Washington University in St. Louis School of Medicine
Ninth Annual Research Training Symposium & Poster Session
October 21, 2014
Farrell Learning and Teaching Center

12:30 – 12:45 pm Connor Auditorium
Welcome and Opening Remarks

Bradley Evanoff, MD, MPH
Richard A. and Elizabeth Henby Sutter Professor of Occupational, Industrial and Environmental Medicine
Director, Division of General Medical Sciences
Director, Institute of Clinical and Translational Sciences
Assistant Dean for Clinical and Translational Research
Washington University in St. Louis School of Medicine

12:45 – 1:45 pm Connor Auditorium
Keynote Address

Susan S. Huang, MD, MPH
Associate Professor, Infectious Disease
Medical Director, Epidemiology and Infection Prevention
University of California, Irvine

1:45 – 3:00 pm Connor Auditorium
Oral Presentations

1:45 – 2:00 pm	Bradley Fritz, BS
2:00 – 2:15 pm	Anne Drewry, MD
2:15 – 2:30 pm	Kerry Bommarito, PhD, MPH
2:30 – 2:45 pm	Brendan Lucey, MD
2:45 – 3:00 pm	Carlos Santos, MD

3:00 – 5:00 pm FLTC Atrium & Hearth
Poster Presentations

3:00 – 4:00 pm	Poster Session I
4:00 – 5:00 pm	Poster Session II

This symposium is made possible by the Clinical Research Training Center (CRTC), a component of the Washington University Institute of Clinical and Translational Sciences (ICTS). The ICTS is part of a national consortium of medical research institutions, funded through the Clinical and Translational Science Awards (CTSA) that includes sixty medical research institutions in thirty states and the District of Columbia, working together to improve the way biomedical research is conducted across the country. The CTSA consortium shares a common vision to reduce the time it takes for laboratory discoveries to become treatments for patients, and to engage communities in clinical research efforts. It is also fulfilling the critical need to train the next generation of clinical researchers. The CTSA initiative is led by the National Center for Advancing Translational Sciences (NCATS) at the National Institutes of Health. The CRTC is supported by NCATS Grant Numbers UL1 TR000448, KL2 TR000450, and TL1 TR000449, Washington University in St. Louis School of Medicine, and Barnes-Jewish Hospital Foundation.

This symposium & poster session is co-sponsored by the Office of Medical Student Research, Washington University in St. Louis School of Medicine.

We gratefully acknowledge the support of Dr. Larry J. Shapiro, Executive Vice Chancellor for Medical Affairs and Dean, Washington University in St. Louis School of Medicine.

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Programs Represented

AHBR Master of Science in Applied Health Behavior Research
The Master of Science in Applied Health Behavior Research is a 33-credit multidisciplinary, applied skills-based program designed primarily for working professionals, junior faculty and training award recipients pursuing studies on a part-time basis. The AHBR Program focuses on developing the applied skills needed to manage health behavior and research program in academic, clinical, and community settings.
Program Director: Anjali Deshpande, PhD
Website: http://crtc.wustl.edu

Alex's Lemonade Stand Foundation Pediatric Oncology Student Training (POST) Program
Alex's Lemonade Stand Foundation (ALSF) is dedicated to funding pediatric oncology researchers at critical points in their careers. The Pediatric Oncology Student Training (POST) Program is designed for graduate and medical students who have an interest in pediatric oncology research and would like to experience the field first-hand. Students train with a pediatric oncology research mentor. Students may join a research project underway in a mentor's lab or begin an original investigation with the mentor.
Website: http://www.alexslemonade.org/grants/post

American Academy of Child and Adolescent Psychiatry Summer Medical Student Fellowship
The AACAP Summer Medical Student Fellowships offer a chance for medical students to explore a career in child and adolescent psychiatry, gain valuable work experience, and meet leaders in the child and adolescent psychiatry field. The fellowship opportunity provides up to $3,500 for 12 weeks of clinical or research training under a child and adolescent psychiatrist mentor. Participants are required to attend the AACAP Annual Meeting in San Diego, CA, October 20 - October 25, 2014. (Complimentary registration and travel reimbursement for the Annual Meeting are included in addition to the fellowship stipend.)
Website: http://www.aacap.org/AACAP/Awards/Medical_Students_Awards/Summer_Medical_Student_Fellowships.aspx

Center for Health Policy
The Washington University Center for Health Policy conducts research in an effort to improve the future health of Americans by affecting health policy on the federal, regional, state and local levels.
Program Director: William Peck, MD
Website: http://healthpolicy.wustl.edu

Child Neurology Foundation (CNF) Swaiman Medical Scholarship
The CNF Swaiman Medical Scholarship awards 1st- and 2nd-year U.S. and Canadian medical students $3,500 for clinical research in child neurology. Each researcher has a child neurologist mentor who oversees their work throughout the summer. Candidates for the award are asked to submit a two-page application accompanied by a letter from a child neurologist agreeing to be their mentor. These applications are scored by child neurologist members of the CNF Scholarship Selection Committee.
Website: http://www.childneurologyfoundation.org/swaiman-scholarships

Clinical Research Training Center (CRTC) KL2 Career Development Awards
The KL2 Career Development Awards Program at Washington University in St. Louis provides high-quality, multidisciplinary training in clinical and translational research to promote the career development of future clinical investigators. The program is comprised of postdoctoral scholars and junior faculty committed to multidisciplinary clinical research. KL2 Career Development Awards provide financial support and benefits that allow scholars to focus on mentored, multidisciplinary research, supplemented by applicable coursework.
Program Director: Victoria Fraser, MD
Website: http://crtc.wustl.edu

Clinical Research Training Center (CRTC) K12 Paul Calabresi Career Development Awards for Clinical Oncology
The K12 Career Development Awards for Clinical Oncology at Washington University in St. Louis provides high-quality, multidisciplinary training in clinical and translational research to promote career development for future clinical investigators. The goal of the K12 Paul Calabresi Career Development Awards for Clinical Oncology is to train a new generation of highly skilled investigators with specialized expertise who will be well prepared to lead cancer research. The K12 Clinical Oncology program supports the development of postdoctoral scholars and junior faculty through patient oriented cancer research training, curricula, and mentored projects.
Program Director: Ramaswamy Govindan, MD
Website: http://crtc.wustl.edu

Clinical Research Training Center (CRTC) Master of Science in Clinical Investigation (MSCI) Degree Program
The MSCI Degree Program at Washington University is designed as a one to three year full- or part-time degree program for young investigators committed to pursuing academic careers in clinical research. The unique program combines didactic coursework with mentored research and career development opportunities and provides students with the knowledge and tools to excel in the areas of clinical investigation most relevant to their careers.
Program Director: David K. Warren, MD, MPH
Website: http://crtc.wustl.edu

Clinical Research Training Center (CRTC) Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)
The CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI) provides multidisciplinary clinical and translational research training to promote the career development of junior faculty and postdoctoral fellows by helping them become clinical and translational researchers. Through didactic coursework, structured mentorship, and interactions with a diverse peer group of trainees, the MTPCI enables Scholars to learn how to: develop effective research projects, utilize human subjects in clinical trials, collect, analyze and summarize data, apply epidemiologic principles and tools, consider relevant ethical and legal issues, write grants and manuscripts, and compete for research funding.
Program Director: Jane Garbutt, MBChB
Website: http://crtc.wustl.edu

Clinical Research Training Center (CRTC) TL1 Predoctoral Interdisciplinary Clinical Research Training Program
The CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program provides career development for medical and allied healthcare students through didactic coursework, mentored training, work-in-progress research discussions, journal clubs, and conferences. This program supports a select group of trainees as they embark on patient-oriented research careers by teaching them how to: design and conduct clinical research, analyze data, consider relevant ethical and legal issues, write manuscripts and grants, develop and present scientific posters, and compete for research funding.
Program Director: Jay Piccirillo, MD, FACS
Website: http://crtc.wustl.edu

Dames Fellowship
The Dames Fellowship supports a medical student to conduct summer research in cell biology and physiology.
Program Director: Koong-Nah Chung, PhD

David F. Silbert Summer Fellowship
In his memory, the David F. Silbert Summer Fellowship was set up to support short-term research internships for medical, graduate, or other students interested in his area of research. David's research focused on genetic biochemical and/or biophysical approaches to the study of specific membrane lipids in signal transduction pathways and in the assembly and function of eukaryotic cell membranes. Since his death from cancer in 1997, a number of biophysical techniques have been developed that address these issues. These techniques include, but are not limited to, state-of-the-art fluorescence methods, structural determination using NMR or x-ray methods and computational approaches. All these techniques are directed towards understanding the role of macromolecular interactions in cellular function. It is now clear that membrane lipids and membrane proteins are functionally involved in all aspects of the regulation of cellular processes and that these processes must be studied at the level of macromolecular function.
Program Director: Linda Pike, PhD
Website: http://biochem.wustl.edu/resources/archives/awards-fellowships/silbert-fellowship/2012-david-f-silbert-summer-fellowship-research

Dean's Fellowship
This program is designed to provide medical students with a hands-on research experience. This can be a first-time experience or a project related or unrelated to research done as an undergraduate. Excellent mentors from a broad range of basic and clinical sciences are available. A Washington University Summer Research Fellowship can provide a strong background for application to the MA/MD and MD/PhD (MSTP) degree programs, can lead to abstracts at meetings and to publications, and can be important for applications for competitive residencies.
Program Director: Koong-Nah Chung, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

DeNardo Education and Research Foundation Grant
The purpose of the DeNardo Education and Research Foundation is to support education and research in the health sciences, broadly defined, with preference for activities that relate to the field of medicine. DeNardo Summer Research Scholars will be engaged in basic and clinical research during the summer following their first year of medical school. The program gives medical students hands-on laboratory research experience with outstanding investigators and helps prepare them for careers in academic medicine.
Program Director: Koong-Nah Chung, PhD

Forum for International Health and Tropical Medicine (FIHTM)
The Forum for International Health and Tropical Medicine (FIHTM) brings together students and physicians at Washington University who are interested in international health. FIHTM aims to promote understanding of global health by enabling medical students to experience firsthand its locales, modes of delivery, disparities, and cultural manifestations. FIHTM organizes the Global Health Symposium each spring, as well as regular discussion lunch meetings with students and faculty. In addition, the group coordinates Spring Break community service trips for the first and second year medical classes. FIHTM offers financial and logistical assistance to students who wish to gain healthcare experience abroad and helps interested students find mentors within the university.
Program Directors: Kathy Diemer, MD; Gary Weil, MD
Website: http://fihtm.wustl.edu

Foundation for Barnes-Jewish Hospital Student & Faculty Award
The mission of the Foundation for Barnes-Jewish Hospital Student & Faculty Award is to provide financial support to help the hospital fulfill its purpose. Funds are used to support medical research, patient care, education, and community service projects that otherwise would not be available to the hospital.
Website: http://www.barnesjewish.org/?id=6296&sid=4

Howard Hughes Medical Institute Summer Medical Fellows Program (HHMI)
The Summer Medical Fellows Program is primarily aimed at students who later intend to apply for the year-long Medical Fellows Program. Summer Medical Fellows spend 8 to 10 weeks doing full-time research with an HHMI investigator, early career scientist, HHMI professor, or Janelia researcher. Fellows are exposed to high-quality science, have a chance to increase their scientific knowledge and research skills, and interact with world-class investigators in a rich training environment. Fellows can gain insight into a career as a medical scientist and determine if they would like to continue their research training in a year-long program. This program is for medical, dental, and veterinary students attending schools located in the United States. Up to 20 fellowships are awarded annually.
Program Director: Melanie Daubs
Website: http://www.hhmi.org/programs/medical-research-fellows-program/summer-program

Mallinckrodt Institute of Radiology (MIR)
The Mallinckrodt Institute of Radiology Summer Research Program offers undergraduate and medical students an opportunity to conduct research in the following aspects of radiological sciences research: Magnetics resonance imaging, Magnetic resonance spectroscopy, Positron emission tomography, X-ray computed tomography, Contrast agent development, Diagnostic radiology, Molecular imaging, Nuclear medicine, Radiopharmaceutical development, Neuroscience imaging, Cardiovascular imaging, Optical imaging, and Ultrasound.
Program Director: Suzanne Lapi, MD
Website: http://www.mir.wustl.edu/education/internal.asp?NavID=95

MA/MD
Created in 1982, the Master's Degree Program allows medical students to participate in cutting-edge biomedical or clinical research and earn a Master of Arts degree in preparation for a career in academic medicine. The program is highly flexible and is intended not only for those who have previous research experience, but also for students who are novices in research. The objective is to provide an individualized research experience in an excellent environment, and students are encouraged to explore a wide range of research possibilities.
Program Director: Deborah Rubin, MD
Website: http://www.dbbs.wustl.edu/divprograms/mamd/Pages/mamd.aspx

Master of Population Health Sciences (MPHS)
The Master of Population Health Sciences (MPHS) Degree Program equips clinicians and clinical doctorates with the advanced research methods skills needed to design clinical outcomes research, interpret results and apply findings to improve clinical effectiveness. MPHS students establish a wide network of mentors and collaborators by interacting with Washington University medical and public health faculty who are renowned for their teaching, patient care and ongoing cutting-edge research around the world. With no research thesis requirement, the degree can be obtained in as few as ten months, which allows students to easily integrate the training into a clinical career, including during the medical school, residency and fellowship years. The Washington University in St. Louis School of Medicine MPHS Program is one of a few in the country and one of the only in the Midwest that offers population health-based research methods training for clinicians.
Program Director: Graham Colditz, MD, DrPH
Website: http://www.mphs.wustl.edu/

MD5
The One-Year Research without Degree Program (MD5) is available to all Washington University medical students. Students who wish to take advantage of this program should select a research mentor at Washington University and obtain permission to work with him/her for one year. The arrangement should then be approved by the mentor and by the associate dean for medical student research through the application process.
Program Director: Koong-Nah Chung, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

Memorial Sloan Kettering Summer Internship Program
An organization with the size and scope of Memorial Sloan Kettering offers a wide variety of opportunities for learning and growth. Several programs have been created to provide meaningful experiences that will help build the careers of medical students.
Website: http://careers.mskcc.org/college-recruiting/internships

Movement Science Program (MSP)
The Program is an integral member of one of the world's largest academic biomedical research institutions; collaboration occurs with nearly every department in the School of Medicine, as well as with colleagues in biomedical engineering, psychology, and biology. Researchers lead studies in a comprehensive array of topics from the basic physiological mechanisms of tissue injury to studying health interventions at the community level. Investigations involve subjects across the life span. The MSP is supported by NIH training grant T32HD007434.
Program Director: Michael J Mueller, PhD, PT, FAPTA
Website: https://physicaltherapy.wustl.edu/Education/DoctoralEducation/PhDinMovementScience

NIDA T32 Training Program in Epidemiology, Services and Prevention Research
The NIDA T32 pre- and post-doctoral Research Training Program in Drug Abuse Epidemiology, Services and Prevention (DAESP) provides outstanding training for fellows in a range of sub-specialties including epidemiology, biostatistics, psychiatric and behavioral health comorbidity, community implementation science, concerning public health aspects of addiction and addictive behaviors. The Department of Psychiatry also offers biomedical science mentoring in areas of genetics, basic and cognitive neuroscience, psychophysiology and imaging for those public health researchers who wish to integrate biomedical research tools with their research specialty.
Program Director: Rumi Kato Price, MPE
Website: http://www.psychiatry.wustl.edu

Office of the Provost, Diversity & Inclusion Grant
The Washington University, Office of the Provost, Diversity & Inclusion Grant helps train 5 Meharry Medical College students in the Washington University in St. Louis School of Medicine's (WUSM) Summer Research Program each summer. The benefits of the partnership include: 1) Exposing the Meharry medical students to cutting-edge science at WUSM; 2) Benefiting our WUSM faculty's research; 3) Enhancing the culture of diversity at WUSM; and 4) Increasing the pipeline of under-represented medical students into our residency programs.
Program Director: Koong-Nah Chung, PhD
Website: http://provost.wustl.edu/diversity/diversity-inclusion-grants

Otolaryngology NIH T32 Physician Scientist Program (PSP)
This training program provides a pathway directing medically trained individuals toward a successful research career in academic otolaryngology. This research experience is offered at two levels. At the first level, medical students are selected to participate in this program for approximately three months during the summer. Mentored research projects for medical students are conducted by selected trainees to stimulate a general interest in research and specific interest in otolaryngological research. At the second level, residents accepted into the 7-year "Advanced Physician Scholars Program" by a special residency match mechanism perform mentored research in depth, in a contiguous two-year period, free of clinical responsibilities. Funding for this program is provided by a National Institutes of Health (NIH)-National Institute on Deafness and Other Communication Disorders (NIDCD), Ruth L. Kirschstein National Research Service Award (NRSA) Institutional Research Training Grant (T32) entitled "Development of Clinician/Researchers in Academic ENT," 5T32DC000022-22.
Program Director: Jay Piccirillo, MD, FACS
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

Rehabilitation and Participation Science (RAPS) Doctoral Program
The mission of the Rehabilitation and Participation Science PhD program is to develop scientists in the areas of rehabilitation and participation science to improve the human condition. We employ an interdisciplinary approach including the fields of neuroscience, engineering, occupational science, psychology, and environmental science. Our graduates will generate new knowledge to minimize limitations of persons with disability and chronic health conditions and increase their ability to participate in family, work and community life. They will address questions about the relationships among occupation, activity, participation, and health; or examine how bio-behavioral or environmental mechanisms such as sensory, motor, or cognitive function, social support or technology enable daily life performance.
Program Director: Carolyn Baum, PhD, OTR/L, FAOTA

Siteman Cancer Center Leah Menshouse Springer Summer Student Program
The Leah Menshouse Springer Summer Student Program at the Siteman Cancer Center provides opportunities for undergraduate, premed and medical students enrolled at Washington University or other accredited universities to work on cancer research projects during the summer. Opportunities range from basic laboratory research to clinical research to prevention/control and population research.
Program Coordinator: Megan Monahan
Website: http://www.siteman.wustl.edu/contentpage.aspx?id=254

Summer Medical Education Research Fellowship (SMERF)
The Summer Medical Education Research Fellowship supports medical students to conduct summer research in medical education.
Program Director: Koong-Nah Chung, PhD

Summer Research Program in Global Health
The 2014 Summer Research Program in Global Health (SRPGH), from the Global Health Center at the Institute for Public Health offered eight students (from undergraduates to medical students) the opportunity to work closely with outstanding faculty mentors focusing on global health. The goal of the program was to expose young investigators to research in a lab or field-based setting and further their interest in global health. The program included regular seminars and opportunities to establish a career-building network.
Contact: Jacaranda Van Rheenen, PhD
Website: http://publichealth.wustl.edu/news/newsroom/Pages/SRPGH-2014-Summary.aspx

T32 NIH Cardiopulmonary Surgery Training Grant
This program has been continuously funded since 1994. It is anticipated that in the next ten years there will be a shortage of cardiothoracic surgeons. To meet the future needs it is essential that an increased number of academic surgeons are trained. An essential element is training these individuals to be independent investigators. Therefore, the overall aims of the program are to provide a stimulating environment and research training for academic cardiothoracic surgeons. The specific goals are to: 1) attract the most innovative, inquisitive, diverse, and motivated candidates; 2) provide them with the highest possible level of training in the basic science of cardiovascular and pulmonary physiology and pathology; and 3) foster critical thought to prepare the trainees for an independent academic career and leadership role. A strength of the program is its interdisciplinary approach to scientific problem solving in which clinically recognized problems are studied in animal models of human disease at the integrative, cellular, and molecular levels, which can then be translated to clinical solutions. A key component of this training program is the faculty, which includes 26 faculty members with over $22 million of NIH support and extensive experience in research mentoring. They represent four separate departments with a history of collaborative research. Over the last 25 years, the program has trained 72 postdoctoral fellows. Of these, 46 are in academic medicine, six are division chiefs or department chairpersons, and one is a principal investigator at the NIH.
Program Director: Ralph J Damiano, Jr, MD

T32 NIH NIDDK Diabetes Training Grant
The goal of the program is to expose medical students to career opportunities in basic or clinical research related to diabetes and related metabolic diseases.
Program Director: Clay Semenkovich, MD
Website: http://medicalstudentdiabetesresearch.org/

T35 NIH NHLBI Training Grant
This program is designed to provide medical students with a hands-on research experience. This can be a first-time experience or a project related or unrelated to research done as an undergraduate. Excellent mentors from a broad range of basic and clinical sciences are available in research areas related to heart, lung and blood diseases and disorders. A Washington University Summer Research Fellowship can provide a strong background for application to the MA/MD and MD/PhD (MSTP) degree programs, can lead to abstracts at meetings and to publications, and can be important for applications for competitive residencies.
Program Director: Koong-Nah Chung, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

T35 NIH NIDDK Short-Term Training Program
The goal of the trans-NIDDK Short-Term Training Program for Medical Students is to expose medical students to career opportunities in basic or clinical research related to diabetes, obesity, endocrine disorders, metabolic diseases, nutritional disorders, digestive diseases, liver diseases, kidney diseases, urologic diseases and hematological disorders.
Program Director: Thomas J Baranski, MD, PhD
Website: http://medadmissions.wustl.edu/unlimitedopp/studentresearch/Pages/StudentResearch.aspx

Abstracts for Oral Presentations

In the Order Presented

Fritz, Bradley
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Anesthesiology
Division: INQUIRI
Mentor: Michael Avidan, MBBCh

Intraoperative electroencephalogram suppression predicts postoperative delirium

Fritz BA; Kalarickal P; Maybrier HR; Muench MR; Dearth D; Chen Y; Escallier KE; Ben Abdallah A; Avidan MS

Introduction: Postoperative delirium is a common complication associated with longer hospital stays, increased morbidity and mortality, and higher healthcare expenditures. Intraoperative electroencephalogram slowing has previously been associated with postoperative delirium, but the relationship between intraoperative electroencephalogram suppression and postoperative delirium has not been investigated.
Methods: In this observational cohort study, 775 adult patients receiving general anesthesia with planned intensive care unit admission were included. Duration of intraoperative electroencephalogram suppression was recorded from a frontal electroencephalograph channel (FP1 to F7). Delirium was assessed twice daily on postoperative days 1 through 5 using the Confusion Assessment Method for the Intensive Care Unit. Quality of life was reported 30 days after surgery using the VR-12 survey.
Results: Postoperative delirium was observed in 175 (26.5%) of 661 patients assessed. When comparing patients with no electroencephalogram suppression to patients divided into quartiles based on duration of electroencephalogram suppression, patients with more suppression were more likely to experience delirium ($\chi 2(4) = 25$, $p < 0.01$). This effect remained significant after adjusting for potential confounders (odds ratio 1.05 [95% CI 1.01 to 1.09] per 5-minute increase in suppression). Electroencephalogram suppression was not associated with decreased quality of life. Predictors of electroencephalogram suppression included higher end-tidal volatile anesthetic concentration and lower intraoperative opioid dose.
Conclusions: Electroencephalogram suppression is an independent risk factor for postoperative delirium. Future studies should investigate whether anesthesia titration to minimize electroencephalogram suppression decreases the incidence of postoperative delirium.

Drewry, Anne, MD
CRTC Postdoctoral MTPCI; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Anesthesiology
Division: Critical Care Medicine
Mentors: Richard Hotchkiss, MD; Thomas Bailey, MD; Allyson Zazulia, MD

The presence of hypothermia within 24 hours of sepsis diagnosis predicts persistent lymphopenia

Drewry AM; Fuller BM; Skrupky LP; Hotchkiss RS

Introduction: The etiology of hypothermia in septic patients is unknown, and there is limited data to explain why these patients have worse outcomes. One theory is that failure to mount a fever in response to infection may be an early clinical sign of sepsis-induced immunosuppression. Sepsis-induced immunosuppression is associated with apoptotic loss of lymphocytes, and persistent lymphopenia leads to increased risk of mortality and nosocomial infection. The aim of this study was to examine the relationship between hypothermia and persistent lymphopenia in septic patients. We hypothesized that patients who presented with hypothermia within 24 hours of sepsis diagnosis would be more likely to develop persistent lymphopenia than non-hypothermic patients.
Methods: Single-center retrospective cohort study conducted between January 1, 2010 and July 31, 2012. All patients admitted to the hospital with documented bacteremia were eligible for inclusion. Exclusion criteria included: immunological disease or treatment with immunosuppressant medication within 6 months of hospitalization. Patients were divided into two cohorts, hypothermic or non-hypothermic, based on their lowest body temperature within 24 hours of sepsis diagnosis. Hypothermia was defined as a temperature less than 36.0°C. Leukocyte counts were recorded during the first four days following sepsis diagnosis. Persistent lymphopenia was defined as an absolute lymphocyte count less than 1.2 cells/µl x 103 present on the fourth day after diagnosis.
Results: Of the 445 septic patients included, 64 (14.4%) developed hypothermia within 24 hours of sepsis diagnosis. Hypothermia was a significant independent predictor of persistent lymphopenia (adjusted OR 2.70 [95% CI 1.10, 6.60], p =.03) after accounting for age, disease severity, comorbidities, source of bacteremia, and type of organism. Compared to non-hypothermic patients, hypothermic patients had higher 28-day (50.0% vs. 24.9%, p < .001) and 1-year mortality (60.9% vs. 41.5%, p < .001).
Conclusions: Hypothermia is associated with higher mortality and an increased risk of persistent lymphopenia in septic patients, and it may be an early clinical predictor of sepsis-induced immunosuppression.

Bommarito, Kerry, PhD, MPH
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Internal Medicine
Division: Infectious Diseases
Mentors: Margaret Olsen, PhD, MPH; Jeffery Peipert, MD, MPH, MHA
Readmissions with endometritis in California 2004-2010
Bommarito KM; Fraser VJ; Olsen MA
Introduction: Endometritis (EMM) is the most common maternal infectious postpartum complication. Previous studies focused only on the delivery admission may have missed EMM diagnosed after discharge.
Methods: We used the 2004-2010 Healthcare Cost and Utilization Project California State Inpatient Database to determine the incidence of endometritis and 6-week readmission rates in women following vaginal (VAG) and cesarean (CSEC) delivery. Risk factors for EMM were identified using ICD-9-CM diagnosis and procedure codes and demographic variables. Logistic mixed effects models were performed, stratified by type of delivery.
Results: A total of 2,305,110 deliveries (32.2% CSEC, 67.7% VAG) were identified. 0.63% of CSEC deliveries were coded for EMM during the delivery hospitalization and 0.24% were coded for EMM during a readmission within 6 weeks of the delivery discharge. 0.15% of VAG deliveries were coded for EMM during the delivery hospitalization and 0.15% were coded for EMM during a readmission within 6 weeks of the delivery discharge. Mean days to readmission with EMM were 7.6 in VAG and 7.0 in CSEC patients. The median total costs of readmission(s) with EMM were $4749 in VAG and $6185 in CSEC patients. CSEC patients were 2.9 (CI, 2.82-3.04) times more likely to have EMM than VAG delivery patients. When controlling for covariates, chorioamnionitis was associated with increased risk of EMM after VAG (RR=3.42; CI, 3.08-3.81) and CSEC (RR=1.74; CI,1.61-1.89). Group B streptococcus was associated with decreased risk of EMM after VAG (RR=0.77; CI, 0.67-0.79) and CSEC (RR=0.74; CI, 0.68-0.80) deliveries.
Conclusions: By including readmissions, the overall incidence of EMM after VAG doubled to 0.30% and after CSEC increased from 0.63% to 0.87%. The risk of EMM was higher in patients with chorioamnionitis after VAG than after CSEC delivery. Group B was protective in both CSEC and VAG, likely due to prophylactic antibiotic utilization.

Lucey, Brendan, MD
CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Neurology
Division: Sleep Medicine
Mentors: Randall J Bateman, MD; Paul J Shaw, PhD
Relationship between Aβ42 kinetics, age, and amyloid on the amplitude of the Aβ42 diurnal pattern
Lucey BP; Mawuenyega KG; Patterson BW; Elbert DL; Ovod V; Kasten T; Jasielec MS; Xiong C; Morris JC; Bateman RJ
Introduction: Recent studies have found that the concentration of amyloid-β (Aβ) fluctuates with the sleep-wake cycle and the amplitude of this diurnal pattern is attenuated with age and amyloid deposition. The relationship of Aβ kinetics to the Aβ diurnal pattern has not been well understood.
Methods: To determine the relationship between Aβ kinetics, age, amyloid, and the amplitude of the Aβ diurnal pattern in humans, we measured Aβ concentrations and kinetics in adults 60-90 years old. Amyloid status was assigned based on cerebrospinal fluid (CSF) Aβ42:40 concentration ratio (amyloid+ = Aβ42:40 < 0.12). Cosinor analysis of each participants' serial CSF Aβ concentrations generated an mesor, amplitude, and acrophase for each participant. The sleep-wake cycle was not monitored.
Results: We found a significant association between age and Aβ42 amplitude (p=0.009), with amyloid- individuals exhibiting a significant decrease between 60-80 years (p=0.0026) but not amyloid+. In addition, the predicted average amplitude level was significantly higher in amyloid- individuals relative to amyloid+ individuals between the ages of 65 and 75, testing by 5 years (all p<0.01). We also found that increased Aβ42 fractional turnover rate (FTR) and age were independently associated with decreased Aβ42 amplitude. However, Aβ42 FTR was no longer significantly associated with Aβ42 amplitude in a multivariable linear regression model with age, Aβ42 FTR, and amyloid-/+ status, along with an interaction between amyloid status and age.
Conclusions: Sleep is hypothesized to be the primary driver of the Aβ diurnal pattern. Aging is associated with changes in sleep that may mediate effects on the Aβ diurnal pattern. Decline in Aβ42 amplitude due to amyloid is likely due to altered Aβ42 kinetics. This study suggests the previously reported effects of age and amyloid on Aβ42 amplitude are at least partially dependent on each other due to interaction between age and amyloid. Future studies will be needed to explore if there are age-related changes in Aβ42 kinetics that also affect the diurnal pattern.

Santos, Carlos, MD
CRTC KL2 Career Development Awards; MPHS Degree Program
Washington University in St. Louis
Department: Internal Medicine
Division: Infectious Diseases
Mentors: Margaret Olsen, PhD, MPH; Daniel Brennan, MD

Incidence, risk factors and outcomes of delayed-onset Cytomegalovirus Disease in a large retrospective cohort of lung transplant recipients

Santos CAQ; Brennan DC; Yusen RD; Olsen MA

Introduction: Cytomegalovirus (CMV) replication and disease commonly occur in lung transplant recipients after stopping anti-CMV prophylaxis. The epidemiology of CMV disease is not well-studied given difficulties in assembling representative study populations with prolonged follow-up. We hypothesized that delayed-onset CMV disease (> 100 days post-transplant) occurs more commonly than early-onset CMV disease in lung transplant recipients, and is associated with an increased risk of death.

Methods: We assembled a large cohort of lung transplant recipients using 2004 to 2010 ICD-9-CM billing data from 3 Agency for Healthcare Research and Quality (AHRQ) State Inpatient Databases (SID), and identified demographics, comorbidities, CMV disease coded during hospital readmission and inpatient death. We used Cox proportional hazard multivariate analyses to assess for an independent association between delayed-onset CMV disease and death.

Results: In the cohort of 1,528 lung transplant recipients from 12 transplant centers, delayed-onset CMV disease occurred in 13.7% (n=210) and early-onset CMV disease occurred in 3.3% (n=51). Delayed-onset CMV pneumonitis was associated with inpatient death > 100 days post-transplant (aHR 1.6, 95% CI 1.1-2.5), after adjusting for transplant failure/rejection (aHR 2.5, 95% CI 1.5-4.1), bacterial pneumonia (aHR 2.8, 95% CI 2.0-3.9), viral pneumonia (aHR 1.5, 95% CI 1.1-2.1), fungal pneumonia (aHR 1.8, 95% CI 1.3-2.3), single lung transplant (aHR 1.3, 95% CI 1.0-1.7) and idiopathic pulmonary fibrosis (aHR 1.4, 95% CI 1.0-1.8).

Conclusions: Delayed-onset CMV disease occurs more commonly than early-onset CMV disease among lung transplant recipients. These results suggest that delayed-onset CMV pneumonitis is independently associated with an increased risk of death. Future studies should focus on whether prolonged anti-CMV prophylaxis can lead to an enduring decrease in CMV disease even after prophylaxis is discontinued, and whether such preventive strategies will lead to a decreased risk of allograft failure and improved long-term survival.

Abstracts for Poster Session

Alphabetically by Training Program and Author

AHBR Master of Science in Applied Health Behavior Research

088 **Kinghorn, Anna, MS**

AHBR Master of Science in Applied Health Behavior Research
Washington University in St. Louis
Department: Internal Medicine
Division: General Medical Sciences
Mentor: Jaime Strickland, MA

Workplace influences on eating and physical activity: a qualitative study of low-wage workers

Kinghorn AM; Strickland JR; Schenk JB; Evanoff BA

Introduction: The number of overweight and obese adults continues to grow in the United States. While many employers offer wellness programs, they are not always available or accessible to all workers, particularly low-wage workers. The purpose of this study was to examine workplace determinants of obesity and participation in workplace wellness programs among hospital and retail workers in the St. Louis area.

Methods: Focus groups were conducted among low-wage employees from two partner organizations: a healthcare employer and a union representing retail workers. The groups discussed worksite factors that support or constrain healthy eating and physical activity, as well as barriers to participating in workplace wellness programs. The focus groups were transcribed and coded using Nvivo 10 software to identify main themes that impact obesogenic behaviors.

Results: Nine focus groups were conducted between the two organizations. Workers identified job characteristics that affect their eating habits and participation in physical activity, including the physical and mental demands of their work, stress, the physical work environment, and work organization. For example, irregular work schedules inhibited healthy exercise and eating routines, and food offered to employees at meetings or as incentives was usually unhealthy. Company programs and priorities were also identified as having an impact on worker behaviors, although this varied by worksite. Retail workers reported few available programs, while many hospital workers were unaware of existing programs. Workers noted barriers to participation in available programs, including cost, schedules, and home responsibilities.

Conclusions: Our study identifies opportunities for obesity interventions at the worksite that go beyond traditional approaches. Although employers typically focus on workers' personal choices as determinants of health behaviors, modifying the physical and social work environment to support healthy eating and physical activity may encourage workers to adopt healthier behaviors. Better tailoring of existing worksite wellness offerings are needed to meet the unique needs of low-wage workers.

