone (UAldo)>12 mcg/24hr. Previous work has shown that aldosterone stimulates insulin resistance. This led us to hypothesize that PA patients have a higher prevalence of type 2 diabetes mellitus (T2DM). To test our hypothesis, we retrospectively analyzed the EMR of RHTN patients who had been worked-up for PA. Patients taking spironolactone, have end-stage renal disease (ESRD), or had incomplete urine collections were excluded. Those included in the analysis (n=2043) were categorized into two groups, PA (n=442) and non-PA (n=1601). Prevalence of T2DM was assessed for both groups if they meet one of the following criteria: 1) previous diagnosis or current anti-diabetic medication(s), 2) fasting glucose≥126 or, 3) HbA1C≥6.5. Statistical analysis revealed that PA patients have a significantly higher prevalence of T2DM than non-PA patients (22.1% vs. 15.4%, p=0.0001). Therefore, PA may be a predictor of T2DM risk in patients with RHTN. This clinical study provides a basis for further exploration into how these disease processes interact. Ultimately, it may help in the development of more effective therapeutic treatments for targeting these chronic conditions.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Thomas Ryan Abstract Approved By Advisor: Yes

Co-Authors: Yongliang Huo and Thomas Ryan

Title: Cure of Humanized Mouse Model of Cooley's Anemia by Non-cytoreductive Bone Marrow Transplantation from a MHC-mismatched Donor

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

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

We hypothesized that by exploiting the naivety of the newborn immune system and survival advantage of healthy donor erythroid cells, stable HSC engraftment could be achieved by transplant in a non-conditioned neonate. Here BMT was performed on neonatal humanized CA mice without cytoreductive conditioning. Immune modulation was tested in recipients by anti-CD122 and anti-CD40L antibody treatments. Low levels of donor chimerism were achieved and animals were rescued from lethal anemia. Most notably, we have demonstrated rescue of CA mice by non-cytoreductive conditioning in an instance of total MHC-mismatch with no evidence of graft-versus-host disease.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Victor Darley-Usmar Abstract Approved By Advisor: Yes

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Title: Platelet Mitochondrial Metabolism is Disrupted by 4-Hydroxynonenal: Implications for Thrombus Formation in Atherosclerosis

4-hydroxynonenal (HNE), a reactive lipid peroxidation product, has been implicated in the pathophysiology of numerous disease states including atherosclerosis. Platelets play a key role in modulating the pro-inflammatory response and the dysregulated thrombus formation in atherogenesis. With thrombus formation being a highly ATP dependent process, this study tests the hypothesis that HNE disrupts platelet metabolism that plays a role in dysregulation of platelet thrombus formation. To first determine if HNE causes dysregulated platelet thrombus formation, light transmission aggregometry utilizing stored human platelets with thrombin as an agonist was performed. A dose dependent decrease in thrombin mediated platelet aggregation was observed in the presence of HNE. At the highest dose of HNE (30 µM), a 95.6% decrease in aggregation was observed compared to control (n=4 donors). Then, to determine if HNE disrupts platelet mitochondrial bioenergetics, extracellular flux analysis was performed. In HNE (30 µM) treated platelets, a 62.2% decrease in maximal mitochondrial oxygen consumption rate compared to control was observed. Therefore, in the presence of HNE, platelet mitochondrial respiration is inhibited leading to decreased energy production required for proper platelet activation and thrombus formation. This study warrants the further investigation in determining the mechanism by which HNE disrupts mitochondrial function. These studies could elucidate novel therapeutic targets in combating atherosclerotic disease as well as other HNE mediated disease processes.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Richard Shelton, M.D. Abstract Approved By Advisor: Yes

Co-Authors: Nona Nichols, Michael Falola, M.D., MPH, and Richard C. Shelton, MD

Title: The Role of Visceral Obesity-Induced Systemic Inflammation in Depression

Introduction: It is well known by clinicians and described in the literature that obesity and depression are often co-morbid conditions (Allison et al, 2009). The literature suggests a bidirectional association between depression and obesity, with prior obesity increasing risk of depression and prior depression increasing risk of obesity (Shelton and Miller, 2010). One potential link between these two disease states is inflammation. Some researchers have conceptualized depression as an inflammatory state, as there are observed increases in serum inflammatory markers, namely TNFa, IL-6, and CRP in medically-healthy patients with Major Depressive Disorder (Howren, et al, 2009). Adipose tissue is a major producer of inflammatory cytokines, including IL-1, IL-6, and TNF-a (Shelton and Miller, 2010). Among sites of adipose tissue, intra-abdominal white adipose tissue produces the greatest effect on systemic inflammation (Shelton and Miller, 2010). Our study seeks to further explore the relationship between inflammation, obesity, and depression.
Methods: A total of 128 MDD patients and 35 controls were recruited from the Birmingham community and elected to participate in this study. Psychiatric diagnoses were verified using the SCID for DSM-IVTR Axis I Disorders- Patient Version (SCID-I), with symptom severity assessed using the MADRS and QIDS assessments. Serum was extracted from each participant and assayed for IL-1β, IL-2, IL-5, IL-6, IL-8, IL-10, IL-12p70, IL-17, IFNγ, TNFα, CRP, Leptin, and Adiponectin using single- or multi-plex human immunoassay kits. The analyses compared biomarker levels between 4 groups: non-obese (BMI<30) controls, obese (BMI$\geq$30) controls, non-obese MDD, and obese MDD.
Results: For IL-6 and CRP, the obese MDD group was significantly greater than the non-obese control and non-obese MDD groups, but not obese controls, suggesting that elevations in these factors were associated with obesity. There were no differences for TNFα. The level of IL-2 was also higher in the obese and non-obese MDD than both obese and non-obese controls indicating that the effect was related to MDD and not obesity.
Conclusions: Higher levels of IL-6 and CRP appear to be associated with obesity, while higher levels of IL-2 appear to be associated with MDD independent of obesity. These results further support a relationship between inflammation, obesity, and depression, and may provide greater insight into future use of cytokines as biomarkers for MDD.

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Project Length: Short Prior Research Experience: No

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Dr. Fernando Ovalle Abstract Approved By Advisor: Yes

Co-Authors: Fernando Ovalle, MD

Title: The Clinical and Biochemical Characterization of Pancreatic Diabetes

Pancreatic diabetes is a phenotype of diabetes mellitus that is caused by pancreatic destruction. Disorders that lead to this condition include, among others: chronic pancreatitis, cystic fibrosis and pancreatectomy. Presently, this disease has not been well characterized and we believe that by analyzing the data of patients with pancreatic diabetes we will discover distinct parameters that will aid in the diagnosis of the disorder and will help clinicians distinguish it from other types of diabetes, most importantly types 1 and 2 diabetes. The data of 1257 consecutive patients from their first visit to a tertiary care center diabetes specialty clinic was recorded and the date from 27 patients who were diagnosed with pancreatic diabetes was compared to that from a matched group of patients diagnosed with type 1 and type 2 diabetes. The type 1 and 2 patients used for comparison were matched based on gender, race, and duration of diabetes. The results show that patients with pancreatic diabetes have similar BMI, systolic blood pressure, diastolic blood pressure, and HDL levels to those with type 1 diabetes, while their triglyceride levels were similar to patients with type 2 diabetes. C-peptide levels were distinct in patients with pancreatic diabetes and islet cell autoantibodies were frequently present in patients with pancreatic diabetes probably representing an epiphenomenon. These novel findings could help clinicians avoid making a wrong diagnosis of autoimmune diabetes in these patients.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Candace Floyd Abstract Approved By Advisor: Yes

Co-Authors:

Title: Oxidative Stress in a Porcine Model of Spinal Cord Injury

Many advancements and new understandings of spinal cord injury have occurred in the past few years, which have led to many new possible treatments for the disorder; however, there is still no definitive treatment to preserve or enhance neurological function after a person undergoes spinal cord injury (SCI). To date, small animal models have been utilized to comprehensively study the pathobiology of SCI, as well as therapeutic targets; however, this is not always an ideal approach to long-term research for SCI treatments in humans. Due to these findings, a porcine model of SCI was developed as a translation intermediary. Using Yucatan miniature pigs, a T10/11 spinal cord injury was induced using a weight drop. To date, only male pigs have been used in the porcine model of SCI. Through this study, we wished to determine if there are sex differences in functional recovery and inflammatory response in the porcine model to SCI. Using the Porcine Thoracic Injury Behavior Scale (PTIBS) to determine locomotive recovery after SCI was used to help distinguish recovery based on sex. The PTIBS scores have strongly correlated with locomotive improvements in female scores versus male scores. Sex differences may show variability recovery of SCI in the porcine model.

Ma, Elizabeth Yean (Elizabeth)

Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: W. Timothy Garvey Abstract Approved By Advisor: Yes

Co-Authors: Nanlan Luo, Ling Tian, Wei Zhang, Dennis Steverson, Jr., Yuchang Fu

Title: Role of MicroRNAs -150 and -33 in Human Insulin Resistance

Insulin resistance plays a key role in Metabolic Syndrome, and risk for future Type 2 Diabetes and cardiovascular disease. However, the mechanism linking insulin resistance with cardiometabolic disease pathophysiology is unclear. Based on miRNA profiling, we previously discovered that microRNA-150 (miR-150) was upregulated during the transformation of THP-1 macrophages to foam cells, and that miR-150 knockout mice exhibited reduced adipose tissue mass and inflammation together with enhanced glucose tolerance and insulin sensitivity.

To assess the role of miR-150 in humans, we studied 10 overweight or obese adults (ages 26-57 years) placed on a very low calorie diet (VLCD), which we have shown increases insulin sensitivity and reduces intramyocellular lipid (Metabolism 57:1-8, 2008). Subjects were first equilibrated for 1 week on an isocaloric diet (50% carb, 30% fat, 20% protein), then studied before and after a 1-week VLCD (800 kcal/day for females, 1000 for males) of the same macronutrient distribution. Body composition was assessed by DEXA; insulin sensitivity by OGTT and Matsuda index; and circulating miR-150 was measured by RT-PCR in fasting blood. After the 1-week VLCD, patients experienced significant weight loss ($p<.001$), decreased waist ($p=.039$), and reduced fat mass ($p<.001$). There was also an increase in insulin sensitivity ($p=.012$) that was accompanied by a marked 58.375% reduction in miR-150 from baseline ($p<.001$). We also measured plasma miR-33, which has been implicated as a marker for atherogenesis, and found that the VLCD also reduced fasting miR-33 levels by 42.94% ($p<.001$).

In conclusion, a short-term VLCD increases insulin sensitivity and leads to pronounced reductions in circulating concentrations of miR-150 and miR-33. When considered in light of our miR-150 data in cultured macrophages and knockout mice, the data indicate that microRNAs could play a significant role in the regulation of human metabolism and in the pathophysiology of insulin resistance and cardiometabolic disease.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Straughn Abstract Approved By Advisor: Yes

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Title: Is observation reasonable in older patients with early stage uterine papillary serous carcinoma and clear cell carcinoma?

Objectives: Early stage uterine papillary serous carcinoma (UPSC) and clear cell (CC) carcinoma have 5-year survival rates as low as 38%. The decision to use adjuvant therapy is influenced by patient and tumor characteristics. We sought to determine whether adjuvant therapy after primary surgery for the treatment of stage I-II UPSC and CC improves progression-free and overall survival.

Methods: A single institution, retrospective cohort study of women diagnosed with stage I-II UPSC or CC endometrial cancer from January 2000 – December 2009 was performed. All patients underwent primary surgery followed by either observation (OBS) or adjuvant therapy including radiation therapy (RT) or chemotherapy (CT). CT patients were treated with 4-6 cycles of paclitaxel and carboplatin. RT patients were treated with whole pelvic radiation therapy (WPRT), brachytherapy (BT), or both and were considered collectively. Statistical analysis included Fisher's exact and Student's *t*-test as appropriate. Kaplan-Meier analysis was used to evaluate (PFS) and overall survival (OS).

Results: 118 patients were identified. 74 patients were stage IA, 23 were IB, and 21 were stage II. 52 patients underwent OBS and 66 received adjuvant treatment. 49 patients (74%) received CT, 10 patients (15%) received RT, and 7 patients (11%) received both. Although the OBS group was older (70.2 vs. 63.2 years; p=0.0009), the two groups were otherwise similar in demographics, tumor characteristics, and surgical management. Nine patients (17%) recurred in the OBS group compared to 17 (26%) in the adjuvant group (p=0.37). 2-year PFS was similar between adjuvant group and OBS (82% vs. 70%; p=0.82). While median OS favored adjuvant treatment, 65.4 months (95% CI 33.2-97.6) compared to OBS 41.6 months (95% CI 35.3-47.8), this was not statistically significant (p=0.61).

Conclusions: In this cohort with early stage UPSC and CC endometrial carcinoma, adjuvant therapy did not improve PFS or OS. Observation may be reasonable in a subset of older patients who may not tolerate adjuvant therapy.

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Project Length: Long Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Joseph Biggio Abstract Approved By Advisor: Yes

Co-Authors: Amelia L. Sutton, Jaya R. Madhav, Tate R. Nice, Scott Anderson, Cherry L. Neely, Jeffrey M. Szychowski, and Joseph R. Biggio

Title: Sonographic predictors of outcomes in prenatally-diagnosed gastroschisis

Objective: Gastroschisis is typically associated with favorable outcomes, but up to 1/3 of cases can have complicated gastroschisis, with an increased risk of perinatal mortality and morbidity. We sought to determine if antenatal ultrasound findings, such as bowel or stomach dilatation, bowel thickening, or herniation of other viscera, were associated with adverse postnatal outcomes.

Methods: We performed a retrospective cohort study of patients with prenatally-diagnosed gastroschisis cared for at our institution from 2004-2012. Ultrasound images from each visit were reviewed, and maximal bowel and stomach dilatation and bowel thickness were measured. Each fetus was categorized as having either simple (no additional findings) or complex gastroschisis (bowel dilatation >10 mm, bowel thickness of >2 mm, stomach dilatation of >25 mm, or herniation of stomach, liver, or other viscera). Prenatal records were linked to a pediatric database of postnatal outcomes. The primary composite outcome included either stillbirth or death <1 year, bowel perforation or necrosis, or sepsis.

Results: Of the 137 fetuses identified, 71 were categorized as complex gastroschisis and 66 as simple. The baseline demographics were similar between the two groups. There was no significant difference in the primary composite outcome between the two groups. While infants with prenatally-diagnosed complex gastroschisis had a length of stay and duration of silo and TPN treatment similar to those with simple gastroschisis, those with prenatally-diagnosed complex gastroschisis had a significant delay in the initiation of enteral feeds (20 vs. 16 days).

Conclusions: Prenatal ultrasound findings of complex gastroschisis are not associated with an increased risk of perinatal mortality, serious bowel complications, or sepsis, but are associated with delayed feeding in these infants. Further studies are warranted to determine if specific ultrasound findings predict postnatal outcomes and to guide obstetrical management of fetuses with gastroschisis.

Mascia, Katherine Louise (Katherine)

Project Length: Short Prior Research Experience: Yes

Source of Funding: Genetics Fellowship

Faculty Advisor: Nathaniel H. Robin, MD. Abstract Approved By Advisor: Yes

Co-Authors:

Title: Attitudes of Deaf individuals towards genetic testing of genes known to cause deafness

Introduction: Congenital deafness is one of the most common birth defects in the human population. Approximately 70% of congenital deafness is non-syndromic, and 80% of non-syndromic hearing loss (NSHL) results from an underlying genetic cause. *Middleton et al*'s groundbreaking 1998 study highlighted the negative attitudes of culturally Deaf individuals towards genetic testing for genes known to cause deafness. After a thorough literature review was conducted, we found that while recent studies concerning genetic testing for deafness genes reference Middleton's study, to our knowledge a re-evaluation of the attitudes of Deaf individuals towards genetic testing has not been conducted. Since recent studies have shown changes in the opinions of members of the Deaf community towards cochlear implantation of children, it follows that attitudes towards genetic testing for deafness genes may have undergone similar changes. The purpose of this study is to establish the current attitudes of Deaf individuals towards genetic testing of genes known to cause deafness.

Methods: A short, computer-based questionnaire will be distributed to members of the Deaf community. The questionnaire contains approximately 30 questions, and will assess demographic information as well as attitudes of Deaf individuals towards genetic counseling, genetic testing, and prenatal testing of genes known to cause deafness. Responses of participants will be statistically analyzed as they are completed.

Results: The questionnaire is being revised and a member of the Deaf community has been contacted in order to facilitate the distribution of surveys to culturally Deaf individuals.

Conclusion: Our study plans to re-evaluate the opinions of culturally Deaf individuals towards genetic testing for genes known to cause deafness. An update on these cultural attitudes is essential for future studies concerning genetic testing of deafness genes. Since the computer-based questionnaire is being revised, there are currently no results to this study.

Massey, Julia Dickinson (Julia)

Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: Dr. William Holman Abstract Approved By Advisor: Yes

Co-Authors: R. Baxter, MS4; J. George, PhD; M. Kukreja; J. Kirklin, MD

Title: Outcomes of cardiac surgery in adult renal transplant recipients

Cardiovascular complications are a major cause of morbidity and mortality in renal transplant recipients. This study accesses pre-, peri-, and postoperative risk factors for mortality and long-term outcomes in renal transplant recipients who subsequently underwent cardiac surgery. Patients with a functioning renal allograft at the time of their cardiac surgery at the authors' institution between 1989 and 2012 were analyzed. Data were obtained by retrospective medical record analysis.

Cardiac procedure categories included coronary artery bypass grafting, isolated valve surgery, combined coronary artery bypass grafting and valve surgery, and other (including aortic procedures). Patients with multiple organ transplants were excluded from the study. Preliminary data collection is still ongoing. Using multivariate analysis, we plan to access and compare the early and late-phase risk factors for death in each type of cardiac procedure (CABG, valve only, bypass + valve, other).

These data may help identify patients at higher risk of developing surgical complications and suggest a lower threshold for aggressive treatment during their post-operative course. Additionally, these data may allow clinicians to provide renal transplant patients with more accurate operative risk assessments.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. William Jordan, Dr. Marc Passman Abstract Approved By Advisor: Yes

Co-Authors: Dr. Zdenek Novak, Dr. Roan GLocker, Dr. Thomas Matthews, Dr. Mark Patterson, Dr. Benjamin

Pearce, Dr. Marc Passman, Dr. William Jordan

Title: Clinical Practice Trends of Vena Cava Filter Utilization at a Single Tertiary Care Center over a 12 Year Period

Objectives: Increasing volume of inferior vena cava filter (IVCF) placement and low retrieval rates nationwide have prompted a closer evaluation of IVCF use. Our study aims to investigate the clinical practice trends of IVCF utilization over a 12-year period at a single institution and to identify potential factors that may affect clinical decision for IVCF placement and patient care follow up for retrieval.

Methods: An institutional database was reviewed for all IVCFs placed between 2000-2012. Data relating to filter type and placement indications were evaluated for annual practice trends. Patient demographics including gender, ethnicity, age, distance, and insurance type were evaluated with respect to patient follow up and IVCF retrieval. Statistical analyses, Chi squared and logistical regressions, were performed.

Results: A total of 3054 IVC filters were placed from years 2000-2012, including 865 (28.3%) permanent and 2189 (71.6%) retrievable. There was a steady increase of IVCF placement from year 2000 to 2009 peaking in 2010 followed by a steady decline through 2012. IVC filter utilization based on indications showed trends of increasing prophylactic filter use, while use for patients with documented deep venous thrombosis (DVT) and or pulmonary embolism (PE) declined. For patients with eligible retrievable IVCFs (1924), overall IVCF retrieval rate was 5.5%, but was virtually nonexistent prior to 2007 and has shown a mean rate of 12.7% (±4.7) from 2008-2012. Significant factors contributing to a low institutional retrieval rate included patient follow up based on insurance type, discharge instructions and location, distance traveled, age, income, and difference in specialty placing IVCF; however, there was no significant difference in ethnicity or gender.

Conclusion: Despite expansion of IVCF utilization during the 12 year time period, a downward trend over the later portion reflects changes in clinical decision making that may parallel national trends. However, overall institutional retrieval rate remained low reflecting variation in specialty practice patterns and poor patient follow-up.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. John Hartman Abstract Approved By Advisor: Yes

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Title: Evolution of 5-Fluorouracil Resistance in Saccharomyces cerevisiae

5-fluorouracil (5-FU) is a nucleoside analog used to treat colon and other forms of cancer. Understanding mechanisms of resistance to 5-FU could help improve its efficacy. Yeast and humans have similar *de novo* and salvage pathways for uracil. In yeast, the Ura5 and Ura10 proteins convert orotate to orotidine-5-phosphate, which is a substrate for Ura3 to produce uridine monophosphate (UMP), while in humans UMP synthase (UMPS) is a bi-functional enzyme that catalyzes both reactions. Ura6 (UMP-CMP kinase in humans) converts UMP to uridine diphosphate (UDP). In the salvage pathway, Fur1 (UPRT in humans) converts uracil and phosphoribosyl pyrophosphate (PRPP) to UMP. We devised a strategy called "selective cycling" to investigate whether 5-FU resistance could emerge while maintaining pyrimidine biosynthesis. A stop mutation in URA3 conferred uracil auxotrophy and resistance to 5-fluoroorotic acid (5-FOA), however selection for uracil independence was subsequently possible, for example, by reversion of the stop mutation. Selective cycling gave rise to "mutation/reversion lineages". Forty mutation/reversion lineages were obtained for 5-FOA resistance and uracil prototrophy, called "dual survivors". Nine out of 40 lineages evolved dual survivors, which could proliferate on both 5-FOA media and media lacking exogenous uracil. In some lineages URA3 mutations did not explain the phenotypic selection, so genomic sequencing was performed, revealing a mutation in URA6 in one dual survivor. Mutations in conserved residues were discovered in 7 of the 9 dual survivor lines by targeted sequencing. No mutations were identified in FUR1. Examination of the crystal structure of URA6 revealed mutations to be near the substrate-binding site, further implicating Ura6 in the dual survivor phenotype. Further experiments are ongoing to assess whether analogous mutations in human UMP-CMP kinase could be a mechanism of 5-FU resistance in cancer.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Tim Townes, Dr. Troy Randall Abstract Approved By Advisor: Yes

Co-Authors:

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

The laudable advances made in cancer therapies are often stymied in practice by recurrence and metastasis of the primary tumor, inherently negatively impacting patient outcomes. Here, malignant cells downregulate surface antigens or upregulate alternative intracellular pathways, thereby rendering initial therapies ineffective. If, however, multiple surface antigens were targeted simultaneously, rather than individually, the likelihood of escape would be dramatically reduced. Furthermore, such a strategy can target a profile of antigen expression, allowing for markedly enhanced selectivity. Chimeric antigen receptors (CARs), fusion proteins consisting of an extracellular specificity-directing antibody fragment tethered to 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 tumor antigen or profiles thereof. Second, dedifferentiating patient fibroblasts 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.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Lindy Winter Abstract Approved By Advisor: Yes

Co-Authors: Dr. Nancy Tofil

Title: Rapid Cycle Deliberate Practice: Implementing a New Approach to Team Building and Education in Neonatal Resuscitation Team Training

Background: The purpose of this pilot study is to utilize a new educational method, Rapid Cycle Deliberate Practice (RCDP), to train hospital staff in Neonatal Resuscitation Program (NRP). RCDP differs from the traditional debriefing approach in that it halts progression of the scenario once an error is encountered to allow for immediate acknowledgment and correction of the error. This allows for opportunities to perform a specific skill combined with rapid expert feedback to master those skills. Our hypothesis is that RCDP, when applied to NRP algorithms taught through simulation, will improve individual learning and team performance.

Methods: Neonatal resuscitation workshops were performed in the UAB Regional Neonatal Intensive Care Unit (RNICU). Each session consisted of three simulations with increasing difficulty progressing further down the NRP algorithm decision tree. RCDP was implemented within these simulations as described above. Research study outcomes were measured through surveys administered prior to starting the workshop and upon completion.

Results: Two sessions with 3 participants per session were completed (N=6). Likert scale responses for the 5 competencies measured in the survey were consolidated for each individual and scored as a numerical value from 0 to 25. Mean pre-simulation score was 12.7±5.1 versus mean post-simulation score of 17.7±2.3 ($p = 0.009$). Statistically significant improvement was noted in each competency surveyed.

Discussion: This pilot study was implemented in order to validate our process for investigation of outcomes related to the use of RCDP in teaching NRP. Based on the data presented above, as well as observation of the simulations, we believe RCDP holds considerable promise as a valid teaching method to improve individual confidence and team performance in adhering to standardized NRP algorithm based patient interventions. Further investigation into the utility of RCDP as a learning tool is warranted, with statistical comparison to traditional modes of simulation debriefing.

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Project Length: Short Prior Research Experience: No

Source of Funding: Other

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Co-Authors:

Title: A novel primary care program for homeless veterans: descriptive analysis of the Homeless Patient-Aligned Care Team (HPACT) in Birmingham

Aims: In 2012, the Department of Veterans Affairs (VA) opened Homeless Persons Aligned Care Teams (HPACTs) for primary care of homeless Veterans. We sought to characterize patients served by Birmingham's HPACT, profiling health and service utilization before and after HPACT engagement. This chart review effort continues a quality improvement project among 3 HPACTs (Birmingham, Pittsburgh, Los Angeles).

Methods: This review examined patients entering the Birmingham HPACT 01/17/13-08/13/13 (n=69). It covers these pre-admission variables: chronic medical diagnoses, health service utilization, and housing. For the 6-month period after HPACT entry, health service utilization was assessed. Methods were coordinated with collaborating sites, resulting in a standard operating procedure for future collaborators.

Results: Of 69 persons entering Birmingham's HPACT, 19% were sleeping in hotels, vehicles, emergency shelters, or on the streets, 25% were living with family/friends, 48% were in transitional programs, and 9% were permanently housed. The most common chronic conditions at baseline were: hypertension (44%), chronic pain (37%), and hyperlipidemia (15%), with 63% having at least one condition. The most common mental conditions were: depression/bipolar (55%), anxiety (19%), and post-traumatic stress disorder (14%), with 59% having at least one mental condition. An alcohol/drug issue was found among 48%/35%, respectively.

Among HPACT entrants for whom there was a record prior to entry (n=64), 81% had obtained non-HPACT primary care, 34% had used the ED and 9.4% had inpatient hospitalizations. 6-month utilization of this population was as follows: HPACT, 97%; ED, 35%; and inpatient, 14%.

Conclusions: Patients received by this HPACT had extremely high morbidity. The high percentage with prior primary care suggests heavy reliance on intra-facility referral rather than outreach to "de novo" patients. A reduction in ED/hospital utilization was not observed. HPACTs appear capable of accruing and serving a vulnerable population but future work will be required to measure outcomes and impacts of care.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Mary Hawn Abstract Approved By Advisor: Yes

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Title: Hematocrit, Blood Transfusion, and Outcomes in Patients with Coronary Stents and Cardiac Risk Factors Undergoing Surgery

Introduction: Despite recommendations for conservative transfusion strategies, blood transfusion practices among surgical patients with cardiac risk factors are highly variable. Further, current guidelines do not address transfusion strategies in patients with coronary stents. We hypothesized that patients with coronary stents receive more transfusions than non-stented patients with similar cardiac risk factors and that receipt of transfusion is associated with major adverse cardiac events (MACE).

Methods: We matched patients with coronary stents who underwent inpatient non-cardiac surgery within 24 months of stent implantation to two patients without stents with similar cardiac risks factors undergoing surgery. Our independent variable of interest was post-operative transfusions of 1-4 units. We excluded patients receiving preoperative and intraoperative transfusions or >4 units of blood within three days of surgery to exclude patients with major blood loss. Our primary outcome was MACE within 30 days postoperatively, which included myocardial infarction, coronary revascularization, or death. Outcome rates were stratified by transfusion status, stent presence, and nadir postoperative hematocrit. Associations with adjustment for MACE risk factors were modeled using logistical regression.

Results: We identified 16,885 patients with cardiac risk factors who underwent non-cardiac surgery, of whom 1265 (7.5%) received post-operative transfusions, and 906 (5.4%) experienced MACE. The presence of a bare metal stent (BMS) or drug eluting stent (DES) was independently associated with receiving a post-operative transfusion (BMS OR=1.25, CI 1.07-1.46; DES OR=1.24, CI 1.04-1.47). Overall, patients with postoperative transfusions were more likely to experience MACE on adjusted analysis (OR 1.99, CI 1.60-2.46), but only non-stented patients had statistically significant increased MACE rates (Stented OR 1.79, CI 0.91-3.54; Non-stented OR 2.15, CI 1.63-2.84). When stratified by nadir postoperative hematocrit levels, patients transfused at hematocrits greater than 27 had significantly higher MACE rates after adjustment (Hct 27-30 OR 2.12, CI 1.05-4.27; Hct >30 OR 1.65, CI 1.26-2.15), but patients transfused at hematocrits less than 27 showed no significant increase in MACE rate.

Conclusion: Patients with coronary stents undergoing surgery are more likely to receive postoperative blood transfusion, indicating need for further evaluation of transfusion indications and guidelines in these patients. Among all patients with cardiac risk factors, postoperative blood transfusion is associated with MACE, especially with postoperative hematocrits above 27. This supports the recommendation for restrictive transfusion strategies in the postoperative period for patients with coronary risk factors.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: John Hablitz Abstract Approved By Advisor: Yes

Co-Authors: Mikael Guzman Karlsson, Cassie Holleman, Jeremy Day, John Hablitz, and David Sweatt

Title: Epigenetic Regulation of Homeostatic Synaptic Scaling via DNA Methylation

Activity-dependent alterations in synaptic strength represent a key cellular mechanism of learning and memory. Synapse-specific plasticity, including Hebbian long-term potentiation (LTP) and long-term depression (LTD), has long been thought to play a major role in information storage. However, both LTP and LTD can propagate in a feed-forward manner, disrupting synaptic gain and network equilibrium. Thus neuronal networks utilize homeostatic synaptic plasticity (HSP) to counterbalance these synapse-specific changes. Synaptic scaling, a type of HSP, is characterized by cell-wide modifications of postsynaptic receptor density occuring in response to chronically elevated or depressed neuronal activity. Importantly, during synaptic scaling, changes in postsynaptic receptor density are thought to occur multiplicatively, preserving relative synaptic strengths acquired via synapse-specific plasticity. Mechanisms that regulate synaptic scaling are incompletely understood. However, emerging evidence suggests that synaptic scaling depends on transcriptional and epigenetic regulation. One type of epigenetic mechanism, DNA methylation, has been reliably shown to be important for learning and memory. We hypothesized that synaptic scaling is dependent on DNA methylation. In studies using dissociated cultures of cortical neurons, we have confirmed that synaptic scaling of mEPSCs occurs in a bi-directional, multiplicative manner in response to chronic changes in activity. We then examined molecular changes underlying synaptic scaling and found that chronically changed neuronal activity regulates the expression of enzymes involved in active DNA methylation and de-methylation. Furthermore, the small-molecule, competitive DNA methyltransferase inhibitor, RG108, blocks both the scaling up and down of mEPSCs, demonstrating that bi-directional scaling is dependent upon active DNA methylation. Together, our results suggest a critical role for DNA methylation in homeostatic synaptic scaling.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. David Cleveland Abstract Approved By Advisor: Yes

Co-Authors: Dr. James Kirklin, Dr. Ayesha Bryant, Andrew Watson

Title: Early and late outcomes after surgical correction of anomalous left coronary artery from the pulmonary artery: a 41 year experience

BACKGROUND: Anomalous Left Coronary Artery arising from the Pulmonary Artery (ALCAPA) is a congenital heart defect wherein the left coronary artery does not arise from the aorta. Various surgical repair techniques have been used over the years. The objective of this study was to identify risk factors for early and late morbidity in patients who have undergone surgical repair for ALCAPA.

METHODS: This is a retrospective review of all patients who underwent surgical repair for ALCAPA between 1971-2012 at UAB. Chart reviews and letters/calls to patients were used to obtain follow up data. Patient characteristics, repair technique, operative variables, vital status, and echo data (LV and mitral function) were obtained. Operative repair techniques included: ligation, tunnel, re-implantation, and anastomosis of left subclavian (LSC) to LCA.

RESULTS: Fifty two patients (12 males, median age 6 months) met the inclusion criteria; 18 had an early (intra-operative or 30-day) mortality. On univariate analysis, early mortality was associated with younger age (4 vs. 21 months, p=0.03), lower pre-operative weight (61 vs. 82 kg, p=0.05), and era of operation (p=0.01). On multivariate analysis age and era of operation remained independent predictors of early mortality. Operative mortality was highest for patients that underwent anastomosis of LSC to LCA (3/5 patients, 60%) and tunnel (8/24 patients, 33.3%). Patients alive beyond the 30-day operative period (n=33) had a 15-year Kaplan-Meier survival of 95.5%. Pre- and post-operative LVED size was (4.2 vs. 3.6 cm, p=0.16, respectively).

CONCLUSION: Younger age at time of operation and operations performed during the early era (prior to 1992) were associated with early mortality in patients who underwent repair for ALCAPA. Long term follow up shows a trend of improvement in cardiac function. Amongst patients surviving the initial post-operative period, long term survival rates are excellent.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Valerie Davis Abstract Approved By Advisor: Yes

Co-Authors: Dr. Valerie Davis, Dr. Kathy Monroe

Title: Pediatric Emergency Department Asthma Pathway Effect on Length of Stay

Asthma is one of the most common complaints seen in a Pediatric Emergency Department (ED) and families can often spend hours in the ED while their child receives treatment. In March 2012, the Children's of Alabama ED started a clinical pathway to standardize care that children with asthma receive in the ED. As part of the clinical pathway, children with asthma are immediately assessed by a nurse or respiratory therapist and their treatment initiated without waiting for physician assessment. Additionally, the clinical pathway mandates the use of a pressurized nebulization system (Circulair) which delivers the same medication dose faster than a traditional nebulizer. The effect of this pathway on ED length of stay (LOS) and time to 1st nebulizer treatment is unknown.

We preformed a retrospective chart review to look at LOS and time to first nebulizer treatment for 3 months before and 3 months after pathway implementation. (July 2011/July 2012, October 2011/October 2012, January 2012/January 2013). IRB approval was obtained and a standardized data collection form was utilized. Children age 2-18 seen in the ED with a discharge diagnosis of asthma, asthma exacerbation, or status asthmaticus were included in the study. In total, 745 children met inclusion criteria. Additional information collected included age, sex, inpatient admission, and the number of nebulizer treatments received.