Alex's Lemonade Stand Foundation POST Program

131 **Bacorn, Colin**

Alex's Lemonade Stand Foundation POST Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Hematology and Oncology
Mentor: Todd Druley, MD, PhD

Improving minimal residual disease detection by error-corrected sequencing

Bacorn CT; Young AL; Druley TE

Introduction: Despite its low prevalence, acute myeloid leukemia (AML) is responsible for up to half of pediatric leukemia deaths. Minimal residual disease (MRD) is a metric used to direct treatment and determine prognosis. Error corrected sequencing (ECS) has several advantages over current MRD because of its ability to detect single nucleotide variations and its high sensitivity. ECS's sensitivity may be limited by PCR amplification errors introduced in sample preparation. Additionally, ECS's sensitivity for G→T substitutions is lower than its sensitivity for other substitution classes because oxidative DNA damage preferentially causes G→T substitutions which mask true mutations. Protecting samples with antioxidants during DNA extraction can increase ECS's ability to detect true G→T mutations.

Methods: pUC19 plasmid was purified from E. coli using the QiaPrep Miniprep kit. A region was amplified from the plasmid using 10, 20, 30 or 40 cycles of PCR. To determine the effect of oxidative damage on ECS error, a separate experiment was conducted where cells were lysed in the presence of 8 mM histidine, 3 uM catalase or both reagents in combination. A "no PCR" control was obtained by restriction digest of the same plasmid region; an unmodified lysis reaction was used to obtain this sample. All samples were prepared using the ECS protocol and sequenced with Illumina's bridge amplification platform.

Results: The error rate was on the order of 10-4 to 10-6 errors per base, with significant variation among the substitution classes. There is an initial cost associated with PCR; all amplified samples have higher error rates than the digest control. Two substitution classes (A→T and C→G) showed little dependence on the number of PCR cycles while the other error classes were more frequent as cycle number increased. Significantly, the inclusion of catalase and histidine in the lysis reaction decreased the rate of G→T substitutions six fold.

Conclusions: This study indicates that the sensitivity of ECS MRD is improved by optimizing sample preparation to minimize oxidative DNA damage, by including antioxidants in DNA extraction steps, and by minimizing the number of PCR cycles employed in sequencing library preparation.

American Academy of Child and Adolescent Psychiatry Summer Medical Student Fellowship

No Poster **Gits, Colton**

American Academy of Child and Adolescent Psychiatry Summer Medical Student Fellowship; Dean's Fellowship Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Division: Child and Adolescent Psychiatry
Mentor: Cynthia E Rogers, MD

Maternal smoking, neonatal brain alterations, and risk of ADHD in preterm children

Gits CC; Lessov-Schlaggar CN; Rogers CE

Introduction: Very preterm birth and prenatal nicotine exposure (PNE) are associated with increased risk of behavioral disorders in children, particularly ADHD. The aims of this study are to assess the differences in neonatal brain structure and behavioral outcomes in preterm children born with and without PNE.

Methods: Infants born at 30 weeks gestation or less were recruited from the St. Louis Children's Hospital Neonatal Intensive Care Unit within the first 72 hours of life. MRI scans were performed at term equivalent age (gestational age 36-42 weeks) to obtain morphological and diffusion tensor imaging data. At age 2 and 5 years, diagnoses of child and parent ADHD were obtained by structured interviews, and symptoms of ADHD and executive function were obtained with parent report questionnaires.

Results: A total of 13 preterm infants with PNE were compared against 45 preterm unexposed controls. There were no significant differences in tissue volumes or surface morphology. PNE cases had significantly increased mean diffusivity in the right superior temporal lobe ($p < 0.01$). At 2 year follow up, cases had significantly decreased externalizing scores ($p = 0.01$) and increased frequency of concern for symptoms of attention deficit ($p < 0.01$).

Conclusions: The current study detected minimal differences in brain structure in preterm infants with PNE compared to unexposed preterm controls. Mean diffusion was increased in the right superior temporal lobe in the exposed group. Cases also showed signs of increased behavioral difficulties at age 2. Further follow-up and additional studies are needed.

Child Neurology Foundation Swaiman Medical Scholarship

058 **Mehta, Nehali**

Child Neurology Foundation Swaiman Medical Scholarship; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Division: Pediatric and Developmental Neurology
Mentor: Rafael Galindo, MD, PhD

Neuroprotective role of nicotinamide mononucleotide adenylyl transferase 3 in a mouse model of term-equivalent birth asphyxia

Mehta NM; Galindo R; Holtzman DM

Introduction: Nicotinamide mononucleotide adenylyl transferases (NMNATs) are a group of enzymes with neuroprotective effects in the injured nervous system. Although NMNAT1 and NMNAT2 have been shown to reduce neuronal injury in the adult and immature brain, the protective role of NMNAT3 in the developing central nervous system has not been explored. The goal of this study is to determine whether an increase in the expression of NMNAT3 in the neonatal brain results in a decrease in brain tissue injury following term-equivalent neonatal hypoxia-ischemia (H-I) in mice.

Methods: First, we subjected wildtype mice and transgenic mice overexpressing NMNAT3 to term-equivalent H-I. We quantified injury in the hippocampus, striatum and cortex. Next, we injected P0 mice with a viral vector containing NMNAT3 or a scramble sequence. We performed quantitative PCR and Western blot studies to examine the extent of expression of brain NMNAT3. After performing H-I in a separate group of injected animals, we examined again the extent of injury in the brain. We also investigated the effects of NMNAT3 overexpression on caspase-3 activity, a key step in neuronal apoptosis, following neonatal H-I.

Results: We observed a trend towards a decreased in injury following H-I in transgenic mice compared to wildtype, specifically in the hippocampus and cortex. We also found that both the mice injected with the viral vector containing NMNAT3 showed greater than a 100-fold increase in expression of NMNAT3. However, our results demonstrated wide variability in the injury of the injected experimental and control animals. Lastly, we observed that the transgenic mice showed little caspase-3 activity compared to control wildtype animals.

Conclusions: The NMNAT3 transgenic and caspase-3 experimental results suggest a neuroprotective role of NMNAT3 in injured developing brain neurons through inhibition of apoptosis. The viral transduction studies are also promising, as they indicate high levels of transfection of the vector containing NMNAT3. However, additional studies are being performed to reveal whether overexpression of NMNAT3 through a viral vector can produce significant protection from injury following neonatal H-I.

Clinical Research Training Center (CRTC) KL2 Career Development Awards

No Poster

Fuller, Brian, MD, MSCI
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Emergency Medicine
Division: Critical Care
Mentors: Marin Kollef, MD; Richard Hotchkiss, MD

Acute respiratory distress syndrome in the emergency department: a multi-center, observational, prospective, cross-sectional study

Fuller BM; Mohr NM; Miller CN; Deitchman AR; Levine BJ; Kollef MH

Introduction: Acute respiratory distress syndrome (ARDS) in mechanically ventilated patients is associated with increased mortality, survivor morbidity, and healthcare cost. Compared to the intensive care unit (ICU), ARDS data in the emergency department (ED) is sparse. The ED prevalence of ARDS, to include early factors promoting its development, is relatively unknown. Progression to ARDS in at-risk patients can occur within hours and onset typically occurs shortly after admission. The investigation of ARDS is therefore important in the ED population. The objectives of this study are to determine: (1) the prevalence of ARDS in the ED and the incidence of ARDS after admission; (2) the ED-based risk factors associated with this outcome; and (3) the clinical outcome differences between patients with ARDS versus those without ARDS.

Methods: Multi-center, prospective, observational cohort study of 259 adult patients receiving mechanical ventilation in four academic EDs. Baseline patient characteristics, illness severity scores, and ED process of care variables were collected. To assess predictors of progression to ARDS, an unpaired t-test, Wilcoxon's, Chi-square, or Fisher's exact test, were used. Variables statistically significant in univariate analyses at a $p \leq 0.10$ level were candidates for inclusion in a bidirectional stepwise, multivariable logistic regression analysis.

Results: Fifteen (6.8%) patients had ARDS during their stay in the ED. The incidence of ARDS after admission from the ED was 14.7% (n= 30), with a mean (SD) onset of 2.3 days (1.2). Multivariable logistic regression analysis demonstrated that higher ED illness severity scores and prehospital intubation (compared to ED intubation) were associated with progression to ARDS. Mortality was 51.1% in patients experiencing ARDS versus 28.2% in patients without ARDS (p= 0.004).

Conclusions: A significant minority of patients have ARDS either in the ED or shortly after admission to the ICU. Given the presence of ED-based risk factors and the significant increase in mortality associated with the syndrome, the role of ED-based interventions to prevent ARDS and mitigate its severity should be studied further.

No Poster

Fuller, Brian, MD, MSCI
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Emergency Medicine
Division: Critical Care
Mentors: Marin Kollef, MD; Richard Hotchkiss, MD

The use of mechanical ventilation in the emergency department: a multi-center, observational, prospective, cross-sectional study

Fuller BM; Mohr NM; Miller CN; Deitchman AR; Levine BJ; Kollef MH

Introduction: Initiation of mechanical ventilation in the emergency department (ED) is common, and the ED is the most frequent source of intensive care unit (ICU) admission for the critically ill. Delayed admission to the ICU for ventilated ED patients is increasing in frequency, and is associated with higher mortality. Despite these trends, ED-based mechanical ventilation practices are poorly characterized. The objective of this study is to further characterize ED mechanical ventilation practices.

Methods: Multi-center, prospective, observational cohort study of 259 adults receiving mechanical ventilation in four academic EDs. A subgroup analysis was also performed on patients with acute respiratory distress syndrome (ARDS) while in the ED. Descriptive statistics were used to assess ventilator settings. Ventilator-related variables included ventilator mode, tidal volume, tidal volume indexed to predicted body weight (PBW), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2), monitoring of inspiratory plateau pressure, receipt of lung-protective ventilation, head of bed elevation, and ventilator titration assessment.

Results: The preferred mode of ventilation across centers was assist-control, volume-control ventilation (65.3%). Median tidal volume delivered was 7.6 mL/kg PBW (IQR, 6.9 - 8.9), with a range of 4.3 - 12.2 mL/kg PBW. Lung-protective ventilation was used in 122 (55.7%) patients, and 25 (11.4%) patients were ventilated with a tidal volume > 10mL/kg PBW. Of the 15 patients with ARDS in the ED, 7 (46.7%) received LPV. Inspiratory plateau pressure was recorded in 78 patients (35.6%). The head of bed was elevated in 79 (36.1%) patients while receiving mechanical ventilation in the ED. Mean PEEP was 5.3 (1.3) cm H_2O and mean FiO_2 was .88 (.21).

Conclusions: Based on this analysis, mechanical ventilation in the ED is delivered using: 1) higher than recommended tidal volumes with infrequent lung-protective ventilation; 2) high FiO_2 and low PEEP; 3) infrequent monitoring of inspiratory plateau pressure; and 4) the supine, flat position. Translational research aimed at improving the quality of ED-based mechanical ventilation is needed.

No Poster **Ju, Yo-El, MD**

CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Neurology
Division: Sleep Medicine
Mentors: David Holtzman, MD; John Zempel, MD

Automated slow wave sleep detection and disruption

Ju YS; Ooms S; Holtzman DH; Zempel J

Introduction: Sleep consists of several distinct stages, which serve separate physiological functions. Complete sleep deprivation is one method of studying the functions of sleep, however, this method cannot tease apart the functions of different sleep stages. A method of eliminating a certain sleep stage without interfering with the rest of sleep architecture is necessary to assess the role of that sleep stage. Slow wave sleep (SWS) is the deepest stage of non-REM sleep, and hypothesized to be important in decreasing amyloid-beta levels and other functions. Prior protocols to disrupt SWS have depended upon a person subjectively scoring the electroencephalogram and delivering a variety of stimuli—usually auditory—to awaken a study participant. Due to the variability in scoring, stimuli delivered, and frequency of stimuli during the night, these experiments are not reproducible. There is a strong need for an automated and objective method of SWS disruption.

Methods: We have developed a protocol for automated slow wave sleep disruption. This protocol assesses electroencephalogram data during sleep "live" every 10 seconds. Specified criteria are applied to determine whether the electroencephalogram data represent SWS, and if so, the protocol delivers back to the participant increasing volumes of tones through earphones to disturb the patient out of SWS and into lighter non-REM sleep.

Results: Preliminary testing was performed on a participant, one night with the SWS disruption protocol, and a separate night with a sham protocol. During the SWS disruption protocol night, 1186 tones were delivered. The protocol had 85% sensitivity and 94% specificity for identifying SWS, as compared to the gold standard. Delta power, the spectral power in the slow (0.5 – 4 Hz) band that is a measure of SWS, decreased from 316.1 μV2/s on the sham night to 242.7 μV2/s with the SWS disruption protocol, or by 23%. Total sleep time, time in REM sleep, awakenings, and other sleep indices were not significantly different.

Conclusions: This novel automated method of SWS disruption effectively reduces SWS without affecting other stages of sleep.

No Poster **Kummer, Terrance, MD, PhD**

CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Neurology
Division: Neurocritical Care
Mentor: David L Brody, MD, PhD

Axonal injury in a mouse model of subarachnoid hemorrhage

Kummer TT; Magnoni S; MacDonald CL; Dikranian K; Milner E; Sorrell J; Conte V; Benetatos JJ; Zipfel GJ; Brody DL

Introduction: Subarachnoid hemorrhage (SAH) from the rupture of an intracranial aneurysm shares key mechanical features with traumatic brain injury (TBI), including exposure to a sudden, global pressure wave generated by the arterial jet. It might, therefore, be anticipated that the diffuse mechanical injury of axons central to TBI pathophysiology is also an important component of injury after SAH. Elucidating these connections may lead to novel treatment approaches to both conditions.

Methods: We undertook a parallel diffusion tensor imaging (DTI) and histopathology study to understand the extent of axonal injury following SAH in a mouse model. We quantitatively compared changes in white matter anisotropy indicative of axonal integrity to histological and ultrastructural evidence of axonal injury from the same tissue.

Results: DTI reveals a significant decrement in relative anisotropy in white matter regions close to the site of arterial rupture, with smaller reductions observed in more distant white matter structures. Histological analysis reveals multifocal axonal injury in a large halo surrounding the focus of bleeding. Correlation with behavioral tests suggests that axonal injury may underlie functional deficits observed after SAH. DTI analysis of human patients with SAH reveals similar decrements in anisotropy.

Conclusions: These investigations reveal that axonal injury is a feature of brain injury following SAH, and suggest that similar pathophysiological processes may contribute to human disease. Further analysis of this phenomenon may further illuminate the processes underlying cerebral injury from SAH and TBI, provide new prognostic indicators, and suggest novel treatment modalities for this devastating condition.

099 **Lane, Michael, MD, MPHS, MSc**
CRTC KL2 Career Development Awards; MPHS Degree Program
Washington University in St. Louis
Department: Internal Medicine
Division: Infectious Diseases
Mentors: David Warren, MD, MPH; Margie Olsen, PhD, MPH

Use of 16s rRNA gene PCR for culture-negative prosthetic joint infections

Lane MA; Gu A; Ganeshraj N; Parsaei S; Burnham CA; Warren DK

Introduction: Negative routine cultures are common among those with prosthetic joint infections (PJI) despite overt signs of infection. 16s rRNA gene polymerase chain reaction (PCR) has been proposed to help identify causative organisms among those with culture negative PJI.

Methods: Joint fluid, tissue or bone was collected from patients with PJI who were admitted to Barnes-Jewish Hospital between 9/15/2012 and 4/15/2013. PJI was defined per IDSA guidelines. Patients were considered to be culture negative or positive based on routine microbiological results after 48 hours of incubation. DNA was extracted from samples using the MoBio Bacteremia Kit. Full length amplification of the 16S rRNA gene was performed, and PCR products were visualized using agarose gel electrophoresis. If a PCR product was present, it was sequenced and compared to GenBank and RDP to assign an organism identification per CLSI standards.

Results: We collected 54 samples from 42 unique patients with culture-negative PJI including 28 (51.9%) hip, 18 (33.3%) knee, 7 (13.0%) shoulder, and 1 (1.9%) ankle samples. Sample types included tissue (31, 57.4%), fluid (13, 24.1%), and bone (10, 18.5%). Staphylococcus aureus-specific PCR was negative in all patients with culture negative PJI. 16s rRNA gene PCR was also negative in all patients with culture negative PJI. Samples were collected from 35 patients with culture positive PJI including 18 (51.4%) hip and 17 (48.6%) knee samples. Sample types included 25 (71.4%) tissue, 8 (22.9%) fluid, and 2 (5.7%) bone. S. aureus was the most common organism isolated in routine cultures (n=21). S. aureus-specific PCR correctly identified 12 (57.1%) of samples with S. aureus and incorrectly identified 1 sample. 16s rRNA gene PCR correctly identified 3 samples with S. aureus and 2 samples with Streptococcus spp. Two polymicrobial cultures were identified as mixed while 4 monomicrobial cultures were identified as mixed. Among those with positive cultures for S. aureus, PCR was more likely to be positive from tissue samples than all other tissue types (p=.03).

Conclusions: 16s rRNA gene PCR proved to be an unreliable diagnostic tool for patients with culture positive and negative PJI.

No Poster **Nagasako, Elna, MD, PhD, MPH**
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Internal Medicine
Division: General Medical Sciences
Mentors: W Claiborne Dunagan, MD; Sarah Gehlert, PhD

Social factors collected during routine hospital care: implications for policies on quality measures

Nagasako E; Dunagan WC

Introduction: The recently released National Quality Forum report on Risk Adjustment for Socioeconomic Status or Other Sociodemographic Factors recommends the development of strategies by the NQF and others to "identify a standard set of sociodemographic variables (patient and community-level) to be collected and made available for performance measurement and identifying disparities." This recommendation has received support; however, concerns over the feasibility, relevance, and burden to providers were noted. To inform the current discussion on standardized collection of social factors, we report an analysis of previously collected data on social factors assessed by case managers and social workers at four hospitals.

Methods: Analysis of data from direct observation of 16 case managers and social workers at 4 hospitals within a large hospital system in August 2011. Hospitals varied in patient volume and setting (rural, urban; academic, nonteaching).

Results: Preliminary results found assessment of 34 different types of social and clinical factors, of which age, physical accessibility of housing (e.g., stairs), and primary language were the most common (16 of 16 observations). Across the case managers and social workers observed, the most commonly collected socioeconomic variable was employment status (11 of 16). Income (7 of 16) and educational level (3 of 16) were collected less frequently. Assessment of patient socioenvironmental factors such as household support, housing situation, and transportation availability occurred in the majority of observations. The majority of these factors were collected in the electronic medical record, but not always in the same electronic system as other clinical information.

Conclusions: These preliminary findings suggest that routine clinical interactions are one potential source of data on patient-level social factors; however, a lack of standardization of storage of these data in a form that facilitates retrospective analysis suggests that mandatory standardized collection of these factors may require significant efforts on the part of providers.

076 **Palanca, Ben Julian, MD, PhD**
CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Anesthesiology
Division: Clinical and Translational Research
Mentors: Joseph Culver, PhD; Linda Larson-Prior, PhD; Marcus Raichle, MD

Diffuse optical tomography during natural sleep

Palanca BJ; Eggebrecht A; Wang D; Avidan MS; Larson-Prior L; Culver JP

Introduction: During sleep, dynamic fluctuations in electrical activity in the brain are spontaneously measured through electroencephalography (EEG). It remains unclear how distinct electrical signatures of different sleep stages relate to coordinated activity across the cerebral cortex. Spatial maps of correlated low-frequency (0.1-0.01 Hz) oscillations in hemoglobin oxygenation can be obtained by functional magnetic resonance imaging (fMRI) and by diffuse optical tomography (DOT). While fMRI has revealed weaker correlations among brain regions during slow-wave sleep (SWS), DOT offers the potential to study natural sleep unencumbered by vibrations, noise, and magnetic interference in the EEG. We assessed the feasibility of imaging superficial cerebral cortex using diffuse optical tomography. Our hypothesis is that interhemispheric correlation strength would be reduced during slow-wave sleep compared to wakefulness but would revert to baseline during rapid eye movement (REM) sleep.

Methods: Following selection and screening to exclude occult sleep disorders, healthy human volunteers underwent two overnight polysomnography (PSG) sessions while wearing a cap equipped for DOT. The DOT cap had a field of view over superficial frontal, temporal, parietal, and occipital cortex. A certified sleep technician assigned sleep stage at 30-second intervals according to the 2012 American Academy of Sleep Medicine scoring rules. After alignment of PSG and DOT data and censoring of motion artifacts, epochs of wakefulness, REM, and SWS were analyzed. The strength of interhemispheric connectivity among frontal, temporal/parietal, and occipital brain regions were quantified using Pearson's correlation analysis and underwent paired t-tests for significance testing.

Results: Preliminary analyses of data from six of eight volunteers met criteria for sleep in all three stages. Compared to wakefulness, SWS was associated with a weakening of interhemispheric correlations, particularly for anterior regions under the DOT cap. In contrast, REM and wakefulness showed similar correlation strength.

Conclusions: DOT is a viable tool for imaging correlated low frequency oscillations in neural activity via wearable technology without the need of an fMRI facility or sleep deprivation, opening the door for future studies comparing the dynamics of brain connectivity during the unconsciousness of natural sleep and pharmacologic interventions. Weakening of interhemispheric connectivity during SWS is consistent with a localized mode of neural processing compared to wakefulness and REM.

No Poster **Pusic, Iskra, MD**
CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Internal Medicine
Division: Oncology
Mentors: John F DiPersio, MD, PhD; Mario Castro, MD, MPH; Jane M Garbut, MD

Pilot study of pomalidomide for refractory chronic graft-versus-host disease (cGVHD)

Pusic I; DiPersio JF; Rettig M; Reineck T; Gale RP; Pavletic SZ

Introduction: Data from rodents suggest that thalidomide is active in chronic Graft-versus-Host Disease (cGVHD). Data from humans are more difficult to assess because toxicities precluded the use of thalidomide at doses that were effective in rodents. Pomalidomide (POM) is a novel immune-modulating drug with 4000-fold greater inhibition of TNF-α production than thalidomide and a different side-effects profile. We assessed efficacy and safety of POM in patients (pts) with corticosteroid-resistant, moderate/severe cGVHD.

Methods: POM was given orally at 3 mg/d with dose-reductions to 2, 1, and 0.5 mg/d, and a total of 12 cycles was planned. Pts were assessed for response every 3 cycles, according to NIH criteria. Pts who completed at least 3 cycles were evaluable for efficacy.

Results: Thirteen pts were enrolled. Median time from transplantation was 2.5 yrs (1.8-15) and median time from cGVHD diagnosis was 1.5 yrs (0.5-14). Five pts had de-novo cGVHD, 7 quiescent, and 1 progressive cGVHD. Median number of prior systemic cGVHD therapies was 4 (2-7). First 8 pts were enrolled at 3 mg/d and 7 of them required dose reductions. Subsequent 5 pts were enrolled at 2 mg/d and only 2 required dose reductions. Most common side-effects were muscle cramps, tremors, pain and fatigue. There was no significant bone marrow suppression, neuropathy, or somnolence. One pt developed deep venous thrombosis and pulmonary embolism. Four pts discontinued therapy before cycle 3 because of adverse-effects in the setting of no response to pomalidomide. Six pts were on the study for 3-7 cycles and 3 pts for 10-12 cycles. Two pts had complete response (CR) of mouth cGVHD; 2 pts had CR of skin erythema and 3 pts had partial response (PR) of skin erythema; 1 pt had PR in movable skin sclerosis; 2 pts had CR of GI symptoms; 1 pt had PR and 1 CR of eye symptoms. Overall, no pts met the criteria for overall CR, 7 pts had overall PR and nobody progressed.

Conclusions: POM can be given to pts with advanced corticosteroid-resistant cGVHD at doses of 2 mg/d or less, without toxicities that have limited the use of thalidomide. There is a modest activity of POM in corticosteroid-resistant cGVHD, however larger trials are needed.

145 **Seifert, Michael, MD**

CRTC KL2 Career Development Awards; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Nephrology
Mentors: Daniel Brennan, MD; Keith Hruska, MD; Vikas Dharnidharka, MD, MPH

Antibodies to self-antigens fibronectin and collagen type IV are associated with phenotype of chronic rejection in pediatric kidney transplantation

Seifert ME; Gunasekaran M; Chishti A; Chiang M; Selewski D; Gipson D; Dharnidharka V; Mohanakumar T

Introduction: Chronic rejection (CR) is characterized by cumulative vascular injury that leads to interstitial fibrosis/tubular atrophy (IF/TA) and/or transplant glomerulopathy (TG). Antibodies (Abs) to kidney-associated self-antigens (SAgs) fibronectin (FN) and collagen type IV (Col-IV) have been associated with TG following adult kidney transplantation, but their prevalence in children is unknown. Since FN and Col-IV are expressed on glomerular endothelium, we hypothesized that Abs to FN/Col-IV would also be associated with coexistence of TG and IF/TA (TG+IF/TA) in pediatric kidney CR.

Methods: Preliminary analysis of 24 pediatric kidney transplant recipients enrolled in a multicenter, case-control study of vascular injury in CR. Subjects were assigned to CR if they had biopsy-proven CR (IF/TA and/or TG). Subjects were assigned to No CR if a biopsy < 6 months prior was normal or glomerular filtration rate was > 90 mL/min/1.73m2. Plasma FN and Col-IV Abs were measured using ELISA by a single investigator that was blinded to clinical data. Subjects were positive for FN/Col-IV Abs if levels exceeded 2 standard deviations above the mean of healthy controls.

Results: 13/24 (54%) subjects had biopsy-proven CR; of these, 3/13 (23%) had TG+IF/TA and 10/13 (77%) had IF/TA alone. Overall, 3/13 (23%) of CR were positive for FN Abs versus 0/11 of No CR (p=0.03). Col-IV Abs were positive in 2/13 (15%) of CR versus 0/11 of No CR (p=0.17). Within CR, 3/3 (100%) of TG+IF/TA but 0/10 of IF/TA alone were positive for FN Abs. Similarly, 2/3 (67%) of TG+IF/TA but 0/10 of IF/TA alone were positive for Col-IV Abs. FN and Col-IV Abs were double-positive in 2/3 (67%) of TG+IF/TA but 0/10 of IF/TA alone (P≤0.01 for all tests within CR).

Conclusions: Abs to kidney-associated SAgs FN and Col-IV are strongly associated with a TG+IF/TA phenotype, but not IF/TA alone or normal function. These preliminary findings suggest that the mechanism leading to TG+IF/TA may have a major component of antibody-mediated injury in contrast to IF/TA alone. These findings need to be further validated.

090 **Smith, Gordon, PhD**

CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Internal Medicine
Division: Geriatrics and Nutritional Science
Mentors: Bettina Mittendorfer, PhD; Brian Finck, PhD

Protein ingestion induces muscle insulin resistance independent of leucine-mediated mTOR activation

Smith GI; Yoshino J; Stromsdorfer KL; Klein SJ; Magkos F; Reeds DN; Klein S; Mittendorfer B

Introduction: Amino acids induce insulin resistance but the exact mechanism(s) responsible for the insulin-desensitizing effect of amino acids is unclear and it is not known whether protein ingestion impairs insulin-mediated glucose uptake. We hypothesized that protein ingestion impairs insulin-mediated glucose disposal due to inhibitory leucine-mediated phosphorylation of AKT by mTOR.

Methods: We measured glucose disposal and muscle p-mTORSer2448, p-AKTSer473 and pAKTThr308 contents in 22 women during postabsorptive conditions and during a hyperinsulinemic-euglycemic clamp with and without concomitant ingestion of whey protein (0.6 g per kg fat-free mass; n=11) or with and without an amount of leucine matching that in whey protein (n=11).

Results: Both whey protein and leucine ingestion raised plasma leucine concentration and muscle p-AKTSer473 and p-AKTThr308 contents by ~2-fold and muscle p-mTORSer2448 content by ~30% above their respective control values. Whey protein ingestion impaired insulin-mediated glucose disposal (38.8 [31.3, 61.8] vs. 51.9 [41.0, 77.3] µmol glucose per µU insulin•ml-1•min-1, whey protein vs. control, respectively; P<0.01; data are median [quartiles]) whereas ingestion of leucine did not (52.3 [43.3, 65.4] vs. 52.3 [43.9, 73.2], leucine vs. control, respectively).

Conclusions: Protein ingestion could be an important regulator of postprandial glucose homeostasis. The insulin-desensitizing effect of protein intake is not due to inhibitory leucine-mediated mTOR signaling to AKT.

107 **Wang-Gillam, Andrea, MD, PhD**
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Internal Medicine
Division: Oncology
Mentors: Lee Ratner, MD, PhD; Jason Weber, PhD

Phase I study of temsirolimus and erlotinib in patients with refractory solid tumors

Wang-Gillam A; Waqar S; Govindan R; Suresh R; Morgensztern D; Picus J; Baggstrom M; Naughton M; Van Tine B; Lockhart C

Introduction: This study was conducted to determine the maximum tolerated dose (MTD) and dose-limiting toxicities (DLT) of the combination of temsirolimus (mTOR inhibitor) and erlotinib (EGFR inhibitor) in patients with refractory solid tumors.

Methods: The study uses a classic 3+3 dose escalation design. The starting dose level was temsirolimus at 15 mg weekly and erlotinib at 100 mg daily. Each cycle was 28 days except cycle 1 being 35 days with erlotinib starting 7 days prior to initiating temsirolimus. Patients with tumors harboring specific genetic alterations and squamous histology were included in the expansion cohort.

Results: Between June 2009 to June 2014, 29 patients enrolled in the dose escalation portion of the study, while 10 patients in the expansion cohort. Two patients experienced DLTs (grade 3 dehydration and grade 4 renal failure). The common drug-related adverse events of all grades were mucositis/stomatitis, fatigue, rash, anemia, thrombocytopenia and nausea. The temsirolimus at 25mg weekly and erlotinib 100mg daily were considered as the recommended phase II dose. The longest durable treatment response was 2 years in a patient with refractory head and neck cancer. The results on treatment responses and molecular evaluations will be reported at the meeting.

Conclusions: Temsirolimus and erlotinib is tolerable, and the treatment resulted in clinical benefit. The combination regimen should be further explored in appropriate tumor types.

097 **Yoshino, Jun, MD, PhD**
CRTC KL2 Career Development Awards
Washington University in St. Louis
Department: Center for Human Nutrition
Division: Geriatrics and Nutritional Science
Mentors: Samuel Klein, MD; Nada Abumrad, PhD

Clock genes and diurnal variations in fatty acid metabolism and insulin sensitivity

Yoshino J; Klein S

Introduction: Many metabolic pathways and functions vary according to the time of day. In healthy people, insulin sensitivity with respect to glucose metabolism is lower in the evening than in the morning. The mechanism(s) responsible for diurnal variation in insulin action is not known, but could be related to alterations in 1) clock genes, master regulators for circadian rhythms, and 2) systemic free fatty acid (FFA) availability and muscle fatty acid metabolism. The purpose of the present study was to test the hypothesis that diurnal variations in clock gene expression, plasma FFA availability and skeletal muscle fatty acid metabolism are associated with diurnal variation in insulin-mediated glucose metabolism.

Methods: We measured plasma FFA concentration, palmitate kinetics, and skeletal muscle expression of genes involved in fatty acid metabolism at breakfast (0700 h) and dinner (1900 h) in 13 overweight (BMI = 27.8 ± 1.2 kg/m2), but metabolically-normal, women.

Results: Plasma FFA concentration was ~30 % greater just before consuming dinner than breakfast ($P < 0.05$) and remained greater after dinner than breakfast (FFA areas under the curve: 0.88 ± 0.33 and 0.51 ± 0.09 µmol/mL x 4h, $P=0.001$). However, adipose tissue lipolytic activity was not different in the evening and in the morning. Skeletal muscle expression of genes that regulate fatty acid oxidation were 38-82 % lower, whereas genes involved in de novo lipogenesis were 51-87 % higher before dinner than before breakfast (all $P < 0.05$), and these changes were associated with diurnal variation in muscle expression of core clock genes that regulate fatty acid metabolism.

Conclusions: Metabolically-normal women demonstrate diurnal variations in fatty acid metabolism, manifested by an increase in circulating FFA, presumably derived from previous meal consumption rather than lipolysis of adipose tissue triglycerides, and a shift in muscle fatty acid metabolism from oxidation to lipogenesis. These metabolic alterations could be responsible for the known evening decline in insulin sensitivity.

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology

No Poster **Ademuyiwa, Foluso, MD, MPH**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Internal Medicine
Division: Medical Oncology
Mentors: Matthew Ellis, MB, BChir, PhD; Cynthia Ma, MD, PhD

Genoproteomic discovery clinical trial in triple negative breast cancer patients

Ademuyiwa FO; Ma CX; Luo J; Li S; Ellis MJ

Introduction: Triple negative breast cancer (TNBC) remains difficult to treat partly due to the lack of true targeted agents. Patients have high rates of relapse, due to chemotherapy resistance within the first few years. Although studies have shown that platinum salts have activity in TNBC, molecular biomarkers predictive for activity are lacking. The current trial will evaluate the combination of carboplatin and docetaxel in the pre-operative setting to determine if these drugs will increase pathologic complete response (PCR) rates compared to historical controls. Patient derived xenografts (PDX) will also be simultaneously developed as an in vivo model to explore genomic and proteomic predictors of chemotherapy resistance.

Methods: This is a co-clinical study in which patients with clinical stage 2 or 3 TNBC will receive pre-operative carboplatin AUC 6 and docetaxel 75 mg/m2 q3 wks x 6, followed by surgery. Tissue collection will occur at baseline (for xenografting), cycle 1 day 2/3, and surgery. The primary objective is to determine the PCR rates, defined as the absence of invasive cancer in breast or nodes at definitive surgery. Exploratory objectives include xenografting rates, association between HRD score and response to preoperative chemotherapy, and evaluation of other unique molecular markers such as NtAI, LST, PAM50, Vanderbilt TNBC subgroups, tumor infiltrating lymphocyte predictor. Genomic and proteomic signatures will be used to identify novel markers of response. 41 eligible patients will be treated to attain a power of 83% to detect the expected PCR of 54% versus 35% historically, based on the two-sided exact Binomial test at the 4.8% significance level.

Results: The study was activated on 7/7/2014 and is currently ongoing. 1 patient has been consented at the time of submission of this abstract.

Conclusions: Achieving a higher PCR rate with this drug combination in patients with TNBC will translate to improved long-term clinical outcomes. In addition, using PDX models as surrogates for originating tumors may allow physician investigators to be able to deeply study the molecular basis for chemotherapy response and ultimately predict response or resistance to chemotherapy based on molecular characteristics of corresponding PDX models. This may allow improved individualization of treatments, in the future, for patients with cancer.

No Poster **Maggi, Leonard, PhD**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Internal Medicine
Division: Molecular Oncology
Mentors: Jason Weber, PhD; Ramaswamy Govindan, MD

Targeting CDKN2A-controlled networks in lung cancer

Maggi LB; Forys JT; Govindan R; Weber JD

Introduction: PIK3CA inhibitors have been used in the clinic in an attempt to inhibit lung cancer growth with limited success. One possible explanation is that PIK3CA mutations cooperate with other genomic alterations to drive disease progression. Our preliminary studies indicate that IFN-beta is produced upon loss of ARF and mutation of p53. Data obtained from the TCGA datasets for squamous cell and adenocarcinoma lung cancer demonstrate that both PIK3CA amplification and IFN-beta-induced JAK activation occur concurrently in a significant number of lung cancer samples. The long-term goal of this project is to develop a dual therapy for NSCLC that targets PIK3CA and IFN-beta-induced JAK activation. We hypothesize that dual treatment with PIK3CA and JAK inhibitors will target lung cancer cells harboring PIK3CA amplification, and JAK activation.