Preliminary analysis shows that with pathway use, the average LOS and average time to 1st nebulizer for all patients improved for 2 of the 3 compared months but it was not a statistically significant change. Subgroup analysis is ongoing. Ideally, the use of an asthma pathway should result in patients receiving treatments quicker and have a shorter LOS. More study is needed to determine the efficiency of this pathway in achieving this goal.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Casey Weaver Abstract Approved By Advisor: Yes

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Title: Transcriptional regulation of Interleukin 10 in autoimmunity

Genome-wide association studies point to the aberrant regulation of genes involved in T cell activation and function as the chief mediator of genetic predisposition to numerous autoimmune disorders, such as Crohn's Disease and Multiple Sclerosis. However, attempts to target such pathways pharmacologically have frequently yielded poor outcomes in patients, suggesting that we have an inadequate understanding of how these transcriptional circuits 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 inflammatory bowel disease (IBD) in the first years of life. Despite the non-redundant function of IL-10 in preventing autoimmunity, an understanding of the complex transcriptional regulation of *Il10* remains in its infancy.

In order to better understand the molecular mechanisms governing gene expression in $CD4^+$ T cells during autoimmune inflammation, we investigated the complexity of *Il10* transcriptional regulation using *in vitro* T cell cultures and *in vivo* models of disease. We identified the transcription factor Growth Factor Independent 1 (Gfi1) as a dominant repressor of *Il10* transcription in multiple lineages of $CD4^+$ T cells. T cells from mice deficient in *Gfi1* produce excess *Il10* mRNA and IL-10 protein upon *in vitro* stimulation, and chromatin immuno-precipitation experiments identified Gfi1 binding sites in several highly conserved regions of *Il10*. Further, *Gfi1*-deficient T cells also contained epigenetic marks indicative of a more active *Il10* locus following stimulation. Finally, we found that mice deficient in *Gfi1* in the T cell compartment are highly resistant to mouse models of IBD and Multiple Sclerosis, and that this reduced disease is dependent upon their increased expression of IL-10. 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.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

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Title: National Characteristics of EMS Care in Frontier and Remote Areas

Objective
While much is known about emergency medical services (EMS) care in urban, suburban and rural settings, only limited data describe EMS care in isolated and sparsely populated frontier regions. We sought to describe the national characteristics of EMS care provided in frontier and remote areas (FAR).

Methods
We performed a cross-sectional analysis of the 2012 National Emergency Medical Services Information System (NEMSIS) data set, encompassing EMS response data from 40 States. We linked the NEMSIS dataset with USDA Economic Research Service-identified FAR areas, defined as a ZIP code >60 minutes driving time to an urban center with >50,000 persons. We excluded intercepts, standbys, interfacility transports, and medical transports. We compared patient demographics, response characteristics (location type, level of care), clinical impressions and on-scene death between EMS responses in FAR and non-FAR areas.

Results
There were 15,005,588 EMS responses, including 983,286 (7.0%) in FAR and 14,025,302 (93.0%) in non-FAR areas. FAR and non-FAR EMS events exhibited similar response (median 5 [IQR 3-10] vs. 5 [3-8] min, $p<0.001$), scene (14 [10-20] vs 14 [10-20] min, $p<0.001$) and transport times (11 [5-24] vs 12 [7-19] min, $p<0.001$). Air medical (1.51% vs 0.42%; OR 4.15 [95% CI: 4.03-4.27]) and Advanced Life Support care (62.4% vs 57.9%; OR 1.25 [1.24-1.26]) were more common in FAR responses. FAR patients were more likely to be of American Indian or Alaska Native race (3.99% vs 0.70%; OR 5.04, 95% CI: 4.97-5.11). Age, ethnicity, location type, and clinical impressions were similar between FAR and Non-FAR responses. On-scene death was more likely in FAR than non-FAR responses (12.2 vs. 9.6 deaths/1,000 responses; OR 1.28, 95% CI: 1.25-1.30).

Conclusions
Approximately 1 in 15 EMS responses in the US occur in FAR areas. FAR EMS responses are more likely to involve air medical or ALS care as well as on-scene death.

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Project Length: Short Prior Research Experience: No

Source of Funding: CaRES Program

Faculty Advisor: Dr. Susan Nozell Abstract Approved By Advisor: Yes

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Title: The Consequences of MicroRNA-31 Deletions in GBM

Glioblastomas (GBMs) are deadly tumors of the central nervous system. Within GBM, there exists a population of cells, glioma stem cells (GSCs), that are capable of self-renewal and tumor propagation. It is postulated that therapies targeting the GSC population may reduce the reoccurrence of GBMs. Most GBM exhibit homozygous deletions of chromosome 9p21.3. Herein, we report the identification of microRNA-31, a novel non-coding tumor suppressor positioned at 9p21.3. In neural precursor cells (NPCs) and gliomas, stem cell factors (SCFs) are abundant and maintain the GSC, and coincidentally miR-31 levels are low or absent. However, when NPCs or glioma cells are differentiated, SCFs are reduced and miR-31 levels are increased. Herein, we report that in undifferentiated cells, SCFs suppress miR-31 expression in order to avoid differentiation. Additionally, upon FBS-induced differentiation, miR-31 levels increase and this reduces the levels of SCFs. These data suggest that miR-31 regulates differentiation, which may explain, in part, how GSCs are maintained in GBMs that lack miR-31. Indeed, GBM growth is reduced upon miR-31 restoration. Collectively, our data suggest that miR-31 may be useful for the treatment of GBM.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Louis Burt Nabors Abstract Approved By Advisor: Yes

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Title: Complementary Therapy and Survival in Glioblastoma Multiforme (GBM)

Introduction: Vitamin and supplement use as complementary and alternative therapy (CAM) is common in GBM patients. However, their association with GBM outcome is not well studied. **Methods:** The analysis was based on 470 patients with primary GBM treated with current standard of care treatment that participated in a clinic-based case-control study. Information on current use of CAM was collected in structured interviews conducted a median of 6 weeks following GBM diagnosis. Proportional hazards regression was used to estimate Hazard Ratios (HR) for GBM-related death according to the use of individual supplements with multivariate adjustment for known prognostic factors including age, Karnofsky Performance Status (KPS), and extent of tumor resection (ESR). **Results:** Use of CAM agents was common with 77% of the cohort reporting CAM usage. Use of multivitamins was reported by more than half of patients CAM (55%). Other frequently reported supplements included Omega 3 fatty acids (DHA and EPA, 15%), Vitamin D (13%), and Vitamin E (5%). No mortality association was observed with the use of multivitamins (HR: 0.96; p = 0.66) or Omega 3 fatty acids (HR: 1.06; p = 0.68). Patients taking Vitamin D as an individual supplement (containing higher dosages than in a multivitamin) had reduced mortality when compared to nonusers (age-adjusted HR: 0.73; p = 0.04). However, the association was diminished after adjustment for KPS and ESR (HR: 0.76; p = 0.20). Vitamin E users had a nonsignificantly higher mortality when compared to nonusers adjusting only for age (HR: 1.54; p = 0.06); the association attained significance (HR: 1.78; p = 0.01) with adjustment for other prognostic factors. **Conclusions:** Use of CAM is common in GBM patients. These exploratory analyses suggest no mortality association with the use of Multivitamins or Omega 3 fatty acids. Associations observed with Vitamin D and E merit further investigation.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Colin Martin Abstract Approved By Advisor: Yes

Co-Authors: Scott Tanner, Taylor Berryhill, Robin G. Lorenz, Colin Martin

Title: Environmental Mediated Intestinal Restitution

Introduction: The intricate process of cell turnover and migration is disturbed in many gastrointestinal diseases including necrotizing enterocolitis (NEC), preventing the tissue from performing essential roles and or self-repair or restitution. The aryl hydrocarbon receptor (AhR) is a basic-helix-loop transcription factor that, when stimulated by exogenous pollutants, microbial products, and dietary components, activates downstream transcription factors that are known to be important for intestinal homeostasis and immunity. The mechanisms responsible for remains unknown.

Hypothesis: AhR signaling plays a central role in enterocyte proliferation and migration after injury.

Methods: C57B/6 wild type (WT) and C57B/6 $AhR^{-/-}$ (KO) were subjected to intestinal injury by exposing them to a lethal dose of radiation (12 g). Mice were harvested 3.5 days later. 12 hours prior to harvest, they were injected with 5-bromo-2'-deoxyuridine (BrdU). Crypt regeneration was determined as the percent of crypts per section with ≥5 BrdU positive cells. Histology was also analyzed to measure tissue injury, villus height, and crypt depth. Results were analyzed by the student's unpaired T-test and expressed as the mean ± standard error of the mean.
Results: KO mice subjected to radiation have a higher percentage of regenerative crypts than WT mice (49.4 ±8.4% vs 17.69 ±10.2%, p=.053). In addition, KO showed a trend of having deeper crypts compared to WT (26.28 ±2.8 μm vs 17.8 ±2.2 μm, p=0.075). There were no differences in villus height and histologic tissue injury.

Conclusion: Preliminary studies suggest that AhR deficient mice have higher rates of regenerative crypts compared to WT mice suggesting that AhR signaling may lead to worse intestinal repair after injury. Further studies are needed to verify these results, as well as clarify the mechanism responsible for these findings. Specifically, we will look at apoptotic markers in the system.

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Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. James Johnston

Abstract Approved By Advisor: Yes

Co-Authors: Daxa M. Patel MD, Emily Shelton, Brandon G. Rocque MD MS, Robert Russell MD, MPH, Jean-Francois Pittet MD, James J. Johnston MD

Title: Predictors of outcome and mortality following traumatic brain injury in children

Introduction: In pediatric traumatic brain injury (TBI), outcomes can often be difficult to predict and many children experience death or disability as a result of this type of injury. In light of this, there is a need for exploration of factors that contribute to mortality and poor outcome in this setting.

Methods: Our group performed a retrospective study in order to determine independent predictors of mortality and poor outcomes in pediatric TBI. Factors that were considered in this study included age, initial Glasgow Coma scale score (GCS), hypoxia upon admission, mechanism of injury, presence of coagulopathy and injury severity score (ISS) among others. The study included 262 children admitted to a tertiary care center for TBI between 2001 and 2010, and assessed outcome based on Glasgow outcome scale score (GOS). GOS ≤ 3 was included as a poor outcome. Marshall and Rotterdam scores were given to patients with available CT scans.

Results: Overall, mortality rate was 14% and 72% of cases were motor vehicle accidents. Average presenting GCS was 9, with injury severity score average of 20. Coagulopathy, anemia, hyperglycemia, hypoalbuminemia, cardiac arrest, seizures, bradycardia, hypotension, diabetes insipidus were present in 30.0%, 16.7, 56.5%, 18.7%, 4.6%, 11.8%, 5.0%, 4.6%, and 4.2% cases, respectively. Preliminary analysis of these data indicates that coagulopathy (INR > 1.2), GCS (threshold of 6), ISS (threshold of 22), and hypoxia on arrival are all independent predictors of mortality and poor outcome.

Conclusion: Coagulopathy, GCS, ISS, and hypoxia on arrival are all independently associated with death and poor outcome in children with TBI. Further investigation of each of these predictors and their management will be a future step in searching for ways to decrease mortality and poor outcomes in pediatric TBI.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Richard Shelton Abstract Approved By Advisor: Yes

Co-Authors: Austin Luker, Dr. Richard Shelton

Title: Pro-inflammatory markers: A link between obesity and depression?

Major depressive disorder (MDD) affects up to 8% of the American population each year and is the biggest reason for Americans collecting disability. While no single cause of MDD has been determined, previous research has noted effects of depression on the body; specifically, the presence of systemic inflammation with elevated cytokines including IL-6, TNF-alpha, and C-reactive protein (CRP), among others, despite lack of systemic disease (which is normally associated with such inflammation) has been noticed. Studies have also shown that depressed patients are more likely to become obese and gain increased intra-abdominal adipose tissue (the presence of which is associated with systemic inflammation). This project sought to compare systemic inflammation markers (particularly IL-6, TNF-alpha, and CRP) in obese versus non-obese depressed patients as well as controls to determine if obesity could be contributing to the inflammation in depressed patients. The obese participants (both controls and depressed) were hypothesized to have more inflammatory factors than non-obese with depressed obese participants being predicted to have the highest levels overall. To determine this, blood samples were collected from both MDD patients and controls, and the serum was extracted. The serum was then assayed for IL-6, TNF-alpha, and IL-2, primarily, though other biomarkers were also assayed for exploratory studies. Obese depressed patients and obese controls have significantly higher levels of CRP than lean depressed and controls. There is higher IL-6 in obese depressed than obese and non-obese controls and lean depressed participants. Ultimately, results obtained from this study could greatly aid in the understanding of the pathology of depression and creating improved treatments.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Christina Muzny Abstract Approved By Advisor: Yes

Co-Authors: Dr. Christina Muzny, Dr. Jane Schwebke, Dr. Erika Austin, Dr. Jeffrey Szychowski

Title: Correlation of Nugent score with vaginal symptomatology among sexual risk behavior groups of women

BACKGROUND:
Bacterial vaginosis (BV) is the most common vaginal infection. BV is most commonly diagnosed in clinical settings using a combination of physical exam and laboratory findings (Amsel criteria). In research settings, BV is more rigorously defined by Gram staining of vaginal fluid to determine the Nugent score. To date, vaginal symptomology and Nugent score have not been correlated.

The objective of this study is to correlate Nugent score with vaginal symptomatology among a cohort of African American women who have sex with women (WSW), women who have sex with women and men (WSWM), and women who have sex with men (WSM). We hypothesize that vaginal symptoms will be more likely to be present in women with very high Nugent scores due to a larger predominance of anaerobic micro-organisms.

The secondary objective of this study was to compare the distribution of Nugent scores among African American WSW and WSWM to an age-matched group of African American WSWM. We hypothesize that there will be significantly greater intermediate and BV Nugent score cases in WSW and WSWM compared to WSM due to differences in behavioral factors such as sexual practices.

METHODS:

Secondary analysis of clinical and laboratory data collected from African American WSW participating in the Women's Sexual Health Project (n=165) at the Jefferson County Department of Health STD Clinic and African American WSM participating in a longitudinal study of vaginal flora at the JCDH STD clinic (n=500).

RESULTS AND CONCLUSION:

Results and conclusion are expected the second week of September and will be sent in to amend this abstract accordingly.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Monika Safford Abstract Approved By Advisor: Yes

Co-Authors:

Title: Attitudes and Beliefs about Diabetes Medications and Illness Acceptance in the Rural Black Belt

The Black Belt Action Committee reported that diabetes mortality was 38.7/100,000 population, contrasted to the US rate of 24.6/100,000 in 2007. Among Alabama's rural African American population, the rate is 50% higher compared to whites. Furthermore, studies show that people living with diabetes in this population report almost two times higher medication non-adherence than the national average. The Chronic Illness Trajectory Model by Corbin and Strauss posits that a feeling of wellness is achieved when there is a balance between 3 central domains: Body, Biography, and Conception of Self (the BBC Chain). Diagnosis of chronic illness, such as diabetes, can profoundly destabilize this BBC Chain, making it difficult for patients to accept their illness and understand the role of medications in living healthy lifestyles long-term. To gain insights into community members' lived experience of diabetes and barriers to acceptance of illness and medication adherence, we conducted focus groups in Alabama's low income Black Belt area. Using modified Grounded Theory, a focus group topic guide was created, eligible participants were recruited through respondent driven sampling, and focus groups were moderated, transcribed, and analyzed using Nvivo 10 software and open coding. Common themes were revealed throughout these focus groups, which will help inform the development of a peer support program that aims to improve diabetes medication adherence and health outcomes using peer storytelling and diabetes education. Major themes included: 1) low knowledge and misperceptions of both diabetes as a disease entity and the efficacy of diabetes medication; 2) disease acceptance and improved medication adherence triggered by a physical exacerbation of the participants' physical diabetes complications; 3) improved medication adherence with the realization that pharmacologics were a vital link to the maintenance of a participants' sense of biography and conception of self by preserving body functions that could not be controlled solely through self-management behaviors (e.g., diet and exercise); and 4) the impact that observing close family and friends who suffered from diabetes had on participant's disease acceptance and improved medication adherence. Further focus groups will be conducted until no new themes emerge and saturation is reached. Education to address diabetes and medication misperceptions as well as focused storytelling addressing these themes will be integrated into the intervention arm of the study.

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Project Length: Short

Prior Research Experience: No

Source of Funding: CaRES Program
Faculty Advisor: John Hartman IV

Abstract Approved By Advisor: Yes

Co-Authors: Sean Santos

Title: Quantitative high throughput cell array phenotyping of Bortezomib in Saccharomyces cerevisiae

We are working on discerning the genes and to what extent those genes interact with Bortezomib. Our methods include quantitative high throughput cell array phenotyping (Q-HTCP), recursive expectation-maximization clustering (REMc), and Gene Ontology (GO) analysis. Q-HTCP is a robotic method to collect growth curve data and is applied to the entire collection of *S. cerevisiae* deletion strains, yielding cell proliferation parameters (CPPs) for measuring gene interaction, which are in turn subjected to REMc followed by hierarchical clustering. The workflow provides automated generation of clusters with heat maps and biological annotation by GO Term Finder (GTF). In this study, we are comparing the gene interaction landscape for Bortezomib targets using a yeast gene deletion strain library that has a background of the double knockout of PDR1 and CYC8. Q-HTCP provided CPPs, which were used to calculate gene interaction values, and the resulting matrix was passed through the clustering workflow. Heat maps revealed distinct patterns for each cluster and GTF reported enrichment in cellular functions shared by genes within each cluster. While the data will continue to be analyzed, Cluster 2-0.0-6 contained genes related to the GO Term proteoasomal ubiquitin-independent protein catabolic process, which contains the *SCL1, PRE1, PRE6, and PRE8* genes. The next step for our study is to further analyze this data by performing a similar experiment with cyclohexamide (a protein synthesis inhibitor) and integrating the cell proliferation parameters (L and K) into REMc with the Bortezomib data followed by GO term analysis.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Michelle Olsen Abstract Approved By Advisor: Yes

Co-Authors: Vishnu Anand Cuddapah, Sinifunanya E Nwaobi, Natasha L Pacheco, Chelsea Thompson

Title: Altered astrocyte function in a mouse model of Rett Syndrome

Background: Rett Syndrome (RTT), a neurodevelopmental disorder affecting girls, is caused by mutations in methyl-CpG-binding protein 2 (MeCP2). RTT is characterized by normal development until 6-18 months of age, when motor and communicative skills regress and hand stereotypies, autonomic symptoms, and seizures present. Several of these deficits were recently reversed in a murine RTT model in which MeCP2 function was selectively restored to astrocytes, the most numerous cell type in the CNS. The mechanism of this phenotypic rescue, however, remains to be elucidated.

Astrocytes serve a critical homeostatic role in the brain by regulating extracellular K^+. This process is mediated by a glial specific potassium channel, Kir4.1. Kir4.1 mediated K+ buffering attenuates neuronal excitability. In the context of disease, astrocytic dysfunction may lead to hyperexcitability and seizures. Given that >80% of patients with RTT experience seizures, we hypothesized that MeCP2 dysfunction in astrocytes may lead to aberrant K^+ homeostasis.

Methods: Western blot and qPCR was performed using cortical tissue obtained from symptomatic MeCP2 deficient mice and WT controls. Whole-cell, voltage clamp recording from cortical astrocytes was performed to examine Kir4.1 mediated currents and K^+- sensitive microelectrode was performed to examine K^+ dynamics in WT and MeCP2 deficient mice. Finally, to determine if the loss of Kir4.1 in astrocytes altered neuronal excitability and network properties, we performed neuronal whole cell electrophysiology and voltage dye recording.

Results: Astrocytes from RTT mice demonstrate significant reductions in Kir4.1 mRNA and protein relative to controls. RTT mice exhibit >50% deficiency in Ba2+ - sensitive Kir4.1-mediated currents and elevated extracellular K+. Neurons from the cortex of MeCP2 deficient mice are hyperexcitable which is due in part to loss of Kir4.1 in astrocytes.

Conclusions**:** MeCP2-mediated astrocytic dysfunction, specifically in the form of aberrant Kir4.1 expression and activity, may play a role in seizure genesis in RTT.

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: James George Abstract Approved By Advisor: Yes

Co-Authors: Kayla D. Isbell, Manisha Kukreja, James F. George, James K. Kirklin, David C. Cleveland

Title: A Forty-three Year Experience with Surgical Correction of Transposition of the Great Arteries with Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction

Purpose: The Rastelli procedure was first performed in 1968 to correct dextro-transposition of the greater arteries (d-TGA), ventricular septal defect (VSD), and left ventricular outflow tract obstruction (LVOTO). Blood is directed from the LV to the aorta through the existing VSD and from the RV to the pulmonary artery via an extra-cardiac conduit. Alternative procedures exist, including the Nikaidoh and *reparation a l'etage ventriculaire*; however, which is best is still debated. Results will be compared to those following other methods of repair, in hopes of better informing future patient care.

Methods: All patients at UAB who underwent the Rastelli operation between 1969 and 2011 were identified and their charts obtained (n=87). Non-US residents (n=9) were excluded. Charts were reviewed for mortality and morbidity post-Rastelli. Attempts were made to contact all surviving patients via telephone to ascertain health status. Subjects were divided into 3 eras (Historical: 1969-1980, Middle: 1980-1990, and Modern: 1990-present).

Results: Actuarial survival for the entire cohort at 5, 10, 15, 20 and 30 years was 67%, 64%, 61%, 53% and 36% respectively. All cause mortality for the historical, middle, and modern eras were 68.3%, 50.0%, and 18.6% respectively. Kaplan-Meier analysis showed increased overall survival for each successive era (p=0.03). Hazard modeling showed an early constant phase with a slight rise in hazard for mortality after 15 years. Among survivors, freedom from arrhythmia at 1,5, 10, 20 and 25 years was 95%, 95%, 88%, 82%, and 54%, respectively. Freedom from reoperation for conduit replacement at 1, 5, 10, and 20 years was 100%, 88%, 52%, and 28% respectively.

Conclusion: Further investigation into cause of death is warranted to better elucidate factors contributing to late decrease in survival. These outcomes following Rastelli procedure should serve as a basis for comparison with alternative corrective procedures for d-TGA, VSD, and LVOTO.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Alexander Lo Abstract Approved By Advisor: Yes

Co-Authors: Alexander Lo, Tammie Quest, Marie Bakitas, M. Robertson Pearce, Vera A. Bittner, Cynthia J. Brown

Title: Emergency Department-Based Palliative Care Needs Assessment of Adults with Heart Failure

Heart failure (HF) is a common and costly public health problem with approximately 6 million cases, 1 million hospitalizations and over $50 billion in total costs annually. Nearly one million HF patients seek care in the Emergency Department (ED) each year, with 80% hospitalized and 25% readmitted within 30 days. Studies report that the majority of HF readmissions may be preventable. Given the national healthcare priority of reducing HF readmission under the Affordable Care Act, it is critical to identify those underlying causes of readmission that may be amenable to intervention. We sought to investigate the impact of symptom burden and mobility on healthcare utilization among adults with HF. We hypothesize that individuals with greater HF symptom burden and more unmet care needs return to the ED or are readmitted to the hospital more frequently. During this pilot feasibility study, we approached any ED patients 50 years or older with a documented history of HF and sought to enroll them in the study, which consisted of a brief survey that measured clinical data (medical history and diagnostic tests), mobility as measured by Life-Space, and symptom burden using a validated ED-based palliative care screening questionnaire. Participants also agreed to be contacted 30 days after the index ED visit to determine if they had been re-hospitalized or returned to an ED after the index visit. We divided each week into 21 time slots (day/evening/night over the 7 days), and targeted 3 participants in each of the 21 slots, thus accounting for temporal variations in health care utilization. We do not as of yet have our results, but we hope that the data will show that HF patients who report unmet care needs, poor mobility, or higher symptom burden are associated with increased ED return visits or hospital readmissions.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Cunningham Fellowship

Faculty Advisor: Dr. Ambika Ashraf Abstract Approved By Advisor: Yes

Co-Authors: Pelham JH, Hanks LJ, Ashraf AP

Title: Analysis of Dyslipidemia in Children with Type 2 Diabetes Mellitus

Background: Patients with Type 2 Diabetes Mellitus (T2DM) are at high risk for cardiovascular disease (CVD) and CV mortality. T2DM dyslipidemia is complicated by hypertriglyceridemia and elevated LDL. Thus, debate still exists whether LDL or non-HDL is the correct lipid measure to identify CV risk. Few studies of dyslipidemia in pediatric patients with T2DM exist. 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 lipid profiles. We also evaluated whether LDL was comparable to Non-HDL as a risk factor in children with T2DM.

Methods: A retrospective electronic chart review of patients with T2DM (169 subjects with regular lipid profile, 45 with vertical autoprofile at initial visit). A total of 214 subjects (31% male) were included, 77% African American (AA) and 23% European American (EA).

Results: AA subjects had numerically though non-significantly higher hemoglobin A1C (HbA1C), total cholesterol, LDL, HDL 2 and 3, and lower VLDL3. EA were younger and weighed less than AA, had lower HDL, and had higher HDL:TC. Females had a numerically but non-significantly higher LDL, apoB, HDL 2 and 3. Males were older than females, weighed more, were taller, and had marginally higher HbA1C, and lower HDL. BMI was not associated with any of the liprotein measures, after controlling for age and sex. Patients with an HbA1C >7% had a higher TC, LDL, apoB, non-HDL, and VLDL.

When LDL was >130 mg/dl, non-HDL was >160 mg/dl in 96% of the participants. **Conclusions:** HbA1C is the main determinant of adverse lipid profiles in children with T2DM, indicating the need for stricter glycemic control in CV risk reduction. BMI was not a determinant of adverse lipid profiles in our group. For children with T2DM, an LDL based treatment cutoff is sufficient for assessing dyslipidemia.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Adam R Wende Abstract Approved By Advisor: Yes

Co-Authors:

Title: A Systems Biology Approach to Understanding the Metabolic Origin of Diabetic Cardiomyopathy

Objective: Diabetic cardiomyopathy is described as diabetes-induced changes in the myocardium independent of other confounding factors, such as hypertension. Diabetes is associated with both hyperglycemia and hyperlipidemia. One change that occurs in the heart with diabetes is a derangement in cardiac mitochondrial substrate utilization. A number of earlier studies have focused on the loss of flexibility within the heart to switch between glucose and fatty acids. Part of this dysfunction is thought to occur by a transcriptional reprogramming. Recently studies have found changes in DNA methylation in diabetes associated with altered gene expression. This project seeks to identify new metabolic genes and to determine if there is a specific substrate dependence of this gene regulation. To begin to dissect the contribution of glucose in disease progression we have employed a transgenic model of glucose transporter 4 (GLUT4) expression and insulin dependent Type 1 Diabetes. Using bioinformatics to compare transcriptomics and DNA methylation from hearts of these animals we have identified a number of novel hyperglycemia-regulated genes. These targets have pointed to new pathways that will aid in understanding the mechanism of this disease. One of these novel targets, 4-aminobutyrate aminotransferase (Abat), is described here.**Methods:** Microarray, RNA-sequencing, and bisulfite DNA-sequencing were performed to determine gene expression and DNA methylation changes in the left ventricles of hearts form streptozotocin-induced diabetic and cardioc-specific inducible GLUT4 overexpression mouse models. Targets that were had significant changes in all three platforms were subjected to additional analysis. Specifically, qRT-PCR was used to confirm changes in gene expression and western blotting was performed to determine changes in gene product protein levels.**Results:** RNA sequencing analysis revealed a number of gene transcripts, including 4-aminobutyrate aminotransferase (Abat), are significantly overexpressed or underexpressed in diabetes and the myc-GLUT4 overexpression mouse models. To cross-validate these highly sensitive -yet notoriously nonspecific- findings in RNA sequencing, microarray analysis was performed to generate a list of transcriptionally regulated genes with higher specificity. As a result, Abat mRNA levels were shown in both modalities to display a significant decrease in STZ-induced diabetic mice and myc-GLUT4 overexpressing mice. Follow-up with qPCR provided “gold-standard” support that both transcript variants of Abat are significantly decreased. Finally, Western blotting analysis showed that the changes in RNA transcript levels confer a drastic decrease in ABAT protein levels. To begin the process of understanding why Abat expression is decreased, methylation status was assessed at highly conserved regions of the Abat promoter. These sites, several of which are differentially methylated, suggest that the decrease in Abat expression are the result of DNA methylation.
Conclusions/Broader Impacts: These data identify the repression of Abat in the left ventricle of diabetic mice and suggest a glucose-mediated mechanism via altered DNA methylation. ABAT has recently connected the anaplurotic reaction of the TCA cycle and oxidative phosphorylation in neurons, though it has never been studied in the heart. ABAT metabolizes gamma-aminobutyrate (GABA) into succinate semialdehyde. in the cell. These findings support an intriguing hypothesis, wherein GABA-mediated changes in cardiac performance may contribute to the decreased contractile performance of diabetic hearts.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Henry E. Wang, MD, MS and David G. Warnock, MD Abstract Approved By Advisor: Yes

Co-Authors: John P. Donnelly, MSPH, Henry E. Wang, MD, MS, David G. Warnock, MD

Title: Characteristics of Patients with Acute Kidney Injury (AKI): Resolving Community-Acquired AKI (CA-AKI) compared to Hospital-Acquired AKI (HA-AKI)

Introduction: AKI is associated with poor outcomes. AKI present upon hospitalization is not well characterized. We compared persons whose serum creatinine (sCr) improved after admission to those who developed AKI during hospitalization.

Methods: We analyzed 2011-2012 University of Alabama at Birmingham Hospital (UAB) discharge and sCr data for inpatients with ≥3 sCr measurements. We excluded patients with age <18 years, end-stage renal disease or kidney transplant. We defined CA-AKI as sCr decrease ≥0.3mg/dl from first inpatient sCr. We defined HA-AKI as sCr increase ≥0.3mg/dl from the lowest of the first three sCr or inpatient dialysis. We analyzed the first 22 days of hospitalization or 60 sCr. We analyzed patient characteristics, AKI incidence, and inpatient mortality for CA-AKI compared to HA-AKI and No-AKI.

Results: Analysis included 35,693 admission events. Individuals with CA-AKI (10,607) and HA-AKI (8,347) compared to those with No-AKI (16,739) were older (58 and 59** vs 55*), had longer length of stay (6 and 7** days vs 4 days*), higher baseline sCr (1.8 and 1.6** vs 0.9*), higher peak sCr (1.9 mg/dl and 2.3** vs 1.0 mg/dl*), were more likely to be male (58% and 52%** vs 50%*), be Black (37% and 40%** vs 32%*), and spend time in an Intensive Care Unit (37% and 43%** vs 18%*). Inpatient mortality was greater for CA-AKI compared to No-AKI (4.3% vs 1.1%*), but less than HA-AKI (4.3% vs 10.8%**). CKD was more common with CA-AKI compared to HA-AKI (62% vs 47%**), as well as to No-AKI (62% vs 15%*). (*P<0.01 for CA-AKI and HA-AKI vs No-AKI; **P<0.001 for CA-AKI vs HA-AKI)

Conclusions: CA-AKI and HA-AKI are associated with increased length of stay, ICU admission, and mortality. CA-AKI has different demographics and reduced mortality than HA-AKI. CKD appears to be a greater risk factor for CA-AKI.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Sara Cooper, Richard Myers Abstract Approved By Advisor: Yes

Co-Authors: Sara Cooper, Richard Myers, Marie Kirby, Karin Bosma

Title: Metabolomic Analysis of Serum and Urine from Pancreatic Ductal Adenocarcinoma Patients

Pancreatic ductal adenocarcinoma (PDAC) ranks 4th in U.S. cancer mortality and has a dismal 6% five year survival rate. Surgical resection remains the best treatment, yet less than 20% of patients are eligible for surgery upon diagnosis. New drug development and mechanisms for earlier detection are required to improve these outcomes as PDAC tumorigenesis begins an average of 17 years prior to diagnosis. Recent studies have identified metabolite profiles unique to primary tumor and serum of PDAC patients using a non-targeted metabolomic approach. We have conducted a pilot study to determine if similar metabolite profiles can be identified in both urine and serum. To improve upon the clinical utility of previous analyses, we compared samples from PDAC patients (n=45) across a wide range of tumor stage and progression to both healthy controls (n=18) and chronic pancreatitis (CP) patients (n=47). As expected, two-dimensional gas-chromatography with mass spectrometry revealed that metabolite patterns of CP and PDAC patients were more closely related than normal controls. Nonetheless, our analysis did identify significantly altered levels of a small subset of metabolites in the serum and urine of PDAC patients compared to both control groups. When compared to healthy controls, PDAC patient serum and urine contained significantly lower levels of several fatty acids. Furthermore, fatty acid and branched chain amino acid levels seemed to be more drastically altered in a subset of PDAC urine and serum from patients with biopsy confirmed lymphovascular invasion. Significant findings from our metabolomic analysis also seem to agree with concurrent transcriptomic analysis of normal and primary cancer tissue from PDAC patient biopsies (n=26). Our preliminary findings indicate that work is still needed to find suitable biomarkers for early PDAC diagnosis; however, our minimally invasive, metabolomics based approach has demonstrated promise in uncovering the complex metabolic landscape of PDAC.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Bradford Woodworth Abstract Approved By Advisor: Yes

Co-Authors: Jessica Grayson, Shaoyan Zhang, Dan Skinner, James Fortenberry, Eric Sorscher, Bradford Woodworth

Title: In Vitro and In Vivo Models of Acute Inflammation Demonstrate Acquired Defects in Transepithelial Cl- Transport

Introduction: Decreased mucociliary clearance is a major contributing feature to chronic rhinosinusitis (CRS). The objectives of the present study were to test models of acute inflammation for acquired defects in transepithelial Cl^- secretion.

Methods: Primary murine nasal septal epithelial (MNSE) cultures were exposed to lipopolysaccharide (LPS) or an ultrafiltrate of PAO1 *Pseudomonas aeruginosa* (bacteria-free preparation from 20 hour log-phase growth). Basal media was collected from airway cell monolayers and analyzed for murine CXCL1/KC (human IL-8 analogue) by ELISA to confirm activation of NFKB mediated inflammatory signaling. Cultures were mounted in Ussing chambers for ion transport measurements.