Methods: A number of biochemical, molecular biological and immunological techniques will be utilized to investigate the activation of the Type I IFN response resulting from ARF loss in lung cancer cell lines. Additionally, the effects of dual inhibition of PI3KCA and JAK on lung tumor cell growth and proliferation in vitro will be assessed.

Results: In human lung cancer samples in which ARF is lost, the Type I IFN response is activated as demonstrated by increased ISG15 staining. Lung cancer cell line data demonstrates that ARF loss in conjunction with p53 inactivation and PI3KCA activation leads to up regulation of IFN-beta and ISG15 – hallmarks of the Type I IFN response. Importantly, only lung cancer cell lines that have lost ARF in the context of p53 loss and PI3KCA activation are sensitive to the dual inhibition of JAK and PI3KCA. In cell lines in which ARF is present, inhibition of JAK has little to no effect. Restoration or knockdown of ARF in the opposite context alters the Type I IFN response in lung cancer cell lines.

Conclusions: Our preliminary in vitro results using lung cancer cell lines demonstrate a promising potential for inhibition of both PI3KCA and JAK in treating a subtype of lung cancer. Immunohistochemical staining of lung cancer sections on tissue microarrays demonstrate a strong correlation of ARF loss and ISG15 staining. Further preclinical studies in mouse xenograph models will assess the in vivo potential for this combined therapy and will pave the way for clinical trials to begin.

No Poster **Waqar, Saiama, MBBS**
CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology
Washington University in St. Louis
Department: Internal Medicine
Division: Medical Oncology
Mentors: Ramaswamy Govindan, MD; Mark Watson, MD, PhD

Molecular genetics of brain metastasis from lung cancer

Waqar SN; Govindan R; Watson MA

Introduction: The molecular mechanisms underlying the development of brain metastasis are not well understood and there are no reliable biomarkers to predict brain metastasis in patients with lung cancer. We hypothesize that metastasis-competent tumor cells already reside within a subpopulation of cells present in the primary tumor. The objective of this proposal is to study the molecular determinants of brain metastasis, through direct comparison of the molecular changes seen in paired primary non-small cell lung cancer (NSCLC) and brain metastasis tumor specimens.

Methods: We performed exome sequencing on patient matched primary NSCLC and brain metastatic lesions with the goal of identifying genomic variants enriched in brain metastatic lesions with putative clinical or biological significance. We also performed quantitative RNA sequencing on a subset of these paired specimens in order to further prioritize genomic variants with gene expression consequences, and to integrate differential gene expression data with exome sequence data. We plan to validate the prognostic significance of these somatic genomic variants by performing targeted, deep sequencing in an independent cohort of primary lung tumors from patients with and without the development of eventual brain metastases.

Results: We have completed exome sequencing of 30 paired primary lung and brain tumors. We have also performed RNA sequencing on 8 paired specimens. We have identified a large number of high quality somatic variants that are recurrent across patients and/or enriched in metastatic lesions relative to their primary tumors, including mutations in FES, FOXD4L1 and clinically actionable mutations in PIK3CA and MAPK4. The prognostic significance of additional candidate variants is being validated by deep targeted sequencing in an independent cohort of 96 primary NSCLC tumors from patients with and without the development of eventual brain metastasis.

Conclusions: This study would lead to biomarker-based strategies to identify patients at high risk for brain metastasis, and possibly facilitate the development of novel molecularly-targeted therapies for patients with lung cancer who have brain metastasis.

108 **White, Brian, PhD**
CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology
Washington University in St. Louis
Department: Internal Medicine
Division: Oncology
Mentors: Daniel Link, MD; Matthew Walter, MD

Mutant U2AF1 alters splicing in hematopoietic cells in vitro and in vivo

White BS; Shirai CL; Okeyo-Owuor T; Kim S; Wadugu B; Chatrikhi R; Laird KM; Kielkopf CL; Graubert TA; Walter MJ

Introduction: Mutations in the U2AF1 splicing factor occur in ~11% of patients with myelodysplastic syndromes (MDS), with most affecting codons S34 or Q157. Though these might be expected to perturb U2AF1 recognition of the 3' splice acceptor site, their effect has not been fully elucidated. This study aims to determine whether and how these mutations disrupt splicing.

Methods: Statistical analysis was performed on three transcriptome sequencing data sets: (1) primary human CD34+ hematopoietic cells transfected with WT (n=3) or mutant U2AF1(S34F;n=3); (2) common myeloid progenitor cells from mice transplanted with donor bone marrow derived from transgenic animals expressing U2AF1(WT;n=3) or U2AF1(S34F;n=3); (3) AML patient samples harboring U2AF1 S34(F/Y;n=6) mutations or without any splicing factor mutations (n=108).

Results: 1,594 splicing junctions were significantly dysregulated (FDR < 5%) in primary human CD34+ cells. Their sequence context suggests that U2AF1(S34F) has a decreased affinity for uridine at the -3 position upstream of the AG dinucleotide splice acceptor site. These findings were confirmed in 460 dysregulated junctions (FDR < 5%) in mouse samples and in 1,655 altered junctions (|log fold change| > 1) in AML patient samples. They were validated experimentally by titration of fluorescein-labeled RNAs with purified U2AF1(WT) or U2AF1(S34F), which showed that U2AF1(S34F) bound a representative oligo harboring UAG less avidly than U2AF1(WT) and that this reduced binding was rescued by mutating UAG to CAG. This sequence context specificity was not exhibited in a U2AF1(Q157P) AML patient sample. We identified homologous junctions significantly dysregulated in all three datasets in two genes previously implicated in cancer and stem cell biology: H2AFY and MED24. These were validated by RT-PCR using MDS patient bone marrow samples with U2AF1(WT) or U2AF1(S34F; $p<0.001$, n=5-6).

Conclusions: These results suggest that U2AF1(S34F) dysregulates splicing by altering spliceosome binding affinity to uridine at the 3' splice acceptor site. Further, specific targets are consistently dysregulated, including genes of potential relevance to MDS pathogenesis.

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)

113 **Diedrich, Justin, MD**
CRTC Postdoctoral MTPCI; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Generalist Division
Mentors: Jeffrey Peipert, MD, PhD; Tessa Madden, MD, MPH
Preliminary findings of LUCID (Long-term Utilization and Continuation of Intrauterine Devices)
Diedrich JD; Madden TM; Peipert JF
Introduction: As use of intrauterine devices (IUDs) in the United States increases, data on long-term use and satisfaction are necessary. Reports of long-term continuation of IUDs in the US are lacking. The goal of this study is to update estimates of continuation with long-term (3- to 5-year) use of the two IUDs available in the US.
Methods: This is a retrospective cohort study of women who participated in the Contraceptive CHOICE Project, which provided no-cost birth control methods to women in the St. Louis area. A random sampling of women who received either the copper- or progestin-containing IUD was included in this analysis. Participants completed a telephone survey asking about continued IUD use as well as factors which may be associated with continuation. Those discontinuing to get pregnant were censored in survival analysis and Cox regression models.
Results: As of preliminary analysis, 227 of 460 women have been contacted (125 copper-IUD users and 102 progestin-IUD users). Continuation at years 3, 4, and 5 did not vary significantly by IUD type. Among copper IUD users, continuation was 52%, 36% and 30% at 3, 4 and 5 years, respectively. Among progestin IUD users, continuation was 60.5%, 41.5% and 30% at 3, 4 and 5 years, respectively. Race, socio-economic status, parity, IUD type, and BMI were not associated with continuation. On binomial logistic regression, age at insertion was strongly associated with continuation. Those age 30 and greater were 3-4 times more likely to continue at 5 years than those 21 years of age and below (OR= 3.7, 95% CI 1.5 - 9.5).
Conclusions: More than half of participants were continuing to use their IUD at 3 years, while approximately one-third continue use at 5 years. Older age at insertion is associated with continuation, regardless of IUD type, demographics and socioeconomics.

059 **Guilliams, Kristin, MD**
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Washington University in St. Louis
Department: Neurology
Division: Pediatric Neurology
Mentor: Jin-Moo Lee, MD, PhD
Infarct distributions differ in pediatric sickle cell patients with or without large vessel vasculopathy
Guilliams KP; Ragan DK; Fields ME; McKinstry RC; Shimony JS; Vo KD; Hulbert ML; An H; Lee JM; Ford AL
Introduction: Children with sickle cell disease (SCD) have a high risk of ischemic strokes in diverse spatial distributions, but mechanisms responsible for these different patterns are unclear. Vasculopathy is a known risk factor for stroke in SCD, but whether it impacts infarction distribution is unknown.
Methods: MRIs and MRAs from 2006-2014 were retrospectively collected on SCD children with an overt stroke history. Hemispheres were categorized based on presence or absence of large vessel vasculopathy (Vsc) on MRA. Manually delineated infarcts on FLAIR were individually co-registered to the corresponding T1 MPRAGE maps, and then co-registered onto a common space. Left and right hemispheres were separated with a mask in the common space. Hemispheres were flipped so all with Vsc were oriented as right hemispheres, and those without Vsc as left. Co-registered infarct maps were warped into the final anatomic space and averaged to create a lesion density map. A cerebral blood flow (CBF) map was created from average pseudocontinuous arterial spin labeled measurements prospectively collected on 7 children with SCD and no Vsc.
Results: Of 22 children with SCD and overt stroke history (median 15.5y, 41% male), 14 had Vsc (median 16 y, 50% male) in 19/44 hemispheres. Both non-Vsc and Vsc hemispheres had infarct hot-spots in a predominantly deep white matter watershed distribution, but Vsc hemisphere infarcts were more numerous, more extensive and encompassed more gray matter. Hot-spots overlapped with regions of lowest flow within the deep white matter on the CBF map. Vsc hemispheres also had infarcts in classic large artery territories, not seen in non-Vsc hemispheres.
Conclusions: The etiology of ischemia in SCD is likely multifactorial, involving reduced oxygen delivery (anemia), impaired CBF (Vsc), and possible associated thrombosis (Vsc with low/turbulent flow distal to stenosis). Differential patterns of infarction reflect these different layers of compromise. Prospective studies are needed to further understand these interactions and improve stroke prevention.

114 Hagemann, Andrea, MD

CRTC Postdoctoral MTPCI; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Gynecologic Oncology
Mentor: Brian Gage, MD, MSc

Efficacy and safety of preoperative venous thromboembolism (VTE) prophylaxis in high-risk gynecologic surgery patients

Hagemann AR; Corr BR; Winter AM; Chu CS; Gage BF

Introduction: VTE remains a common complication of high-risk gynecologic surgery. The American College of Chest Physicians suggests routine use of preoperative thromboprophylaxis, yet there remains low compliance nationally for pharmacologic thromboprophylaxis due to perceived risk of bleeding complications. The dual purposes of this study are: 1) to determine if single-dose preoperative subcutaneous heparin combined with two weeks of postoperative low-molecular weight heparin (extended prophylaxis) reduces the rate of VTE in a high-risk gynecology population compared to inpatient thromboprophylaxis alone, and 2) to evaluate if this perioperative prophylaxis increases bleeding or infectious complications.

Methods: We performed a retrospective cohort study of 527 patients undergoing major surgery at a single institution's gynecologic oncology service over a thirty-month interval in which a uniform practice change of post-operative VTE prophylaxis was implemented. We compared rates of VTE pre- and post-intervention as well as bleeding and infectious complications. A time-to-event analysis was performed using the method of Kaplan Meier.

Results: Prior to the intervention (N=345), there were 23 VTE events (6.67%): 8 deep vein thrombosis (DVTs) and 15 pulmonary emboli (PEs). Post intervention (N=182), there were 5 VTE events (2.7%), 3 DVTs and 2 PE s ($p=0.056$, RR=0.4). Time-to-event analysis showed a significantly higher incidence of VTE events in the pre-intervention group compared to the post-intervention group (Chi-square 4.25, $p = 0.039$). There were no significant differences in bleeding or infection complications between groups for any outcome ($p > 0.2$ for all comparisons): length of surgery, estimated blood loss, post operative hemoglobin drop, number of individuals requiring blood product transfusion, hospital length of stay or wound infection rate.

Conclusions: Preoperative single-dose heparin, combined with two weeks of VTE thromboprophylaxis may decrease VTE events without increasing bleeding or infection complications in a high-risk gynecologic surgery population. Consideration should be made for standardization of preoperative pharmacoprophylaxis administration in this group of patients.

140 Hesemann, Laura, MD

CRTC Postdoctoral MTPCI; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Nephrology
Mentor: Vikas Dharnidharka, MD, MPH

Antibodies to kidney-associated self-antigens occur at high rates at early time points after kidney transplantation in children

Hesemann L; Subramanian V; Mohanakumar T; Dharnidharka V

Introduction: Chronic rejection is the leading cause of graft loss after kidney transplantation in children. Our group has shown a strong association between the development of antibodies (Ab) to self-antigens and the development of chronic rejection after lung transplantation and kidney transplantation in adults. The rate of Ab production has not previously been studied in children. In the current study, we measured Ab to the kidney-associated self-antigens (KASA): Collagen IV (Col IV), Fibronectin (Fn); and Angiotensin II Receptor Type I (ATR1) in a cohort of children following kidney transplantation.

Methods: Using ELISA, we measured titers of Ab to Col IV, Fn, and ATR1 in saved sera samples from a prior study. Our cohort included 27 subjects, age 1-18 years, M:F=16:11, 59% white, 30% black, 11% Hispanic, 19% living donor, 81% deceased donor. The study protocol included sampling in months 1-12 post-transplant, though samples were not available at each month for all subjects.

Results: We analyzed 20 pre-transplant samples for Ab to Col IV and Fn and 27 for Ab to ATR1. None had Ab to Col IV or Fn. Three subjects had low levels of Ab to ATR1. We tested 83 post-transplant samples for Ab to Col IV, 81 for Ab to Fn, and 144 for Ab to ATR1. Ten of the twenty subjects developed high levels of Ab to any one KASA. Four samples, all from 1 subject, were weakly positive for Ab to Col IV. Three subjects developed Ab to Fn; 8 serial samples from 3 subjects were strongly positive, and 3 serial sera from 2 of these subjects were weakly positive. The subject with reactivity to Col IV was also positive for Ab to Fn. Sixty-five samples from 9 subjects had low levels of ATR1 Ab, including 2 of the subjects with Ab to Fn. Twenty-five samples from 8 subjects had high levels of Ab to ATR1 including the subject with Ab to Col IV and Fn. The earliest development of any Ab was 16 days post-transplantation.

Conclusions: Half of the subjects developed high levels of Ab to kidney-associated self-antigens Col IV, Fn, or ATR1 in the first year after kidney transplantation; a higher rate of early Ab development than expected. Further study is required to assess whether these Ab are associated with development of chronic rejection.

057 **Longbrake, Erin, MD, PhD**

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Department: Neurology
Division: Neuroimmunology
Mentors: Anne H Cross, MD; Robyn S Klein, MD, PhD; Jane Garbutt, MD

Impaired color vision as determined by Farnsworth Munsell 100 Hue testing is tightly associated with retinal thinning in multiple sclerosis

Longbrake EE; Lancia S; Tutlam N; Naismith RT

Introduction: Color vision abnormalities are common among patients with multiple sclerosis (MS), particularly in the setting of past optic neuritis. This has been established using a variety of screening instruments including Hardy Rand Ritler (HRR) plates, Lanthony D-15 desaturated tests (LD15), and the Farnsworth Munsell 100 Hue Test (FM-100). Villoslada, et al (2012) previously demonstrated Pearson correlation coefficients of 0.594 for HRR plates and -0.424 for LD15 screening tests of vision with average RNFL thickness. The FM-100 is often considered the definitive test for impaired color vision, but it is time-consuming to administer and has not been comprehensively assessed in conjunction with modern visual testing including retinal nerve fiber layer (RNFL) thickness as measured by optical coherence tomography (OCT), visual evoked potentials (VEP), high contrast visual acuity (HCVA), low contrast visual acuity (LCVA) and quantitative visual field testing. Moreover, real-world correlates of these visual function measures in the form of quality of life data is lacking. We sought to determine the relationship between the FM-100 and other visual outcome measures in MS patients who had previously suffered optic neuritis. We then correlated these measures with self-reported visual quality of life.

Methods: Forty six MS patients with stable ON for at least 3 months were enrolled as part of a clinical trial. They underwent comprehensive visual analysis, including high- and low-contrast visual acuity (HCVA and LCVA) testing, visual evoked potentials (VEPs), OCT, Humphrey visual field testing, and FM-100 testing during two separate visits over 8 weeks. The National Eye Institute Visual Function Questionnaire (VFQ-25) was administered to participants at each visit.

Results: The majority of MS eyes (86% of ON eyes and 64% of non-ON eyes) had abnormal color vision as determined by FM-100. FM-100 scores correlated strongly with other measures of visual function, including HCVA, LCVA, RNFL thickness, visual field indexes, and VEP 60-minute amplitudes. FM-100 scores did not correlate with P-100 latencies on VEP testing or with visual function quality of life testing. VFQ-25 scores did correlate with RNFL thickness and Humphrey visual field index.

Conclusions: FM-100 scores correlate strongly with other quantitative measures of visual function. However, abbreviated screening tests for color vision may give similar results when compared to the FM-100. Of the quantitative measures of visual function studied, RNFL thickness and Humphrey visual field index correlated most strongly with patient-reported visual function quality of life.

011 **Nam, Denis, MD**

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Washington University in St. Louis
Department: Orthopaedic Surgery
Division: Joint Preservation, Resurfacing, and Replacement
Mentor: Robert L Barrack, MD

The impact of custom cutting guides on patient satisfaction and function following total knee arthroplasty

Nam D; Nunley RM; Berend KR; Lombardi AV; Barrack RL

Introduction: Custom cutting guides (CCGs) in total knee arthroplasty (TKA) use 3-dimensional imaging to manufacture cutting guides specific to each patient's anatomy. However, their impact on patient-perceived outcomes and satisfaction has not been evaluated. The purpose of this study was to evaluate the impact of CCGs versus standard alignment guides on patient satisfaction following TKA.

Methods: Two centers contributed a consecutive series of patients who underwent TKA using a MRI-based CCG system or standard intramedullary or extramedullary alignment guides. All patients received the same, cemented, fixed-bearing, cruciate-retaining prosthesis. Data was collected by an independent, third-party survey center blinded to surgical technique, who administered questionnaires about patient satisfaction and residual symptoms using a previously published survey instrument. Age, gender, minority status, education level, income, length of follow-up, and pre-arthritic University of California at Los Angeles (UCLA) scores were accounted for using multivariate logistic regression analyses.

Results: 107 CCG TKAs and 341 with standard instrumentation were analyzed. There was no difference in postoperative UCLA scores (6.8 + 1.7 vs. 6.6 + 1.6, p=0.27), and only 74% in the CCG cohort and 78% in the standard cohort reported their knee to feel "normal" (p=0.37). The incidence of residual symptoms, including knee stiffness (37% CCG versus 28% standard, p=0.08) and difficulty getting in and out of car (34% CCG versus 30% standard, p=0.40) remained relatively high in both cohorts. Only 74% in the CCG cohort and 76% in the standard cohort reported the complete absence of a limp (p=0.66). Multivariate regression analyses demonstrated no significant differences between the two cohorts for both patient satisfaction and the presence of residual symptoms (odds ratios 0.72 to 1.48; p=0.10 to 0.81).

Conclusions: When interviewed by an independent, blinded third party, the use of custom cutting guides in total knee arthroplasty did not improve patient satisfaction and the presence of residual symptoms when compared to the use of standard alignment guides.

123 **Roland, Lauren, MD**

CRTC Postdoctoral MTPCI; T32DC00022; CRTC MSCI Degree Program
Washington University in St. Louis
Department: Otolaryngology
Division: Otolaryngology
Mentors: Jay Piccirillo, MD; Jonathan Peelle, PhD

The effect of mindfulness-based stress reduction therapy on subjective bother and neural connectivity in chronic tinnitus

Roland LT; Lenze EJ; Hardin FM; Kallogjeri D; Nicklaus J; Wineland AM; Fendell G; Peelle JE; Piccirillo JF

Introduction: Chronic tinnitus is a common problem in otolaryngology. Mindfulness-Based Stress Reduction (MBSR) is thought to improve symptoms in tinnitus patients. In a variety of different conditions, MBSR is associated with alterations in neural connectivity in default mode networks as seen on resting-state functional connectivity MRI (rs-fcMRI). The objective of this study was to evaluate the impact of an MBSR program in patients with chronic bothersome tinnitus on the 1) perception and severity of symptoms of tinnitus and 2) functional connectivity in neural attention networks as measured by rs-fcMRI.

Methods: A total of 13 adult participants with a median age of 55 years, suffering from subjective, non-pulsatile bothersome tinnitus for at least 6 months participated in this study. Intervention included an 8-week MBSR program, conducted by a trained MBSR instructor. The primary outcome measure was the difference in patient-reported symptoms of tinnitus using the Tinnitus Handicap Index (THI) and Tinnitus Functional Index (TFI) between pre-intervention, post-MBSR, and 4-week post-MBSR follow-up assessments. Secondary outcomes included assessment of change in measurements of depression, anxiety, mindfulness and cognitive abilities between pre- and post- MBSR time points. Functional connectivity MRI was performed at pre- and post- MBSR intervention time points to serve as a neuroimaging biomarker of cortical networks.

Results: Scores on the THI and TFI showed statistically significant and clinically meaningful improvement over the course of the study with a median ΔTHI of -16 and median ΔTFI of -14.8 between baseline and 4-week follow-up scores. Except for depression, there was no significant change in any of the secondary outcome measures. Analysis of the rs-fcMRI data showed overall increased connectivity in the post-MBSR group in attention networks but not the default network.

Conclusions: These findings demonstrate that participation in an MBSR program is associated with significant improvements in tinnitus symptoms, depression, and connectivity changes in neural attention networks. We believe MBSR is a promising treatment option for chronic bothersome tinnitus that is both noninvasive and inexpensive.

092 **Sheshadri, Ajay, MD**

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Washington University in St. Louis
Department: Internal Medicine
Division: Pulmonary and Critical Care Medicine
Mentors: Mario Castro, MD, MPH; Jane Garbutt, MD, MPH; Jonathan Green, MD

Reducing field of view in multi-detector quantitative computed tomography improves accuracy of measures of airway wall remodeling

Sheshadri A; Rodriguez A; Chen R; Kozlowksi J; Burgdorf D; Wilson B; Schechtman K; Castro M; Fain S; Gierada D

Introduction: Multi-detector computed tomography (MDCT) of the chest offers a non-invasive way to measure airway remodeling in obstructive lung disease. Most methods used to quantify airway remodeling typically overestimate wall area (WA) and wall thickness (WT). Reduced reconstructed field of view (FOV) will increase the number of image pixels across the airway structures, potentially improving automated digital measurement. This study investigates whether reducing the MDCT reconstruction FOV improves accuracy of measures of airway remodeling.

Methods: 30 well-characterized adults (13 normal, 7 non-severe asthma (NSA), 10 severe asthma (SA)) underwent MDCT scanning (supine, maximum bronchodilation, TLC). The COPDGene phantom was used to compare the accuracy of MDCT measures of remodeling with the known dimensions of three artificial airways. Human and phantom MDCT images were reconstructed at full (30 cm), 15 cm, and 10 cm FOV. Measures of airway remodeling (WT, WA, wall area percent (WA%), and square-root wall area at Pi10 (Pi10)) were compared at each FOV for the phantom and specific airway segments (RB1, RB10, LB1, and LB10) using Airway Inspector v2.8 (www.airwayinspector.org). The MDCT remodeling measures at each FOV were compared with mixed-model repeated measures analysis of variance with Tukey's post-hoc correction using SAS v9.3 (SAS Institute, Cary, NC).

Results: As observed previously subjects with SA were older than subjects with NSA or normal (46.8±7.7 vs. 30.4±14.8 and 24.9±6.8 years, $p<0.001$) and had lower lung function before and after bronchodilator (BD) (pre-BD, %predicted: SA, 67.3±18.3 vs. NSA, 99.3±12.3 and normal, 102.6±9.4, $p<0.001$; post-BD, %predicted: SA, 73.5±18.3 vs. NSA, 109.3±11.0 and normal, 106.5±9.9, $p<0.001$). For phantom experiments the MDCT remodeling measures were most accurate at the 10 cm FOV, followed by increasing overestimation for 15 cm and Full FOV (Table 1). MDCT remodeling measures in humans followed a similar pattern and progressively decreased with decreasing FOV (ANOVA $p<0.001$, 10 cm vs 15 cm FOV $p=0.01$-0.005, 10 and 15 cm FOV vs. Full FOV, $p<0.001$).

Conclusions: MDCT measures of airway remodeling in the phantom were progressively more accurate as reconstructed FOV decreased, suggesting that a reduced FOV strategy for measures in human subjects would be effective. Indeed, a similar pattern of smaller measured values of airway remodeling was observed in human subjects, though the improvement in accuracy is small. Future studies should consider the use of a smaller FOV when using MDCT measures of airway remodeling as clinical endpoints.

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Compliance with follow-up cultures in Staphylococcus aureus bacteremia: Opportunity for quality improvement

Thomas BS; Jafarzadeh SR; Marschall J; Fraser VJ; Warren DK

Introduction: Treatment failure in uncomplicated Staphylococcus aureus bacteremia (SAB) occurs in 20-30% of cases. Published guidelines recommend follow-up blood cultures (cx) to document clearance of SAB within 72 hrs of treatment initiation. We hypothesized that not all patients (pts) with SAB would have follow-up blood cultures done & that pts without documented clearance would have higher in-hospital mortality.

Methods: We performed a retrospective cohort study of adult pts with their first episode of SAB from 2008-2012 at a large academic medical center. Pts were excluded if they left AMA, were discharged to hospice, or had a blood cx's obtained <72 hours from discharge or death. We used logistic regression to study the association between SAB clearance (≥1 negative cx collected >1 hour after the last positive cx) & mortality. We estimated the causal risk difference of documenting SAB clearance versus failure to do so using the g-computation approach.

Results: We identified 1,437 pts with SAB; 873 pts met study inclusion criteria. Study pts median age = 57 (IQR: 46-67) yrs, were predominantly male (60.1%, n=525), Caucasian (60.1%, n=525) & the median Charlson score = 2.0 (IQR: 1.0-5.0). The median length of stay = 14.0 (8.0-25.0) days & 48.8% (n=426) had an ICU admission. 88.4% of SAB were healthcare-associated. 45.0% (n=393) of pts had a CVC. 33.1% (n=289) were hemodialysis pts, 11.1% (n=97) had endocarditis & 6.4% (n=56) had pneumonia. The mean duration of SAB = 1.1 (±4.6) days & duration of antibiotics = 10.2 (±12.5) days. Failure to perform follow-up cx to confirm clearance occurred in 11.5% (n=100) of pts. In-hospital mortality was greater in pts without documented clearance [27/100 (27%) w/o vs. 67/773 (8.7%) w/ clearance]. Failure to document SAB clearance (OR = 5.4, 95% CI: 2.7, 10.0), Charlson comorbidity score (OR = 1.3, 95% CI: 1.1, 1.4), ICU admission (OR = 8.1, 95% CI: 4.2, 15.7) & pneumonia (OR = 2.6, 95% CI: 1.1, 5.9) were independent predictors of mortality. The estimated causal risk difference of mortality per 100 SAB pts without documented clearance was 18.9% (95% CI: 17.4%, 20.5%) compared to those with documented clearance.

Conclusions: A lack of repeat cx to document clearance of SAB occurred in 11% of pts & was independently associated with poor outcomes.

116 **Trudell, Amanda, DO**

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Development of a clinical prediction model to identify pregnancies at risk for stillbirth

Trudell AS; Tuuli MG; Cahill AG; Macones GA; Odibo AO

Introduction: Stillbirth (SB) complicates nearly 26,000 pregnancies each year in the United States. Our goal was to develop a clinical risk prediction model for SB to be used as a maternal risk stratification tool following second-trimester anatomy survey.

Methods: We performed a retrospective cohort study of all singleton pregnancies presenting for second trimester anatomic survey between 2000-2009. Pregnancies with incomplete follow-up were excluded. The primary outcome was antepartum SB > 20 weeks gestation. Backward stepwise logistic regression was used to create models for the prediction of SB. Candidate predictors were identified from the literature and from univariate analysis of maternal characteristics. ROC curves were generated and the area under the curves (AUC) with 95% confidence intervals (CI) compared to identify the most discriminatory model. A stratified analysis was performed excluding fetal anomalies and aneuploidy. To assess SB prediction at periods of potential clinical intervention two additional models were developed to predict the risk of SB >23 weeks and >28 weeks and compared to the overall model for the prediction of SB >20 weeks. The final model was internally validated using bootstrapping with 1,000 repetitions.

Results: Of 73,661 pregnancies meeting inclusion criteria 639 (0.87%) SBs occurred. Coefficients for significant risk factors for SB are shown in the Table. The model with the greatest AUC was for the prediction of SB >28 weeks (AUC 0.701, 95% CI (0.67-0.74)). The most discriminative model for the prediction of SB at >20 weeks had an AUC of 0.687 (95% CI 0.66-0.71) When fetal anomalies and aneuploidy were excluded, the model with the greatest AUC had a reduced discriminative value for SB >20 weeks AUC=0.644 (0.62-0.67).

Conclusions: Although significant risk factors for the prediction of SB were identified, the discriminative ability of even the best model was modest. Our study calls for continued efforts at developing prediction models for SB including the identification of biomarkers that can improve these models.

042 **Tucker, Natalia, MD**

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Axillary ultrasound accurately excludes clinically significant lymph node disease in patients with early stage breast cancer

Tucker N; Cyr A; Ademuyiwa F; Tabchy A; Jin J; Margenthaler J; Gao F; Sanati S; Gillanders W

Introduction: The current standard of care for patients with newly diagnosed breast cancer is sentinel lymph node biopsy (SLNB) for axillary staging. SLNB is not a risk-free procedure. Axillary ultrasound (AUS) has also been used to identify spread of disease to the axilla. We believe that AUS may be a potential alternative to SLNB for preoperative axillary staging, possibly allowing the avoidance of SLNB.

Methods: Patients who underwent AUS between January 2007 and March 2013 were identified using a prospectively maintained surgical database at Washington University School of Medicine. The negative predictive value (NPV), sensitivity, and specificity of AUS were calculated using pathology as the gold standard. Axillary recurrence and disease-free survival were also assessed. Univariate analyses were performed to determine if any patient and/or tumor characteristics affect AUS NPV. A blind review was also performed.

Results: 653 patients diagnosed with breast cancer (T1, T2, clinical N0) underwent AUS at our institution between January, 2007 and September, 2013. 271 patients had abnormal AUS. Of those, 155/268 (57%) had axillary disease on surgical pathology. 382 patients had normal AUS. Of those, 61/382 (16%) were found to have axillary disease on surgical pathology. Overall AUS sensitivity and specificity were 72% and 73%, respectively. AUS NPV was 84%. 21/61 (34%) of patients with false-negative AUS had micrometastatic disease only (< 2 mm). For detection of macrometastatic disease, AUS had a sensitivity of 77% and NPV of 90%. Agreement between the actual treatment received and blind reviewer treatment recommendations ranged from 62-77%.

Conclusions: AUS accurately excludes patients with clinically significant axillary disease in 90% of patients. Given current paradigms in breast cancer treatment, where (1) biomarker profile and other predictors of tumor biology are increasingly used as a major factor in medical decision-making and (2) sentinel lymph node biopsy is not considered therapeutic, AUS may provide a non-invasive alternative to surgical lymph node staging.

038 **Vouri, Scott, PharmD, BCPS, CGP**

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Validating acute urinary retention using diagnosis and procedural codes

Vouri SM; Olsen MA; Strope SA

Introduction: With a lack of existing validation studies, we evaluated the accuracy of diagnosis and procedural codes used to identify acute urinary retention (AUR).

Methods: This was a retrospective, cross-sectional validation study conducted at a single medical institution within the emergency department (ED) and the outpatient urology clinic (OUC) in men ≥45 years. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes 788.20, 788.21, 788.29 for AUR and Current Procedural Terminology (CPT) codes 51701, 51702, 51703 for urinary catheterization were used to identify men with potential AUR. Four algorithms using ICD-9-CM and CPT codes were compared against the gold standard blinded chart review. Sensitivity (Sn), specificity (Sp), positive predictive values (PPV), and negative predictive value (NPV) were determined for both the ED and OUC.

Results: A total of 162 men in the ED and 245 men in the OUC were identified using these codes. Of the four algorithms, the use of any ICD-9-CM diagnosis codes for AUR was the preferred algorithm. The Sn, Sp, PPV, and NPV were, 0.84, 0.96, 0.90, and 0.93 in the ED. The Sn, Sp, PPV, and NPV were 0.86, 0.87, 0.69, and 0.95 in the OUC.

Conclusions: The algorithm which used ICD-9-CM diagnosis codes for AUR most accurately identified acute urinary retention. Based on this, ICD-9-CM codes for AUR can be reliably used in claims data.

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

045 **Adebayo, Moses**
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Department: Neurosurgery
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A detailed investigation of the role of the vestibular system in idiopathic scoliosis
Adebayo MA; Dorward IG
Introduction: Adolescent idiopathic scoliosis (AIS) is the abnormal curvature of the spine seen in adolescents of ages 10-16. Multiple studies have suggested a correlation between dysfunction of the vestibular system and the development of AIS. However, the nature of the relationship between the vestibular system and the development of AIS remains poorly understood. We will attempt to elaborate the relationship between vestibular dysfunction and scoliosis along a spectrum of severity, as well as to determine if operative correction of the spinal deformity impacts the degree of vestibular dysfunction.
Methods: Subjects will undergo standard radiographic assessments on upright long-cassette x-rays, to characterize their degree of deformity. We will then assess vestibular dysfunction utilizing the bucket test which utilizes a simple apparatus to assess subjective visual vertical (SVV). Deviations of SVV have been shown to indicate dysfunction in the otoliths of the vestibular system. Subjects who proceed to surgical correction of their deformity will then undergo repeat radiographic and SVV measurements at several postoperative time points. We will then assess our measurements for correlations between various elements of spinal deformity and the degree of vestibular dysfunction both before and after surgery.
Results: Pending.
Conclusions: We would anticipate a strong positive correlation between severity of spinal deformity and severity of vestibular dysfunction. Further, we anticipate that operative intervention will result in a significant improvement of all radiographic parameters of spinal deformity, but will not lead to any improvement in vestibular function.