Results: MNSE cultures incubated with PAO1 filtrate or LPS (100 nM) for 24 hours produced significantly elevated CXCL1/KC (PAO1, 1267.4+/-54.3 pg/ml and LPS, 1774+/-159.4 pg/ml) when compared to controls (660+/-139.5 pg/ml) ($p<0.05$). CFTR-mediated Cl^- transport [change in short-circuit current, ΔI_{SC} ($\mu A/cm^2$)] measured using forskolin (20 □□) was significantly decreased compared to controls (PAO1, 9.7+/-0.5; LPS, 9.6+/-1.6; control, 13.8+/-0.9, $p<0.05$). Quantitative PCR (reported as relative mRNA levels+/-S.D.) showed significant inhibition of CFTR mRNA expression when cultures were incubated with PAO1 (0.76+/-0.03) and LPS (0.69+/-0.19) when compared to controls (1+/-0.19) ($p < 0.05$).

Conclusions: Exposure to LPS or PAO1 extract in primary airway epithelial cells led to acquired defects in transepithelial Cl^- transport. These findings indicate that acute inflammation or infection in sinonasal epithelia may create acquired defects in CFTR, reduce MCC, and create a localized cystic fibrosis environment.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Omer Lee Burnett, III Abstract Approved By Advisor: Yes

Co-Authors: Andrew M. McDonald, Craig J. Baden, Rojymon Jacob, Omer L. Burnett III

Title: Factors associated with increased incidence of toxicities following administration of yttrium-90 resin microspheres.

Purpose

To further define variables associated with increased incidences of hepatic, constitutional, gastrointestinal, and lung toxicities following administration of yttrium-90 (90Y) microspheres in a sequential cohort of heterogeneous patients.

Materials and Methods

Sixty-five patients undergoing 86 treatments were assessed for toxicity incidence following 90Y administration. Post-treatment clinical and liver function test (LFT) toxicities were assessed using the Common Terminology Criteria for Adverse Events version 4.03 (CTCAE v4.03). Univariate analysis of variance was used to evaluate the effect of variables on toxicity incidence. A multivariate linear regression model was performed using all variables with a $p < 0.10$ on univariate analysis for each toxicity.

Results

Hepatic toxicities, including LFT toxicities, were present following 48.8% of treatments, while gastrointestinal and constitutional toxicities were present following 51.8% and 54.7% of treatments, respectively. Lung toxicities were present following only 5.9% of treatments. Multivariate analysis revealed that hepatocellular carcinoma (HCC); increased pre-treatment alanine aminotransferase, international normalized ratio, and alkaline phosphatase; increased pre-treatment white blood cells; and decreased Karnofsky Performance Status were statistically significant ($p < 0.05$) important predictors for increased toxicities.

Conclusions

In order to avoid toxicities and improve quality of life following 90Y treatment, more attention should be given to patients with increased pre-treatment LFTs and HCC. Patients may also experience better post-treatment quality of life if 90Y is administered earlier in the disease course before functional status declines too much.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Harald Sontheimer Abstract Approved By Advisor: Yes

Co-Authors: SM Robert, SL Campbell, SC Buckingham, S Robel, KT Holt, T Ogunrinu-Babarinde, P Province Warren, DM White, MA Reid3, JM Eschbacher, ME Berens, AC Lahti, LB Nabors, H Sontheimer

Title: Gliomas upset the excitatory/inhibitory balance in the brain, creating tumor-associated excitotoxicity and seizures

Seizures are a common symptom of brain tumors. In the non-pathological brain, there exists a delicate balance between excitatory glutamate and inhibitory GABA signaling, and this balance is disrupted during seizures. In glioma research, past studies have identified an important role of the cystine/glutamate exchanger, System x_c^- (SXC), in glioma biology and tumor-associated seizures (TAS). Using tissue micro-array samples of matched glioma and uninvolved brain from 45 patients, we found heterogeneous SXC expression, which we then modeled using a mouse-propagated patient-derived xenoline model of glioma (PDXg). We found that SXC-mediated glutamate release created neuronal excitotoxicity, measured as large increases in neuronal $[Ca^{2+}]_i$, peritumoral neuronal death, and shortened survival in SXC-expressing, glioma-implanted mice. Interestingly, we also found that GABAergic inhibition was altered in the peritumoral brain of mice implanted with both SXC-expressing and non-SXC-expressing gliomas. In the mature, non-pathological brain, GABA receptor activation causes a hyperpolarizing inflow of Cl^-. This effect occurs due to the action of KCC2, which keeps $[Cl^-]_i$ low. We have found that in the peritumoral brain, however, KCC2 expression is decreased, and intracellular $[Cl^-]$ is increased. Therefore, when GABA binds peritumoral neuronal receptors, Cl^- leaves, depolarizing the cell and creating excitatory signaling. These findings suggest that regardless of SXC-expression, gliomas alter inhibition, but only those with SXC-mediated glutamate release initiate seizures. We then used Magnetic Resonance Spectroscopy (MRS) to measure peritumoral glutamate in patients with biopsy-determined SXC-expression. Following administration of the SXC-inhibitor Sulfasalazine, peritumoral glutamate levels were reduced in patients with SXC-expressing gliomas, suggesting that SXC is responsible for glutamate release underling tumor-associated seizures. These findings suggest SXC-expressing gliomas comprise an excitotoxic glioma subtype, with a poorer prognosis and increased incidence of TAS. Defining subpopulations of gliomas is an important first step for a personalized medicine approach to treatment of these devastating tumors and their side effects.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Dr. Amos Bailey

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Living with Life-Limiting Illness: Exploration of the Life of the Terminally-ill through Narrative Medical Blogging in Tamil Nadu, India

BACKGROUND: Understanding the grieving process of different world regions allows medical specialists to better care for patients of all backgrounds. Comparing and contrasting the way people grieve in various populations elucidates whether grief relating to death and dying is the same, regardless of any society. This medical-humanities based research intends to contribute two key aspects to the field of medicine: (1) to explore the grief of fifteen patients facing the end-of-life while analyzing what factors into their coping mechanisms. (2) To understand and assess the therapeutic efficacy of interviewing and communicating with patients. METHODS: Q&A sessions with fifteen different oncology patients will be conducted to also assess a vital component of the medical field: whether communication itself is a form of therapy which may help medical professionals better provide care for suffering patients. Study design includes an online web-blog relaying each patients' interview anonymously and a post-interview survey to qualitatively assess whether each interviewee may have benefited from communication therapy. RESULTS/CONCLUSIONS: After two months of extensive patient interviews and four months of survey data collection/blog posts, conclusions drawn from this research demonstrate that certain aspects of grieving appear to be consistently prevalent across cultures. All patients of various backgrounds (when comparing with other grief literature) generally worry about the following: monetary aid for treatments, family support, life after death, and questionings of religion. In addition, post-interview surveys of each patient in this study elucidated that overall, communication therapy (ex: conversing with medical specialists for at least thirty minutes daily) has proven beneficial to their overall mood. Thirteen out of fifteen patients answered that they felt better relieved and more satisfied with their health conditions post-interviews because they were able to speak about their medical experiences and address feelings concerning death and dying.

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Project Length: Short Prior Research Experience: No

Source of Funding:

Faculty Advisor: Jennifer F. De Los Santos Abstract Approved By Advisor: Yes

Co-Authors: Robert M. Conry

Title: Neoadjuvant Vemurafenib Followed by Aggressive Local Therapy for Surgically Unresectable Stage III Melanoma

Background*:* The use of BRAF inhibitors (BRAFi) in patients with BRAF mutated melanoma has resulted in significant improvements in overall response rates (ORR), and median durations of response as compared with dacarbazine chemotherapy, and has the potential to downstage unresectable primaries to disease amenable to local therapyThis retrospective study reviews our experience treating patients with surgically incurable stage III melanoma treated with neoadjuvant BRAF inhibition and radiation.

Methods and Materials*:* Forty-four patients with BRAF mutated melanoma treated with BRAFi and radiation therapy at UAB between January 2010 and February 2014 were identified. Of these, 6 patients had surgically incurable stage III disease. Patient, tumor, and treatment factors were abstracted from the charts. We compared progression free survival and recurrence patterns in this group to published data from phase III randomized clinical trials of vemurafenib alone for similar stage melanoma.

Results*:* Six patients received neoadjuvant vemurafenib for a median treatment duration of 5.83 months (range 3.5-8.3 months). Two patients had complete radiographic response following 3 months of Vemurafenib, with the remaining four achieving a radiographic partial response by RECIST criteria. Two patients underwent surgical resection of regional disease following vemurafenib, one with complete pathologic response. All patients received radiation therapy following BRAFi, with an average dose of 57.43 Gy (range 36-66.6 Gy). 4 patients obtained complete response and remain disease free at primary site at a median follow up of 21.7 months (range 3.67-31.37 months). 4 patients remain free of distant disease at last follow up. Mean progression free survival following treatment was 20.9 months (range 9.1-36.97 months).

Conclusions*:* Patients with stage III surgically unresectable BRAF mutated melanoma treated with neoadjuvant BRAFi and aggressive local therapy achieved mean progression free survival of 20.9 months with the median PFS not yet reached. Radiation therapy +/- surgery provided excellent local control, as the only recurrence occurred distant from the treatment field. Compared to the common practice of indefinite BRAFi until progression, use of BRAFi neoadjuvantly followed by aggressive local therapy allowed patients to enjoy a prolonged interval off treatment. Further studies are warranted to confirm the benefit of short-term neoadjuvant BRAFi in treating surgically unresectable stage III melanoma.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Peter Mannon Abstract Approved By Advisor: Yes

Co-Authors: Jaskirat Sethi, Peter Mannon

Title: Identifying Cell Source of IL-13 Production in Ulcerative Colitis

Ulcerative Colitis is a chronic, relapsing, idiopathic inflammation of the colonic mucosa. Recent studies have associated this inflammation with the excess production of IL-13 in both mouse models of colitis and in human disease with production coming from natural killer T cells. A novel cell subset, the innate lymphoid cell type 2 (ILC2), was described as a source of IL-13 in response to epithelial cell-derived cytokines. We hypothesized that the ILC2 cell might play a role in pathologic IL-13 production in UC.

We tested for the contribution to IL-13 production in UC by ILC2 cells, seeing whether they were present in the blood and in lamina propria mononuclear cells of the colon. Peripheral blood mononuclear cells (PBMCs) and LPMCs were incubated with polyclonal T-cell stimuli (anti-CD2 + anti-CD28) and ILC2 stimuli (IL-25 (10 ng/mL), IL-33 (10 ng/mL, TSLP (50 ng/mL)) for 24 hours. Supernatants were assayed for IL-13 cytokine production using an ELISA.

The average production of IL-13 in PBMC and LMPC samples with active UC and TSLP stimulation was 3.66 and 6.74 pg/mL, respectively. One patient had IL-13 production with the lamina propria mononuclear cell sample, while the other patient had IL-13 production with the peripheral blood mononuclear cell sample. In addition, there was IL-13 production in PBMC samples with UC in remission following exposure to IL-25 and IL-33 stimulation. Average production of IL-13 using IL-25 and IL-33 stimulation was 5.99 and 7.03 picograms, respectively. There was no IL-13 production using cells isolated from Crohn's patients.

These data suggest that there may be an association with active UC and IL-13 production with TSLP stimulation as well as remission UC an IL-25 and IL-33 stimulated IL-13 production. Furthermore these data suggest that further work should be done to confirm ILC2 cells as an alternative source of IL-13 in UC pathogenesis

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Dr. Martin Young Abstract Approved By Advisor: Yes

Co-Authors: Dr. Kirk Habegger and Dr. Martin Young

Title: Targeted Disruption of the Skeletal Myocyte Circadian Clock Markedly Impacts Skeletal Muscle Insulin Sensitivity and Metabolism

Background: Molecular, cellular, and animal based studies have recently exposed circadian clocks as critical regulators of energy balance. Invariably, mouse models of ubiquitous genetically manipulated circadian clock components display alterations in cardiometabolic parameters, including lipid/fatty acid metabolism and adiposity, as well as both insulin secretion and responsiveness. However, relatively little is known regarding the relative roles of cell autonomous circadian clocks in distinct metabolically active peripheral tissues *in vivo*. .

Hypothesis: The skeletal myocyte circadian clock directly regulates skeletal muscle metabolism and insulin sensitivity.

Methods: In order to test this hypothesis, we generated a novel mouse model wherein the circadian clock was genetically disrupted specifically in skeletal myocytes, through muscle creatine kinase promoter driven expression of a dominant negative Clock mutant protein (termed SMCM mice).Soleus muscles were isolated from 16 week old wild-type (WT) and SMCM littermate mice for ex vivo assessment of glucose and fatty acid (oleate) metabolism, under basal and insulin-stimulated conditions. A sub-maximal insulin concentration (100uU/ml) was utilized to facilitate investigation of insulin sensitivity, as opposed to maximal insulin responsiveness.

Results: No significant differences were observed in the weight of soleus muscles isolated from WT versus SMCM mice. Under basal conditions (i.e., in the absence of insulin), lactate release was lower in soleus muscles muscles from SMC versus WT mice. In contrast, no genotype specific differences were observed for glucose or oleate oxidation under basal conditions. Somewhat surprisingly, insulin stimulated lactate release and glucose oxidation, as well as repressed oleate oxidation, to a greater extent in soleus muscles isolated from SMCM versus WT mice.

Conclusions: These data suggest that the skeletal myocyte circadian clock is a novel modulator of insulin–mediated regulation of metabolism. Future studies are required to determine the mechanisms by which skeletal myocyte circadian clock influences insulin signaling.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Dr. Tiffany Carson Abstract Approved By Advisor: Yes

Co-Authors: Helen Kidane, Dr. Tiffany Carson

Title: Examining the relationship between socioeconomic status (SES), stress, and dietary intake of women in the Deep South

Low SES has been associated with increased risk for chronic disease and cancer, poorer health outcomes, and less overall wellness. Data from previous studies support the inverse relationship between SES and energy-dense, nutrient-poor diets. Lower SES is also linked to higher levels of stress hormones and stress-related health problems. Additionally, stress levels have been associated with snacking, as well as over- and under-eating suggesting a complex interplay between SES, stress, and dietary intake. The purpose of this study was to evaluate these relationships among a sample of racially diverse non-obese and obese women. We hypothesized that lower SES would be associated with poorer dietary habits and higher stress levels overall. We also hypothesized that the association between SES, stress, and diet would differ by racial group. Black (n=58) and white (n=46) women who were community volunteers provided the following data: demographics (race, age, household income, education, and marital status); anthropometrics (height, weight, and waist circumference; body mass index (BMI) was calculated from measured height and weight); psychological measures of stress using validated surveys; and dietary intake via interviewer-administered 24-hour dietary recall using the National Cancer Institute's ASA24. Mean age and BMI of participants were 39.6 years and 31.0 kg/m^2, respectively. Additional analyses are currently ongoing to measure the independent effects of individual SES proxy variables (e.g., income, education) and stress level on dietary patterns. Additionally, we will test for effects of SES-by-stress interactions on dietary patterns. If our hypothesis is supported, we expect to find that women with lower SES will have poorer diets with more refined grains, added sugars, and added fats. Those who report higher stress levels will have a higher proportion of snacks. The findings of this study will inform future research regarding the development interventions for stress and dietary management in low socioeconomic groups.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Casey Weaver Abstract Approved By Advisor: Yes

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

Title: Rorgt Positive Innate Lymphoid Cells are Important for Neonatal Intestinal Barrier Development

Neonatal Late-Onset Sepsis (NLOS) is a clinical syndrome seen primarily in preterm infants characterized by non-specific sequelae from underlying bacteremia and systemic infection. Between 20-30% of all Very Low Birth Weight (VLBW) infants are affected. While Gram-positive infections are often treatable with antibiotics, Gram-negative and fungal species still causes septic shock in 45% of patients with mortality rates reaching 20-74% and 32-50% respectively. The Gram-negative organisms cultured from patient blood suggest translocation across an immature intestinal barrier as the major mechanism of pathogenesis in Gram-negative NLOS. However, little is known about the immunologic events that govern normal development of the intestinal barrier following birth. We hypothesize that

Here we characterize a novel model of Gram-negative NLOS in the newborn mouse using *Klebsiella pneumoniae*. While adults are colonization resistant prior to weaning, newborns show age dependent susceptibility to bacterial translocation and subsequent induction of sepsis. Interestingly, we find no evidence of overt intestinal inflammation, or reduced weight gain during *Klebsiella* colonization prior to sepsis suggesting that our model recapitulates many important features of the human disease. Using luminex-based cytokine array assays and pharmacologic inhibition studies, we also identify *Rorgt* positive Innate Lymphoid Cells (ILC3s) as the most likely cell type involved in preventing bacterial translocation in early life. These results not only establish a novel model for studying a devastating disease of infancy, but shed light on how the mammalian intestines stave off opportunistic pathogens during the period of initial postnatal colonization.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Foundation for Anesthesia Education and Research

Faculty Advisor: Dr Nina Kraguljac/Dr Michael Froelich Abstract Approved By Advisor: Yes

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Title: Subanesthetic Ketamine as Model for Psychosis - A Preliminary Analysis

Background: Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist which is used for starting and maintaining general anesthesia. At lower doses, NMDA receptor antagonists are also shown to produce a broad range of symptoms, behaviors, and cognitive deficits that resemble aspects of endogenous psychoses, particularly schizophrenia. Schizophrenia is a chronic mental illness, characterized by three complexes of clinical features. Positive symptoms present as hallucinations, delusions and disorganized thoughts or behaviors. Negative symptoms include lack of motivation, social withdrawal, diminished expression of emotions, and poverty of thinking and speech. Impaired cognition includes problems with attention and memory. In prior work, we have found evidence that at least some of the pathology and symptomatology of schizophrenia may result from a dysfunction of the glutamatergic system which can be modelled by use of NMDA receptor antagonists. We will use ketamine as a model for schizophrenia to examine the relationship between two symptom domains of schizophrenia, positive symptoms and cognitive deficits.

Methods: We will recruit 25 healthy subjects of any ethnicity aged 19-40 with no prior psychiatric history and no current medical condition. Subjects will perform a Continuous Performance Task (CPT) task, a neuropsychological test that measures a person's sustained and selective attention, before and during ketamine administration. Ketamine will be administered by a bolus (0.27mg/kg) over ten minutes then followed by a continuous infusion of 0.25 mg/kg/hr for sixty minutes. Positive symptom severity will be assessed by the Brief Psychiatric Rating Scale.

Results: We will present results of a preliminary analysis of subjects enrolled in this study and examine the relationship between CPT scores and BPRS positive symptom subscale scores. We expect to find that attention deficits are independent of psychosis severity, as cognitive deficits are independent of positive symptom severity in schizophrenia.

Conclusion: The results will help clarify if the relationship between symptom domains induced by ketamine resemble those of schizophrenia.

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Project Length: Short Prior Research Experience: Yes
Source of Funding: MSTP NIH Training Grant T32GM008361-23

Faculty Advisor: Daniel A. Gorelick Abstract Approved By Advisor:

Co-Authors: Daniel A. Gorelick

Title: Creating an inducible CRISPR-Cas9 system for spatiotemporal genome editing

CRISPR-Cas9 technology can create targeted DNA mutations in diverse organisms. A short guide RNA (gRNA) hybridizes to a complementary DNA sequence and recruits the Cas9 nuclease, which induces a double-stranded break (DSB) in the target DNA. Nonspecific repair of the DSB causes the insertion or deletion of nucleotides that modifies protein synthesis or function. However, existing Cas9 systems lack temporal and spatial control, valuable attributes for modeling human diseases that affect a subset of cells within a particular cell type. We sought to achieve spatiotemporal control by generating an inducible Cas9 system. Cas9 protein contains several discrete domains, including a recognition domain that binds gRNA and a nuclease domain that cuts DNA. Thus, Cas9 may be split into two discrete molecules with the ability to selectively interact. If the split proteins lack constitutive nuclease activity, then they may be fused to conditionally interactive domains, such as light- or ligand-inducible domains, that selectively restore Cas9 activity.We tested this strategy by injecting zebrafish embryos with either Cas9 recognition or nuclease domains together with gRNA targeting an exon within the *cyp19a1b* gene. We observed targeted mutations in < 5% of embryos, compared to 90% of embryos injected with full length Cas9. This suggests that the efficacy of the individual split Cas9 proteins is significantly lower than full length Cas9. Next, we injected embryos with both pieces of split Cas9 together with gRNAs targeting four different genes. 12% of embryos had mutations in *cyp19a1b*, yet no embryos had mutations in the other targets (*esr2a*, *esr2b*, *pr*). This suggests that split Cas9 activity varies depending on the gRNA and that split Cas9 displays lower activity compared to full length Cas9 at multiple genetic loci. Future work will determine whether split Cas9 proteins regain activity when rejoined via the addition of interacting domains.

Comment [DAG1]: note that this is a simplified version of the actual experiment, because part of the nuc domain is contained in the rec domain half. you should point this out in the poster, but not enough space to explain this detail in the abstract

Comment [DAG2]: another way to spin this positively is to say that split cas9 is capable of spontaneous recombination and exhibiting targeted nuclease activity in vivo, but at lower frequency than full length cas9. which means that bringing the split cas9 pieces together artificially, ie with interacting domains, is likely to increase the frequency of targeted mutations. in contrast, if split cas9 had 0 activity, one might worry that no amount of forced interaction could ever restore activity and that the two separate pieces could never function as the full length protein. something to think about when you're presenting your poster.

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Project Length: Short Prior Research Experience: No

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: William E. Neway M.D. Abstract Approved By Advisor: Yes

Co-Authors: Steven M. Theiss M.D. and William E. Neway M.D.

Title: Civilian Gunshot Injuries to the Spine: Application to Current Spinal Injury Classification Systems that were Designed for Blunt Force Trauma.

PURPOSE: To investigate whether classification systems (such as the Thoracolumbar Injury Classification and Severity Score (TLICS) and Denis Classification) can be applied to spinal injuries obtained as a result of gunshot wounds as well as blunt force trauma.

METHODS: Using ICD-9 codes from 2003-2014, we found 32 patients who had spinal gunshot injuries. We retrospectively evaluated each patient for the type of injury, neurological involvement, stability, treatment, and follow-up status. We then tried to apply each classification system to evaluate ease of application and usefulness.

RESULTS: Out of 20 patients with neurological involvement, 17 of those had fractured posterior columns, as per Denis classification. Out of all 32 patients, only one had received surgical treatment. This patient had a disruption of all three columns, but nine other patients with three column injuries did not receive surgery. The nine patients who did not receive surgery had no long-term changes except for three patients who developed minor to mild scoliosis after short-term follow-up. Long-term follow-ups on all patients were stable.

CONCLUSIONS: An ideal classification system will provide descriptive as well as prognostic information on an injury. Although TLICS can provide prognostic information, it was difficult to apply to gun shot wounds since the fracture patterns are not the same as blunt force trauma. The three-column approach (Denis) was easy to apply for descriptive purposes and was effective for predicting neurological involvement, but provided no prognostic or management information. It is our opinion that a new classification system needs to be designed to specifically include the injury patterns seen from a gunshot wound that can also guide injury management. Also, despite the location or fracture pattern, we found abstaining from a surgical treatment rarely causes any significant short or long-term problems for the patient neurologically or mechanically.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Eddy Yang Abstract Approved By Advisor: Yes

Co-Authors: Stanley JA a,b, Nowsheen S, Cooper T, Forero A, LoBuglio AF, Yang ES

Title: Novel interaction between EGFR and PARP1 may modulate DNA repair in human triple negative breast cancer

Background/Objectives
Few therapeutic options are effective for triple negative breast cancers (TNBCs), thus necessitating novel approaches. We reported a novel synthetic lethality with combined EGFR and PARP inhibition, due to a homologous recombination (HR) repair defect induced by EGFR inhibition. As EGFR has no DNA binding domain, we hypothesize it may exert its effects on repair through nuclear translocation and interaction with essential repair proteins, like PARP1, and thereby sensitize TNBC cells to the combination of EGFR and PARP inhibition.

Methods
TNBC cells, MDA-MB-231 and MDA-MB-468, were used as TNBC models *in vitro*. EGFR inhibition was achieved through the treatment of cells with 1uM lapatinib. MALDI-TOF mass spectroscopy was utilized to ascertain protein-protein interactions. Confirmation of interaction data and determination of subcellular location was accomplished through immunoprecipitation and subcellular fractionation, Dou-link *in situ* proximity ligation, and *in vitro* binding assays. To determine if interactions were dependent on DNA, Ethidium Bromide and DNAse were used. Kinetics of EGFR subcellular localization was investigated via immunofluorescence.

Results
Interestingly, mass spectroscopy identified a novel interaction between EGFR and PARP1. These interactions were not found upon EGFR inhibition with lapatinib. Furthermore, we validated the EGFR and PARP1 interaction with reciprocal immunoprecipitation, Duo-link, and *in vitro* protein binding assays. Additionally, these proteins were found to interact in the nucleus, independent of DNA. Lastly, DNA damage increased nuclear levels of EGFR, which was attenuated by lapatinib.

Conclusions
These results dissect the mechanism behind combined EGFR and PARP inhibition contextual synthetic lethality, and may implicate EGFR in regulation of DNA repair via interaction with the repair protein, PARP1. Further investigation of how EGFR regulates DNA repair may shed light on novel roles of EGFR in the nucleus and help determine future targets that can be exploited in the treatment of TNBCs.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Marjorie Lee White Abstract Approved By Advisor: Yes

Co-Authors: White ML, Peterson DT, Watts P, Hall R, DeMoss J, Epps C

Title: PILOT OF MASTER'S OF SCIENCE IN HEALTH ADMINISTRATION STUDENT PARTICIPATION IN SIMULATION-BASED EDUCATION

Background/Objectives: Hospital administrators are individuals that act as the central point of control within hospitals. Training competent health administrators to be prepared for situations they will commonly be presented with in the hospital can be a challenge. The goal of this case was to expose Masters' of Science in Health Administration (MSHA) students to clinical scenarios that they will potentially face in the future. By using simulated cases, the goal is for students to have the opportunity to experience an uncomfortable situation in a controlled environment.

Setting and Participants: This study took place in the Pediatric Simulation Center located at Children's of Alabama and the Center for Patient Safety and Advanced Medical Simulation located at University of Alabama at Birmingham Hospital. Students participated on several different dates between January and April 2014 to allow exposure to as many health administration students possible. Other participants of the simulations included medical and nursing students; however, the study specifically focused on the experience and learning outcomes among MSHA students.

Description/Methods: Data was collected by using program evaluations completed at the conclusion of the simulation experience by the participating health administration students. Each evaluation contained seven statements about the experience with the options of agree, neutral, or disagree. Participants were also asked to describe what they believed was most beneficial about the experience based on what they learned as well as what they felt could be improved.

Evaluation/Results: All participants of the control group (N=18) felt that their simulation experience was a valuable learning experience and the overwhelming majority of participants (N=17) felt that this experience will help improve their care of patients in the future. Many students commented that these cases also helped them realize how important it is to have interdisciplinary communication and collaboration. Simulations were the most valuable to MSHA students when there were defined questions relating to legal issues because these cases had higher engagement of administrators. The MSHA students' evaluations demonstrate the desire for further education and management of controversial patient scenarios in a controlled environment.

Reference: Boet S, Bould MD, Layat C, Reeves S. "Twelve tips for a successful interprofessional team-based high-fidelity simulation education session. Med Teach. 2014 Jul 15:1-5. [Epub ahead of print]

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Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Matthew Delaney

Abstract Approved By Advisor: Yes

Co-Authors:

Title: Observing and Comparing the Effects of Dilaudid, Morphine, and Low Dose Ketamine in Severe Pain Patients

In this study, the focus was to observe and rate to level of pain and side effects patients experienced in the UAB Department of Emergency Medicine before, during, and after given a dose of pain medication. Three pain medications were selected to observe the effects in order to compare their usefulness and results. Pain medications under observation in this study are morphine, dilaudid, and ketamine. Patients were selected by severity and cause of pain and with signed consent, agreed to participate in study. During the study, the patients level of pain, side effects, and desire whether or not to be administered more medication was recorded in progressive intervals over a total of two hour observation. Other patient information, including history of pain, surgery, and medication was recorded and also the physicians rate of the patient's pain. The goal of this research is to observe the effects of ketamine and conclude whether or not it is a good candidate to substitute the administration of dilaudid in sickle cell patients during a sickle cell crisis.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Frances Lund Abstract Approved By Advisor: Yes

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

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

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

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Project Length: Prior Research Experience:

Source of Funding:

Faculty Advisor: Abstract Approved By Advisor:

Co-Authors:

Title: Impact of the LRRK2G2019S Mutation on Alpha-Synuclein Aggregation

Parkinson's Disease (PD) is a neurodegenerative disorder characterized by loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc), the midbrain. Mutations in the alpha-synuclein gene, SNCA, are linked to increased susceptibility of PD. Another autosomal dominant mutation leading to late-onset PD is the G2019S mutation in leucine-rich repeat kinase 2 (LRRK2). 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. We use a novel system to model Lewy body and Lewy neurite formation, which uses pre-formed alpha-synuclein fibrils to induce formation of phosphorylated aggregates from endogenous alpha-synuclein. Our lab has shown that alpha-synuclein aggregates are markedly increased in LRRK2G2019S primary neurons when compared to nontransgenic neurons. We have shown in vivo that aggregates are found in distinct inter-connected brain regions. We are currently in the process of determining if LRRK2G2019S mutants have enhanced alpha-synuclein aggregation in vivo by comparing aggregates found 8 weeks post-injection of pre-formed fibrils in LRRK2G2019S rats to those in nontransgenic rats.

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Project Length: Short Prior Research Experience: No

Source of Funding: T35

Faculty Advisor: Robert Russell Abstract Approved By Advisor: Yes

Co-Authors: Michelle Shroyer MPH, Ann B. Douglas RN, MSN, Robert T. Russell MD, MPH

Title: Risk Factors for Pediatric Surgical Readmissions: An Analysis of the Pediatric NSQIP Database

Unplanned hospital readmissions are associated with significant and often avoidable expenditures of healthcare resources. The characterization of unplanned readmissions following pediatric surgery can better define risk factors for preoperative counseling and help identify potential improvements in surgical practice and clinical management.

Data from a portion of pediatric surgical cases from fifty hospitals are collected annually in the National Surgery Quality Improvement Program registry. From the 2012 NSQIP pediatric database, 18,642 pediatric general surgery cases were queried and analyzed; 1,111 of these cases involved readmission within 30 days. Univariate and multivariate logistic regression were used to identify the patient characteristics and comorbidities associated with unplanned readmission. Variables in the analysis not predictive of readmission were race, a preoperative diagnosis of diabetes, cerebral palsy, chronic lung disease, cystic fibrosis, major/severe cardiac risk factors, enteral or parenteral nutritional support at the time of operation, a history of prematurity, and emergent/urgent operation. We found that patients in older age groups (>30 days-old) were more likely to be readmitted than those <30 days-old. Developmental delay and asthma were also associated with readmission. Higher pre-operative American Society of Anesthesiologists physical status classifications (ASA classes 3-5) were associated with an increased risk of readmission. Cases involving dirty, infected, or contaminated wounds (Class IV) were also associated with readmission. While health care providers may not be able to directly mitigate these risks, they can use them to preoperatively counsel high-risk patients and to tailor their postoperative care to reduce the chance of readmission.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Department of Medicine Fellowship

Faculty Advisor: Dr. Andrea Cherrington Abstract Approved By Advisor: Yes

Co-Authors: April Agne, Matthew Carle, Morgan Lepard, Margaret Meehan, Lynn Andreae, Heidi Beck, Ariann Nassel, Wei Su, Andrea Cherrington

Title: Social Determinants of Obesity: Recruitment Methods, Strategies, and Challenges for a Health Survey among Latino and Non-Latino Individuals in Albertville, AL

Background: The Social Determinants of Obesity Study in Albertville, AL is a population-based, cross-sectional pilot study seeking to understand the interpersonal, community, and environmental influences of obesity in a sample of 100 Latinos and 100 non-Latino whites.

Methods: Participants were recruited using a CDC-designed cluster sampling approach and GIS technology to generate random samples of census blocks. Eligible participants have to reside in the blocks sampled, self-identify as Latino or non-Latino white, speak fluent Spanish or English, be 19 years or older and not pregnant. A multi-prong approach was used to inform residents of the upcoming survey, including distributing flyers in Spanish and English to businesses, registering the study with the local police and city hall, and publishing an article in the local newspaper and online with a study team photo.

Results: There were 429 households screened. Eighty-two surveys were completed, in which 29.4% were Hispanic and 63.5% were female. The study team experienced recruitment difficulties during business hours with a high number of “No Answer” (n=250). In response, teams extended hours to afternoons and weekends, when residents were more likely to be home. Blocks were also revisited at different dates/times. Another obstacle was the number of declines (n=86); reasons included survey length (90 minutes), being too busy, and not interested. To facilitate survey completion, interviewers offered to reschedule. Some elderly participants had hearing impairments. In response, larger font showcards were used. Driving time between houses also limited recruitment. Some blocks had a large “count number,” or number of houses between two targets homes. For efficiency, the count number was reduced by half in these blocks.

Conclusions: Eighty-two surveys were completed from the 429 households screened. Many challenges were encountered, and adjustments were made in response. As a result, the study team has reached nearly 50% of the targeted sample.