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Mentor: Catherine Lang, PT, PhD
Affected upper limb activity in chronic stroke: An examination of potential modifying factors
Bailey RR; Birkenmeier RL; Lang CE
Introduction: Adults with chronic stroke experience disability in everyday activity despite intervention-related improvement in motor function. Recent studies fail to support the assumption that improved motor function measured inside the clinic leads to improved motor function that occurs outside of the clinic. Factors other than motor function may influence affected (i.e. hemiparetic) upper extremity (UE) activity. The purpose of this study was to characterize affected UE activity and examine potential modifying factors of affected UE activity in community-dwelling adults with chronic stroke.
Methods: Forty-six adults with chronic stroke (i.e. >6 months) wore accelerometers on both UEs for 25 hours and provided information about potential modifying factors (time spent in sedentary activity, cognitive impairment, depressive symptomatology, number of comorbidities, motor dysfunction of the affected UE, age, independence in activities of daily living (ADLs), and living arrangement). Accelerometry was used to quantify duration of affected and unaffected UE activity. The ratio of affected-to-unaffected UE activity was also calculated. Associations between duration of affected UE activity and potential modifying factors were examined.
Results: Mean hours of affected and unaffected UL activity were 5.0 ± 2.2 and 7.6 ± 2.1 hours, respectively. The ratio of affected-to-unaffected UE activity was 0.64 ± 0.19, and hours of affected and unaffected UL activity were strongly correlated ($r=0.78$). Decreased severity of motor dysfunction was moderately associated with increased affected UE activity ($\rho=0.49$, $p<0.01$). Affected UE activity was greater in adults who were independent in ADLs (5.4 ± 2.1 hours) versus dependent (3.0 ± 1.3 hours, $p < 0.01$). No other factors were associated with affected UE activity.
Conclusions: Severity of motor dysfunction and dependence in ADLs should be addressed when setting goals for UE activity in people with chronic stroke. Given the strong, positive correlation between affected and unaffected UE activity, future research should examine if encouragement to increase activity of the unaffected UE leads to increased activity of the affected UE.

No Poster **Cartmill, Christopher**

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The pathophysiology of perioperative myocardial infarction: a coronary angiographic investigation

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Introduction: Perioperative Myocardial Infarction (PMI), a serious complication experienced by patients undergoing non-cardiac surgery, is a significant concern, particularly among high cardiac risk patients. While myocardial infarction in non-surgical patients often results from plaque rupture (type I MI), the pathophysiology of PMI is unclear and is likely to involve more cases of supply and demand mismatch (type II MI). Using coronary angiography, our study's goal is to determine the exact etiology of PMI.

Methods: This retrospective cohort study includes 141 patients who received a coronary angiogram as a result of PMI in the past 5 years. These patients are identified using the BJC patient database to identify patients that had non-cardiac related surgery and subsequently received a coronary angiography within two weeks after surgery at Barnes-Jewish Hospital. The patients were screened to ensure that the coronary angiography was indeed performed as a result of MI. These angiographs will then be analyzed by an interventional cardiologist and classified by the etiology of the PMI.

Results: These findings will be used to determine the pathophysiology of PMI and used to identity predictors of Type I (plaque rupture) versus Type II (supply and demand mismatch) PMI. Multivariate logistic regression analysis will be performed to assess clinical predictors for the specific angiographic findings. Based on past studies, PMI is strongly correlated with supply demand mismatch and associated ST segment depression on EKG, which is consistent with our initial findings. This study will give a better understanding of all types of PMI. Additionally, the majority of the patient population had other comorbidities, with high ASA scores, indicating that certain surgeries might put undue stress on these patients.

Conclusions: The results of this study will lead to a better understanding of the pathophysiology of PMI. This understanding will then be used to better predict, prevent and treat patients at risk for this serious surgical complication, leading to a decreased rate of morbidity and mortality in non-cardiac surgery patients.

078 **Chen, Yulong**

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Amnesia of the operating room in the B-Unaware and BAG-RECALL clinical trials

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Introduction: Patient perioperative memories have implications for assessing patient satisfaction with anesthesiologists, for timing of informed consent, and for provision of medical information.

Methods: This was a retrospective study of patients from 2 clinical trials (n=8100) on intraoperative awareness. Patient descriptions of last preoperative and first postoperative memories at 1-3 and 30 days postop were analyzed and coded into perioperative locations. The proportions of patients who did not remember perioperative locations of interest at 30 days postop were ascertained. Logistic regression analyses were performed for patients not remembering the OR before surgery and for patients remembering the OR after surgery, both at 30 days postop. To assess memory stability, coded locations were compared between 1-3 and 30 days postop.

Results: Most patients did not remember the OR before and after surgery ($P < 0.0001$, 54%, 2187/4067; 95% CI, 52.2% to 55.3%). Fifty-six percent of patients did not remember the OR before surgery (3353/5990; 95% CI, 54.7% to 57.2%) and 95% did not remember the OR after surgery (4327/4564; 95% CI, 94.1% to 95.4%). Midazolam dose and age predicted not remembering the OR before surgery. No variable predicted remembering the OR after surgery. Forty-one percent of patients (2077/5122; 95% CI, 39.2% to 41.9%) changed their answer regarding last preoperative location between 1-3 and 30 days postop, and 40% of patients (1388/3517; 95% CI, 37.9% to 41.1%) changed their answer regarding first postoperative location.

Conclusions: Patient perioperative amnesia may argue against assessing patient satisfaction with anesthesiologists as well as obtaining consent and providing information close to surgery.

103 **Chiang, Leslie**

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Geriatric assessment as predictors of hospital readmission in senior adults with cancer

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Introduction: Hospital readmission is a common, costly problem. Little is known on risk factors for readmission in older adults with cancer. This study aims to identify factors associated with 30-day readmission in a cohort of older medical oncology patients.

Methods: This is a retrospective cohort study of adults over age 60 hospitalized to an Oncology Acute Care for Elders Unit at Barnes-Jewish Hospital. Standard geriatric screening tests were administered in routine clinical care. Clinical data and 30-day readmission status were obtained through medical record review.

Results: 696 patients met the inclusion criteria. 77% were white and 52% were male. Thoracic (32%), hematologic (20%), and gastrointestinal (18%) malignancies were most common. The 30-day unplanned readmission rate was 35.9%. Multivariate analyses identified complete dependence in feeding (odds ratio [OR], 3.95; 95% confidence interval [CI], 1.38 - 11.30), and some dependence (1.61, 1.07 - 2.43) and complete dependence (2.70; 1.74 - 4.17) in housekeeping, prior to admission, as associated with higher odds of readmission. Age < 75 (1.54; 1.08 - 2.21), African-American race (1.69; 1.14 - 2.53), potentially inappropriate medications (1.52, 1.05 – 2.19), and higher-risk reasons for admission (1.92; 1.34 - 2.74) also increased odds of readmission. These factors were organized into a prognostic index.

Conclusions: Hospital readmission was common and higher than previously reported rates in general medical populations. We identified several previously unrecognized factors associated with increased risk for readmission, including some geriatric assessment parameters, and developed a practical tool that can be used by clinicians to predict 30-day readmission.

115 **Demaree, Devyn, MHS**

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Do neonatal outcomes after spontaneous versus indicated preterm birth differ?

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Introduction: It is known that there is an increased incidence of neurological and developmental delays in infants born prematurely. However, little is known regarding whether there are different neonatal outcomes of these infants if they were born by spontaneous birth or indicated preterm delivery (PTD). The purpose of this study is to determine if there is any significant difference in the neonatal outcomes of premature infants born either by spontaneous birth or indicated birth. Discovering these outcomes will help physicians counsel families facing PTD.

Methods: A retrospective cohort study was performed on all consecutive live preterm deliveries at Barnes-Jewish Hospital between 2004 and April 2008. Selected neonatal morbidities and mortality for spontaneous versus indicated PTD were compared within gestational age strata, and adjusted for fetal gender and birth weight <10th percentile for gestational age (GA).

Results: Of 1,318 PTDs during the study period, 69% (n=915) were spontaneous and 31% (n=403) were indicated. Distribution by GA: 24-25 weeks, n=127; 26-29 weeks n=257; 30-33 weeks n=553; 34-37 weeks n=379. All respiratory morbidities and lengths of hospitalization were significantly higher in indicated PTD compared to neonates born from spontaneous PTD. However, cesarean mode of delivery was a possible confounder. Adjusting for mode of delivery attenuated the significant results for most of the respiratory outcomes. However, number of ventilator days remained significant. A variable called extended ventilation was created and defined as >3 days of ventilation. Extended ventilation was significantly increased in indicated compared to spontaneous preterm birth (33% vs. 21.6%) after adjustments (aOR 1.8, 95%CI 1.3-2.6), p<0.01). Neurological and other morbidities didn't differ by indication for delivery.

Conclusions: In conclusion, all clinical factors including gestational age and underlying reason for preterm birth should be considered when counseling patients facing preterm delivery. The precise mechanism for why respiratory morbidities appear more severe in neonates born after indicated preterm birth should be an area of future research.

034 **Feely, Megan, MSW**

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Well-being for child welfare involved children: Social skills deficits

Feely MA; Kohl PL

Introduction: More child welfare involved children (CWIC) experience deficits in the well-being domains of health, cognitive development and emotional development than the general population. However, despite research demonstrating its importance little is known about CWIC's social skill deficits. This study is part of larger research project examining the comorbidities of deficits in well-being. Specifically, this study aims to answer the following questions: (1) How many children experience deficits in at least one domain of well-being, including social skills? (2) Are demographic characteristics associated with these deficits?

Methods: This study utilizes the second cohort of the National Survey of Child and Adolescent Well-Being, and includes children 0-17 years old (n=5,872). The sample is weighted to be nationally representative of children investigated for maltreatment. Most measures administered were standardized scales and the parent, current caretaker or was child the respondent. The demographic characteristics used are age, race/ethnicity and gender. Measures will be categorized by domain and all measures will be dichotomized into the categories "above clinical threshold" or "below clinical threshold". Having at least one measure in the domain with a score below the clinical threshold classifies the child as having a deficit in that domain. For measures without a clinical threshold, following precedent, two standard deviations below the population norm will be considered the clinical threshold. Bivariate analyses will include t-tests and chi-square tests to assess for differences by group.

Results: These analyses are on-going, but the number of children experiencing a deficit in each of the main domains (physical health, cognitive development, emotional development and social skills) will be presented along with associations between demographic characteristics and deficits.

Conclusions: The result of this study will help inform practice by identifying the number of children with deficits in their social skills. These deficits are critical as they may influence children's academic engagement and success and their ability to have a stable placement.

105 **Fuest, Stephen**

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Novel bi-specific therapeutics in AML

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Introduction: Dual Affinity Re-Targeting (DART) molecules are an investigational immunotherapy for the treatment of acute myelogenous leukemia (AML). These target T cells to upregulated CD123 on AML blasts. There are indications that PD-1, a cell surface protein expressed on activated T cells, is activated by blasts with PD-L1. The effects of mAb blockade of PD-1 concurrent with DART administration were studied to potentially increase the efficacy of DART therapy.

Methods: Primary human AML samples were treated with various concentrations of DART and anti-PD-1 monoclonal antibody. Levels of PD-1 on T cells and PD-L1 on blasts expression were measured in addition to T cell numbers to determine T cell survival, activation, and proliferation. Effects were analyzed with flow cytometry.

Results: There was a statistically significant difference in the outcomes of treating all the huAML samples with differing DART, anti-PD-1 mAb, and control Ab. Post hoc analysis with Wilcoxon signed rank tests did not indicate significance for any combination of these groups. After 5 days of incubating human AML sample UPN924073, the trends of T cell number were higher for the blocking antibody group as compared to controls with a statistically significant difference (Friedman test, $X2(7) = 16.556$, $p = 0.020$). The number of T cells expressing PD-1 was decreased by the anti-PD-1 blocking antibody relative to the control. This group was also statistically significant ($X2(7) = 19.667$, $p = 0.006$). PD-1 expression increased with increased DART exposure. The increased PD-1 expression on CD4 T cells from peripheral blood samples from the DART clinical trial indicates that activation of T cells due to DART treatment also occurs in vivo.

Conclusions: PD-L1 expression levels varied in primary AML samples yet increased after IFN-γ exposure. DART treatment induced increased surface expression of PD-1 on T cells when incubated with CD123+ AML cells. Initial studies on blocking the PD-1/PD-L1 axis with anti-PD-1 mAb showed trends towards augmented T cell proliferation without statistical significance. Lastly, preliminary data in vivo suggested enhanced PD-1 expression in the first patient enrolled in CD123xCD3 DART trial.

017 **Garrett, Tasha, MS**

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Importance of timing in surgical treatment of clinical stage I non-small cell lung cancer: A retrospective study

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Introduction: Lung cancer is the leading cause of cancer deaths among men and women worldwide and is classified as small cell carcinoma or non-small carcinoma. Standard of care for stage 1 non-small cell lung cancer (NSCLC) is surgical resection. This retrospective study focused on whether a delay of surgical resection in the treatment of clinical stage I NSCLC has an effect on overall survival, recurrence of the lung cancer, and pathological upstaging while employing the null hypothesis that delay in operation does not lead to a higher incidence of pathologic upstaging or lower long-term survival in patients undergoing surgery for clinical stage I lung cancer.

Methods: Analysis of Washington University's Society of Thoracic Surgeons General Thoracic Surgery Database was performed in order to identify patients who were treated for stage I NSCLC with surgical resection between January 1, 2000 and December 31, 2012. Patient charts were reviewed to obtain relative information such as surgery dates, dates of initial diagnosis, postoperative complications, lung cancer recurrences, and overall survival. Patients were then divided into two groups: early surgery term (surgery within 8 weeks of initial diagnosis of lung cancer) and delayed surgery term (surgery greater than 8 weeks after initial diagnosis). Initial diagnosis is defined as 1) documentation of biopsy; or 2) date of the CT or PET scan on which the nodule was first seen. The two groups were compared using t-tests and chi square tests in SPSS version 22.0 in order to assess the significance of the aforementioned information.

Results: The data shows that the following variables have a significant relationship with late surgery term: clinical stage T1, ACE score, congestive heart failure, hypertension, coronary artery disease, and myocardial infarction.

Conclusions: Limitations included incomplete medical files and inability to obtain follow-up. More results are still pending so the null hypothesis cannot be proven or disproven at this time. This study will hopefully provide a better understanding of surgical treatment potentially affecting patient survival and aid future research.

035 **Glasheen, Megan, MS**

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Mentors: Graham Colditz, MD, DrPH; Adetunji Torioloa, MD, PhD, MPH

The effects of NSAID use on pancreatic cancer risk and mortality

Glasheen ME; Toriola A

Introduction: Pancreatic cancer is the 4th leading cause of cancer death, and there were over 46,000 new cases reported in 2014. Furthermore, most patients are not diagnosed until they have reached an advanced stage of the disease, resulting in limited treatment options and high mortality rate. Chemoprevention would be beneficial and greatly improve outcomes for patients with a pancreatic cancer diagnosis, and for those at risk for developing the disease. This study will assess the associations of NSAID use with pancreatic cancer risk and mortality among participants enrolled in the NIH-AARP Diet and Health Study cohort.

Methods: Participants were asked on the Risk Factor Questionnaire of the past 20 years, how many total years they took analgesic medications at least once per week. The analgesic medication options were aspirin, acetaminophen, anti-inflammatory pain relievers, Vioxx, Celebrex, or Bextra. Outcome variables of the study are incident exocrine pancreas cancer and pancreatic cancer mortality. Time to incident exocrine pancreas cancer is determined by date of entry into baseline study and date of cancer diagnosis as provided on follow-up questionnaire. Pancreatic cancer mortality is determined based on date of death with pancreas cancer confirmed as cause of death as obtained from cancer registry returns, follow up questionnaire, National Death Index, or Social Security Death Master File.

Results: Since study commencement, 2,022 participants have developed pancreatic cancer and 1,898 have died. An extensive analysis of the effect of NSAIDs on pancreatic risk and mortality on this population will contribute to the existing knowledge on this subject.

Conclusions: Studies on the effects of NSAID use and pancreatic cancer risk and mortality have produced conflicting results. Some have observed no association, while others have reported inverse associations of NSAIDs with both risk and mortality. This study will assess this controversial relationship in one of the largest cohorts that have been examined thus far, and will provide further insight on the possibility of the use of NSAIDs as chemopreventive agents in pancreatic cancer.

048 **Greenberg, Jacob**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentor: David Limbrick, MD, PhD

The Chiari Severity Index: a preoperative stratification tool for Chiari Malformation Type 1

Greenberg JK; Yarbrough CK; Radmanesh A; Godzik J; Yu M; Jeffe DB; Smyth MD; Park TS; Piccirillo JF; Limbrick DD

Introduction: To develop evidence-based treatment guidelines for Chiari Malformation Type 1 (CM-1), preoperative prognostic indices capable of stratifying patients for comparative trials are needed. Therefore, we developed a preoperative Chiari Severity Index (CSI) integrating the clinical and neuroimaging features most predictive of long-term, patient-defined improvement in quality of life (QOL) after CM-1 surgery.

Methods: We recorded preoperative clinical (e.g. headaches, myelopathic symptoms) and neuroimaging (e.g. syrinx size, tonsillar descent, clivus-canal angle) characteristics. Brief follow-up surveys were administered to assess overall patient-defined improvement in QOL. We used sequential sequestration to develop clinical and neuroimaging grading systems and conjunctive consolidation to integrate these indices to form the CSI. We evaluated statistical significance using the Cochran-Armitage test and discrimination using the c-statistic.

Results: There were 158 patients in the study. Sequential sequestration identified headache characteristics and myelopathic symptoms as the most impactful clinical parameters. These characteristics produced a clinical grading system with improvement rates ranging from 81% (grade 1) to 58% (grade 3) ($p=0.01$). Based on sequential sequestration, the neuroimaging system included only the presence (55% improvement in QOL) or absence (74% improvement in QOL) of a syrinx ≥ 6 mm ($p=0.049$). Integrating the clinical and neuroimaging indices, improvement rates for the CSI ranged from 83% (grade 1) to 45% (grade 3) ($p=0.002$). The combined CSI had better discrimination ($c=0.66$) than the clinical ($c=0.62$) or neuroimaging ($c=0.58$) systems alone.

Conclusions: Integrating clinical and neuroimaging characteristics, the CSI is a novel tool that predicts patient-defined improvement in QOL following CM-1 surgery. The CSI may aid preoperative counseling and stratify patients in comparative effectiveness trials.

No Poster **Han, Rowland, MSE**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Division: Adult Epilepsy
Mentor: Luigi Maccotta, MD, PhD

Neuropsychological correlates of rsfMRI connectivity modulations in unilateral TLE

Han RH; Maccotta L

Introduction: Unilateral temporal lobe epilepsy (TLE) is often considered a disorder of neural networks with neuropsychological sequelae in functions that extend beyond the primary seizure focus. Resting state functional MRI connectivity is a powerful measure for studying effects of disorders on networks that cover wide cortical regions, yet few studies have examined cognitive decline driven modulations in inter- and intra-resting state network connectivity in patients with unilateral TLE.

Methods: We analyzed data from 20 subjects comprised of 10 men and 10 women between the ages of 24 and 69, who have had 8 to 18 years of education. There were 17 right-handed and 2 left-handed patients; one patient was ambidextrous. 12 of the subjects had left localized TLE, and 8 had right TLE.

Results: Results using 169 anatomical regions of interest showed that the neuropsychological meta-variables extracted bidirectional changes in connectivity within and between specific networks, and that these network modulations make sense given the major cognitive domains captured in the meta-variables. Extension of these results to a voxel-wise analysis is ongoing.

Conclusions: To our knowledge, this is the first study that investigates cognitive decline driven connectivity modulations in TLE by examining so-called meta-variables summarizing neuropsychological scores across various cognitive domains, and their correlations with functional connectivity, without a priori focus on specific networks or cognitive functions.

003 **Housten, Ashley, MPA, OTD/S**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Occupational Therapy
Washington University in St. Louis
Department: Occupational Therapy
Mentor: Allison King, MD, MPH

Sickle cell disease & sexual health education for youth: A social skills model

Housten AJ; Abel RA; King AA

Introduction: Youth with sickle cell disease (SCD) do not receive adequate SCD genetic inheritance and sexual health education. As more individuals with SCD live into childbearing years, education is needed. To assess interest in a SCD inheritance and sexual health education program, we conducted a single center pilot study among youth with SCD. Secondarily, we studied the feasibility of program implementation.

Methods: We used a mixed methods approach. Patients aged 11-19 years were approached in an urban hospital. Semi-structured interviews were conducted, recorded and transcribed. Qualitative data were analyzed and coded to identify themes. These results served as drivers for content of a social skills-based education program. Sisters Informing Sisters about Topics on AIDS (SISTA) also provided a framework for the curriculum. The program was assessed using member-check. Feasibility was measured and defined as at least 50% of individuals consenting to participate.

Results: Twenty of 35 youth (57%) consented. All participants from the qualitative analysis demonstrated knowledge deficits and/or interest in SCD genetic education. Nineteen (95%) demonstrated deficits in sexual health knowledge and/or requested education. Seventeen (85%) demonstrated knowledge gain in SCD genetics and/or sexual health. Twelve (60%) reported engaging in sexual activity, seven (35%) in risky behaviors, and three (15%) reported past STI diagnosis. An education program and pre/posttest measures were created and assessed using member-check.

Conclusions: Youth with SCD lack understanding of both SCD genetic inheritance and sexual health. With feasibility supported, the next phase of research will address the efficacy of implementing a genetic and sexual health education program.

070 **Ibiebele, Abiye**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Mentor: Laura Bierut, MD

A return of genetic ancestry results to a smoking population

Ibiebele A; Olfson E; Hartz SM; Bierut LJ

Introduction: With the rise of personalized medicine and direct to consumer genetic testing companies, more research is needed on how participants respond to genetic results. The purpose of this descriptive study is to examine attitudes towards the return of genetic results in a smoking population and whether these results can be used as an incentive for research participation.

Methods: 578 subjects enrolled in a genetic study on smoking in St. Louis were asked to rate their interest in receiving 1) genetic ancestry results and 2) genetic results related to health risks. Chi Square goodness of fit was used to examine differences in interest based on gender, race, high school diploma status, and health literacy.

Results: Of the 578 participants, 485 (83.9%) reported a high interest in receiving genetic ancestry results. Subgroup analysis of those reporting having a high interest shows no significant effect between males (82.6%) and females (86.6%); p=.07. There was also no significant effect between African-Americans (82.6%) and Caucasians (87.6%); p=.18. There was a significant effect for high school diploma (86.9%) and none (80.5%); p = .04. There was also a significant effect for limited health literacy (79.6%) vs competent health literacy (88.7%); p=.003. Further analysis will also be done on interest in receiving health information.

Conclusions: Preliminary results show that participants are interested in receiving genetic results, and therefore it may be a potential incentive for research participation. This study is unique because we examined returning genetic results to an underserved, understudied population, compared to previous studies looking at the return of genetic results. Preliminary results show that regardless of a participant's gender, race, education, or health literacy, a majority of people have a high interest in receiving their genetic ancestry information when participant in a genetic study however there is a significant difference based on high school education and health literacy.

005 **Keglovits, Marian, OTD, MSCI**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Occupational Therapy
Washington University in St. Louis
Department: Occupational Therapy
Mentor: Susan Stark, PhD, OTR/L, FOATA

The in-home occupational performance evaluation for providing assistance

Keglovits MA; Somerville EK; Stark SL

Introduction: Caregiving can be physically and emotionally taxing, placing caregivers at risk for negative health consequences. Home modifications such as grab rails near toilets can improve the functional abilities of people with disabilities and may reduce strain for caregivers. The impact home modifications have on reducing caregiver strain is understudied, with no assessments currently available to measure the impact on caregivers. The aim of this study is to investigate the psychometric properties of a new evaluation to assess caregiver support and describe problematic activities and environmental barriers to caregiving.

Methods: In this cross sectional study, two occupational therapists completed the new assessment with 31 caregivers. Interrater reliability, internal consistency, and correlations with existing measures were investigated for the new assessment. Descriptive statistics of caregiving activities and environmental barriers were also investigated.

Results: Caregivers were primarily female (68%) with an average age of 61 years. Interclass correlation coefficients of the 5 subscales ranged from .94-1.0. The self-efficacy subscale was positively correlated with the Caregiving Inventory (confidence in caregiving) r=.504, p=.006 and Caregiver Competence Scale r=.391, p=.040. The Functional Independence Measure demonstrated a negative correlation with the base activity score r=-.395, p=.028 and barrier severity score r=-.340, p=.061, indicating that the number of activities the person assists with and the number of barriers were correlated with poorer function. The most problematic caregiving activities included providing assistance up/down steps, in/out of the car, in/out of the home, in/out of the bath or shower, and responding to an emergency. The most frequent barriers to providing assistance in the home include lack of hand support, characteristics of the transfer surface, malfunctioning/lack of adaptive equipment, weight of items, presence of steps, and a lack of signal or cues in the environment.

Conclusions: The new assessment demonstrated the potential to guide home modification interventions and measure the impact on informal caregiving in the home.

091 **McKenzie, Matt**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Pharmacy
St. Louis College of Pharmacy
Department: Center for Clinical Studies
Division: Asthma and Airway Translational Research Unit
Mentor: Mario Castro, MD

A prospective observational study of biopredictors of bronchial thermoplasty response in patients with severe refractory asthma (BTR Study)

McKenzie M; Castro M; Sheshadri A

Introduction: Asthma continues to be a major health concern for 25 million people in the United States. Although the current treatment of asthma has improved control, many severe asthma patients still have difficulties. Bronchial thermoplasty, a device-based approach to reduce airway smooth muscle has been shown to improve asthma-specific quality of life. However, predictors of response were not investigated in the past, so this study attempts to evaluate the different markers that may predict clinical response to bronchial thermoplasty.

Methods: We obtained data from 34 willing participants whose clinicians felt that they should have bronchial thermoplasty for severe refractory asthma. At baseline, demographic, physiologic, AQLQ, medication use, and healthcare utilization data were collected. Baseline Multi Detector CT scans of the chest were analyzed using automated airway evaluation software to measure airway remodeling at various airway segments and lung density. Follow-up AQLQ, medication use, steroid use, and healthcare utilization data were collected for 12 months post-thermoplasty. A clinical response by AQLQ was defined as a 0.5 increase in the individual participants score from baseline visit to 12 month visit. Logistic regression model was used to identify the factors associated with AQLQ increase and steroid reduction.

Results: Two areas were predictive of response: shorter duration of asthma (20.1 ± 15.4 vs 44.5 ± 8.7, p=0.001) and history of severe exacerbations in the year prior to thermoplasty (22 vs 3 p=0.064). Also three specific areas that were not predictive of response included: airway remodeling (WA%), lower air trapping at FRC, and lower emphysema-like lung. Three variables were predictive of steroid reduction: age at the time of the first BT (54.9 ± 8.0 vs. 42.6 ± 11.5, p=0.009), baseline AQLQ (2.8 ± 1.0 vs. 4.0 ± 1.0, p=0.005), and OCS dose (10.0 ± 13.9 vs. 1.7 ± 6.7, p=0.03).

Conclusions: Our study suggests that clinical response from bronchial thermoplasty can be predicted with baseline demographic and imaging data. Further studies with larger number of subjects could allow careful selection of patients with severe refractory asthma that would benefit from bronchial thermoplasty.

112 **Milman, Kelly**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Family Planning
Mentor: Jeff Peipert, MD, PhD

Changes in insurance status in CHOICE Project participants

Milman KS; Diedrich J; Peipert JF

Introduction: The Contraceptive CHOICE Project was a prospective cohort study which provided 9,256 women with no-cost contraception. This elimination of the cost barrier helped to increase use of highly-effective long-acting reversible methods of contraception (LARC), which have higher up-front costs than other methods and are thus the least affordable methods for low-income women. Access to health insurance has been shown to be associated with increased use of LARC methods and use of these methods has been shown to be associated with lower rates of unintended pregnancy and abortion. The present analysis aims to describe the changes in insurance status of participants in the CHOICE Project between enrollment in the CHOICE Project in 2008-2009 and during follow-up in 2014.

Methods: Project participants who initiated IUD use between January 1, 2008 and June 30, 2009 were contacted for a follow-up telephone survey which included questions about insurance status. We compared the insurance status at the time of enrollment to insurance status at follow-up (median follow-up time 68.90 months). A related samples McNemar test was used to analyze the change in insurance status in these women over this time period.

Results: We randomly selected 436 women from the cohort of 2,002 potentially eligible CHOICE participants to participate in this follow-up study. This preliminary analysis includes the first 219 women who completed the survey. Participants contacted had an average age of 33.6 years, 51.1% were white, 46.1% had completed college, and 19.2% had a household income below 100% of the federal poverty level. The analysis reveals a statistically significant change in insurance status over this time period (41.6% uninsured at time of enrollment, 24.2% uninsured at time of follow-up; $p<0.001$).

Conclusions: Women in this study were more likely to gain insurance than lose insurance between enrollment in the CHOICE Project and the time of the 2014 phone follow-up. Since use of the most effective methods of contraception (long-acting reversible contraception or LARC) has been shown to be associated with decreased unintended pregnancy and abortion rates, this improvement in insurance status is promising.

007 **Nemanich, Samuel**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Movement Science
Washington University in St. Louis
Department: Physical Therapy
Division: Movement Science Program
Mentor: Gammon Earhart, PhD, PT

After-effects following stepping on a rotating surface: A comparison of people with Parkinson disease with and without freezing of gait and healthy controls

Nemanich ST; Earhart GM

Introduction: People with Parkinson disease (PD) have gait difficulties that impair mobility and increase risk for falls and accompanying injuries. About one-third of people with PD experience an especially disabling condition termed freezing of gait (FOG), where the individual is unable to advance his feet despite the intention to walk. Previous research suggests that people with PD+FOG may have differences in connectivity of motor networks in the brain. One way to probe the capacity of the motor system is by examining motor adaptation, which is the flexibility of the brain to alter movement patterns in response to sensory perturbations. Therefore, we wished to examine if individuals with PD+FOG are impaired during a motor, specifically a locomotor, adaptation task compared to people with PD without FOG (PD-FOG). We predicted that after-effects would be diminished in the PD+FOG group, reflecting decreased storage of the adapted motor pattern. Furthermore, since healthy aging has been shown to impact motor adaptation capacity, we will compare the results from PD participants to groups of healthy older and younger adults.

Methods: Five healthy young (Y), 6 healthy old (O), 5 PD-FOG, and 3 PD+FOG adults stepped in place on a rotating disc (45 deg/s) for 15 min (training phase), followed by 10 min. of stepping in place at a fixed cadence (2 Hz) on a stationary surface (after-rotation phase). Rotational velocity of the pelvis during the after-rotation phase was measured using an 8-camera motion capture system.

Results: Preliminary results show that the maximum rotational velocity was as follows: Y>O>PD-FOG>PD+FOG. All groups showed a consistent asymptote of velocity which also followed the order: Y>O>PD-FOG>PD+FOG.

Conclusions: While our sample to date is small, these results suggest that younger adults store the newly learned locomotor pattern to a great extent, while PD+FOG have lower storage or retention of the locomotor patterns. Older adults have lower retention overall, but PD and FOG may further impair adaptive capacity. Future rehabilitation and training approaches for older adults with and without PD may be informed by these data.

022 **Ochieng, Peter**
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Surgery
Division: Minimally Invasive Surgery
Mentor: Corey R Deeken, PhD

Novel scaffold development via electrospinning and 3-D printing

Ochieng PT; Thompson DM; Est SV; Castile RY; Deeken CR; Lake SP

Introduction: In the United States, over $1 billion is spent on hernia repair meshes and fixation every year. However, some of these meshes do not meet the criteria needed for optimum hernia repair. The goal of this study was to combine electrospinning and 3D printing to produce a simple and inexpensive novel scaffold with appropriate physiomechanical properties suitable for use in hernia repair, breast reconstruction or wound repair.

Methods: A 3D printer was utilized to make scaffolds out of polycaprolactone (PCL). Electrospinning was then done on top of the scaffold using a polymer concentration of 10% PCL for different time intervals (60, 30, 15, 7.5 minutes). Ball burst testing, biaxial testing and two-strip biaxial tests were also done.

Results: Ball burst testing showed that electrospinning provided a slight increase in the overall strength of the mesh. All of the meshes showed similar mechanical properties. The scaffolds showed isotropic properties and little effects with cyclic loading ($P > 0.05$). All tested meshes had a Poisson's ratio near zero and showed similar peak membrane values from the 1-3 & 2-4 two-strip biaxial testing ($P > 0.05$).

Conclusions: The results of this study show that it is possible to combine 3D printing technology with electrospinning to produce mesh that has similar pre-failure mechanical properties to some of the commercially available meshes (DUALMESH® and INFINIT®). Developing mesh using 3D printing and electrospinning will allow for personalized medicine by matching host tissue and mesh. This would have a significant impact in healthcare and importantly, help the general surgeon with choosing the appropriate mesh for each hernia repair situation.

No Poster **Olfson, Emily**
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: MD/PhD
Washington University in St. Louis
Department: Psychiatry
Mentor: Laura Bierut, MD

Common, low frequency, and rare coding variants in CHRNA5 contribute to nicotine dependence in European and African-Americans

Olfson E; Saccone NL; Fox L; Rice J; Goate A; Bierut LJ

Introduction: The functional nonsynonymous variant rs16969968 in the α5 nicotinic receptor subunit gene (CHRNA5) is the strongest genetic risk factor for nicotine dependence in European Americans (frequency=35%), and contributes to risk in African-Americans (frequency=6%). The goal of this study was to comprehensively assess the influence of CHRNA5 coding variation on nicotine dependence risk using targeted sequence data from approximately 3,000 unrelated cases and controls.

Methods: Community-based recruitment enrolled subjects aged 25-45. Cases had a Fagerstrom Test for Nicotine Dependence score of ≥4 and controls had a score of 0 or 1. Custom next-generation sequencing with mean on-target coverage of 180X was performed on the CHRNA5 gene. Logistic regression was used to model case-control status with the variables sex, age, ethnicity, individual common variants (frequency≥5%), individual or aggregate low frequency variants (5%>frequency≥0.5%), and aggregate rare variants (frequency<0.5%).

Results: Sequencing identified 24 nonsynonymous variants and 2 frameshift deletions in CHRNA5. The well-studied rs16969968 was the only common variant among these, and the minor allele was associated with increased risk of nicotine dependence (OR=1.28, p=0.0007). Three low frequency variants individually trended in the risk direction and the aggregate term was significant (OR=1.45, p=0.01). The remaining 22 coding variants were rare (each occurred in 1-4 individuals), and similarly, the aggregate term revealed a risk effect (OR=2.39, p=0.03). Nagelkerke's adjusted R2 was used to assess the proportion of nicotine dependence variation explained by CHRNA5 variants. In European Americans, the well-studied rs16969968 gave an R2 of 0.9%, and the addition of all CHRNA5 coding variants increased the R2 to 2.4%. In African-Americans, rs16969968 gave an R2 of 0.2%, and adding all coding variants increased the R2 to 0.8%.