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Project Length: Short

Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Adrie Steyn

Abstract Approved By Advisor: Yes

Co-Authors: Adrie Steyn, Rajhmun Madansein

Title: Proteomic atlas of the human tuberculous lung

In South Africa, tuberculosis (TB) is an epidemic. Fueled by the country's huge HIV burden, it is South Africa's leading cause of death. The province of Kwazulu-Natal is the heart of the epidemic. It has the highest rates of HIV and TB co-infection, and in 2005, was the site of the first documented outbreak of extensively drug-resistant (XDR) TB. The Kwazulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) seeks to address the growing problem by focusing on the biomedical science underlying the mechanisms of TB and HIV. The scientists at K-RITH work closely with the clinicians at Inkosi Albert Luthuli Central Hospital, affording the researchers access to TB-infected human lung samples. Patient 27's resected right lung had clear areas of infected, intermediate, and uninvolved lung, which presented a unique opportunity for further study. The human body's response to TB infection is one of the most important mediators of destruction of the lung in active TB, but broad analysis of the proteins at play has never been performed in human samples. With this in mind, we set out to establish a proteomic profile and identify the up and down-regulated human proteins in the infected, intermediate, and uninvolved portion of patient 27's lung. The samples were prepared appropriately, run on SDS-PAGE gels, and sent to UAB's proteomics facility for liquid chromatography-mass spectrometry analysis. The results provided a list of 127 statistically significant top-hit proteins that were up and down-regulated in the healthy versus infected tissue. Many of the proteins are structural, which is consistent with the extensive fibrosis seen in the infected region. Many others point to important pathways that are potentially involved in the human response to TB. This profile will be instrumental in providing direction for further study as well as identifying proteins of interest for drug targeting and treatment.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: O'Brien Center Fellowship

Faculty Advisor: Anupam Agarwal

Abstract Approved By Advisor: Yes

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Title: HEME OXYGENASE -1 EXPRESSION PREVENTS DOXORUBICIN-INDUCED CARDIAC TOXICITY

Heme oxygenase-1 (HO-1) is an inducible enzyme that degrades pro-oxidant heme into carbon monoxide, biliverdin, and iron. The role of HO-1 in delayed onset heart failure (DOHF) caused by the chemotherapeutic agent doxorubicin (DOX) is unknown. We hypothesized that HO-1 expression protects against DOX-induced DOHF by preventing mitochondrial toxicity in caradiomyocytes. We used DOX to model DOHF in mice (18 mg DOX per kg of body weight, administered IV over one week as three 6 mg/kg doses). HO-1 overexpression in humanized transgenic (HBAC) mice prevents systolic dysfunction (ejection fraction 67% vs 51% in WT mice, $P<0.05$, n=5) at day 14 after DOX treatment. DOX-induced DOHF is characterized by left ventricle dilation (3.22 mm vs 3.55 mm in WT mice, $P<0.05$, n=5) and wall thinning (0.89 mm vs 0.61 mm in WT mice, $P<0.05$, n=5), which is prevented by HO-1 overexpression. Histological evaluation demonstrated that global and cardiac-specific overexpression of HO-1 prevents cardiomyocyte death, evidenced by a reduction in cytoplasmic vacuolization and loss of myocyte striations. Transmission electron microscopy (TEM) demonstrated that mice with cardiac-specific overexpression of HO-1 (CS-HO-1 mice) ameliorates DOX-mediated ultrastructural changes to cardiomyocytes by preventing dilatation of the sarcoplasmic reticulum, cytoplasmic vacuolization, and myofibrillar disarray at days 14 and 60 after treatment. TEM also revealed mitochondrial fragmentation and damaged mitochondria in autophagic vacuoles in DOX treated WT and HO-1 deficient mice ($HO\text{-}1^{-/-}$) but not in cs-HO-1 mice. Quantitative analysis revealed a significant increase in the number of mitochondria per field in $HO\text{-}1^{-/-}$ mice which was accompanied by a significant decrease in average mitochondrial area when compared to CS-HO-1 mice at day 14 after DOX treatment. WT mice also showed significantly more mitochondria per field 60 days after DOX treatment when compared to CS-HO-1 mice.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Marjorie Lee White, MD Abstract Approved By Advisor: Yes

Co-Authors: Kandi M.Wise, BSN, RN, J. Lynn Zinkan, MPH, BSN, RN, Amber Q. Youngblood, BSN, RN, Dawn Taylor Peterson, PhD, Marjorie Lee White, MD, MEd MPPM, Nancy M. Tofil, MD, Med.

Title: FIRST FIVE MINUTES OF THE CODE

Background: We sought to improve the response of bedside personnel during the crucial first few minutes of an emergency by developing a simulation-based training targeted at personnel on units with limited exposure to resuscitative measures.

Hypothesis: We hypothesized that simulation is an effective tool for identifying breaches to delivering appropriate care at our institution, educating nurses on their strengths and weaknesses and preparing them to apply this knowledge in the future.

Methods: Each mock code was followed by debriefing session during which major components of effective child resuscitation were discussed. A qualitative assessment questionnaire was given to each participant at the end of the debriefing session. This study was approved by the IRB at the University of Alabama at Birmingham.

Results: There was tremendous variability in responses collected. Four areas of strength that seemed to overlap the most were the following- initiating CPR (29.5%); good assessment (21%); good CPR technique (17%); and effective communication within the team (11.5%). When asked about barriers to delivering timely and effective care 56% of people stated that there were no barriers. However, 78% of responses to the next question identified some area that participants would like to improve and will do differently during the next code. All 100% of participants found the activity to be helpful in preparing them to contribute to better patient care.

Conclusion: Based on the survey data obtained from mock codes, it is evident that there are numerous areas for improvement in delivering timely and appropriate care to pediatric patients in the event of arrest. The fact that 100% of the participants found their mock code experience valuable and 78% of participants reported that they would do a better job during subsequent codes leads us to believe that simulation is an effective tool for improving patient care.

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Project Length: Short Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. Cynthia Brown Abstract Approved By Advisor: Yes

Co-Authors: Courtney Williams

Title: Resiliency: Factors that Contribute to Recovery in Community-Dwelling Older Adults

Background: For older patients, hospitalizations are common and have been associated with a number of adverse outcomes including high rates of functional decline and loss of community mobility. Functional decline is common just prior to and during hospitalization, with many patients failing to recover by discharge. There is an important relationship between resilience and function after an adverse event such as hospitalization[1]. Factors that predict resilience have not been well described but may include community and social support[2] as well as optimism and having fewer cognitive problems[3]. Determining factors that influence recovery to baseline function (resilience) may provide targets for interventions to reduce the observed functional decline and loss of community mobility. This project aims to determine, among a cohort of older adults who are independent at baseline, what proportion experience a hospitalization and what proportion recover to near-baseline levels. We also examined factors that predict recovery to near baseline levels.
Methods: The UAB Study of Aging (SOA I) is designed to understand person-specific factors that predispose older adults to mobility decline. Participants were a random sample of Medicare beneficiaries at least 65 years of age who lived in central Alabama, stratified by race, sex and rural/urban residence. Potential participants for our study included all participants in the UAB Study of Aging who had at least one hospitalization over the course of the study. The SOA I collected data by telephone every 6 months from 1999-2008 including demographics, functional ability, self rated health and an assessment of community mobility measured by the UAB Life-Space Assessment (LSA). The LSA measures mobility based on the distance through which a person reports moving during the four weeks preceding assessment. Questions establish movement to six specific life-space levels ranging from within one's dwelling to beyond one's town. For each level, persons were asked how many days within a week they attained that level and if they needed help from another person or from assistive devices to move to that level, based on the assumption that persons able to get to a level by themselves are the most independent, that using equipment represents a mid-level of independence, and requiring personal help represents dependence. Among this cohort of older adults who are independent at baseline we determined the proportion who experienced a hospitalization and what proportion of those persons subsequently recovered to their previous life-space level. Hospitalizations included any other overnight hospitalization or longer for both medical and surgical indications. We defined "recovery" as reaching within ±5 points of pre-admission LSA score within one year from the time discharged from hospital. In addition, using step-wise logistic regression we examined factors that predicted near recovery or recovery to prior life-space levels (resiliency).
Results: Three-hundred and thirty nine participants had at least one hospitalization during the 8.5 years of study. Mean age of the group was 75.4 (s.d. 6.6) years, 44% African American and 48% female. The mean Mini Mental State Examination (MMSE) score was 25.8 (s.d. 4.1) and the Geriatric Depression Scale score was 2.3 (s.d. 2.3) indicating the group was cognitively intact and not depressed. In bivariate analysis comparing those with a good recovery to those without a good recovery only age and church attendance were statistically significant. Using logistic regression we examined variables that were independently associated with having a good recovery of life-space after hospitalization. In the full model which included demographics, physical function and Comorbidities/ general well-being 3 variables were independently associated with a good recovery after hospitalization, age (p=.004), adl ability (p=.03) and church attendance (p=.001). A limitation of the study was that questions regarding social support were only asked at year 4 of follow-up, so church attendance was used in lieu of a more specific gauge of social support.
Conclusions: Age, ADLs, and church attendance were significant predictors of good recovery in the third model, whereas physical factors such as number of comorbidities or BMI were not significant in predicting good recovery. ADL ability suggests that at least some level of independence with daily activity is needed for resilience. Female gender lost significance once ADLs was added in model 3, suggesting some interaction

between gender and ADL ability. Results suggest greater emphasis on social support may improve recovery of community mobility after hospital discharge among community dwelling older adults.

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Project Length: Short

Prior Research Experience: No

Source of Funding: Other

Faculty Advisor: Candace Floyd

Abstract Approved By Advisor: Yes

Co-Authors: Candace Floyd

Title: A New Therapuetic Approach to Managing the Aftermath of Traumatic Brain Injury: Manipulation of O-GlcNAcylation via Thiamet-G

Traumatic brain injury (TBI) is a serious public health problem in the U.S, but there are currently no FDA-approved pharmacologic treatments. It has been shown that the O-linked attachment of ß-N-acetyl glucosamine (O-GlcNAc) to cytoplasmic proteins plays a critical role in the acute regulation of neuronal cell survival. Increasing O-GlcNAcylation enhances cell survival, while decreased levels of O-GlcNAcylation have been associated with increased cell death. Inhibition of O-GlcNAcase (OGA), an enzyme that catalyzes the removal of O-GlcNAc from proteins, has been shown to increase O-GlcNAcylation. A specific inhibitor of OGA, thiamet-G, has recently become available, and post-TBI administration of thiamet-G to animals has been shown to increase O-GlcNAc levels and attenuate neuronal cell death in the hippocampus, a region of the brain susceptible to TBI-induced cell death. Therefore, we hypothesized that post-TBI administration of thiamet-G protects against cognitive deficits caused by TBI. TBI was induced in rats using the lateral fluid percussion model. Post-injury, animals were given low-dose thiamet-G, high-dose thiamet-G, or saline. The cognitive performance of injured animals was then assessed using the Morris Water Maze (MWM) hidden platform task latency times and compared to that of uninjured sham animals. After the acquisition phase of MWM testing, animals were subjected to a probe trial in which the MWM platform was removed. We then measured the time animals spent in the target quadrant and the number of platform annulus crossings. There were no statistically significant differences in escape latency times, time spent in the target quadrant, or the number of platform crossings. Therefore, our findings suggest that post-TBI administration of thiamet-G does not protect against cognitive deficits as assessed in this study. We will conduct further work analyzing MWM search strategies in an effort to better distinguish cognitive performance differences between animals.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Departmental or Mentor Funds

Faculty Advisor: Dr. Duraid Younan Abstract Approved By Advisor: Yes

Co-Authors: Russell Griffin

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

Introduction: Firearm injuries have accounted for more than 15% of trauma cases every year for 3 decades, making the care of firearm victims integral to the trauma surgeon's practice. In 2010, piercing objects caused an estimated 2.4 million non-fatal injuries and 2,600 fatal injuries. This study presents 5 years of data covering penetrating limb injury (PLI) from an urban Level-1 trauma center in an attempt to gain further insight into patient outcomes with modern course of treatment.
Methods: A retrospective analysis was conducted of 1,218 patients presenting with penetrating limb injuries from 2005 – 2009. Information was gathered on demographics, mechanism and location of injury, any associated injuries, Injury Severity Score (ISS), hospital stay, mortality, and functional status at discharge. The data were analyzed utilizing ANOVA and chi-square test for continuous and categorical variables, respectively.
Results: Most patients with PLI were male (86.7%) having an average age of 34.2±12.1 years. Firearm assault was the most common cause of injury (60.1%) followed by stabbing (16.7%). Average ISS was 10.4±11.3 on presentation. Location of limb injury was evenly divided between upper (45.2%) and lower (42.3%) extremity; 12.6% of the patients sustained injuries to both upper and lower extremities. 83.5% of patients were discharged from the ED with good functional outcome scores. Only 4.8% of patients required amputations, and less than 10% required a vascular operation. Mortality rate was 5.3%, most commonly due to exsanguination from other injuries.
Conclusions: The overwhelming majority of PLI patients do not require operative intervention to save life or limb. Our data show that the overwhelming majority of patients who present to our ED with a penetrating limb injury are discharged home in good condition. Most of the danger faced by these patients arises from associated injuries to areas like the abdomen, thorax, or head, so care needs to be taken when assessing these patients because if they have associated injuries, they are much more likely to receive an operation or die from the injury.

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Project Length: Short

Prior Research Experience: No

Source of Funding:

Faculty Advisor: Dr. John Waterbor

Abstract Approved By Advisor: Yes

Co-Authors: Dr. Aly Padilla, Dr. John Waterbor

Title: Methods for Longitudinally Tracking Graduates of a Short-Term Cancer Research Training Program

The National Cancer Institute's (NCI) R25E Cancer Education Grant helps support students to complete short (10-12 week) cancer research projects with a faculty advisor. The long-term goal is to encourage program participants to consider pursuing cancer-related professions in the future. The career choices that program alumni choose will not be evident until several years after program participation, when further education and training are complete. Therefore, valuable and efficient methods must be used in order to determine if the program is achieving its long-term goal. Each program graduate must be located and information on his or her current institution, job title, and professional achievements must be gathered via questionnaire and reviewed for cancer content. At the University of Alabama at Birmingham, the NCI-funded R25E program called "CaRES" has operated since summer 1999 and has supported over 500 students, two-thirds of them are entering or first-year medical students, and the rest are master's students in public health. In summer 2014, we tracked CaRES graduates from summers 1999 through 2013, noting which search methods worked best. We posted our tracking questionnaire on the CaRES website so program alumni could enter their information easily. Our institutional electronic directory and faculty contacts were the most reliable sources to locate past program participants. After being contacted, program alumni typically accessed and completed the questionnaire within the same day. Social media was helpful in identifying past program participants, but did not bring about questionnaire completion. Telephone calls were not an efficient means of contact. Posting the short tracking questionnaire on the website, and using current email addresses to contact program alumni, was the best approach for longitudinal tracking of our R25E graduates.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: Marilyn Crain, MD, MPH; Michelle Khan, MD, MPH Abstract Approved By Advisor: Yes

Co-Authors: Alan Tita, MD, MPH, Ph.D.; Mickey Parks, NP

Title: Pregnancy Outcomes in Alabama Women with HIV1 Infection

Introduction: HIV infection during pregnancy is associated with potential adverse health outcomes for mother and infant. We wished to describe the population of HIV+ women giving birth at UAB Hospital between 2009-2013 and their pregnancy outcomes.

Methods: A list of HIV+ women who delivered at UAB between January 1, 2009 and December 31, 2013 was generated using UAB's Obstetrics Automated Record; data from UAB's electronic health records were entered onto a Microsoft Excel spreadsheet for tabulation. Descriptive statistics (and chi-square analysis) were performed using Stata SE version 11.

Results: 92 HIV+ women with 106 pregnancies and 108 live births presented during the study period (12 women with 2 pregnancies; 1 with 3). There were 5 sets of twins (4.9%) and 3 stillbirths (rate 29.4/1000). The majority were unmarried (62.3%), Black (83%), overweight/obese, (18.9%/35.8% respectively, mean BMI 30.0), and had Medicare/Medicaid (79.2%); median age was 28.4y (range 16.9-41y). 34% reported substance use. 45 pregnancies (42.5%) had detectable (>40 copies/ml) viral loads in the first trimester (median 1950 copies/ml, range 56-119,000 copies/ml); 31 (29.2%) had detectable virus at delivery, with 7 exceeding 1000 copies/ml, meeting criteria for elective Cesarean-section to prevent vertical HIV transmission. Median gestational age at delivery was 38.3 weeks (25% pre-term); median birth weight was 2809 g (25% were <2500g).

Conclusions: Overall, these women are at high risk for pregnancy-related morbidity and poor neonatal outcomes with 25% LBW and 25% <38 weeks gestation. These numbers are higher than reported for all Alabama women and Black women delivering between 2009-2012.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Tanja Dudenbostel and Suzanne Oparil Abstract Approved By Advisor: Yes

Co-Authors: Mingchun Liu, Bin Zhang, Peng Li

Title: Prevalence of metabolic syndrome in patients with and without primary aldosteronism

Objective

Obesity and primary aldosteronism (PA) are associated with resistant hypertension (RHTN). Obesity is associated with insulin resistance on peripheral glucose and fatty acid utilization, often leading to type 2 diabetes(T2DM). Obesity, hyperglycemia, dyslipidemia (HLD) and hypertension as metabolic risk factors have been termed metabolic syndrome (MetS). Obesity has been also associated with increased aldosterone levels. We evaluated whether MetS was associated with PA.

Methods:

We retrospectively studied 2043 patients referred to the UAB Hypertension Clinic for evaluation and treatment of RHTN. PA was defined as aldosterone renin ratio (ARR) >30 and urinary aldosterone (UAldo) > 12 mcg/24h, MetS was defined according to the NCEP ATP III guidelines.

Results:

Patients with PA versus patients without PA were significantly younger (54.7 vs 57.7%), more male (56.8 vs 36%), more African American (54.8 vs 67.6%), and had a higher BMI (32.5 vs 30.6 kg/m^2%). Biochemically higher serum aldosterone levels (18.1 vs. 8.6 ng/dl), ARR(29.2 vs 8.6), UAldo (19.7 vs 7.2 mcg/24hr), urinary cortisol (UCort)(153.2 vs 141.8 mcg/24hr) urinary potassium (UK^+) (mEq/24hr), urinary sodium (UNa^+) levels (199.0 vs. 170.6 mEq/24hr) and lower serum potassium levels (3.8 vs. 4.1 mEq/dL) were found in patients with PA.