Conclusions: Our findings suggest that common, low frequency, and rare coding variants in CHRNA5 are associated with increased risk of nicotine dependence. Coding variation in CHRNA5 accounts for over 2% of the nicotine dependence variation in European Americans and close to 1% in African-Americans.

136 **Osborne, Ashley**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Cardiology
Mentor: Charles Canter, MD

Variation in surveillance biopsy protocols for pediatric heart transplant recipients

Osborne AD; Zinn MD; Canter CE

Introduction: Endomyocardial biopsy (EMB) is widely accepted as the gold standard to monitor for allograft rejection in pediatric heart transplant recipients. However, a best practice for using EMB surveillance has not been established and there has been little research on this topic. The purpose of this study is to describe the variation in surveillance biopsy protocols amongst centers in the United States.

Methods: We administered a multiple choice survey to the 46 centers enrolled in the Pediatric Heart Transplant Study. The survey consisted of 9 questions for each era: 1995-2004 and 2005-present. Each center was also asked about any changes made during these 2 eras, and if changes occurred, to describe the changes. We used a two-tailed Fisher's Exact Test for statistical analysis.

Results: 34/46 centers completed the survey. In the first year post transplant, different centers performed "0" to "more than 8" biopsies with 30.3% and 50.0% of centers responding "more than 8" for 2005-present and 1995-2004, respectively (p=0.18). Total biopsies in the 2nd-5th year post-transplant ranged from "0" to "5 or more" with 64.7% in 2005-present and 50.0% in 1995-2004 performing 4 or less (p=0.30). There was a statistically significant increase in centers that routinely check NT-pro BNP or BNP levels from 2005-present compared to 1995-2004 (46.9% vs. 23.1%, p=0.03). Additionally, more centers use blood tests in 2005-present than in 1995-2004 to evaluate for acute rejection, although this difference was not statistically significant (21.9% vs. 7.8%, p=0.17).

Conclusions: The results of this study illustrate the wide variation in centers' surveillance EMB protocols and that this variation has not been resolved between the 2 eras. Although it appears more centers are taking advantage of new technologies to monitor for allograft rejection, there is still a need for a consensus on a best practice. Continuing need for investigation into optimal surveillance strategies is warranted.

084 **Patel, Parth**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Internal Medicine
Division: Gastroenterology
Mentor: Deborah Rubin, MD

Understanding the mechanisms by which tis7 and Hedgehog signaling interact to regulate crypt cell proliferation

Patel PA; Swietlicki E; Rubin DC

Introduction: Small bowel diseases including Crohn's disease, radiation enteritis, and celiac sprue may result in short bowel syndrome, either due to poor intestinal function due to extensive disease involvement, or following small bowel resection to remove severely diseased intestine. Post-operatively, patients have reduced total small bowel absorptive surface area. Therapies to enhance small bowel surface area and improve absorptive function are lacking; to address this, our laboratory seeks to identify the pathways that regulate gut epithelial cellular proliferation following small bowel resection. We addressed the hypothesis that Hedgehog signaling increases myofibroblast tis7 expression, which then signals to the crypt to increase proliferation. The overall goal of my project was to understand the mechanisms by which tis7 and Hedgehog signaling interact to regulate crypt cell proliferation.

Methods: Myofibroblasts were isolated and cultured in presence and of Indian hedgehog (Ihh). We isolated myofibroblasts from tis7-/- and wild type (WT) intestine; both myofibroblast cell types were incubated with Ihh, and their proliferation will be measured by immunohistochemical detection of Ki67 expression. In addition, crypt organoid cultures isolated from WT intestines were co-cultured with WT and tis7-/- myofibroblast cells, and incubated with Ihh ligand.

Results: Myofibroblasts exposed to Ihh had increased expression of tis7. Crypt organoid surface area was increased in response to Ihh in co-cultures with WT myofibroblasts but not in co-cultures with tis7-/- myofibroblasts.

Conclusions: The results suggest that tis7 expression is regulated by and is downstream of Ihh, and myofibroblast tis7 expression is required for Ihh induced proliferative effects on WT organoids. The significance of our studies is their potential to identify new therapeutic agents, by characterizing novel tis7 target genes, and understanding signaling pathways that enhance crypt-villus surface absorptive area following resection.

055 Phillips, Katherine

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Pharmacy
St. Louis College of Pharmacy
Department: Knight Alzheimer's Disease Research Center (ADRC)
Mentors: John Morris, MD; Catherine Roe, PhD

Seizures in Alzheimer disease: prevalence, risk factors, and anti-epileptic drugs

Phillips KM; Babulal GM; Roe CM; Morris JC

Introduction: Recent studies have noted a greater incidence of unprovoked seizures in Alzheimer disease (AD) than the general population. The literature does not agree on the actual incidence or prevalence of seizures in AD, nor on the risk factors for seizures, whether they are related to dementia severity, duration, or age of onset. We compared the prevalence of seizures in persons with symptomatic AD versus cognitively normal persons, evaluated the likelihood of seizures by Clinical Dementia Rating stage, and described the effects of anti-epileptic drug (AED) use on cognitive course and survival.

Methods: This retrospective cohort study used the National Alzheimer's Coordinating Center database. Participants were aged 50+ years and were cognitively normal or had a baseline clinical diagnosis of AD. Logistic regressions tested the association of the likelihood of seizures with dementia presence and dementia stage. Analyses adjusted for age, sex, race, and education, and were repeated adjusting for APOE4 genotype. Cox-proportional hazard models tested the association of baseline seizures and use of AEDs with time to death while simultaneously adjusting for age, sex, race, and education. Mixed linear models tested baseline associations between seizures and AEDs with change in cognition over time.

Results: Participants with AD at baseline were more likely to have a seizure history than those with normal cognition (OR=1.79, 95% CI=1.45, 2.21). Compared to those with normal cognition, the likelihood of having seizures increased in a dose-dependent manner with increasing dementia severity ($p<.001$). Within the normal cognition group, having seizures or taking AEDs at baseline was unrelated to cognitive decline with time. Within the AD group, people without seizures at baseline on an AED had a slower decline on cognitive tests over time compared to those not taking a seizure drug. Those with untreated seizures at baseline had a faster rate of decline than those not having a seizure regardless of whether they were taking an AED or not.

Conclusions: This study suggests the importance of treating seizures and a possible benefit of AED use on cognition in AD. More study is needed on the effect of specific AEDs in AD.

015 Rogalski, Brandon

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Orthopaedic Surgery
Mentor: Robert Brophy, MD

Descriptive epidemiology of surgical patients at the Orthopedic Outpatient Center - a retrospective review

Rogalski BL; Brophy RH

Introduction: Surgical site infection (SSI) is a potentially major complication with variable costs and a significant burden for patients, providers and the healthcare system. However, there has been little data collected on the risk factors that contribute to surgical site infections following outpatient orthopedic surgery. The purpose of this study is to identify SSI risk factors so that orthopedic surgeons can better serve their patients and ultimately decrease the incidence of SSI's.

Methods: We retrospectively reviewed the charts of approximately 22,000 patients who underwent orthopedic surgery at the Outpatient Orthopedic Clinic in Chesterfield, Missouri between the opening of the center in July of 2005 through May 31st, 2014.

Results: Based on preliminary data, we expect the overall incidence of surgical site infections within our population to be approximately 3-5 SSI's per 1000 patients. Further, we anticipate that diabetes mellitus status and length of surgery will be statistically significant predictors for an increased risk of SSI incidence.

Conclusions: The preliminary results of this study suggest that the absolute risk of surgical site infection following outpatient surgery is very low, however; the total number of SSI's still represents a significant cost to patients and providers alike. After compiling the data, we hope to identify statistically significant indicators of SSI's and use our findings to help surgeons recognize at-risk patients. Further research on techniques to minimize the effects of these risk factors will be warranted.

052 **Roubakha, Mikhail**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentor: Ian Dorward, MD

Determinants of costs and complications in long-segment spinal fusion procedures in adults

Roubakha M; Dorward I

Introduction: We would like to determine if a difference in outcomes exists between patients undergoing spinal procedures at academic versus private centers, and if outcomes differ between patients who are privately insured and those who are insured through Medicare or Medicaid. We will examine the impact of factors such as patient age, comorbidities, academic vs. community center, payor, and surgeon experience. We will also compare posterior vs. anterior and posterior approach, and posterolateral fusion only vs. circumferential fusion.

Methods: A task order will be submitted to CADR at WUSM. Patient records containing procedural variables for thoracic and lumbar spinal fusions of greater than 7 levels and diagnoses including idiopathic scoliosis or lumbar/thoracic spondylosis, among others, will be requested. Outcome variables such as comorbidities, hospital readmissions, stroke, and pneumonia for these patients will be examined. Once data has returned, statistical analysis will be performed to determine if differences between various cohorts exist.

Results: We hypothesize that there will be lower complications and costs at academic medical centers compared with community centers. Also, longer-segment spinal fusions are predicted to have lower complication rates after 2 years than shorter-segment procedures.

Conclusions: The reasons for differences in outcomes following long-segment spinal fusions should be identified and targeted for improvement. Additionally, determining long-term outcomes following long-segment spinal fusions will help surgeons decide if the procedure is right for their patient.

006 **Sarrami, Behnaz, MS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Pharmacy
Creighton University School of Pharmacy and Health Professions
Department: Occupational Therapy
Mentor: Susan Stark, PhD, OTR/L, FAOTA

Medication taking behavior in the medically underserved community dwelling older adults

Sarrami B; Murphy M; Hu Y; Stark S

Introduction: With increased age and functional loss, adherence to prescription medication becomes a complex daily activity. Declined cognitive ability, limited access to healthcare, lack of transportation, management of multiple medications that are for age-related illnesses and lack of health literacy all contribute to the complexity of the daily routine. These complexities are barriers for older adults who are home-bound and reside in medically underserved communities. Inappropriate medications are also prescribed to these groups which increases their risk of falls, fractures, mortality, cognitive impairment, and hospitalization.

Methods: A cross-sectional descriptive study of medically underserved older adults was conducted on 28 participants that underwent an in-home performance based assessment to screen for environmental, functional, and cognitive abilities. A sub-sample of 6 underwent an in-home Medication Management Performance-Based Assessment (MedicAPE) to identify potential barriers to adhering to their medication and the use of inappropriate medications.

Results: The sample was 100% African-American with an average age of 80 years of which 32% were taking inappropriate medication. Among the sub-sample of participants,100% had barriers to medication adherence, all got their medication from more than one doctor, 67% forgot to take their medication, 33% used multiple pharmacies, and 50% had no current medication list to show their physician at every visit. Only 50% had no transportation to pick up their prescription. This is an ongoing research and we anticipate to find all the barriers for older adults' medication adherence, the inappropriate medications prescribed, and be able to individually tailor interventions and find its future use as a guide for healthcare providers.

Conclusions: There is a high prevalence of inappropriate medications prescribed to this sample of underserved African-Americans and a numerous of barriers that make adhering to medication a difficult daily task. Intervention strategies to remediate these barriers are necessary for this population to be able to continue to reside in their own home more independently and effectively.

No Poster **Schachter, Michael, MD**
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Tel Aviv University
Department: Surgery
Division: Pediatric Surgery
Mentor: Jacqueline Saito, MD, MCSI

Integrated management of acute abdominal pain in children

Schachter MP; Saito JM

Introduction: Appendicitis is the most common atraumatic diagnosis requiring surgical intervention in children over the age 2. It accounts for 94,000 ED visits per year in the United States. But, because of the often vague and non-specific presentation, diagnosis can be difficult. Concerns over CT use in children have been raised because it exposes children to ionizing radiation. A recent study showed that cancer incidence increases by 24% in children exposed to ionizing radiation. While ultrasounds involve no radiation exposure, the sensitivity is operator dependent. While recent studies have attempted to validate diagnostic protocols for use of these imaging modalities in diagnosing appendicitis, they tend to lack generalizability to non-pediatric hospitals. This is highly problematic because recent studies show that the majority of children are treated at community. We hypothesize that CT scanning is more heavily utilized in the diagnostic workup of children presenting to ED with acute abdominal pain in hospitals with lower pediatric volume and higher tendencies to transfer pediatric patients to a children's hospital for definitive care. Because of the known risks associated with radiation exposure, we hope to establish a method of identifying and triaging the patients most at highest risk in an effort to reduce the number of CT scans while maintaining the same quality of care.

Methods: This study is a retrospective review of data regarding children evaluated for acute abdominal pain during 2011 in a single metropolitan area. Data will be extracted from each subject's medical record in order to compare subject characteristics, presenting symptoms, imagining modalities utilized, hospital type, volume of pediatric care, and resource availability. The targeted enrollment is 425 patients.

Results: Results will quantify variation in the type and frequency of imaging technology applied for pediatric acute abdominal pain evaluation across subject characteristics, hospital type, volume of pediatric care, and resource availability.

Conclusions: By characterizing and quantifying the use of imaging in relationship to patient and hospital demographics, we will be able to use this information to eventually develop a decision analytic model for evaluating pediatric acute abdominal pain. This will result in more less exposure to potential harmful diagnostic tools, quicker diagnostic evaluations, fewer complications, and less spending.

016 **Shaw, Neil**
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Medicine
Saint Louis University
Department: Orthopaedic Surgery
Mentor: Charles Goldfarb, MD

Prevalence of congenital upper extremity anomalies from 1992-2010: A total population study of New York State

Shaw NB; Goldfarb CA

Introduction: There are only a few epidemiological studies regarding congenital upper extremity anomalies and none from the United States. These data provide important information to health care professionals and affected families to help guide health care planning and future research. The purpose of this investigation was to examine the prevalence of various congenital upper extremity anomalies in the total birth population of New York State over an 18-year period utilizing the New York Congenital Malformations Registry (NYCMR) database.

Methods: The NYCMR documents diagnoses codes for children with at least one congenital upper extremity anomaly diagnosed by two years of age. We scrutinized these diagnosis codes for specific anomalies, including polydactyly, syndactyly, reduction defects, clubhand malformations, and syndromes involving upper limb anomalies.

Results: Between 1992 and 2010, there were 4,883,072 live births in New York State. The overall prevalence of the congenital upper extremity anomalies we counted was 0.31% or 31 cases per 10,000 live births. Polydactyly was the most common anomaly with 12,418 cases and a prevalence rate of one per 393 live births. Syndactyly (1463 cases) and reduction defects (1030 cases) were the next most common anomalies. Specific syndromes were quite rare; however, when combined as a category of syndromes involving upper limb defects (215 total cases), they are more common with a prevalence rate of about one per 23,000 live births.

Conclusions: The NYCMR data demonstrated that congenital upper extremity anomalies are more common than previously believed. Specifically, the prevalence of polydactyly at one per 393 live births is higher than reported. While passive registry data are imperfect, such epidemiological figures are helpful in monitoring prevalence rates over time, identifying potential causes of or associations with the anomalies, and guiding health care planning and future research.

008 **Sorensen, Christopher, MS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Movement Science
Washington University in St. Louis
Department: Physical Therapy
Mentor: Linda Van Dillen, PT, PhD

Is lumbar curvature angle in standing related to low back pain development

Sorensen CJ; Norton BJ; Hwang CT; Callaghan JP; Van Dillen LR

Introduction: Previous studies have used an induced-pain paradigm in back-healthy people to understand risk factors for developing LBP during prolonged standing. The purposes of this study were to (1) compare lumbar lordosis in back-healthy participants who develop LBP symptoms (Pain Developers, PDs) during 2 hours of standing to those who do not develop LBP symptoms (Non Pain Developers, NPDs), and (2) examine the relationship between lumbar lordosis and LBP symptom intensity.

Methods: Participants stood while the positions of the markers placed on 1st, 3rd and 5th lumbar vertebrae were recorded using a motion capture system. Participants then stood for 2 hours while performing 4 different simulated, light work tasks, randomly presented every 15 minutes. At baseline and every 15 minutes during standing, participants rated their LBP symptom intensity on a visual analog scale (VAS). PDs were participants that reported any symptoms following the baseline VAS measure and maintained symptoms throughout standing. Lumbar lordosis angle was calculated using the trigonometric method. An independent samples t-test was used to test for a difference in lumbar lordosis angle in PDs and NPDs. A Pearson correlation coefficient was calculated for lumbar lordosis angle and maximum VAS scores during standing in PDs.

Results: There were 24 (44%) PDs and 33 (56%) NPDs. Lumbar lordosis was significantly larger in PDs compared to NPDs (Mean difference=4.4°; 95% CI=0.9^{o} to 7.8°). The correlation coefficient between lumbar lordosis and maximum VAS during standing was 0.46 (p=0.02).

Conclusions: The results of this study suggest that standing in more lumbar lordosis may be a risk factor for LBP symptom development in back-healthy people who participate in activities that require prolonged periods of standing. A proposed mechanism for LBP symptom development is large tissue stress concentrations on the innervated posterior elements of the spine (e.g. facet joints) that give rise to pain. Identifying characteristics that increase risk for developing LBP symptoms informs strategies for preventative as well as therapeutic interventions.

009 **Tinius, Rachel, MS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Movement Science
Washington University in St. Louis
Department: Physical Therapy
Mentors: Todd Cade, PT, PhD; Alison Cahill, MD, MSCI

The influence of physical activity on labor and delivery outcomes in obese pregnancy

Tinius RA; Cahill AG; Cade WT

Introduction: Maternal obesity during pregnancy is a significant public health issue as it is associated with labor and delivery complications. In normal weight women, regular physical activity during pregnancy leads to shorter labor time and lower incidence of medically necessary cesarean deliveries; however, the impact of physical activity during pregnancy on labor and delivery outcomes in obese pregnant women has not been studied. The purpose of the study is to examine the effect of physical activity during pregnancy on labor and delivery outcomes in obese pregnant women.

Methods: A retrospective chart review was performed on women who received prenatal care at the Women's Health Center at Barnes-Jewish Hospital between 2009 and 2013. Inclusions included: 18-44 years of age, pre-pregnancy BMI >30kg/m2, and delivery of a full-term infant (37+weeks) at Barnes-Jewish Hospital. Exclusions included: history of chronic hypertension or diabetes, prior or scheduled cesarean delivery, current smoker, and current illegal drug or alcohol consumption. Exercise levels were subjectively reported through clinic visit questionnaires and confirmed through personal telephone calls.

Results: Inactive obese women were more likely than active obese women to request an epidural (100% vs. 92%, p=0.04). Adjusting for labor induction/augmentation and parity, inactive obese women had a tendency to spend more total time in labor (16.3±9.2 hours vs. 11.8±9.3 hours, p=0.09). Inactive pregnant women had a tendency to spend more time in stage 2 of labor (57.3± 60.5 minutes vs. 45.8±49.0 minutes, p=0.37) compared to active women. Inactive women also had a slightly lower likelihood to develop gestational hypertension/preeclampsia compared to active women (40% vs. 27%, p=0.19). Comparing women who progressed to stage 2 of labor (pushing), inactive women were more likely to require a cesarean section during the process of pushing (22.5% vs. 5.6%, p=0.08). Cesarean section frequency was similar between groups (31% vs. 25%, p=0.49).

Conclusions: Obese women who reported exercising during pregnancy may have improved labor and delivery outcomes; however, more research in this area is needed.

010 Tinius, Rachel, MS

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program
Current Doctoral Program of Study: Movement Science
Washington University in St. Louis
Department: Physical Therapy
Mentors: Todd Cade, PT, PhD; Alison Cahill, MD, MSCI

The role of physical activity in maternal and neonatal metabolic outcomes in obese pregnancy

Tinius RA; Cahill AG; Cade WT

Introduction: Both maternal obesity and physical inactivity during pregnancy are independently associated with unfavorable maternal and neonatal metabolic outcomes. Previous research in non-gravid adults suggests physical activity provides protection from many chronic diseases irrespective of body weight. This study will examine this hypothesis in pregnancy. The goal is to determine if maternal outcomes (lipid oxidation, insulin resistance, inflammation, oxidative stress) and neonatal outcomes (insulin resistance, inflammation, oxidative stress, body composition) are more attributable to physical activity levels or maintenance of a healthy body weight.
Methods: Three groups of pregnant women (n=45), lean (LG), obese (OBG), and obese-physically active (OPAG), will be compared between 32-37 weeks gestation. Body composition, predicted fitness level, dietary composition, and objectively-measured weekly physical activity levels will be assessed. Lipid oxidation, insulin resistance, oxidative stress, inflammation, and circulating free fatty acids will be measured at baseline, during a 30-minute bout of moderate exercise, and during a 1-hour recovery period. Cord blood will be collected at delivery to measure neonatal substrates, inflammatory markers, insulin resistance, and oxidative stress levels. Within 48 hours of delivery, infant body composition will be measured.
Results: Data has been collected on 14 LG, 10 OBG, and 8 OPAG women. The OPAG spends more time in moderate physical activity (16.8%) compared to the OBG (9.9%, $p<0.001$) and the LG (14.2%, $p=0.16$). The OPAG has higher predicted fitness levels (33.4±7.6 ml/kg/min) compared to the OBG (23.7±4.9ml/kg/min, $p=0.01$) and the LG (29.9±6.3ml/kg/min, $p=0.46$). Inflammatory marker (CRP) is elevated in the OBG (9.2±4.9) compared to the LG (2.4±2.0, $p<0.001$) and the OPAG (5.5±2.1, $p=0.09$). Similar trends are emerging among triglyceride and HDL levels. Maternal and neonatal data collection is ongoing and results are pending.
Conclusions: Preliminary data suggests physical activity during pregnancy can improve maternal metabolic health irrespective of body weight.

077 Wang, David

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program
Current Doctoral Program of Study: Medicine
Saint Louis University
Department: Anesthesiology
Division: Clinical and Translational Research
Mentor: Ben Palanca, MD, PhD

Feasibility of diffuse optical tomography during overnight polysomnography

Wang D; Palanca BJ

Introduction: Sleep involves spontaneous changes in the conscious state that appear critical for survival. The similarity between sleep and altered conscious states induced during sedation and general anesthesia remain unclear. Sleep is subdivided into different stages using electrical signals recorded from the scalp via electroencephalography (EEG). Current imaging modalities such as functional magnetic resonance imaging (fMRI) have limitations for studying sleep. fMRI introduces noise and vibration artifacts, interferes with simultaneous EEG recordings, and is costly. Diffuse optical tomography (DOT) is a novel method that uses near infrared light to image superficial brain activity using a wearable cap. Like fMRI, DOT relies on low frequency oscillations in hemoglobin oxygenation as a surrogate of brain activity. This study was undertaken to assess the feasibility of quality polysomnography (PSG) recordings and DOT imaging of healthy sleeping volunteers.
Methods: We recorded DOT and PSG during two overnight sleep sessions from seven volunteers. PSG included six-channel EEG, chin electromyography (EMG), and bilateral electrooculography (EOG). A certified sleep technician assigned sleep stage at 30 second intervals. After alignment of PSG and DOT time series, EEG data quality was assessed visually and by power spectral analyses. Strength of interhemispheric connectivity among brain regions was quantified using Pearson's correlation analysis.
Results: Volunteers were able to sleep to varying degrees while undergoing simultaneous DOT and PSG (sleep duration in minutes: M = 387, SD=113). Characteristic EEG motifs of K-complexes, sleep spindles, and slow waves combined with EMG and EOG traces facilitated staging. Power in the delta (0.5-4 Hz) and gamma (30-50 Hz) frequency bands differed between wakefulness and slow wave sleep. Preliminary analyses showed weakening of bilateral connectivity during slow wave sleep compared to wakefulness.
Conclusions: Although tolerability of the DOT cap varied across subjects, simultaneous EEG and DOT are feasible during overnight sleep sessions, supporting the potential of DOT for imaging brain activity during natural sleep.

Dames Fellowship

129 **Xiao, Qi**

Dames Fellowship; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Chemistry; Pathology and Immunology
Mentor: Michael Gross, PhD

New methodology of data analysis for fast photochemical oxidation of protein (FPOP)

Xiao Q; Zhang H; Rempel D; Rohrs H; Gross M

Introduction: Fast Photochemical Oxidation of Proteins (FPOP) is a mass-spectrometry-based protein footprinting method that modifies proteins on the microsecond time scale to reveal regional and even amino-acid structural changes. Highly reactive •OH oxidatively modifies the side chains of approximately one half the common amino acids on this time scale. Finding all of the radical •OH-labeling sites requires LC/MS/MS analysis of a proteolyzed sample, but data processing is daunting without the help of automated software. In this project, we demonstrated a systematic means for achieving a comprehensive residue-resolved analysis of footprinting data using a MathCad software written by Don Rempel.

Methods: A syringe containing 10 uM CBP or ACTR, glutamine, H2O2, PBS buffer, was infused through silica tubing contained a transparent window and intersected by a 248-nm pulsed KrF eximer laser beam (5 Hz) to photolyze H2O2 and label the protein. The flow rate was adjusted to give an exclusion volume of 15% and prevent over-labeling. The photolyzed sample was collected in an Eppendorf tube containing methionine and catalase for scavenging remaining H2O2 and radicals. Analysis of the modified protein was done with a Thermo LTQ FT mass spectrometer. Raw data from the experiment provided the input for the new software.

Results: We employed the new algorithm to extract the quantitative information on the protein level. The spectrum of FPOP IDP proteins was converted into simple m/z and intensity files. The isotopic distribution for each charge state as well as multiple modifications can be resolved using our analysis, even if the isotopic distributions of modifications overlap. The customized algorithm contains all known FPOP modifications and the data fitting process generates the all protein peaks based on the sequence. The calculated spectrum is used to fit the experimental data and the peak envelop of modification from fitting is used to generate the quantitative information.

Conclusions: This new software was found to be a viable alternative to the traditional analysis method. The new software also provided a more straightforward data analysis workflow. The results of this study confirmed that FPOP can be used to rapidly obtain structural information for protein complexes.

David F. Silbert Summer Fellowship

046 **Aum, Diane**
David F. Silbert Summer Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentors: Albert Kim, MD, PhD; Amit Gujar, PhD
Effects of NamPT inhibition on tumor initiating cells of Glioblastoma Multiforme
Aum DJ; Kim AH; Gujar A
Introduction: Alterations in cell metabolism and regulatory pathways are believed to have a significant role in Glioblastoma multiforme, the most malignant and aggressive of brain tumors. NAD^+, an important molecule involved in metabolic activity which is critical for cancer cell function, likely plays important roles in the self-renewal and tumorigenesis of Glioblastoma multiforme.
Methods: Self-renewing tumor initiating cells were cultured from five different Glioblastoma tumors. These cells were then treated with FK866, a NAMPT inhibiting drug, and observed for changes in proliferation, cell death, and transcriptional regulation. Cell death assays were visualized with Hoechst and propidium iodide staining.
Results: A cell death assay with FK866-mediated NAMPT inhibition resulted in two groups of cell lines—one with high susceptibility and the other with resistance to treatment. Upon further analysis, resistance to NAMPT inhibition was correlated with higher basal NAMPT expression.
Conclusions: These results show the importance of NAMPT activity and intracellular NAD levels on tumor initiating cell growth and also demonstrate another aspect of molecular heterogeneity found in Glioblastoma. Studying the role of NAD could elucidate important mechanisms in the pathogenesis of Glioblastoma multiforme which could lead to new therapeutic approaches for this challenging disease.

128 **Zou, James**
David F. Silbert Summer Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pathology and Immunology
Division: Immunobiology
Mentor: Marco Colonna, MD
Generation of monoclonal antibodies against human IL-26, Pyhin1, and Reg3G
Zou J; Colonna M
Introduction: Antibodies are a useful tool in both research and clinical medicine, capable of assisting in the diagnosis of disease, localizing molecules of interest, and treating or alleviating a number of conditions. However, because mice are one of the most common model organisms for research, most artificial antibodies target murine molecules. The purpose of my project was to generate monoclonal antibodies against three human proteins: Pyhin1, a member of the HIN-200 interferon-inducible proteins that acts as a tumor suppressor; Reg3G, an anti-bacterial protein that targets Gram-positive bacteria; and IL-26, a cytokine that is recognized by epithelial cells and helps promote antimicrobial functions and cell survival. All three of these proteins are involved in mucosal immunity, an important area of study because the human mucosal immune system is poorly understand, and tools allowing for its analysis are scarce.
Methods: The genes encoding human IL-26, Pyhin1, and Reg3G were amplified using PCR and then purified using gel electrophoresis followed by gel extraction. The purified DNA was passed through chemically competent bacteria for antibiotic screening and sequencing. The satisfactory DNA was then purified from the bacteria and ligated into expression vectors before being transformed into J558L mouse myeloma cells (IL-26 and Reg3G) or BL21 E. coli (Pyhin1) for protein expression.
Results: J558L myeloma cells expressing IL-26 and Reg3G and BL21 E. coli cells expressing Pyhin1 are currently in the process of being screened for the production of the proteins of interest. Cells that test positive will be isolated and cultured to promote the unadulterated production of adequate amounts of IL-26, Reg3G, or Pyhin1. Mice will then be immunized with these proteins of interest.
Conclusions: Currently, no conclusions can be drawn.

Dean's Fellowship

142 **Badu, Asante**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics, Dr. von Hauner's Children's Hospital, Germany
Mentor: Max Witzel, MD
A novel mutation in SWI/SNF complex as a potential candidate in severe congenital neutropenia
Badu A; Witzel M
Introduction: Severe congenital neutropenia (SCN) is a condition characterized by an absolute neutrophil count of below .5x10^9/L. As neutrophils are critical for innate immune response and mediating inflammation, this deficiency almost always results in recurrent infections and often death in children. While the genetic bases of 60% of SCN cases have been identified, the pathogenesis of 40% of cases remains unknown. This study attempts to link a defect in a component of the SWI/SNF chromatin remodeling complex that affects assembly to SCN pathogenesis.
Methods: Exome sequencing in 8 patients with SCN was conducted to identify potential gene candidates underlying their condition. Once a gene of interest was identified, shRNAs were used to knockdown the gene in AML-NB4 cells and IP, ChIP, and qPCR experiments were conducted to see how the knockdown affected SWI/SNF complex assembly and what regions of the DNA the complex binds to.
Results: Results were inconclusive as the knock down was insufficient in cells treated with ATRA.
Conclusions: Once cells have been treated with ATRA, the shRNAs must be less effective. The experiments need to be conducted with knockout cells in order to determine whether SWI/SNF component assembly is affected by defects in the gene of interest. As chromatin remodeling complexes are critical for determining gene expression, a defect in a component of one of these complexes could have large ramifications that may underlie the pathogenesis of SCN.

068 **D'Amelio, Giuseppe**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Division: Child and Adolescent Psychiatry
Mentor: Anne Glowinski, MD, MPE
Preliminary examination of M-CHAT performance in an English-speaking twin sample
D'Amelio GS; Glowinski AL; Constantino JN
Introduction: Autism Spectrum Disorder is a pervasive developmental disorder whose prevalence seems to be increasing over the last several years. The Modified Checklist for Autism in Toddlers (M-CHAT) has shown success as a screening tool for early detection of ASD. However, recent studies have found that Spanish speakers fail the M-CHAT at a disproportional rate. The purpose of this study is to conduct a preliminary examination of data, which will eventually be used to investigate the effect of language and ethnicity on M-CHAT performance.
Methods: 304 twin families were recruited through the Missouri Family Registry. Data was collected via mail home packets and phone interviews. ANOVA and Chi Square analyses were conducted to investigate differences in M-CHAT performances based on ethnicity, race, and maternal education levels.
Results: Differences in M-CHAT performance based on ethnicity were not statistically significant. Differences in performance based on race were significant, $F(4,263)=6.576$, $p=.00$, but this was due to an outlier score. Differences in performance based on maternal education were significant, $X2=15.753$, $p=.046$ with responses to questions 18, 20, and 21 differing by maternal education as well.
Conclusions: These results support trends that previous literature has found. Race and ethnicity do not seem to be related to M-CHAT failures. However, maternal education level seems related to M-CHAT performance, with lower maternal education level corresponding with higher rates of M-CHAT failure. This examination found that children whose mothers have graduated high school or received an associate's degree had higher failure rates compared with children whose mothers had some college or higher. This preliminary examination suggests that variables such as maternal education should be controlled for in the final study in order to truly examine the effect of language on M-CHAT performance.

040 **Fernandez-Maldonado, Amarilys**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery, Icahn School of Medicine at Mount Sinai
Division: Vascular Surgery
Mentors: Rami O Tadros, MD; Luis A Sánchez, MD, FACS

A retrospective study on the effects of an elective or urgent indication on the outcomes of endovascular thoracic aortic aneurysm repair

Fernandez-Maldonado A; Tadros RO

Introduction: Thoracic aortic pathologies, such as dissections, penetrating ulcers, aneurysms, and traumatic injuries, are life threatening medical conditions that require close observation and many times interventions. Thoracic endovascular aortic repair (TEVAR) was pioneered in the 1990s as a less invasive alternative to conventional open repair. The purpose of this study is to determine if having either an elective or urgent indication for TEVAR affects the outcomes of the procedure.

Methods: A retrospective review of a maintained database was performed on all patients undergoing TEVAR at Mount Sinai Hospital from 2001 to 2013. Patients were categorized as having either an elective or urgent procedure. Demographics, preoperative adjunctive procedures, and intra-operative procedure details were collected for each patient in addition to intraoperative parameters, follow-up visits, complications, endoleak rates and types, reinterventions, and overall mortality.

Results: Complication rates (intraoperative, perioperative, and late onset) tripled in the urgent group (36.4%) when compared to the elective (11.0%) (P=0.001). Length of hospital stay was doubled in the urgent group (16.3 ± 13.4 days) when compared to the elective group (8.3 ± 20.9 days). However, there was no relationship between an urgent indication and an elevated rate of endoleaks. There was also no relationship between indication and mortality rates. There was however, a statistically significant relationship between age and mortality rates. Mortality rates more than doubled in patients 70 years and over (53.7%) when compared to patients under the age of 70 (20.5%) (P=0.001).

Conclusions: Having an urgent indication for TEVAR affects the outcomes of the procedure by doubling the complication rate when compared to patients who had an elective procedure. A bigger sample size is needed to evaluate more specific characteristics. With this information, it may be possible to plan ahead necessary precautions such as placing a spinal drain or providing blood transfusions to reduce the incidence of complications in high-risk groups such as patients having an urgent indication.