Metabolic syndrome was found in 65% of patients with PA. Patients with PA had significantly higher prevalence of T2DM (23% vs. 15.4%, $p<0.0001$) compared to patients without PA. Additionally, patients with T2DM had a significant higher proportion of HLD than patients without T2DM (55.4% vs 55.1%, $p<0.0001$). Multivariate logistic regression showed that T2DM and HLD significantly predict PA.

Conclusions

The high co-occurrence of MetS in resistant hypertensive patients with PA and the association of T2DM and HLD with PA support a possible pathophysiological link between aldosterone and individual components of MetS other than hypertension. Better understanding of the mechanisms underlying this connection might be useful for prevention and treatment of the MetS.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: T35

Faculty Advisor: David C. Cleveland, MD Abstract Approved By Advisor: Yes

Co-Authors: David C. Cleveland, James K. Kirklin, Ayesha Bryant, John Merriman

Title: Early and late outcomes after surgical correction of anomalous left coronary artery from the pulmonary artery: a 41 year experience

BACKGROUND: Anomalous Left Coronary Artery arising from the Pulmonary Artery (ALCAPA) is a congenital heart defect wherein the left coronary artery does not arise from the aorta. Various surgical repair techniques have been used over the years. The objective of this study was to identify risk factors for early and late morbidity in patients who have undergone surgical repair for ALCAPA.

METHODS: This is a retrospective review of all patients who underwent surgical repair for ALCAPA between 1971-2012 at UAB. Chart reviews and letters/calls to patients were used to obtain follow up data. Patient characteristics, repair technique, operative variables, vital status, and echo data (LV and mitral function) were obtained. Operative repair techniques included: ligation, tunnel, re-implantation, and anastomosis of left subclavian (LSC) to LCA.

RESULTS: Fifty two patients (12 males, median age 6 months) met the inclusion criteria; 18 had an early (intra-operative or 30-day) mortality. On univariate analysis, early mortality was associated with younger age (4 vs. 21 months, p=0.03), lower pre-operative weight (61 vs. 82 kg, p=0.05), and era of operation (p=0.01). On multivariate analysis age and era of operation remained independent predictors of early mortality. Operative mortality was highest for patients that underwent anastomosis of LSC to LCA (3/5 patients, 60%) and tunnel (8/24 patients, 33.3%). Patients alive beyond the 30-day operative period (n=33) had a 15-year Kaplan-Meier survival of 95.5%. Pre- and post-operative LVED size was (4.2 vs. 3.6 cm, p=0.16, respectively).

CONCLUSION: Younger age at time of operation and operations performed during the early era (prior to 1992) were associated with early mortality in patients who underwent repair for ALCAPA. Long term follow up shows a trend of improvement in cardiac function. Amongst patients surviving the initial post-operative period, long term survival rates are excellent.

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Project Length: Long Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Eddy Yang Abstract Approved By Advisor: Yes

Co-Authors: Tiffiny Cooper, Hoa Q. Trummel, James A. Bonner, Eben L. Rosenthal, Eddy S. Yang

Title: Defects in repair of DNA double strand breaks and sensitivity to PARP inhibition in HPV-positive oropharyngeal squamous cell carcinoma.

Although tobacco-associated head and neck cancers (HNCs) are declining in incidence, HNC rates are escalating overall due to increasing prevalence of human papillomavirus (HPV)-associated tumors, especially oropharyngeal squamous cell carcinomas (OPSCC). HPV-positive OPSCC express two viral oncoproteins, E6 and E7, which functionally disrupt cell signaling pathways by altering stability and interactions of regulatory proteins, leading to carcinogenesis. Clinically, patients with HPV-associated cancers have improved overall survival and increased response to therapy, especially agents which act by damaging DNA. Based on these observations, we *hypothesized* that HPV-positive OPSCC harbors a defect in DNA repair activity and will be sensitive to DNA repair-targeted therapy. Consistent with our hypothesis, *in vitro* disease models demonstrated delayed resolution of radiation-induced DNA double strand breaks (DSBs) as assessed by γH2AX foci staining and neutral comet assay. Investigation of the two main DSB repair mechanisms, non-homologous end joining (NHEJ) and homologous recombination (HR), indicated intact activation of both pathways but strikingly diminished recruitment of downstream repair factors DNA-Pk (NHEJ) and BRCA2 (HR) to sites of damage. In addition, protein expression of both DNA-PK and BRCA2 was decreased in HPV-positive compared to HPV-negative HNC cell lines. We next studied susceptibility of HPV-positive OPSCC to PARP inhibition, a class of anticancer agents which block DNA repair signaling pathways and have proven effective clinically in DNA repair deficient cancers. *In vitro* colony formation assays revealed a negative effect on cell survival in HVP-positive but not HPV-negative HNCs treated with the PARP inhibitor veliparib. Importantly, these results were confirmed *in vivo* in both cell line-derived xenografts and a patient-derived xenograft. In summary, our findings demonstrate the presence of a significant DNA DSB repair defect in HPV-positive OPSCC, encompassing both NHEJ and HR repair, and suggest therapies targeting DNA repair pathways may provide a means to improve treatment of this disease.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: NIH Medical Scientist Training Program

Faculty Advisor: Dr. Farah D. Lubin Abstract Approved By Advisor: Yes

Co-Authors: Timothy J. Jarome, Jasmyne S. Thomas

Title: Histone ubiquitination is a critical epigenetic regulator of memory formation

The formation of long-term memories requires *de novo* gene transcription in neurons, which is necessary to transfer labile short-term memories to stable long-term memories, a process referred to as memory consolidation. In the past decade, numerous studies have implicated epigenetic changes such as histone methylation and acetylation, and DNA methylation in transcriptional regulation during the memory consolidation process (Jarome & Lubin, 2014). For example, tri-methylation of histone H3 at lysine 4 (H3K4me3), a transcriptional activator, is critical for the consolidation of contextual fear memories in the hippocampus, suggesting that histone methylation is a critical regulator of memory formation in neurons (Gupta et al. 2010). However, while the role of some epigenetic mechanisms has been extensively studied in the context of memory formation, no study to date has examined the role of histone ubiquitination in this process. Recently, our lab has collected preliminary data demonstrating that monoubiquitination of histone H2B at lysine 120 (H2BubiK120), a transcriptional activator, accompanies increases in H3K4me3 in the CA1 region of the hippocampus following contextual fear conditioning. Thus, we hypothesized that inhibition of H2BubiK120 in the CA1 region of the hippocampus would impair memory for a contextual fear association.

Rats were stereotaxically infused with an Accell siRNA targeting *Rnf20*, the ubiquitin E3-ligase for H2BubiK120; *MLL1*, the histone methyltransferase for H3K4me3; or a negative control siRNA. Five days later, all groups were trained in a contextual fear conditioning task in which a novel environment was associated with a series of electric shocks. The following day, animals were returned to this environment and freezing behavior was measured as an indicator for fear memory of the context-specific stimulus. Twenty-four hours following behavioral testing, the animals were sacrificed, and their brains were dissected for CA1 and nearby control regions. Histones and RNA were extracted, and relative expression of *Rnf20* and *MLL1* were determined by rt-qPCR. H2BubiK120 and H3K4me3 levels were examined using western blotting.

We confirmed successful knockdown of *Rnf20* mRNA in the CA1 region of the hippocampus, which was associated with a significant impairment in memory for the contextual fear conditioning task compared to controls. Additionally, we found a strong trend for a reduction in memory for the task in animals infused with the *Mll* siRNA, confirming our previous result with a genetic knockout of *Mll* in mice (Gupta et al. 2010). Collectively, these results suggest a critical role for histone ubiquitination in the regulation of memory consolidation in neurons and provide the first evidence that H2BubiK120 is involved in activity-dependent synaptic plasticity.

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Project Length: Short Prior Research Experience: Yes

Source of Funding: Diabetes Research and Training Center Fellowship

Faculty Advisor: Dr. Monika Safford Abstract Approved By Advisor: Yes

Co-Authors: Title: Qualities of Diabetes Patients with Medication Adherence in Rural Alabama

Diabetes is one of the most prevalent diseases in the United States, affecting an estimated 8.3% of the U.S. population in 2010. In rural Alabama, diabetes is compounded by medication non-adherence, which was found to be a problem in 56% of the population in these areas. One model of chronic illness that may explain non-adherence is Corbin and Strauss's illness trajectory framework, which posits that disease states disrupt the balance between three elements – body, biography, and conception of self – that, when aligned, creates a sense of well being. In disease states such as diabetes, where the individual experiences a body failure, the conception of self must be reconfigured. This process may be especially stressful and lead to denial of the disease, negatively impacting optimal self-management behaviors. To understand the influences that allowed individuals with diabetes to move past their body failure toward achieving a balance with their new biography and conception of self, we interviewed four individuals from rural south Alabama who reported being adherent to their medications. These interviews revealed several common qualities among adherent participants, including both internal and external qualities. Internal qualities noted among participants included a high level of self efficacy and an internal locus of control. They also believed that the complications of diabetes were severe and that they themselves were susceptible to these complications. Adherent participants had a high belief that the medication would help to prevent diabetes complications. With regard to external qualities, these patients had strong social support networks and had heard about others' experiences with diabetes. These findings reveal attitudes and beliefs regarding diabetes and diabetes medications that may be helpful for future interventions. Further work with non-adherent patients is needed in order to compare the qualities of non-adherent participants to those of adherent patients found in this study.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: CaRES Program

Faculty Advisor: Rojymon Jacob Abstract Approved By Advisor: Yes

Co-Authors: Jessica Whitaker, Andrew McDonald, MD

Title: Efficacy of Treatment Options for Metastatic Neuroendocrine Tumors

Abstract:

Neuroendocrine tumors (NETs) represent a rare subset of malignant tumors in which the tumors spontaneously produce hormones that are native to the body; however, it is the overproduction of hormones that causes patients to become symptomatic. NETs have a high rate of metastasis, specifically to the liver and brain. Because the tumors are rare, treatments options span techniques designed to decrease symptoms rather than cure the disease. In this retrospective chart analysis of twenty four patients treated at the University of Alabama at Birmingham, the treatment options included radiofrequency ablation (RFA), surgical resection of the tumor(s), transarterial chemoembolization or bland embolization (TACE/TAE), and Yttrium-90 radioembolization. Patients qualifying for this analysis were provided from an institutional database of patients receiving Sirspheres and minimally invasive intravascular therapy for hepatic neoplasms and metastasis. Treatment options were compared on the basis of efficacy measured by symptom progression or decline, time between treatment options, and remarkable changes in lesion size.

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Project Length: Intermediate Prior Research Experience: No

Source of Funding:

Faculty Advisor: Tom Harris Abstract Approved By Advisor: Yes

Co-Authors: Staci Self, Tom Harris

Title: Caregiver Response to CF Carrier Identification in the Alabama CF New Born Screening Program

Background: Newborn screening for CF offers benefits such as early disease detection and intervention before irreversible consequences develop that are felt to outweigh the consequences of false positive screens to CF carriers and caregivers. Evaluating caregiver response offers an opportunity to improve communication and limit unintended consequences.

Hypothesis: Identification of CF carrier status by Alabama's NBS program induces caregiver anxiety and ongoing health concerns in caregivers.

Methods: Caregivers of newborns identified for follow-up CF testing by IRT/ DNA NBS and CF negative by sweat test through the Children's of Alabama/UAB pediatric CF center were provided a 36 item telephone survey. Multiple-choice questions assessed (1) understanding of carrier implications (2) perceptions of child health (3) impressions of healthcare providers (4) satisfaction with clinic staff and (5) family planning. Anxiety was scored on a Likert scale.

Results: 119 families were identified. 45 were contacted, of which 35 participated. 86% of respondents were mothers, and 72.2% were Caucasian. Most respondents experienced high anxiety as a result of their notification but thought the information was delivered appropriately. Anxiety increased while awaiting sweat testing. Everyone experienced relief after negative sweat testing, though 15% reported residual anxiety. Caregivers retained more information regarding carriers' health than specific genetics. 8% reported ongoing concern about the child's health. Only 6% changed their family planning as a result of the information, but 97% plan to tell the child of their status.

Conclusions: NBS's benefits outweigh the negative effects on carrier families. Initial identification induces anxiety that typically resolves after negative sweat testing. Caregivers retain appropriate understanding about carrier health, and almost all plan to inform the child. Many caregivers express satisfaction with the NBS process and clinic. Addressing anxiety between NBS notification and sweat chloride testing will be a major quality improvement initiative to limit negative consequences of testing.

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Project Length: Intermediate Prior Research Experience: Yes

Source of Funding: Other

Faculty Advisor: Melanie Tucker, PhD Abstract Approved By Advisor: Yes

Co-Authors: Melanie Tucker, PhD, CHES (Assistant Professor; Director of Clinical Investigations); Lloyda Williamson, MD, DFAPA (Associate Professor, Department of Psychiatry and Behavioral Medicine)

Title: The Art of Empathy: Does Exposure to a Humanities-Based Extracurricular Activity Affect Empathy Changes in Third-Year Medical Students?

Empathy is defined as a cognitive attribute that involves an understanding of patients' experiences, concerns, and perspectives combined with a capacity to communicate this understanding. Defined in this way, empathy is always beneficial in the patient-physician relationship and leads to personal growth, career satisfaction, and optimal clinical outcomes. Studies have shown that empathy declines significantly throughout medical training, particularly during medical school. One study has cited that the most substantial decline occurs during the third year – a time when the curriculum begins to shift almost exclusively toward patient care. The purpose of this research study was to determine whether exposure to a humanities-based extracurricular activity, "The Art of Medicine Rounds," at the University of Alabama School of Medicine – Tuscaloosa campus – affects changes in empathy among third-year medical students. This study sought to answer the following questions: 1) Does participation in "The Art of Medicine Rounds" affect empathy changes in third-year medical students? 2) If so, does it correlate with positive or negative change? 3) Is there a correlation between the number-of-times attended to "The Art of Medicine Rounds" and scoring on the empathy scale? This study surveyed incoming, treatment-naïve, third-year medical students and utilized a validated empathy scale for medical students, the Jefferson Scale of Empathy – Student version, in order to assess changes in empathy over a 6-month and 12-month period. Students were monitored for number-of-times attended to "The Art of Medicine Rounds." Preliminary results are pending. In conclusion, empathy is a vital component of a medical student's professional development. Understanding that significant declines occur during the third-year of medical school can lead to timely interventions during this critical time point. Although integrating humanities into the curriculum has been shown to generally improve empathy in medical students, almost no research has specifically targeted and evaluated its use in third-year students.

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Project Length: Short Prior Research Experience: Yes

Source of Funding:

Faculty Advisor: Brent A. Ponce, MD Abstract Approved By Advisor: Yes

Co-Authors: Brent A. Ponce, MD (1) Mariano E. Menendez (1)

Title: Risk Factors for Pulmonary Embolism Following Shoulder Arthroplasty

Pulmonary emboli (PE) are associated with significant morbidity and mortality in arthroplasty patients; therefore, it is important to establish predictors for perioperative (PE) following shoulder arthroplasty. We used the Nationwide Inpatient Sample to gather a sample of 422,372 patients who underwent shoulder arthroplasty between 2002 and 2011. This population was divided into two cohorts based on those who experienced perioperative PE (0.25%) and those who did not. We then accounted for confounding patient characteristics and comorbidities to establish the top 4 independent predictors for PE following shoulder arthroplasty: primary diagnosis of proximal humerus fracture, deficiency anemia, congestive heart failure, and chronic lung disease. Other pertinent risk factors include: age, subsequent days of post-operative care, undergoing TSA rather than HA, fluid and electrolyte abnormalities, and obesity. It is important for patients and surgeons to understand the risk factors reported here because they may be useful in deterring morbidity and mortality from surgical complications.

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Project Length:

Prior Research Experience:

Source of Funding:

Faculty Advisor:

Abstract Approved By Advisor:

Co-Authors:

Title: Individual differences in novelty-seeking and emotional reactivity: noradrenergic activation in the brainstem following forced-swim stress

Purpose: Mood disorders arise from a complex interaction between genetics and environmental factors. Outbread rats can be classified as either "High Responders" (HR) or "Low Responders" (LR) based on their level of activity in a novel environment, a trait that is related to emotional reactivity. We selectively bred each type of rat, establishing strains of rats that preserved their behavioral features. Using this HR/LR model, we sought to examine neurochemistry that may correlate with either vulnerability or resistance to the development of anxiety- and depression-like behaviors. The present study tested the hypothesis that activation of noradrenergic circuits in the hindbrain/brainstem would be accountable for differences in depression-like behavior, tested by the forced swim test (FST).

Methods: Animals were exposed to FST protocol, where greater immobility is interpreted as depression-like behavior and an indicator of behavioral despair. Subjects were sacrificed 1.5 hours following FST, and hindbrain tissue was collected and immunohistochemically stained for c-Fos protein, a marker for neuronal activation, and tyrosine hydroxylase (TH), the rate-limiting enzyme required for noradrenaline synthesis.

Results: As previously reported, LR animals exhibited high immobility during FST. LR rats had a significantly higher percentage of c-Fos expression in noradrenergic A2 neurons ($p=0.0329$) compared to HR rats. However, these differences in activation did not individually correlate with the behavioral differences observed during FST.

Conclusions: These findings confirm that LR animals are more susceptible to stress-induced depressive behaviors compared to HR animals. In addition, our results suggest that HR and LR rats possess distinct noradrenergic circuits which may be responsible for their behavioral differences. While the observed differences in A2 activation are not significantly correlated with FST behavior, other behavioral measures related to emotional reactivity may be influenced by these differences.