095 **Ge, Tianjia**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Radiology, Stanford University
Mentors: Sanjiv Gambhir, MD, PhD; Ophir Vermesh, MD, PhD

Toward real-time in vivo detection of circulating biomarkers: Antibody-gold nanoparticle conjugates for in vivo homogeneous immunoassays

Ge TJ; Vermesh O; Gambhir SS

Introduction: Detection of circulating biomarkers, ranging from protein markers to circulating tumor cells, is desirable for the detection and monitoring of various disease processes such as tumor metastasis. In vitro immunoassays designed to detect these biomarkers require separation steps that introduce additional time, error, and repeated blood draws for the patient. An in vivo, homogeneous immunoassay that delivers information through the surface plasmon resonance (SPR) properties of gold nanoparticles (AuNPs) would provide more real-time monitoring of these circulating biomarkers.

Methods: Antibodies were conjugated to 20 nm AuNPs by multiple methods. Conjugate functionality was characterized by dot blot immunoassay. SPR peaks were measured by UV-Vis spectroscopy. Aggregate sizes were determined by dynamic light scattering (DLS).

Results: Antibodies were directionally attached to AuNPs by linking the Fc region of the antibody to the gold nanoparticle surface. Characterization revealed functional antibody-nanoparticle conjugates capable of antigen detection with minimal non-specific protein binding. These properties were also seen in conjugation to nanoparticles of other sizes and morphologies. A one-step, homogenous immunoassay is under development using capture and detection antibodies conjugated to AuNPs. Antigen could be detected at picomolar concentrations using DLS, with a dynamic range of 5 to 50-fold excess of conjugate concentration. The dynamic range of this immunoassay can thus be adjusted by simply varying the concentration of the nanoparticle conjugates. Antigen specificity was demonstrated by the absence of aggregation with addition of off-target antigen.

Conclusions: The antibody-nanoparticle conjugates are capable of forming aggregates of predictable size in the presence of antigen. The current characterization method of dynamic light scattering, however, is not suited to in vivo applications. Future work is needed to exploit the SPR properties of gold nanoparticles, in which the close presence of neighboring particles detectably alters the absorption peak. Different sizes and shapes of nanoparticles will shift the SPR peak to the clinically useful near-infrared range.

132 **Hanson, Eric**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Hematology and Oncology
Mentors: Shalini Shenoy, MD; Jeff Bednarski, MD, PhD

Outcomes of stem cell transplantation using reduced intensity conditioning for non-malignant disorders

Hanson E; Shenoy S; Bednarski J

Introduction: Traditional, myeloblative stem cell transplants have been successfully used for decades to treat a range of diseases. Traditionally, stem cell transplants were reserved as last case treatments or for treating malignant diseases with no other cure. Recently, advanced survival and efficacy of stem cell transplants has allowed for treatment of non-malignant diseases such as hemoglobinopathies and immunodeficiencies. Due to the nature of these diseases, transplants don't need to completely replace host stem cells to effectively cure the disease. Instead, donor stem cells just need to engraft enough to replace the deficit that exists in the donor. As a result, the chemotherapy given before transplant can be reduced in intensity, which leads to less side effects, while still allowing for successful engraftment of donor cells. In this multi-centered study, patients were given the same reduced-intensity chemotherapy, Campath, prior to transplant.

Methods: Patients with non-malignant disorders that could benefit from transplant and had suitable donors were enrolled on the study. Patients enrolled were followed for 2 years post-transplant. Relevant data was extracted from the database and from case report forms submitted by participating institutions. Data was compiled into specific databases and prepared for publication using Excel and similar programs.

Results: The results indicate the reduced-intensity regimen used in this study has a high engraftment rate with early immune reconstitution and provide a cure from disease (hemoglobinopathy). The pace of immune reconstitution results in fewer infections after the first few months post transplant with improving immune reconstitution. Mixed chimerism was present, but these patients had no significant differences in eradication of disease.

Conclusions: This research is immediately applicable for patients with a NMD such as thalassemia, sickle cell disease, metabolic disorders, bone marrow failure, and immune deficiency. The conditioning prior to transplant is less intensive and is tolerated better with fewer early and late toxicities.

069 **Holttum, Jessica**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry, University of Washington
Mentor: Susan Collins, PhD

Extended-release naltrexone and harm-reduction counseling: perception of treatment among chronically homeless patients with alcohol dependence

Holttum JK; Blacker BF; Collins SE

Introduction: This study is a qualitative analysis of exit interviews conducted in the context of a single-arm pilot that assessed the initial feasibility, acceptability and alcohol outcomes following a combined pharmacobehavioral intervention involving extended-release naltrexone (XR-NTX) and harm-reduction counseling for chronically homeless people with alcohol dependence. The goals of the present study were to document participant perceptions of the medication, counseling, and assessment aspects of the parent study as well as suggestions for how to improve these procedures in the future.

Methods: Participants were currently/formerly homeless individuals with alcohol dependence (N = 24) who participated in the parent study. Measures included participant responses to semi-structured interview prompts administered after completion of treatment. A conventional content analysis was conducted by reviewing interview transcripts, systematically coding participants' statements for each of these aspects of the study, and classifying them into coding categories.

Results: Participants reported interest in the study primarily due to a desire to reduce their drinking. They also reported general satisfaction with study assessments, counseling, medical procedures, and medication, as well as fulfillment of prior expectations regarding the study. Negative perceptions of study components were most often due to medication side effects or emotional discomfort with one or more study components. Participants also provided recommendations for improving study protocol, which included logistical suggestions and ways to manage side effects. Reporting of posttreatment experiences focused mainly on maintaining reduced drinking and meeting personal goals.

Conclusions: Participants reported generally positive experiences with the study and also provided constructive criticism for how to improve future studies. These findings are therefore critical for continuing to improve treatments for alcohol dependence among chronically homeless individuals.

109 **Hritz, Shannon**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Adolescent and Pediatric Gynecology
Mentor: Laura Parks, MD

Survey of the perceptions and knowledge of breastfeeding among adolescents and young adults in an urban setting

Hritz SL; Parks L

Introduction: Breastfeeding has significant health and developmental advantages for infants, including optimal nutrient content, maternal antibodies to fight infections, and important bonding interaction between mother and child. Previous studies of adolescent experiences with breastfeeding have shown that younger women are less likely to breastfeed their babies than older women, and have dealt primarily with populations of university students. This study seeks to test the claim that adolescents in an urban environment will have more negative attitudes and misconceptions about breastfeeding than individuals in an older and more affluent setting as well as to explore why this may be the case.

Methods: This study was is a cross-sectional survey investigating prior exposure to breastfeeding, intent to breastfeed in the future, access to breastfeeding programs, and ease of breastfeeding in the work or school environment. The sample population consisted of walk-in visitors to the SPOT youth center. Participants were given a survey containing 39 questions regarding knowledge and attitudes toward breastfeeding and 9 about breastfeeding experience and exposure.

Results: Preliminary data have shown that adolescents and young adults in an urban setting are generally positive about breastfeeding, although they tend to think that breastfeeding is less convenient, can be painful, and is associated with increased maternal dietary restrictions. Further survey collection and statistical analysis are required to determine the significance of these trends. Long term, this study will be used to identify common misconceptions in this demographic group.

Conclusions: Since breastfeeding is so important in infant development, the results of this study will be useful to identify areas for future public health intervention.

012 **James, Michael**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Orthopaedic Surgery
Mentors: John Clohisy, MD; Megan Killian, PhD; Stavros Thomopolous, PhD

A novel model for the induction of hip dysplasia in the developing murine hip

James MG; Killian ML; Thomopoulos S; Clohisy JC

Introduction: Developmental dysplasia of the hip (DDH) is one of the most common and challenging childhood orthopaedic conditions, and is the focus of worldwide efforts in disease screening and treatment. Despite the clinical significance of DDH, there is a paucity of animal models to investigate the critical signaling pathways and mechanical cues that mediate the formation of a dysplastic hip. The current study utilized a newly developed murine instability model to investigate the role of postnatal connective tissue laxity and femoral head unloading on acetabular and proximal femur maturation. We hypothesized that altering joint stability and loading prior to joint maturation via destabilization of the murine hip will cause acetabular dysplasia.

Methods: Under anesthesia, 3-week old pups were subjected to titrated unilateral surgical destabilization, via iliacus/iliopsoas tenotomy, capsulotomy, and/or ligamentum teres transection, for the induction of acute instability and lateralization of the femoral head. Mice were scanned using in vivo micro-computed tomography at 2, 6, and 8 week time points.

Results: Hips subjected to mild instability appeared normal and did not have noticeable changes in Norberg angle, FH coverage, or qualitative bone shape at 2, 6, or 8 weeks post-injury. For mice subjected to moderate instability, lateralization of the proximal femur with decreased Norberg angles and decreased FH coverage were observed. Severe instability led to altered structure of the proximal femur, such as sclerotic bone accumulation proximal to the greater and lesser trochanters, which translated to increased proximal femur total volume in this group.

Conclusions: This is the first study to explore titrated levels of surgical hip instability in a mouse model for the development of a small animal analogue of post-natal hip dysplasia. In this study, we identified a level of muscle and ligament unloading that induces lateralization of the femoral head without dislocation (i.e., moderate instability). Future work using this model will explore the role of abnormal mechanical loading, specifically acetabular rim overload and instability, on mechanobiological regulation of hip maturation during adolescent growth.

013 **Khan, Taleef**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Orthopaedic Surgery
Mentor: Luke Zebala, MD

Long-term outcomes of transforaminal lumbar interbody fusion in spine surgery

Khan T; Zebala L

Introduction: Transforaminal Lumbar Interbody Fusion (TLIF) is a posterior based spine surgical technique that allows the surgeon to create structural support for the anterior side. The purpose of this study was to determine the effectiveness of this surgery after a number of years following operation.

Methods: The study conducted was a retrospective review of patients who had undergone the TLIF procedure at Barnes-Jewish Hospital. While not all patient data was utilized, since only 349 patients were reviewed in the limited time frame, many cases from Washington University were excluded. Those included in our database were adult patients, all above the age of 18, who underwent back surgery with at least 1 level of vertebrae having the TLIF being performed on it, along with at least 2 years of follow up.

Results: The results showed that of the 349 patient cases that were reviewed, 97 patients reported adjacent level degeneration following the procedure (27.7%). Additionally, 15 patients (4.3%) suffered from a nonunion, meaning the levels did not fuse following surgery and required follow up and sometimes further surgery. Furthermore, days the patient stayed following surgery varied from 4 to 87 days, with only 5 patients experiencing post operative infections (1.4%).

Conclusion: The results of the study suggest that the TLIF surgery is a relatively safe procedure with most patients healing without any significant complications. Most operative complications were observed following at least a 10-year period. Future research is needed on the many other TLIF surgeries.

014 **Li, Kevin**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Orthopaedic Surgery
Mentor: Denis Nam, MD

Patient reported metal allergies as a potential risk factor for poor outcomes in total joint arthroplasty

Li KK; Nam D

Introduction: Total Joint Arthroplasty (TJA) of the hip and knee are highly successful procedures performed to give patients relief of pain, improve function, and increase quality of life. Despite their success, some patients inevitably express dissatisfaction after surgery, which is reflected in their patient reported outcomes. Metal allergy has been reported as one cause of persistent pain and poor outcomes. Recent studies have shown that reporting of multiple drug allergies are associated with poorer perceived outcomes following TJA. To our knowledge, the impact of specifically self-reported metal allergies on perceived TJA outcomes has not yet been studied. Patients who report metal allergy receive nickel-free implants, but whether these implants improve outcomes remains unclear. The purpose of this study is to 1) to identify the overall incidence of patients who self-report having a metal allergy who present for TJA, 2) assess the impact of reporting a metal allergy on patient outcomes following TJA, and 3) to determine if use of nickel-free implants leads to improved outcomes in this patient population.

Methods: A retrospective review of patients undergoing elective primary TKA or THA at this institution in the interval 2009 - 2011 was performed to obtain allergy information and survey data. Outcomes scores of patients reporting metal allergy were compared to those of patients who did not report metal allergy.

Results: Incidence of metal allergy reporting was found to be 3.01%. Self-reporting of metal allergy was found to have no significant impact on outcomes measures, with the exception of decreased Short Form Health Survey Mental Component scores preoperatively (in knee replacement patients) and postoperatively (in hip replacement patients).

Conclusions: The results suggest that while metal allergy reporting does not correlate with decreased perceived surgical outcomes, it may be associated with increased anxiety or depression before or after TJA. Further research with larger patient numbers is needed to verify these results and clarify the relationship between metal allergy and perceived outcomes.

096 **Moseley, Anna**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Mentors: Garry Fathman, MD; Linda Yip, MD

Dysregulated Reg: new clues to the etiology of type 1 diabetes

Moseley, AC; Fathman G; Yip L

Introduction: Type 1 diabetes mellitus (T1D) is an autoimmune disorder that causes progressive destruction of pancreatic beta cells, leading to an inability to produce insulin and regulate blood glucose. However, the etiology of this disease is not well understood, and it is difficult to determine if individuals at risk for T1D will eventually progress to the disease, and if so, how long until symptoms will appear. The goal of our research was to identify potential biomarkers for T1D to aid in staging its progression in patients and predicting future outcomes, as well as to gain more insight into the disease's etiology.

Methods: We isolated RNA from the pancreatic islets of 4-week and 12-week old female non-obese diabetic (NOD) mice, a model of type 1 diabetes. We then performed a microarray comparing NOD RNA expression levels to those of controls to identify any dysregulated genes. QPCR was conducted confirm these findings. We then performed an in vitro proliferation assay to determine whether addition of the dysregulated protein caused macrophage proliferation. Proliferation was measured at 0, 24, and 48 hours via cell counts, digital imaging, and RNA expression of Mki67 (a proliferation marker).

Results: We identified four genes in the Reg protein family - Reg2, 3a, 3b, and 3g - that have significantly different expression in the islets of pre-diabetic NOD mice vs. controls. QPCR analysis trended toward these findings, with more precise results at 12 than 4 weeks. The proliferation assay showed gross morphological changes, but decreased cell counts and Mki67 levels for Reg-treated cells.

Conclusions: We concluded that dysregulation of genes in the Reg family may be associated with the development of T1D in NOD mice (specifically, upregulation at 4 weeks and downregulation at 12 weeks). Additionally, the addition of Reg did not appear to promote cell proliferation in vitro, suggesting the protein has a different function. Future studies will focus on elucidating the role of Reg proteins in the progression of T1D, with the eventual goal of translating these findings to humans so that individuals at risk of developing T1D can obtain faster and more effective treatment.

071 **Mulvey, Bernard J**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Mentor: Andrey Anokhin, PhD

Adolescent history of ADHD traits predicts ERP impairments in adulthood

Mulvey BJ; Peng C; Anokhin AP

Introduction: Attention-deficit hyperactivity disorder (ADHD) is a highly prevalent disease in children, affecting up to 5% of the child and adolescent population worldwide. Numerous alterations in brain activity in the short term—on the scale of hundreds of milliseconds—have been repeatedly demonstrated in children. However, very limited research on small cohorts has been done to identify whether these changes persist into adulthood for ADHD patients.

Methods: A large cohort of adolescent twins (n=145) from the population were scored by parents on ADHD traits at age 14, just past the age at which ADHD is thought to be developmentally "set" (age 12). At age 20, these same subjects performed a complex flanker task while having electroencephalogram data recorded. EEG data was then averaged into ERN-Pe (error-related negativity and error positivity, respectively) and N2-P3 waveforms for statistical analysis of these event-related potentials (ERPs) .

Results: Numerous correlations were generated between ERPs and performance of a complex flanker task to quantify existing theoretical research on their roles task performance. Correlation of the task-elicited ERPs at age 20 to parent-reported ADHD symptoms of the subjects at age 14 found that inattentive symptoms in early adolescence were significantly predictive of deficient neural processes of error-detection and error-awareness/adaptation, signified by the ERN and Pe, respectively. Similarly, a history of hyperactive symptoms predicted impaired neural activity associated with behavioral inhibition/stalling, signified by the N2 wave. No correlation was found between attention-switching or behavioral execution processes (P3) and adolescent ADHD symptoms, although impairments of the P3 are well-documented in children.

Conclusions: Collectively, these results suggest that ADHD-like impairments of anterior cingulate cortex-produced activity (ERN, Pe, and N2) persists into adulthood, whereas P3 impairments generated in temporal and parietal brain structures do not. Our findings suggest differential development of local brain regions, which may explain the partial, but not full, remission of most ADHD cases in adulthood.

025 **Rosenberg, Elizabeth**

Dean's Fellowship
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Plastic and Reconstructive Surgery
Mentors: Albert Woo, MD; Gary Skolnic, MD

Lay assessment of deformity as related to facial asymmetry and scarring after post cleft lip repair

Rosenberg ED; Skolnic GB; Woo AS; Nguyen DC; Naidoo SD; Patel KB

Introduction: Patients with repaired cleft lip can often be sensitive and self-conscious about the residual scarring and deformity in their own faces. However, it is unclear how perceptive an individual without facial deformities perceive the same abnormalities. We aim to determine how quantitative deformities in the nose, upper lip, or vermilion relate to lay perceptions.

Methods: Frontal and worm's- eye view photographs were taken of 19 patients, between 11-17 years old, with repaired cleft lip. Photos of 2 teenagers without cleft lip history were used as controls. Three objective measurements were obtained from the photographs: 1) bilateral asymmetry of nasal area, 2) appraisal of scarring, and 3) philtral asymmetry. The frontal view photographs were then included in a survey soliciting the overall level of deformity, the location, and the specific nature of the most prominent defect. Two images were included twice to allow examination of intra-respondent reliability.

Results: There were 103 participants in the survey. The patient images were rated as normal 22% (range 2-47%) of the time, while normal control images were rated as normal 89% of the time. There was poor agreement in categorization of deformity severity (generalized Fleiss' Kappa = 0.15). Individual respondents were also internally inconsistent, rating the severity of deformity of repeat images differently 33% of the time. Further analysis is continuing and we are working to compare objective measures of deformity to the layperson survey results.

Conclusions: Although lay people recognize deformity, their categorization of its severity is inconsistent. The relationship between quantitative asymmetries, the specific physical features which catch a layperson's eye and lay assessment of deformity are knotty. Surgeons can use this information to focus their efforts while operating, aiming to place the results of the surgeries within ranges of asymmetry and scarring measurements to be the least noticeable to laypeople. Patients with cleft lip and palate will also be able to use this information for reassurance that their own deformities are not as noticeable to the average people around them as to themselves.

031 **Schloemann, Derek**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentor: Graham Colditz, MD, DrPH

Accelerated partial breast irradiation through brachytherapy for ductal carcinoma in situ: Observational study of influencing factors and risks of second breast tumors

Schloemann DT; Liu Y; Lian M; Colditz GA

Introduction: Despite the lack of evidence from phase III clinical trials demonstrating equivalent benefit in local control with whole breast irradiation (WBI), the use of accelerated partial breast irradiation through brachytherapy (APBIb) has been increasingly used since 2002 for early invasive breast cancer. Little is known about APBIb utilization for ductal carcinoma in situ (DCIS) or its associated risk of second breast tumors. The purpose of this study was to examine the utilization patterns, influencing factors, and outcomes for APBIb vs. WBI in women with DCIS.

Methods: 40749 women with DCIS in the Surveillance, Epidemiology, and End Results database who received breast conserving surgery and radiotherapy between 2002 and 2011 were included. We analyzed utilization patterns and influencing factors of APBIb. Risks of developing second breast tumors were analyzed in 2043 patients with APBIb and 8172 propensity score-matched patients with WBI.

Results: Overall, 2212 (4.5%) of 40749 women received APBIb between 2002 and 2011. Substantial variations in APBIb use were observed over time and across counties. Factors associated with the increased use of APBIb included older age, non-Hispanic white race/ethnicity, smaller tumor size, hormone receptor positivity, comedo subtypes, and urban residence. During the 54-month follow-up, 82 (0.8%) and 141 (1.4%) of 10215 propensity score-matched patients developed ipsilateral and contralateral breast tumors, respectively. Compared with WBI, APBIb was associated with a significantly increased risk of ipsilateral breast tumors (HR 1.62, 95% CI 1.05 to 2.62; p=0.03) but not contralateral breast tumors (0.90, 0.58 to 1.39; p=0.64).

Conclusions: This population-based study suggests that APBIb use for DCIS was not only influenced by patient and tumor characteristics, but also by urbanization of residence and major policy related to APBIb. We observed a statistically significant moderate increase in ipsilateral breast tumor risk associated with APBIb versus WBI. This result suggests that APBIb should be used with caution for DCIS before data from the ongoing randomized controlled trial with long-term follow-up are available.

023 **Simien, Adrian**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Des Moines University
Department: Surgery
Division: Minimally Invasive Surgery
Mentors: Corey R Deeken, PhD; Spencer P Lake, PhD

Biaxial strain analysis for the evaluation of hernia mesh materials

Simien AA; Lake SP; Deeken CR

Introduction: Hernia repairs are common in the United States, with nearly one million surgeries performed each year. A vast majority of the hernia repairs are secondary to inguinal hernias which may be caused by a combination of pressure and weakening of the connective tissues and muscles. Although surgical meshes are utilized to reinforce the abdominal wall during surgery, a lack of knowledge remains with regards to the characterization and orientation of the material in the surgical site. The outcome contributes to the high rates of recurrence today. The purpose of this current study was to analyze strain data and compare surgical mesh mechanics of five types of hernia repair material via biaxial tensile testing with a focus specifically on optimizing the method of analysis.
Methods: Strain analysis was performed on five commercially used hernia meshes (BardTM Mesh, VentralightTM ST (C.R. Bard, Inc./Davol, Inc., Warwick, RI); PROCEED®, PROLENE®(Ethicon, Somerville, NJ) and INFINIT®) using MatLabTM automatic tracking. The results were compared using graphical representation of strain patterns.
Results: VentralightTMST(C.R. Bard, Inc./Davol, Inc., Warwick, RI) and PROLENE®(Ethicon, Somerville, NJ) displayed variations from the normal strain pattern expected. VentralightTMST(C.R. Bard, Inc./Davol, Inc., Warwick, RI) strain contained opposite strain patterns with the 2,4 directionality displaying the greatest strain and the 1,3 directionality with the least strain. PROLENE®(Ethicon, Somerville, NJ) hernia mesh analysis was similar to a uniaxial tension strain pattern, with one direction stressed and the opposite direction displaying Poisson's effect. BardTM Mesh, PROCEED®, and INFINIT® analysis correlated to the regular strain pattern usually exhibited with regards to orientation and directionality.
Conclusions: The results of this study suggest that anisotropic characteristics of hernia mesh are important parameters which should be taken into account when performing hernia repairs.

101 **Taiwo, Rukayat**
Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University School of Medicine
Department: Infection and Immunology, U East Anglia, Great Britain
Mentor**:** Tom Wileman, PhD

Utilizing the CRISPR/Cas9 Genome Editing System to engineer silenced MEKK4 cell lines

Taiwo R; Wileman T

Introduction: Autophagy is an integral eukaryotic process that degrades existing cytosolic components to free amino acids for new protein synthesis in times of starvation. Autophagy also plays a critical role in inflammation and disease progression necessitating the need to characterize proteins involved in this complex machinery. MEKK4, a 180 kD serine/ threonine kinase, has been implicated in protein interactions essential for the formation of a mature autophagosome however a specific role for this protein is yet to be elucidated. The purpose of this study was to determine the effects of MEKK4 silencing on autophagy.
Methods: To characterize the role of MEKK4 in autophagy, the RNA-guided Cas9 nuclease from the microbial clustered regularly interspaced short palindromic repeats (CRISPR) system was used to selectively knock out MEKK4 in eukaryotic cell lines. This method was employed to increase the efficiency of MEKK4 silencing in comparison to siRNA-mediated knock down used in previous experiments.
Results: Presented data show on average, about a 30% reduction in MEKK4 expression when comparing protein levels in wild type cell lines to those transfected with the CRISPR genome editing plasmid.
Conclusions: The CRISPR genome editing tool has been used successfully in the literature to completely silence both copies of a gene. Thus, the results obtained in this study can be attributed to the polyclonality of cells used in the protein expression assays. Further experimentation with monoclonal cell lines will need to be conducted to accurately determine the efficiency of the CRISPR/Cas9 genome editing tool in MEKK4 silencing.

106 **Tobias, Ethan**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Oncology
Mentors: Matthew Ellis, MB, BChir, PhD; Jieya Shao, PhD

Characterizing the activity of estrogen-receptor alpha fusions found in endocrine therapy resistant estrogen-receptor positive breast cancer

Tobias EM; Shoa J; Crowder R; Ellis M

Introduction: Breast cancer is one of the leading causes of cancer in women and estrogen-receptor positive cancer is the most common form of breast cancer. Unfortunately, treatment of estrogen-receptor positive breast cancer is often frustrated by de novo or acquired endocrine therapy resistance. Recently, genetic mutations and chromosomal abnormalities involving the estrogen receptor have been discovered that mediate endocrine therapy resistance and growth. Here we seek to examine in-frame gene fusions resulting from chromosomal translocations found in endocrine resistant breast cancer.

Methods: Gene constructs containing the in-frame gene fusions, the C-terminal fusion partner alone, and YFP as a control were introduced into an estrogen-receptor positive breast cancer cell line. Cells were then grown in hormone-stripped media with or without the selective estrogen receptor downregulator, Fulvestrant. By determining the growth of cells in this estrogen-deprived environment, we could assay the relative ability of each gene fusion, and its C-terminal portion alone, to mediate the endocrine resistance seen in the clinic. We then sought to determine whether cell lines containing these in-frame estrogen-receptor fusions, would be susceptible to the cyclin dependent kinase 4 and 6 inhibitor, Palbocicblib.

Results: Here, we show that one such fusion gene, ESR1-POLH has a positive effect on growth of estrogen deprived cells, as does the 3' fusion partner alone. We also show evidence that another fusion gene ESR1-Nop2 has a limited effect on cellular growth. Finally, we were interested in determining if endocrine resistant growth in these gene fusions could be inhibited by the cyclin dependent kinase 4 and 6 inhibitor, Palbociclib. Our results indicate that the ESR1 fusions are sensitive to this form of inhibition, especially at high concentrations, but that there appeared to be some degree of resistance compared to the control line.

Conclusions: Our study has shown that the ESR1-POLH gene fusion mediates endocrine-therapy resistance when introduced into an endocrine-therapy susceptible cell line. This lends further credence to the finding that gene fusion events play an important role in mediating endocrine therapy resistance and establishes the need to determine downstream effectors as second-line therapeutic targets in estrogen positive breast cancer.

053 **Varman, Rahul**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentors: Eric Arias, MD; Gregory Zipfel, MD

Impact of management options on development of delayed cerebral ischemia following treatment of aneurysmal subarachnoid hemorrhage

Varman RM; Arias E; Zipfel GJ

Introduction: Subarachnoid hemorrhage (SAH) due to cerebral aneurysm is a serious condition necessitating proper medical attention. Appropriate treatment and management are aimed at alleviating symptoms of the hemorrhage to preserve health. However, severe complications can often arise following treatment. Delayed cerebral ischemia (DCI) is a large cause of death and disability in patients following management for aneurysmal SAH. We sought to examine the association and impact of various medical management options with regards to development of DCI.

Methods: Retrospective analysis was done for 224 patients who were admitted to Washington University in St. Louis Department of Neurosurgery between the years 2009 and 2013. Patient specific data including mental status at various points during management were collected along with diagnostic imaging data from CT and cerebral angiograms. Factors noted during management included specific complications from various procedures during management and appropriate treatments and changes in health status at those times.

Results: We anticipate that there will be certain factors from aneurysmal SAH management that may be more associated with development of delayed cerebral ischemia.

Conclusions: From a clinical perspective, determining factors in management that may contribute to DCI development would be useful since it would allow for changes in protocol to allow for optimal management to decrease risk of DCI complication following treatment of aneurysmal SAH.

027 **Yen, Debra**

Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Plastic and Reconstructive Surgery
Mentors: Albert Woo, MD; Gary Skolnick, MD

Evaluation of direct surgical remodeling of frontal bossing in patients with sagittal synostosis

Yen DW; Skolnick GB; Nguyen DC; Patel KB; Smyth MD; Kane AA; Woo AS

Introduction: The need for surgical correction of frontal bossing in patients with sagittal synostosis is currently debated. We retrospectively analyzed frontal bossing in patients with isolated, nonsyndromic sagittal synostosis who underwent calvarial remodeling with and without frontal craniotomy and compared with control subjects.

Methods: We analyzed computed tomography (CT) scans of patients with sagittal synostosis < 9 months of age (6.2±1.6 months) who underwent modified-pi procedure either with frontal craniotomy (FC, n=16) or without frontal craniotomy (NFC, n=10). Only patients treated from 2003-2013 with both preoperative and one-year postoperative CT scans were included. Non-synostotic age-matched control scans were also analyzed. Cephalic index (CI) and three previously validated measures of frontal bossing (bossing angle, horizontal bossing ratio, and vertical bossing ratio) 8 were obtained. Additionally, three-dimensional photographs of ten FC patients were evaluated for frontal bossing between 1-8 years postoperatively.

Results: Preoperatively, no significant differences were found between the two groups ($0.064<p<0.940$). Both groups showed greater scaphocephaly and frontal bossing compared to controls ($p<0.001$). One-year postoperatively, all measures improved but remained significantly different than normal values except: CI of NFC patients ($p=0.296$); bossing angle ($p=0.068$) and horizontal bossing ratio ($p=0.129$) of FC patients. Compared to NFC patients, horizontal bossing ratio was significantly improved in FC patients ($p=0.017$, mean difference of 0.047). No other statistically significant differences were found between the two techniques ($0.127<p<0.637$). In our long-term study of FC patients up to 9 years of age (n=10), we analyzed forehead inclination as our measure of frontal bossing in three-dimensional photographs. A linear regression analysis showed a significant reduction in forehead inclination with age, decreasing 1.3±0.4 degrees per year ($p=0.021$). Forehead inclination for controls did not change significantly with age ($p=0.558$).

Conclusions: At one-year following modified-pi procedure, FC patients approached normalization of their forehead morphology to a greater extent than NFC patients. However, neither group completely normalized during this time period. Frontal bossing in FC patients continued to decrease with age, which reveals the postoperative dynamic nature of frontal bone morphology during childhood for these patients.

DeNardo Education and Research Foundation Grant

018 **Huang, Lingling, PhD**
DeNardo Education and Research Foundation Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentor: Daniel Kreisel, MD, PhD
IRF3 is dispensable in polyI:C-induced transcriptional activation of CXCL-2
Huang L; Kreisel D
Introduction: Neutrophils are important for tissue repair after myocardial ischemia/reperfusion in heart transplantation. When monitoring the neutrophil trafficking in beating murine cardiac grafts during ischemia/reperfusion, we found that wild-type mice receiving hearts deficient in the TLR3-TRIF-IRF3 axis showed severely impaired neutrophil adhesion, whereas neutrophils in mice receiving hearts from MyD88 knockout failed to transmigrate after normal adhesion. These data suggested that TLR3-TRIF-IRF3 axis and MyD88/NF-κB signaling regulate different stages of neutrophil extravasation. When chemokine CXCL2 was neutralized in recipients, we noticed a similar phenotype of impaired neutrophil adhesion as found in recipients deficient in TLR3TRIF-IRF3 axis. These findings suggested that CXCL2 may be regulated by mechanisms other than NF-κB signaling in this circumstance. This is particularly interesting because no studies have reported a relationship between IRF3 and CXCL2. This study aims to test whether IRF3 directly regulates CXCL2 transcriptional activation by modulating CXCL2 promoter activity.
Methods: Lentiviral-shRNAs were used to knock down IRF3 in HEK293-TLR3 cells. Expression of CXCL2 mRNA after polyI:C stimulation was assessed by quantitative PCR in these cells. CXCL2 promoter activity in IRF3-knockdown cells was also examined using a luciferase reporter system.
Results: Two independent shRNAs caused 70%-80% reduction of both IRF3 mRNA and protein in HEK293-TLR3 cells. Depletion of IRF3 did not affect the polyI:C-induced upregulation of CXCL2 mRNA. Consistently, luciferase reporter assay showed that IRF3-deficient cells produced similar levels of CXCL2 promoter activity induced by polyI:C.
Conclusions: Our data collectively demonstrate that IRF3 is dispensable for polyI:C-induced CXCL2 transcriptional activation, and hence they do not act in a simple linear fashion to regulate neutrophil adhesion. Therefore, we will start to investigate alternative hypotheses.

043 **Liang, Zhe**
DeNardo Education and Research Foundation Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Mentor: Michael Awad, MD, PhD
The effect of patient obesity on minimally invasive surgeon's muscle fatigue
Liang Z; Wang R; Awad M
Introduction: Laparoscopy has become the treatment of choice for many abdominal diseases requiring surgical intervention. The laparoscopic approach has been associated with significant reductions in morbidity and mortality for a wide range of procedures, including ventral hernia repairs, paraesophageal hernia repairs, bariatric surgeries, and cholecystectomies. However, the benefits to the patient may come at a cost to the surgeon, as this type of surgery creates unique ergonomic challenges with the potential to cause pain or injury, especially in the neck and upper arm region. As obesity rates have remained steadily high in the United States, we sought to quantify how patient BMI might influence these ergonomic stressors.
Methods: Using a Trigno Wireless EMG system, we recorded electrical activity in the biceps, triceps, deltoid, and trapezius muscle groups of five laparoscopic surgeons in a total of 32 abdominal surgeries. These recordings were then used to calculate average muscle activation during the surgery, normalized to a percentage of the maximum voltage of contraction (MVC). As a subjective measure of task difficulty, the subjects also completed the NASA Task Load Index (NASA-TLX or NTLX) survey after each case.
Results: Surprisingly, our initial analysis suggests that average muscle activation during surgery and subjective task difficulty are not correlated with patient BMI. These results suggest that laparoscopic surgery reduces or eliminates potential difficulties of operating on high-BMI patients, possibly though eliminating the need for gross manipulation of body mass by the surgeon.
Conclusions: The result of this study suggests that there is no significant association between patient obesity and surgeon's muscle fatigue. However, due to potential confounding factors such as procedure type and the role of the attending surgeon versus the assisting resident, further detailed analysis should be conducted before any solid conclusions can be drawn.

041 Linkugel, Andrew

DeNardo Education and Research Foundation Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Mentor: Amy Cyr, MD

Staging studies are of limited utility for newly diagnosed clinical stage I-II breast cancer

Linkugel AD; Margenthaler JA; Cyr AE

Introduction: For patients diagnosed with clinical stage I-II breast cancer, treatment guidelines recommend against the routine use of radiologic staging studies in the absence of signs or symptoms suggestive of distant metastasis. However, these tests continue to be used for many early-stage breast cancer patients. This study aims to determine the utilization and yield of these studies.

Methods: Female patients presenting with AJCC 7th Edition clinical stage I-II invasive breast cancer between 1998 and 2012 at Siteman Cancer Center, were identified in a prospectively maintained institutional surgical database. Clinical stage and staging studies performed within 6 months of diagnosis were recorded. Staging studies of interest included computed tomography (CT) of the chest, abdomen, and/or pelvis, bone scan, and positron emission tomography (PET). Results of staging studies and additional diagnostic studies or procedures were recorded. Descriptive statistics were used for the analysis.

Results: A total of 3291 patients were included in the analysis, of which 2044 were stage I and 1247 were stage II. Of these, 882 (27%) received CT of the chest, abdomen, and/or pelvis; bone scan; or PET within 6 months of diagnosis. Of these 882 patients, 312 were stage I (15% of the stage I cohort) and 570 were stage II (46% of the stage II cohort). Of the 882 patients imaged, 194 (22%) required additional imaging (x-ray, CT, bone scan, sonogram, or PET) and/or biopsies to follow up abnormalities seen on the staging studies. However, only 11 of those 194 (6%) were confirmed to have metastatic disease (1.2% of the 882 imaged patients, 0.33% of the total study cohort). Numbers of patients determined to have metastatic disease were too small for comparative analysis.

Conclusions: The identification of distant metastasis among clinical stage I-II patients in this study was rare (0.33% of the total cohort). Even among patients judged appropriate for staging studies (CT, bone scan, and/or PET), only 1.2% were diagnosed with metastatic disease. These findings suggest that staging studies are overused and lead to additional procedures in over 20% of patients.

133 Wondmeneh, Sarah

DeNardo Education and Research Foundation Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Hematology and Oncology
Mentor: Robert Hayashi, MD

Knowledge and perceptions of infertility in adolescent female cancer survivors and parents

Wondmeneh S; Cooper AR; Richardson BE; Morhmann CE; Gettinger KF; Henry J; Hayashi RJ

Introduction: Infertility, a late-effect of cancer treatment, is a major concern for female cancer survivors. Recent advances in fertility preservation have increased options available for survivors with decreased reproductive abilities. However, few studies have assessed the level of knowledge about fertility preservation and attitudes towards fertility in the female adolescent cancer survivor population. The purpose of this study is to quantitatively assess survivor and parent fertility knowledge, parent distress, survivor reproductive concerns and overall quality of life.

Methods: In this pilot study, three validated instruments, designed to assess knowledge, reproductive concerns and quality of life, are administered to female adolescent cancer survivors aged 13-18 years with a treating relationship in the Division of Hematology/Oncology at St. Louis Children's Hospital. Parents are asked to complete the Impact of Events Scale, in addition to the 13-item knowledge scale. It is expected that the accrual period of the study will be completed in a year, with a total of 50 enrolled. Pearson correlation coefficients will be used to determine if there is an association between the knowledge scale of the patients and that of the caregivers, with any of the other 3 outcome scales or, with any socio-demographic variable collected.

Results: Results are pending completion of data collection. We hypothesize that for childhood cancer survivors, limited knowledge on fertility and its relationship to cancer treatment is associated with increased reproductive concerns and increased distress for parents. Furthermore, we expect this group to demonstrate a low quality of life assessment.

Conclusions: This study intends to assess fertility knowledge in adolescent female cancer survivors and their parents, in addition to increasing our understanding of fertility concerns in survivors and the stress parents experience with regards to their child's fertility. This will facilitate the development and implementation of an educational program tailored to their needs. This will hopefully improve the knowledge of patients and families, facilitate future decisions on family planning and, optimize their outlook for the future.

085 **Yeat, Nai Chien**

DeNardo Education and Research Foundation Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Gastroenterology
Mentors: Samuel Klein, MD; Faidon Magkos, PhD

The effect of weight loss on markers of adipose tissue inflammation

Yeat N; Klein S; Magkos F

Introduction: It has been hypothesized that non-infectious inflammation in adipose tissue is involved in the pathogenesis of metabolic abnormalities associated with obesity. Studies of the link between obesity and adipose tissue inflammation in humans have so far been limited to macrophages. Two landmark studies in particular, demonstrated that obesity is associated with increased adipose tissue macrophage infiltration, in conjunction with a switch in macrophage population to a pro-inflammatory state. Recently, data from rodent models suggest that other immune cells found in adipose tissue, including CD4 and CD8 T cells, natural killer T cells, B cells, eosinophils, neutrophils, and mast cells, might also contribute to metabolic dysfunction. We have recently found that T-cell subtypes present in adipose tissue of obese people are closely linked with insulin resistance (unpublished observations). However, the full spectrum of immune cells present in adipose tissue in lean overweight and obese people has not been carefully characterized, and it is not known if adipose tissue has an immune cell phenotype that varies with adiposity and metabolic status.
Methods: A total of 40 men and women between the ages of 21 and 65 years with a BMI of >30 but ≤45 kg/m2 were randomized to the weight loss group or the control group. The weight loss group participated in a dietary intervention with a targeted weight loss of 15%. Adipose tissue biopsies were taken from the weight loss group at baseline, and at the milestones of 5%, 10% and 15% weight loss, whereas the control group was biopsied at baseline, and at a time point corresponding approximately to 10% weight loss in the treatment group. Markers for immune cell infiltration will be quantified by RT-PCR and visualized by immunohistochemistry.
Results: We expect inflammation to be negatively correlated with weight loss. However, a preliminary RT-PCR study using 5 treatment group samples and 5 control group samples showed no statistically significant difference in inflammation between the treatment and control group after 10% weight loss.
Conclusions: We will conduct a second preliminary RT-PCR study using more samples in order to decide whether to proceed with assaying the rest of the samples by PCR, and whether to proceed with immunohistochemistry.

121 **Corbin, Rachel**

Forum for International Health and Tropical Medicine; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Anthropology; Obstetrics and Gynecology, Tunxi District People's Hospital, China
Mentors: Carolyn Sargent, PhD; Shengbo Fang, MBBS

Analysis of the cesarean section rate in Tunxi, Anhui, China

Corbin RS; Sargent C; Fang SB

Introduction: According to the World Health Organization, the maximum optimal cesarean section (CS) rate for any population is 10–15%. The CS rate in urban China, however, was 64.1% in 2008. High CS rates introduce unnecessary risk, thus, it is important to understand the factors that contribute to these rates, and to work to bring them down to the optimal, safest level.

Methods: The CS rate was calculated for patients who received prenatal care at one public hospital in Tunxi, Anhui, China based on the hospital's records. A random sample of 50 women having given birth within the past 6 months in Tunxi were interviewed individually about 9 topics: birth experience, perinatal knowledge, family and friends' advice about birth method, doctor, family, and friends' attitude towards CS, participant's attitude towards CS, reason for birth method choice, participant's birth method recommendation to friends, financial and educational background. Responses were analyzed qualitatively to determine common themes.

Results: The CS rate for women receiving prenatal care at the hospital was found to be 77%. 76.3% of interview participants reported planning to have vaginal birth (VB) prior to their final ultrasound, and 100% reported that VB was better for the baby's health and/or the mother's recovery. However, only 24% gave birth by VB. Commonly cited reasons for choosing CS were doctors' recommendations, patient's fear of pain, and patient's concern for the baby's safety (often despite the doctor recommending VB and despite the fact that only 30% of participants believed that, in an uncomplicated delivery, CS was safer than VB).

Conclusions: The unavailability of epidurals to women choosing VB contributes to the fear of pain, discouraging women from having VB. Spending extra time in the hospital due to early presentation (either because misunderstanding of the nature of due dates or fear of hospital bed shortage) may contribute to women's feeling that they have been in labor for too long or that the baby is too late. Finally, doctors' desire to avoid medical disputes by emphasizing risks of vaginal birth and providing elective CS contributes to the high CS rate.

033 **Krishnan, Sangitha**

Forum for International Health and Tropical Medicine; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentor: Joaquin Barnoya, MD, MPH

Newspaper advertising and consumer promotions of fast-food chain restaurants with delivery service in Guatemala

Krishnan S; Melendez R; Weisel D; Barnoya J

Introduction: Obesity is a widespread epidemic in many countries, including Guatemala. Fast food restaurants serve food with high caloric content and high fat, which contributes to weight gain and leads to obesity. In Guatemala, fast food consumption is a large part of the lifestyle, and many restaurants have delivery services to increase convenience. This project evaluates the prevalence and content of fast food advertising in Guatemalan newspapers in order to provide a framework around which to evaluate the impact of fast food consumption on obesity.

Methods: Fast food advertisements of twelve restaurants that offer delivery services were counted and evaluated in seven major newspapers every day for ten weeks. Various features of the advertisements were recorded, and the food advertised was assessed for additional advertisements and nutritional quality. The data was analyzed using STATA.

Results: There are no results to be presented yet. The results will show that there are food advertisements in each newspaper.

Conclusions: This study provides a baseline for studying the impact of fast food consumption on obesity. Fast food advertising aims to increase consumerism, which leads to unhealthy eating habits in families. Banning fast food advertisements has been shown to decrease the probability of buying fast food in other countries; therefore, banning fast food advertisements in Guatemalan newspapers would decrease exposure and could decrease consumption. This would have a positive, healthy impact on the Guatemalan community and could decrease the prevalence of obesity in the country.

143 Shen, Ching-Chieh

Forum for International Health and Tropical Medicine; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics, National Taiwan University School of Medicine, Taiwan
Mentors: Li-Ming Huang, MD, PhD; Chi-Song Hsieh, MD, PhD

Early Palivizumab treatment on cells infected with respiratory syncytial virus can reduce the adherence of Streptococcus pneumoniae

Shen C; Yeh CW; Huang LM

Introduction: Respiratory syncytial virus is one of the most common pathogens in young children and can cause serious illnesses in certain vulnerable patient populations such as premature infants. Previous studies have shown that certain virally infected cells can enhance the adherence of Streptococcus pneumoniae on human respiratory epithelial cells, but none has investigated the effect of anti-RSV treatment (e.g. Palivizumab) on pneumococcal adherence. This study aims to preliminarily investigate the benefits of prophylactically treating patients with palivizumab for the prevention of S. pneumoniae infection.

Methods: Hep-2 and A549 cells were infected with RSV then inoculated with S. pneumoniae. Bacterial adhesion was measured using colony forming unit adherence assay.

Results: In this study, we confirmed that a preceding respiratory syncytial virus infection of human respiratory epithelial cells can indeed enhance the adherence of Streptococcus pneumoniae. We also investigated whether treatment with an anti-RSV antibody, Palivizumab, can affect bacterial adherence. We observed that early Palivizumab treatment on RSV-infected cells may reduce bacterial adherence, whereas late Palivizumab treatment may further enhance bacterial adherence.

Conclusions: We hope that these experiments would shed light on the mechanism by which RSV enhances bacterial adherence and contribute to the prevention of S. pneumoniae infections.

033 Weisel, Daniel

Forum for International Health and Tropical Medicine; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentors: Renato Meléndez, MD; Joaquin Barnoya, MD, MPH

Newspaper advertising and consumer promotions of fast food chain restaurants with delivery service in Guatemala

Weisel DM; Meléndez R; Barnoya J; Krishnan S

Introduction: In Guatemala, the estimated prevalence of obesity and overweight combined was 41.4% in men and 54.5% in women in 2013. Excessive calorie intake from fast food restaurants is thought to be a major contributor. Fast food chains advertise consumer promotions and delivery service to increase exposure to their product, which promotes overconsumption. The extent to which fast food advertising contributes to obesity in Guatemala is not yet known, but to date, there has been no quantitative analysis of fast food print advertisements in Guatemala, nor of the prevalence or marketing of delivery services of those products. The purpose of this study is to quantify and assess newspaper advertising of fast food chains with delivery service in Guatemala City. In addition, this study will investigate the availability and quality of nutrition information offered in these advertisements.

Methods: For 10 weeks, each daily issue of 7 newspapers was screened for all types of advertisements. Ads from 12 selected fast food chains were analyzed according to size, placement within the newspaper, use of text and images, color, price and nutrition information, and classification as a promotion, reminder, or sponsored ad. Promotions were ordered, and upon delivery, any accompanying flyers or coupons were also analyzed.

Results: We expect most fast food restaurants to utilize advertising and consumer promotions as marketing strategies. Lack of nutrition information in consumer promotions, as well as low nutritional quality is also expected. The price of individual non-promotional items is expected to be more expensive than their combined promotional price.

Conclusions: The results of this study aim to ultimately impact consumption of fast food in Guatemala. The results will be used to advocate for policies that limit advertising and consumer promotions of fast food and increase the accessibility of healthy products. Regulations of portion sizes of unhealthy food will also be sought. The results will be shared with both consumers and researchers to encourage further projects regarding the direct impact of advertising on consumption.

Foundation for Barnes-Jewish Hospital Student & Faculty Award

122 **Wu, Francis**

Foundation for Barnes-Jewish Hospital Student & Faculty Award; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Otolaryngology
Division: Head and Neck Surgery Oncology
Mentors: Brian Nussenbaum, MD; James Duncan, MD, PhD

Auditing adherence to pre-procedure checklists to preserve patient wellness

Wu FS; Nussenbaum B

Introduction: The delivery of medical care is complex and possible errors exist at every step. In particular, there are errors medical providers strive to avoid that are known as "never events," which include wrong-patient and wrong-site surgeries. These errors are avoided in practice by running a pre-procedure check, or "timeout." In spite of this effort, however, these errors persist. Based on previous work done by the pediatric interventional radiology (IR) team at Barnes-Jewish involving auditing timeouts, we believe hospital personnel will decrease their error rates if procedures are recorded and audited for compliance with a timeout checklist and feedback is shared with hospital teams. Establishing a feedback cycle will help promote greater adherence to pre-procedure checks for hospital staff, which in turn should improve patient safety.

Methods: LiveCapture recording systems have been installed in the IR department with an additional one to be installed in the otolaryngology (ENT) operating room, which record timeouts prior to procedures. Until the ENT system is online, live audits are performed. These recordings are reviewed and scored by medical students and hospital personnel with a checklist. Control charts and scatterplots will be used to monitor timeout scores and progress with individual items on the checklist. Inter-observer variation will be assessed using matrix plots.

Results: Preliminary data from the Barnes-Jewish Hospital pediatric IR and general IR departments have found a significant and sustained improvement in timeout performance. We expect that expanding the video recording and auditing process to the ENT department will show a similar improvement.

Conclusions: Errors in healthcare are dangerous, and patients expect hospitals to actively take steps to prevent these adverse events and perceive thorough pre-procedure checks as adherence to high quality care. While timeouts have been a universal requirement in hospitals, they alone have limited success in preventing "never events." Barnes-Jewish is the first institution to combine pre-procedure checklists with video recording, and our hope is to promote a stronger safety culture to prevent "never events" from harming our patients.

Howard Hughes Medical Institute Summer Medical Fellows Program (HHMI)

100 **Macneal, Kenneth**
Howard Hughes Medical Institute Summer Medical Fellows Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine; Molecular Microbiology
Division: Infectious Diseases
Mentors: Dan Goldberg, MD, PhD; Jeremy Mallari, PhD
Functional characterization and substrate identification of a metalloprotease required for the intra-erythrocytic growth of Plasmodium falciparum
Macneal KM; Mallari JP; Goldberg DE
Introduction: Growing artemisinin resistance presents a serious problem for the treatment of Plasmodium falciparum, the causative organism for the deadliest form of malaria, which kills over 600,000 people each year. Despite its extensive impact, much of the biology of P. falciparum remains obscure. This project lays the foundation for the study of a putative zinc metalloprotease, MAL13P1.184 (MAL), which appears to be essential for the parasite's intra-erythrocytic lifecycle.
Methods: Vectors were created for the expression of tagged, wild-type and inactivated protein within the 3D7 strain of P. falciparum as well as within Escherichia coli. These tags could be used for the purification of MAL, which could then be tested for activity against substrates of homologous proteins using an HPLC-based assay.
Results: Both full length wild type and inactivated protein were successfully purified from P. falciparum, and a 76 base pair, N-terminal truncation was successfully purified from E. coli. Both the full length and 76-bp truncations exhibited EDTA-sensitive cleavage of bradykinin, but not of dynorphin, Pz-peptide or neurotensin, demonstrating an unusual level of substrate specificity within this protein family.
Conclusions: The parasite lines, purification protocols and activity assay developed in this project allow for the future in-depth characterization of MAL and its role in the parasite. These tools can be used for the analysis of MAL's substrate specificity, optimal conditions and the development of inhibitors against it. If the protein is indeed essential, this may lead to the development of new malaria treatments, or at the very minimum, provide more information on the complex biology of P. falciparum.

056 **Segura, Abraham, MS**
Howard Hughes Medical Institute Summer Medical Fellows Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurobiology, Harvard Medical School
Division: Cardiology
Mentors: David Clapham, MD, PhD; Nathaniel Blair, PhD
Carvacrol and hydroquinone reveal distinct but interacting desensitization mechanisms in TRPA1
Segura A; Blair NT; Clapham DE
Introduction: Transient receptor potential ankyrin-repeat 1 (hTRPA1) is a non-specific cation channel expressed in sensory neurons that innervates various targets, such as airways, GI, and skin, and may play a role in inflammation. Previous work has shown that numerous chemicals activate and desensitize hTRPA1, though the latter is not fully understood. The aim of this study is to observe the effects of carvacrol, a non-electrophilic agonist, and hydroquinone (HQN), a precursor of the electrophilic irritant p-benzoquinone, on hTRPA1 desensitization.
Methods: Whole-cell patch clamp recordings were obtained from human embryonic kidney (HEK) 293 cells expressing wild-type hTRPA1. Glass pipettes were filled with an internal solution containing Cs-methanesulfonate, $MgCl_2$, EGTA, Tris-creatine phosphate, ATP, NaGTP, and HEPES (pH 7.20, CsOH). The extracellular solution had no added Ca^{2+} and consisted of NaCl, KCl, $MgCl_2$, glucose, and HEPES (pH 7.40, NaOH). Agonists were applied directly on cells using ~200-mm-diameter quartz tubes.
Results: Whole-cell recordings revealed carvacrol elicited weaker activation (peak current 174.6 ± 148.2 pA/pF) and reversible, fast (τ = 4.6 ± 2.3 s) desensitization, whereas HQN had greater activation (1159.2 ± 324.7 pA/pF) and irreversible, slow (τ = 12.5 ± 0.63 s) desensitization. Carvacrol, but not HQN, desensitization reversed with washout and also spontaneously over time during long (>6 min) exposure. Lower concentration HQN resulted in delayed activation of the channel during subsequent exposure to carvacrol but no desensitization. No carvacrol desensitization was observed following prolonged (>3 min) exposure to HQN or carvacrol.
Conclusions: This study suggests non-electrophilic and electrophilic desensitization in hTRPA1 occurs via two different, but interacting mechanisms. Long-term exposure to either class of agonist may promote conformational changes that inhibit further desensitization. Additional drug concentrations should be tested to better understand the dose dependence of this phenomenon. Site-directed mutagenesis studies targeting known residues involved in electrophilic desensitization might uncover potential sites that interact with non-electrophilic agonists.

124 **Chalivendra, Varun**
MA/MD Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Otolaryngology
Mentor: Ravindra Uppaluri, MD, PhD

The role of developmental transcription factor Nkx2-3 in oral cavity squamous cell carcinoma aggressiveness

Chalivendra V; Uppaluri R

Introduction: Squamous cell carcinoma of the head and neck (HNSCC) is the sixth most common cancer worldwide, representing up to half of all malignancies in parts of the developing world. A majority of these tumors arise in the oral cavity. For those patients with advanced carcinogen-associated oral cavity squamous cell carcinoma (OCSCC) 5-year overall survival rate is around 50%. Our laboratory has developed a mouse cell line model (MOC) of carcinogen induced OCSCC in which some lines are non-metastatic and others are metastatic to regional lymph nodes or the lung. A comparative microarray analysis of the MOC lines revealed a distinct molecular signature associated with aggressive tumor growth. The microarray signature revealed that the homeodomain developmental transcription factor Nkx2-3 is selectively upregulated in the aggressive cell lines and thus may be a candidate driver of tumor aggressiveness.
Methods: Nkx2-3 overexpression was enforced using pBABE vector in the indolent locally growing MOC1 line. Nkx2-3 knockdown was accomplished by pooled siRNA. In vivo tumor growth was measured by the two largest diameters upon flank injection in C57BL/6 wild type mice. In vitro growth was measured by the soft agar colony formation assay.
Results: Expression of Nkx2-3 was confirmed by RT-PCR and Western blot. Phenotypic differences between Nkx2-3 overexpressing and control lines were examined in vitro and in vivo. Soft agar assay showed significantly greater colony formation potential for the MOC1 Nkx2-3 overexpression compared to the control (166±44.4 vs. 26.7±10.8 colonies/plate, p=0.038). MOC1 Nkx2-3 overexpressing line also formed significantly larger tumors in wild type mice (2048.9±253.2 vs. 922.6±294.5 mm3 p=0.020).
Conclusions: We have described a murine OCSCC cell line model that parallels human disease in its carcinogen-derivation, mutational landscape, histology, and in vivo behavior. We identified Nkx2-3 as a candidate driver of aggressive growth. Our data show overexpression of Nkx2-3 in the indolent MOC1 cell line produces an aggressive growth phenotype with greater soft agar colony formation, and larger tumors in vivo.

Memorial Sloan Kettering Summer Internship Program

036 Cheng, Jenny Zhao
Memorial Sloan Kettering Summer Internship Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Transplantation Surgery, Memorial Sloan Kettering
Mentor: Wendy Schaffer, MD, PhD

Cardiac stress testing is a poor prognostic indicator for outcomes in allogeneic hematopoietic stem cell transplantation

Cheng JZ; Pham A; Amaruso D; Jakubowski A; Schaffer WL

Introduction: Hematopoietic stem cell transplantation (HSCT), a successful therapy for hematologic malignances and disorders, is also associated with increased risk for short term and long-term cardiovascular complications. Given the limited data available, a retrospective analysis of more recent data was conducted to evaluate the effectiveness of pre-transplant stress testing.
Methods: 284 allogenic HSCT during 1999-2009 were included in the study. 170 patients underwent stress echocardiography (Bruce protocol) whereas 114 underwent stress MUGA (Multi Gated Acquisition Scan).
Results: As measured with stress echo, blood pressure (BP) response, change in ejection fraction (EF), maximal predicted heart rate (MPHR), maximal metabolic equivalents of task (METs), forced expiratory volume in one second (FEV1) and pre-stress test hemoglobin level (Hb) did not correlate with cardiovascular (CV) events, ICU admission, in-hospital death or one-year mortality. Stress MUGA demonstrated that BP response, resting EF, exercise time, maximal METs, change in EF, MPHR, FEV1 and Hb did not correlate with CV events, one-year mortality, in-hospital death or ICU admission. Abnormal BP responses during stress test were not associated (odds ratio < 1) with in-hospital death in MUGA patients with a significant p value (<0.05), showing that normal BP response during stress MUGA result in CV events. Due to the low incidence of CV events in MUGA patients, the maximum likelihood estimation is likely to suffer from small-sample bias. Resting EF and exercise time were associated with in hospital death in echo patients with p values of 0.0116 and 0.0147 respectively.
Conclusions: Most stress test parameters correlate poorly with outcomes of allogenic HSCT, suggesting that neither stress echocardiography nor stress MUGA stress testing is a valid pre-transplant screening test with significant prognostic value. More standardized evaluation of exercise tolerance in the clinical setting and rest echocardiography may be good substitute.

Office of the Provost, Diversity & Inclusion Grant

079 **Bala, David**

Office of the Provost, Diversity & Inclusion Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Internal Medicine
Division: Emergency Medicine
Mentor: Christopher R Carpenter MD

Reducing CMS-defined preventable readmissions: a comparative study of three geriatric friendly emergency department healthcare models

Bala DO; Carpenter, CR

Introduction: The Center for Medicare and Medicaid Services (CMS) recently initiated readmission penalties for a few common diagnoses. The majority of patients affected by this policy are older adults. Recent "Geriatric Emergency Department Guidelines" provide alternative emergency department (ED) management protocols for this population, but these strategies remain largely untested. The objective of this study was to compare three ED models' 60-day hospital readmission rates for patients age 65 or older presenting to the ED following hospital discharge with one of four CMS diagnoses: congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), pneumonia, or myocardial infarction (MI).

Methods: This was a prospective observational trial. A convenience sampling of community-dwelling patients age 65 or older was recruited from the EDs of Washington University, the University on North Carolina-Chapel Hill, and the University of Alabama Birmingham. Inclusion criteria included: discharge from an inpatient facility within the last 60 day with a diagnosis of CHF, COPD, MI, or pneumonia, the patient dwells in the community, and the patient consents to participate. The intervention of this study will be the standard care of the three geriatric healthcare models. RA's (research assistants) will use instruments to screen for common geriatric syndromes. Thirty days after the index visit, RA's followed up with each participant by phone using a scripted interview. The data was analyzed using t-tests.

Results: At the time of this writing 6 participants have been recruited. The mean age was 77.7, 83.3% were male, and 66.7% were non-white. Geriatric screening found that 66.7% of participants were at risk of dementia, but none were at risk of delirium. Only one follow-up call has been completed resulting in no 30 day readmits. It is anticipated that increased geriatric specific intervention, UAB with the highest and Wash U with the lowest, will coincide with lower ED revisits and hospital readmissions.

Conclusions: Once completed the results of this study will aid in developing more effective geriatric ED models that will lower hospital and ED readmissions.

093 **Harris, Kathryn**

Office of the Provost, Diversity & Inclusion Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Internal Medicine
Division: Cardiology
Mentor: Ari Cedars, MD

Care burden of patients with a single ventricle

Harris KO; Cedars A

Introduction: Adult patients with a single ventricle physiology will have significantly higher hospitalization rates than age-matched controls in the general population. Due to increased hospitalization rates and the need for regular cardiac follow-up and testing, the costs of care of adult patients with a single ventricle will be significantly higher compared with age-matched controls.

Methods: In order to evaluate this hypothesis, a single center, retrospective chart review of all patients with a single functional ventricle at the Center for Adults with Congenital Heart Disease at Washington University was undertaken. Patient admissions were categorized according to discharge diagnosis. National estimates and standard errors were derived from the 37th annual report of the US Centers for Disease Control/ National Center for Health Statistics CDC/ NCHS from 2013 by diagnosis, categorized by age: 15-44, 45-64, and 65+. Statistics were generated for the total single ventricle population regardless of admission. Further statistics were generated for subgroups of unplanned admissions and unplanned cardiac admissions.

Results: It was discovered that single ventricle patients are much more likely to be admitted than the general population, specifically for cardiac arrhythmia and congestive heart failure as well as for musculoskeletal reasons and lung disease. Risk factors for unplanned hospitalization of any type among patients with a single ventricle were: age at Fontan, arrhythmias of either atrial or ventricular origin, genetic syndromes, baseline disability and non-cardiac problems. Risk factors for unplanned hospitalization for a cardiac reason were: atrial arrhythmias, baseline creatinine, and evidence of cirrhosis.

Conclusions: Although the Fontan procedure provides an excellent palliation for patients with a single ventricle, the physiology ultimately contributes to progressive circulatory failure. Due to the limited power of this study, it is necessary to repeat this study with multiple institutions. In the future, therapies to reduce failure rates and optimization of the timing for referral for heart transplant should be studied.

037 **Heningburg, Avory**

Office of the Provost, Diversity & Inclusion Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Surgery
Division: Urologic Surgery
Mentors: Gerald Andriole, MD; Steven Brandes, MD

Physician decision impact study of stone patients' nutritional intake

Heningburg A; Desai A; Paradis A; Vetter J; Kuxhausen A; McIntosh L; Juehne A; Andriole G; Benway B; Brandes S

Introduction: Nutrition plays an important role in the development and management of stone disease. We aimed to evaluate physicians' decision making with regards to stone management based on an assay of nutrition and hydration levels generated by an electronic food frequency questionnaire. We sought to determine if a physician's decision making differs based on information reported by the patient via a computerized clinical decision support system (CDSS) versus that obtained during a medical history. In addition, we sought to evaluate alterations in proposed care based on the results provided by the physician.

Methods: We collected 75 food frequency questionnaires over a period of 6 weeks at Washington University Urology Stone Clinic. Two urologists were consented for this study. Each stone patient was given an electronic version of the survey before or after his or her visit in the stone clinic. Following completion of the questionnaire, the physician was asked to complete a brief survey of initial impressions based upon their patient interview, followed by a second bank of questions incorporating the patient-reported electronic results. Statistical analysis was used to compare results of the physicians' responses to the survey.

Results: Hydration score and diet score did not differ significantly across physician. The odds of a diet score change was significantly higher for patients who consumed more sodium ($p = 0.012$) or more fluids ($p = 0.04$). There is no difference in the odds of a change in hydration score for patients who consumed oxalate, calcium, sodium, purine or water. Oxalate consumption was positively correlated with the decision for additional intervention. The following foods have significant relationships with change in score or intervention ($p<0.05$): raspberries, cashews, table salt, smoothies, kale, other caffeinated drinks, pork, restaurant meals, and vegetables.

Conclusions: Information derived from the food frequency questionnaire, CDSS, can have significant impact on a physician's decision for treatment and management of stone disease. Future studies will include more FFQs collected longitudinally. Morbidity factors such as date of diagnoses, race, age, and BMI will be recorded.

072 **Oh, Moo Jin**

Office of the Provost, Diversity & Inclusion Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Radiology
Mentor: Jie Zheng, PhD

Whole-heart cardiac perfusion imaging protocol using PET-MRI system for the diagnosis of coronary heart disease

Oh M; Zheng J

Introduction: Cardiac PET-MRI combines the best qualities of high signal resolution MRI anatomic imaging and PET functional measurements. One problem is the limited spatial coverage for the cardiac perfusion imaging with only 3-4 slices, whereas PET perfusion imaging can cover the entire heart. However, the entire heart usually needs >6 slices to cover so that regional ischemia can be diagnosed correctly. The goal of this study is to evaluate a new technique, such as whole-heart perfusion imaging by MRI part in a clinical setting, and also to compare them to the PET findings acquired simultaneously. Two specific aims are: 1) Optimize MRI whole-heart perfusion imaging protocol and analysis tool in volunteers; 2) Perform preliminary study in patients with coronary artery disease.

Methods: The PET-MRI examinations will include MRI coronary artery imaging, resting and stress 3D perfusion MRI and whole-heart perfusion PET (^{13}N-ammonia) acquisitions, and myocardial viability imaging by MRI only. Both PET and MRI images will be viewed and assessed in consensus by a team of a nuclear cardiologist and cardiac MRI radiologist and graded for the presence or absence of ischemia and infarction in each of the 17-segments in comparison to findings on SPECT-MPI imaging. These three data sets will be de-identified and randomized and presented to the radiologist and cardiologist team on separate days for reviewing.

Results: This demonstrates the coronary artery imaging from one subject at pre-, post-contrast 1, and post-contrast 2. The contrast and signal improved for both post-contrast scans, in comparison with pre-contrast images. The SNR and CNR data suggests that post-contrast 2 provided the best image quality. One set of images from dynamic perfusion image data sets at 6 slices were shown, which indicates the feasibility of whole-heart MRI perfusion imaging in the PET-MRI system.

Conclusions: The feasibility of MR whole-heart coronary artery and perfusion imaging in PET/MRI system was demonstrated. A single bolus injection of contrast agent can allow both contrast studies. Patient study is warranted for clinical applications.

117 **Omambia, Elizabeth On'gera**

Office of the Provost, Diversity & Inclusion Grant, Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Meharry Medical College
Department: Obstetrics & Gynecology
Division: Maternal Fetal Medicine and Ultrasound
Mentors: Allison Cahill, MD, MSCI; Molly Stout MD, MSCI

Estimated fetal weight accuracy in macrosomic babies: Systematic underestimation by more than you think

Stout MJ; Dukes J; Omambia EO; Tuuli MG; Dicke JM; Macones GA; Cahill AG

Introduction: Suspicion of fetal weight > 4000 grams impacts patient counseling of risks regarding labor management, cesarean, and shoulder dystocia. This counseling depends on the accuracy of the estimates of fetal weight obtained before delivery. We aimed to investigate how well estimated fetal weight obtained by ultrasound (EFW) agreed with birth weight (BW) in a cohort of neonates with BW ≥ 4000 grams. In addition, we examined the performance of commonly used Hadlock biometry equations for EFW to assess which equation performed best to maximize EFW and BW agreement.

Methods: From a prospective cohort of full-term live-born neonates from 2010-2012, those with birth weight ≥ 4000 grams and an ultasound for EFW with individual biometry parameters obtained within 21 days of delivery were included. Bland Altman analysis was performed to assess the agreement between EFW and BW. EFWs were calculated using multiple Hadlock equations comprised of 1-4 biometry components. Agreement between calculated EFW from each biometry equation and actual BW was tested to determine which biometry regression equation performs best for prediction of macrosomia. Subgroup analysis by maternal BMI was performed.

Results: In this cohort of 55 infants born with BW ≥ 4000 grams, Bland Altman analysis demonstrated that EFW systematically underestimates birth weight in these infants by an average of 442 grams. Notably, the disagreement between EFW and BW was more severe with increasing maternal BMI. In normal weight women EFW systematically underestimated BW by 310 grams, whereas in obese women BW was underestimated by 475g, and in morbidly obese women BW was underestimated by 605g. The Hadlock equation that performed best (minimized systematic error) included abdominal circumference and femur length, or abdominal circumference alone.

Conclusions: In term fetuses with BW ≥ 4000 grams, ultrasound EFW obtained within 21 days of delivery systematically underestimated actual birth weight with significant clinical magnitude. The risk for underestimation error of ultrasound measurements for EFW when there is clinical suspicion of macrosomia should be considered when counseling these patients.

Otolaryngology NIH T32 Physician Scientist Program (PSP)

126 **Karim, Adham**
Otolaryngology NIH T32 PSP
Current Doctoral Program of Study: Medicine
University of Illinois at Chicago College of Medicine
Department: Otolaryngology
Mentor: Timothy E Hullar, MD
The effect of hearing aids on postural stability
Rumalla K; Karim AM; Hullar TE
Introduction: Falls are the leading cause of injury-related visits to emergency departments in the United States and the primary cause of accidental deaths in people above the age of 65. There is evidence that older people with hearing loss have an elevated risk of falling. The vestibular, proprioceptive, and visual systems are proven to contribute to postural stability, but the contribution of audition to imbalance has not yet been determined.
Methods: We conducted a matched-paired cross-sectional study to measure postural stability in bilateral hearing aid users over the age of 65 with their hearing aids on and off. A total of 14 subjects were enrolled. Balance was assessed using two tests: the tandem stance and the Romberg on foam tests. The balance tests were administered in the presence of a point-source broadband white-noise sound (0-4 kHz) source in both unaided and aided conditions in the dark. Subjective measures of subjects' confidence were performed using the Activities-Based Confidence Scale (ABC) and a questionnaire regarding perception of balance performance.
Results: Performance on the Romberg on foam test was significantly better in the aided than unaided condition ($p = 0.0051$). Performance on the tandem stance test showed a similar improvement ($p = 0.0052$). No statistically significant relationship between improvement in balance and audiologic performance was identified. Subjects did not report that they perceived a difference in balance between the two conditions.
Conclusions: Relative risk of falling was found to decrease 40% when subjects wore hearing aids. This indicates a new treatment modality for imbalance in older adults with hearing loss and suggests a significant public-health benefit for wearing hearing aids in older adults vulnerable to falls.

074 **Tang, Rose**
Otolaryngology NIH T32 PSP; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Anesthesiology
Division: Cardiothoracic Anesthesiology
Mentor: Michael Avidan, MBBCh
Assessment of preoperative falls
Tang RD; Schelble AP; Avidan MS; Ben Abdallah A; Wildes TS
Introduction: Falls are the third leading cause of deaths from accidental or unintentional injuries in the US and represent a major public health problem for all age groups. Even nonfatal falls often result in serious injuries and hospitalizations that can dramatically change one's life trajectory. The purpose of this study was to examine the frequency of falls in the adult surgical population as well as the demographic and health characteristics of fallers. A specific aim was to consider correlates of preoperative falls and assess whether falls in the year preceding surgery are associated with poorer health.
Methods: 2,883 elective surgical patients at the Center for Preoperative Assessment and Planning at Barnes-Jewish Hospital completed a brief baseline survey that included information on fall history and quality of life. Descriptive statistics, chi-squared tests and t-tests were used in statistical analyses.
Results: Overall, 27.53% of participants reported one or more falls during the past year and of those who fell, 44.50% reported sustaining injuries. Fall frequency increased with age with falls occurring in 23.10% of patients aged 44 and under, 28.67% aged 45 to 64, and 32.17% aged 65 and older ($p<0.0001$). Gender, but not racial, differences were found with females more likely to fall (30.40%) compared to males (26.34%) ($p<0.0282$). Falls were more common in participants with worse self-reported health ($p<0.0001$).
Conclusions: The results of this study demonstrated that falls occurred more frequently in females and older adults. However, falls and injuries occurred at a high frequency in all age groups. Furthermore, patients who reported one or more falls in the past year had worse self-reported health. Asking about falls is a simple and quick way to gain a great deal of information about a patient's health. In the future, consideration should be given to including fall history as part of routine preoperative assessment. Additional research regarding the ability of fall history to predict postoperative complications and outcomes is warranted and would make these findings more compelling.

No **Tran, Kayla**

Poster Otolaryngology NIH T32 PSP

Current Doctoral Program of Study: Medicine

University of Cincinnati College of Medicine

Department: Otolaryngology

Mentors: Judith EC Lieu, MD, MSPH; Jay Piccirillo, MD, FACS, CPI

The accuracy of 226 Hz and 1000 Hz tympanometry in children with Down syndrome

Tran KT; Heeren CM; Ead B; Eikenberry G; Karzon RK; Lieu JEC

Introduction: Tympanometry assesses the integrity of the middle ear. However, its accuracy is unknown in children with Down syndrome. This is a prospective study to evaluate the sensitivity and specificity of 226 Hz and 1000 Hz tympanometry in children with Down syndrome, ages six months to five years.

Methods: Seventy-six children with a mean age of 2.59 years, received 226 Hz and 1000 Hz tympanograms by trained audiologists and ear exams by otolaryngologists, both blinded to each other's results. Static admittance at 226 Hz and compensated static admittance at peak pressures of +200 daPa, -200 daPa, and -400 daPa at 1000 Hz were recorded or calculated. Varying cutoff criteria for "normal" values were applied to determine the accuracy.

Results: The greatest agreement between ear exam and static admittance for the 226 Hz probe tone was with a 0.1mmhos cutoff, yielding 68% sensitivity and 83% specificity (K=0.491). The current clinical guideline of 0.3 mmhos resulted in 92% sensitivity and 33% specificity (K=0.273). For the 1000 Hz probe tone, compensated static admittance was most accurate for a peak pressure based on +200 daPa with a 0.7 mmhos cutoff, yield 71% sensitivity and 74% specificity (K=0.433).

Conclusions: Results showed that neither 226 Hz nor 1000 Hz tympanometry accurately differentiate middle ear fluid versus air in children with Down syndrome. However, the 226 Hz static admittance criterion of 0.1 mmhos is more accurate than the current standard of 0.3 mmhos.

Rehabilitation and Participation Science (RAPS) Doctoral Program

001 **Boone, Anna, MSOT**
RAPS Doctoral Program
Current Doctoral Program of Study: Occupational Therapy
University of Central Arkansas
Department: Occupational Therapy
Mentor: Jack Engsberg, PhD
Development of a novel, engaging VR gait intervention for children with CP
Boone AE; Engsberg JR; Iyer SE
Introduction: Cerebral palsy (CP) is the most common motor disorder in children. Many do not walk independently and have slow gait speed, leading to decreased participation in daily life. The purpose of this investigation was to develop a novel, cost efficient virtual reality (VR) gait intervention to motivate children with CP to achieve the high numbers of repetitions necessary for developing increased gait speed.
Methods: The Microsoft Kinect sensor, the Flexible Action Articulated Skeleton Toolkit (FAAST), and online games can be used to convert any body movement into a keyboard event generally required to play online video games. Strategies were applied to this existing method to adapt it as a gait intervention. Games utilized require at least one keyboard command that must continuously be activated. If addressing intervention through the client's current gait pattern, cadence or stride length would be used as the computer input whereas for underlying gait abnormalities the inputs would be hip flexion, knee flexion, or plantarflexion that are characteristic of CP. Data were gathered through the use of a non-disabled user. The number of repetitions, stride length, and motivation level were assessed. Additional demands can be placed on the virtual environment through incorporating additional desired movement thresholds.
Results: Utilizing this VR system a clinically feasible gait intervention was created for addressing multiple levels of gait variables including hip flexion, knee flexion, plantar flexion, cadence, and stride length. Preliminary results show a potential to achieve over 6,000 repetitions, increase stride length and kinematics, and be highly motivating for the client. Future data will be gathered to determine client feasibility, clinical feasibility, efficacy and effectiveness.
Conclusions: A proposed method of addressing decreased gait speed in children with CP through an inexpensive, engaging virtual reality therapy has been created and prepared for participant feasibility testing. Pending successful refinement and testing the intervention potentially could increase gait speed and ultimately children's participation in meaningful activities with peers.

002 **Foreman, Matthew**
RAPS Doctoral Program
Current Doctoral Program of Study: Rehabilitation and Participation Science
Washington University in St. Louis
Department: Occupational Therapy
Mentor: Jack Engsberg, PhD
A virtual environment for distorted reaching in the treatment of hemispatial neglect
Foreman MF; Pioppo A; Connor LT; Carter AR; Engsberg JR
Introduction: Hemispatial neglect is a common condition for persons with stroke that is characterized by decreased awareness towards one side of space. The most common treatment for leftward spatial neglect is prism adaptation therapy (PAT) that uses prism glasses to cause a rightward visual shift during repeated reaching movements. PAT can cause short and long-term effects allowing persons to more readily use and attend to the left side of space following rehabilitation. The purpose of this project is to develop a virtual reality environment (VRE) similar to PAT that combines modern motion capture technology and advanced software to allow the controllable rightward deflection of a virtual arm during the performance of a virtual task.
Methods: Custom software was designed to use the Microsoft Kinect to detect skeletal movement, feed movement into VRE control, initiate virtual events, assess upper extremity movements in real-world coordinates, and initiate rightward spatial deviations of various magnitudes. A Flash program was developed as a simple virtual task involving color-coded reaching targets. Initial data concerning the trajectory of the arm, position of the hand, and success of each reach was recorded using healthy persons and various virtual conditions in order to test feasibility of the VRE.
Results: After initial training of approximately 50-100 reaches, the success rate of targeted reaching without deviation within the VRE exceeded 80% and was invariant across all participants. A similar load of 50-100 reaches was required to reach 80% success with rightward-deviated reaching of all magnitudes. After the removal of deviation, a significant measurable aftereffect, or leftward discrepancy between the virtual arm and the target, was present but varied between participants.
Conclusions: A VRE involving the Microsoft Kinect and a simple virtual task was developed and initial results show that it is capable of causing persons to immediately move toward and attend to the left side of space similar to PAT. Future research will involve further feasibility testing and an initial study involving persons with hemispatial neglect to establish treatment effect and optimum dosage.

004 **Hu, Yi-Ling, MS**

RAPS Doctoral Program
Current Doctoral Program of Study: Occupational Therapy
Washington University in St. Louis
Department: Occupational Therapy
Mentor: Susy Stark, PhD

Medically underserved older adults' perspectives on fall prevention programs: How to enhance recruitment and adoption

Hu Y; Tate J; Stark S

Introduction: Home modifications and Life Style and Functional Prevention Program (LiFE) are effective ways to reduce falls among older adults in Australia. Medically underserved older adults were seldom the target for fall prevention research despite this population's high risk of falling. The purpose of this study is to gain an understanding of the perceptions and concerns of medically underserved older adults toward fall prevention.

Methods: Three focus groups were conducted to gain older adults' perception about the two fall prevention programs in medically underserved area in St. Louis, Missouri. Participants included 17 older adults (35.3% Male; 11.7% Caucasian, 82.3% African-American), aged 60 or older (*M* = 72.6, *SD* = 9.9); all were referred by the St. Louis Area Agency on Aging. Audio recordings from the focus groups were transcribed verbatim and the data was analyzed using constant comparison.

Results: Qualitative analysis revealed that participants recognized the benefit of both fall prevention programs, but several concerns emerged regarding their decision to adopt the programs. Trust, autonomy and cost were the main concerns for home modifications. Concerns for LiFE were: participants manuals needed to be written in plain language, the images of older adults in the participant manuals should represent the participant's race, preparing the participant to a mindset that is ready to act is needed, and group support would enhance motivation of the participants. The participants agreed both of the programs should be tailored into personal conditions and needs.

Conclusions: Medically underserved older adults acknowledge the values of the fall prevention programs, but there are several adaptations needed. The research team will adapt the current programs by reviewing the manual, and pilot testing the programs. Adaptations for the LiFE program include adapting the manual, preparing the participants with needed knowledge, and creating formal or informal networks of older adults to support adherence. For both programs, tailoring the intervention to each older adult's unique personal and environmental characteristics will be important.

Summer Research Program in Global Health

120 **Bliss, Laura**

Summer Research Program in Global Health; Dean's Fellowship
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Mentors: Indira Mysorekar, PhD; Sanjay Jain, MD, PhD; Henry Lai, MD

Cytological analysis of urinary biomarkers may be useful in distinguishing between bladder conditions

Bliss LA; Ma E; Mysorekar IU; Jain S; Lai H

Introduction: The urinary bladder is afflicted by a number of chronic conditions and diseases, including Interstitial cystitis/bladder pain syndrome (IC/BPS), UTIs, and Overactive Bladder (OAB). These conditions affect millions of patients worldwide and are a major cause for concern. Because patients suffering from IC/BPS, OAB, and symptomatic bladder UTIs often report similar symptoms, distinguishing between these disease subtypes can be difficult without the use of invasive techniques. Our objective is to use injury models developed by the Mysorekar lab to decipher the mechanisms by which the bladder repairs itself following injury, define markers of these processes, and test these in humans.

Methods: Urine samples from women suffering from these bladder disease subtypes were examined using cytology and stratified into categories. De-identified samples were obtained from 4 cohorts of women: IC/BPS patients, OAB patients, symptomatic bladder UTI patients, and age matched controls. Samples were examined using cytology and given scores based on levels of inflammation, amounts of superficial cell sloughing, prevalence of crystals, and bacteria levels. These profiles were integrated with clinical data in order to obtain a comprehensive profile for each patient.

Results: Preliminary data has shown that inflammation levels and pain scores do not distinguish the patient conditions. Contrary to past suppositions, most OAB and IC patients had inflammation scores of 1 or lower.

Conclusions: Cytological analysis is an effective non-invasive technique to assist urological clinicians in defining disease parameters. The use of urinary biomarkers may help lay the foundation for developing diagnostic and treatment strategies based on the underlying bladder pathophysiology.

T32 NIH Cardiopulmonary Surgery Training Grant

No Poster

Janjua, M Burhan, MD
T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano, MD; Richard B Schuessler, PhD

Adenosine triphosphate sensitive potassium channel kir subunits implicated in cardioprotection by diazoxide

Janjua MB; Kanter EM; Makepeace CM; Henn MC; Schuessler RB; Nichols CG; Lawton JS

Introduction: Adenosine triphosphate–sensitive potassium (K_{ATP}) channel openers provide cardioprotection in multiple models. Ion flux at an unidentified mitochondrial K_{ATP} channel has been proposed as the mechanism. The potassium channel subunit Kir 1.1 has been implicated as the mitochondrial channel pore forming subunit. We hypothesized that subunit Kir 1.1 is involved in the cardioprotection (maintenance of volume homeostasis and contractility) of K_{ATP} channel opener diazoxide during stress (exposure to hyperkalemic cardioplegia) at the myocyte and mitochondrial levels.

Methods: Kir subunit inhibitor Tertiapin Q was utilized to evaluate response to stress. Mouse ventricular mitochondrial volume was measured in the following groups: 100 µM diazoxide + 200µM ATP + Tertiapin Q (0.5pM, 10pM, 90pM, or 1,000pM). Mouse myocytes were exposed to Tyrode's solution (5 min), test solution (Tyrode's, hyperkalemic cardioplegia (CPG) stress, CPG + diazoxide, CPG + diazoxide + Tertiapin Q, Tyrode's + Tertiapin Q, or CPG + Tertiapin Q), N=12 for all (10 min); followed by Tyrode's (5min). Volume (mitochondrial and myocyte) and myocyte contractility were compared.

Results: Tertiapin Q alone, or with diazoxide, did not alter mitochondrial or myocyte volume. Stress (CPG) resulted in myocyte swelling and reduced contractility that was prevented by diazoxide. Tertiapin Q prevented the cardioprotection afforded by diazoxide (volume homeostasis and maintenance of contractility).

Conclusions: Tertiapin Q did not alter diazoxide – induced mitochondrial swelling, but it did inhibit myocyte cardioprotection provided by diazoxide during stress. Because Tertiapin Q inhibits Kir1.1, Kir3.1, and Kir3.4, these data support that any of these Kir subunits could be involved in the cardioprotection afforded by diazoxide. However, these data suggest that mitochondrial swelling by diazoxide does not involve Kir 1.1, 3.1 or 3.4.

No Poster

Janjua, M Burhan, MD
T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano, MD; Richard B Schuessler, PhD

Cardioprotective diazoxide inhibits succinate dehydrogenase independent of the ATP sensitive potassium channel in mouse and human mitochondria

Janjua MB; Kanter EM; Makepeace CM; Henn MC; Schuessler RB; Nichols CG; Lawton JS

Introduction: Adenosine triphosphate sensitive channel (K_{ATP}) opener diazoxide provides cardioprotection during myocyte stress via an unknown mechanism that has been proposed to involve the inhibition of succinate dehydrogenase and the activation of a mitochondrial K_{ATP} channel (mK_{ATP}). Diazoxide's cardioprotection is eliminated by the prevention of its ability to inhibit succinate dehydrogenase (SDH) and by genetic deletion of K_{ATP} channel subunit SUR1. Interestingly, diazoxide still inhibits SDH in SUR1 deficient mice, suggesting the inhibition of SDH precedes mK_{ATP} activation; however, the relationship between the succinate dehydrogenase enzyme complex and a mitochondrial K_{ATP} channel are unknown. We hypothesized that the addition of mK_{ATP} channel inhibitor, 5 – hydroxydecanoate (5-HD), would alter diazoxide's ability to inhibit SDH.

Methods: Mitochondria were isolated from mouse hearts and human left ventricular specimens using serial homogenization and exposed to test groups: 8 mM malonate (inhibitor of SDH), 100 microM diazoxide (DZX), 100 microM 5-HD, DZX + 5 HD, succinate control, no succinate, and no mitochondria. SDH activity was measured by spectrophotometric analysis for 2-6 dicholoroindophenol reduction at 600nm for 20 min.

Results: Diazoxide inhibited SDH in mouse and human mitochondria (figure demonstrates human SDH activity, percent change in absorbance is inversely proportional to SDH activity) (*$p<0.05$ vs. succinate control). However, SDH activity was not altered by the addition of 5-HD (DZX + 5-HD not significantly different from DZX alone).

Conclusions: Similar to previous results following genetic deletion of mK_{ATP} subunit SUR1, these data are consistent with the inhibition of SDH by diazoxide as upstream to mK_{ATP} activation as diazoxide inhibits SDH despite the inhibition of mK_{ATP} by 5 – HD.

No Poster **Janjua, M Burhan, MD**

T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano Jr, MD; Richard B Schuessler, PhD

Diazoxide cardioprotection is independent of adenosine triphosphate – sensitive potassium channel Kir 6.1 subunit in response to stress

Janjua MB; Zhang H; Henn M; Makepeace C; Kanter E; Schuessler R; Nichols C; Lawton JS

Introduction: Previous work implicated the sarcolemmal adenosine triphosphate sensitive (sKATP) potassium channel (composed of Kir6.2 and SUR2A subunits) in cardiac myocyte volume regulation during stress. Paradoxically, sKATP subunit 6.2 was necessary for detrimental myocyte swelling secondary to stress (hyperkalemic cardioplegia) in a myocyte model of stunning. Two pore-forming Kir 6 subunits may contribute to KATP channels (Kir 6.2 and Kir 6.1) in the heart. We hypothesized that KATP channel subunit 6.1 would also play a role in cardiac myocyte volume regulation in response to stress.

Methods: Isolated mouse myocytes from Wild type mice (WT) or mice lacking the Kir 6.1 subunit (Kir 6.1 (-/-)) were exposed to control Tyrode's solution (TYR) for 20 min, test solution (TYR, hypothermic hyperkalemic cardioplegia (CPG), or CPG + KATP channel opener diazoxide (CPG+DZX)) for 20 min, followed by 20min re-exposure to TYR. Volume and contractility were compared.

Results: Both WT and Kir 6.1 (-/-) myocytes demonstrated significant swelling and reduced contractility during exposure to stress (CPG) that was prevented by DZX (mean % change from baseline volume +/- SEM, Table).

Conclusions: Both WT and Kir 6.1 (-/-) mouse myocytes demonstrated detrimental swelling and reduced contractility in response to stress that was prevented by diazoxide. These data support that the cardioprotective mechanism of action of diazoxide was intact despite elimination of Kir 6.1. In addition, data implicate the surface (sarcolemmal) KATP channel (composed of SUR 2A and Kir 6.2) in myocyte volume regulation in contrast to KATP channels composed of Kir 6.1 pore forming unit.

019 **Janjua, M Burhan, MD**

T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano Jr, MD; Richard B Schuessler, PhD

Gain of function of adenosine triphosphate sensitive potassium channel subunit kir 6.1 results in myocyte volume and contractility rearrangement during stress

Janjua MB; Zhang H; Kanter EM; Makepeace CM; Henn MC; Schuessler RB; Nichols CG; Lawton JS

Introduction: Adenosine triphosphate – sensitive potassium (KATP) channel activity is uniquely linked to cellular metabolism and provides cardioprotection. KATP channel opener diazoxide maintains myocyte volume homeostasis and contractility during stress. KATP channels are composed of pore-forming Kir 6 (6.2 or 6.1) and regulatory SUR (SUR 1 and SUR2) subunits. Gain of function of 6.1 subunits has been implicated in Cantu syndrome in humans (cardiomegaly, lymphedema, pericardial effusions). We hypothesized that gain of function of Kir 6.1 subunits would result in altered myocyte response to stress.

Methods: Wild type (WT) and Transgenic gain of function (GOF) Kir 6.1 mice were exposed to Tyrode's for 20 min, test solution (Tyrode's, hyperkalemic cardioplegia (stress) +/- KATP channel opener diazoxide), followed by Tyrode's for 20 min. Myocyte volume and contractility were compared. Transgenic mice were generated with ATP-insensitive Kir 6.1 subunits.

Results: Both WT and Kir 6.1 GOF myocytes demonstrated significant swelling in response to stress (cardioplegia) (both $p<0.05$ vs. Tyrode's, respectively); although significantly less swelling was seen in Kir 6.1 GOF myocytes (6% vs. 11%, $p<0.05$ Kir GOF CPG vs. WT CPG). Diazoxide prevented swelling secondary to CPG in WT but resulted in a nonsignificant reduction in swelling in Kir 6.1 GOF myocytes. Kir 6.1 GOF myocytes demonstrated significant reduction in contractility during stress that was prevented by diazoxide.

Conclusions: Both WT and Kir 6.1 GOF myocytes demonstrate volume and contractility derangements secondary to stress that are responsive to cardioprotection by diazoxide.

020 **Janjua, M Burhan, MD**

T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano, MD; Richard B Schuessler, PhD

Genetic deletion of adenosine triphosphate – sensitive potassium channel subunit 6.2 paradoxically confers increased tolerance to myocyte stress

Janjua MB; Zhang H; Kanter EM; Makepeace CM; Henn MC; Schuessler RB; Nichols CG; Lawton JS

Introduction: Adenosine triphosphate – sensitive potassium (KATP) channel openers are cardioprotective, mimic ischemic preconditioning, and prevent detrimental myocyte swelling and reduced contractility secondary to stress. Paradoxically, myocyte swelling secondary to stress of hyperkalemic cardioplegia and metabolic inhibition is lacking in channel subunit Kir 6.2 knockout mice. The present study was performed to assess the response of Kir6.2 (-/-) myocytes exposed to osmotic stress.

Methods: Isolated mouse (wild type (WT) or Kir 6.2 (-/-)) myocytes were assessed for volume and contractility changes secondary to osmotic stress using image grabbing software and edge detection. Myocytes were exposed to 1T Tyrodes solution for 20 min, test solution (1T Tyrodes, osmotic stress (0.9T) +/- KATP channel opener diazoxide) for 20 min, followed by 1T Tyrodes for 20 min. Kir 6.2 (-/-) mice were created by disruption of the Kir 6.2 gene.

Results: WT myocytes demonstrated significant swelling ($p<0.05$) that was prevented by diazoxide. Kir 6.2(-/-) myocytes demonstrated less swelling secondary to stress that was unchanged by diazoxide. Myocyte contractility was reduced following stress in both groups, although no statistically significant differences were demonstrated.

Conclusions: Myocytes lacking the KATP channel Kir 6.2 subunit demonstrate resistance to osmotic stress which is consistent with observations following stress of hyperkalemic cardioplegia and metabolic inhibition. These data are consistent with a role of the sarcolemmal KATP channel (composed of Kir6.2 subunits) in detrimental myocyte swelling secondary to stress.

No Poster **Janjua, M Burhan, MD**

T32 NIH Cardiopulmonary Surgery Training Grant
Washington University in St. Louis
Department: Surgery
Division: Cardiothoracic Surgery
Mentors: Jennifer S Lawton, MD; Ralph J Damiano, MD; Stefano Schena, MD

Heparin induced thrombocytopenia (HIT) in cardiac surgery may be associated to continuous rather than occasional previous heparin exposure: A single center study

Janjua MB; Lawton JS; Zhang AJ; Burmeister T; Bell JM; Schuessler RB; Damiano RJ; Schena S

Introduction: Heparin-induced thrombocytopenia (HIT) is an immune-mediated, life-threatening, complication of heparin therapy, occurring in about 2% of patients undergoing cardiac surgery. These patients receive large doses of unfractionated heparin intraoperatively and may receive heparin for other reasons perioperatively. No definitive study, however, explains how heparin exposure triggers heparin-dependent antibodies to induce platelet aggregation. We investigated various risk factors that predispose these patients to HIT.

Methods: We retrospectively reviewed all adult cardiac surgery patients operated at our institution since the beginning of HIT data collection in the STS database, in 2011. Patients with HIT (+ve PF4-antibodies) were compared to NON HIT based on previous exposure (i.e. hemodialysis, redo surgery, unrelated heparin therapy), type of procedure, length of stay (LOS), and mortality. Age, LOS, and categorical data were compared with the unpaired t-test, Mann-Whitney U, and $\chi 2$ test, respectively.

Results: Out of 2507 (1586M/921F) patients, 23 (1%) developed HIT. Redo procedures ($p= 0.06$) or previous unrelated heparin treatment ($p=0.919$) did not increase the incidence of HIT. However, the incidence of HIT was clearly higher for dialysis vs non-dialysis patients (5.7% vs 0.8%, $p<0.001$). Interestingly, the incidence of HIT was lower in isolated CABG, isolated valve, or combined CABG/valve (0%, 0.5%, 0.6%) vs other cardiac procedures (1.6%, $p=0.006$). HIT patients had longer LOS (22 vs 8 days, $p<0.001$), younger age (54 vs 64 years, $p=0.01$), higher perioperative (30.4 vs 7.2%, $p<0.001$) and overall mortality (39.1 vs 10.8%, $p<0.001$).

Conclusions: Chronic heparin exposure (i.e. hemodialysis) is associated with higher risk of HIT than occasional administration (i.e. redo surgery or unrelated treatment) in cardiac surgery patients. The incidence of HIT is still associated with prolonged LOS and higher mortality.

T35 NIH NHLBI Training Grant

104 **Al-Khalil, Bilal**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Oncology
Mentor: Timothy Ley, MD

The patterns of DNA methylation and chromatin accessibility caused by the R882H mutation associated with AML

Al-Khalil B; Spencer DH; Ley TJ

Introduction: Among all patients with acute myeloid leukemia (AML), approximately 25% of patients exhibit mutations in the de novo DNA methyltransferase DNMT3A. The most common mutations affect codon 882 within the catalytic domain, and these mutations have dominant negative activity in vitro. These mutations are associated with hypomethylation at various CpG dinucleotides in primary AML samples. The patterns of this DNA hypomethylation and the effects of said hypomethylation are currently unknown.

Methods: We used an Illumina 450k array platform on 210 AML patients from the TCGA AML cohort. We considered patients with the codon 882 mutation as our experimental group (n = 27) compared to patients with no mutations in any known genes related to DNA methylation and a normal karyotype (n = 28). We used the R packages CpGAssoc, BioConductor, and Biomart to find differentially methylated regions, then identify regions with several differentially methylated CpGs in a cluster. We also carried out whole-genome bisulfite sequencing (WGBS) and transposase-mediated chromatin accessibility profiling (ATAC-seq) on 3 normal karyotype AML samples with the DNMT3A codon 882 mutation and 4 matched AML samples without a DNMT3A mutation. All seven samples had an NPMc mutation but did not have any mutations in genes involved in DNA methylation. We then compared the WGBS data to the ATAC-seq data using DeepTools, and DeSeq2.

Results: Of 456,671 CpG dinucleotides, we found 5,017 differentially methylated CpG dinucleotides. We defined differential methylation as an adjusted p-value of 0.05 or less with a mean difference in methylation value of 0.15 when compared to wild type. We examined DNA regions in clusters of 5 to 19 consecutive CpG dinucleotides as well, and found anywhere from 339 regions for the clusters of 5, to 1 for the clusters of 19. The chromatin areas which were differentially open were plotted against the methylation values and showed that in DNMT3A mutants, there is a significant drop in methylation in areas where chromatin openness is affected between the experimental and control group.

Conclusions: The results of this study have yielded several differentially methylated regions and canonically differentially methylated CpG dinucleotides which may serve as drug targets in the future. It also shows that DNA hypomethylation has a significant impact on the chromatin accessibility of a region, allowing more openness in areas that are affected my hypomethylation, further suggesting the importance of the epigenetic landscape in de novo AML.

061 **Beleckas, Casey**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Mentors: David Gutmann, MD, PhD; Corina Anastasaki, PhD

Novel mouse models with unique NF1 germline mutations affect phenotype in a Ras-independent fashion

Beleckas CM; Anastasaki C; Gutmann DH

Introduction: Neurofibromatosis type I is an extremely variable disease, leaving physicians with no accurate way to perform risk assessments. Recent research suggests that a patient's underlying germline mutation significantly affects their phenotype. The purpose of this study is, using GEM mouse strains with homologs of unique patient germline mutations, to see the effects of the germline mutation on mouse biology, behavior, and disease progression.

Methods: Primary hippocampal neuronal cultures from NF1+/sp21 and NF1+/st18 mice were grown and measured. Ras activity, PKCζ phosphorylation, and neurofibromin expression were also measured and analyzed with unpaired two-tailed students t-test.

Results: Both NF1+/sp21 (20% decrease) and NF1+/st18 (65% decrease) mice showed decreased neurofibromin expression compared to their wildtype littermates. The hippocampal neurite lengths, an indirect measure of Ras activation, were decreased relative to the wildtype controls by equal amounts in the two strains.

Conclusions: The results of this study suggest that the germline mutations cause effects in a Ras-independent fashion. Once the behavior and development of these mice are determined, the results will be able to be used to create a more accurate risk assessment model for physicians.

047 **Bruck, Brent**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentors: Gregory Zipfel, MD; Henry Han, PhD

Vascular Kir6.1-GOF mutations attenuate neurological deficits and vasospasm in subarachnoid hemorrhage

Bruck BS; Vellimana AK; Nelson JW; Zhang H; Han BH; Nichols CG; Zipfel GJ; Han H

Introduction: While subarachnoid hemorrhage (SAH) accounts for only 6-8% of all strokes, it is responsible for about 25% of all cerebrovascular related deaths and years lost due to stroke. Vasospasm induced delayed cerebral ischemia (DCI) is thought to be a major factor contributing to this poor neurological prognosis. Importantly, KATP channels have been implicated in a number of physiological processes that vary by tissue and channel composition. In cerebral vasculature, both vascular endothelial cells (vECs) and vascular smooth muscle cells (vSMCs) contain a KATP channel constituted by Kir6.1 and SUR2B, and these channels are implicated in maintaining cerebrovascular tone. Gain-of-function (GOF) mutations in Kir6.1 elevate KATP channel activity while loss-of-function mutations (LOF) depress its activity.

Methods: vSMC specific GOF, LOF, or wildtype (WT) littermate controls were subjected to SAH or sham procedures and monitored for sensorimotor neuroscore by blinded observers. On day 3 post-SAH, mice were sacrificed and underwent India ink gel perfusion for monitoring of vasospasm in the middle cerebral artery. Similarly, vEC specific GOF, LOF, or WT littermate controls were subjected to the same protocol.

Results: SAH-induced vasospasm was attenuated in vSMC:GOF mice relative to WT mice ($p<0.05$). This reduction in vasospasm in vSMC:GOF mice was associated with improved neurological outcome as assessed by neuroscore ($p<0.05$). No significant difference in vasospasm or neurological outcome was noted between WT and vSMC:LOF mice. Preliminary data from vEC:GOF mice also show protection against SAH-induced vasospasm and neurological deficits, while data from vEC:LOF mice show no significant difference in vasospasm or neurological outcome compared to WT mice.

Conclusions: KATP channel GOF mutations in vSMC and vEC produce robust neurovascular protection in SAH, while KATP channel LOF mutations in vSMC and vEC do not impact SAH-induced neurovascular deficits. The latter likely reflect low baseline KATP channel activity and/or a floor effect for the neurovascular deficits obtained in our SAH model. Overall, our data indicate KATP channels are a promising new therapeutic target for SAH-induced DCI.

111 **Burton, Lindsay**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Family Planning
Mentor: Tessa Madden, MD, MPH

Frequencies of adverse events in teen LARC users

Burton L; Madden T

Introduction: Unintended teen pregnancy remains a major public issue in the United States. Long-acting reversible contraception (LARC)—the IUD and implant—offers women and adolescents highly effective and safe birth control. Despite its superior efficacy, only 4.5% of adolescents use LARC methods. There is concern that teens don't tolerate LARC methods as well and experience more side effects. Our objective was to describe the frequency and type of complaints experienced by teen LARC users in the Contraceptive CHOICE Project (CHOICE).

Methods: Secondary study of CHOICE, which is a prospective cohort study of 9,256 adolescents and women desiring reversible contraceptive methods. 394 teen LARC users reported at least one adverse event. Adverse events were coded and frequencies were run by STATA.

Results: Our cohort of 394 adolescent LARC users experienced 837 complaints. Irregular bleeding was the most common complaint, making up 19.4% of the total complaints. The next most common complaints in descending order were cramping, expulsion (full or partial), vaginal complaints, frequent bleeding, weight gain, heavy vaginal bleeding, mood changes, arm pain or numbness, and patient cannot feel strings.

Conclusions: These results suggest that many of the complaints related to LARC methods are not dissimilar from complaints that would be seen in any type of hormonal birth control, although this study did not assess the severity or duration of these complaints. This information will be useful to health care providers and help them more effectively counsel their patients on the expected and normal side effects. We hope that this research will dispel some of the myths surrounding LARC methods and promote their use in teens.

021 **Chi, Tingying**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Minimally Invasive Surgery
Mentors: Corey Deeken, PhD; Spencer Lake, PhD

Biaxial analysis of synthetic scaffolds for hernia repair in 90-degree and 45-degree orientation

Chi T; Deeken CR; Lake SP

Introduction: Synthetic scaffolds, or surgical meshes, are commonly used in ventral hernia repair (VHR) to reduce post-operational recurrences. Over the past sixty years, more than fifty such meshes have been developed. Typically, surgeons implant these materials in whichever orientation maximizes overlap with the wound, with little regard to the mechanical properties of each mesh type. However, previous experiments have demonstrated that many meshes exhibit anisotropic behavior, or different mechanical properties depending on the direction of applied load. Understanding the mechanical differences of these meshes could thus help surgeons optimize mesh placement for each patient based on relevant parameters like wound dimension and direction of greatest abdominal tension. This experiment specifically aims to compare the anisotropic/isotropic behavior of twenty commercially available meshes in either the 90° or the 45° orientation.

Methods: Equibiaxial, or equal simultaneous loading in both directions, tests were performed on all mesh types. Tension data on both orthogonal axes were collected to compare the peak tension in one direction versus the other.

Results: Out of the twenty meshes tested, twelve out of fourteen mesh types that exhibited anisotropic behavior at 90° began to exhibit more isotropic behavior when oriented at 45°. The change in direction did not seem to significantly affect the remaining six mesh types, which already exhibited isotropic or nearly isotropic behavior at 90° orientation.

Conclusions: Many synthetic meshes are currently used in clinical settings as if they are uniform and interchangeable, when this is not the case. The clinical value of this data would be enhanced if characteristics of the human abdominal wall could be elucidated to provide a comprehensive understanding of the tissue sites where these materials are ultimately implanted.

110 **Chiu, Ami**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Clinical Research
Mentor: Jeffrey Peipert, MD, PhD

Prior use of DMPA and increased amenorrhea in the 3-6 months following LNG-IUS insertion

Chiu AC; Zhao Q; Peipert JF

Introduction: Use of the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena) leads to lighter and less frequent bleeding over time, and many long-term users consider amenorrhea to be a positive bleeding change. To this end, we sought to determine whether use of depot medroxyprogesterone acetate (DMPA; Depo-Provera) in the year before LNG-IUS insertion was associated with more reported amenorrhea in the 3-6 months after insertion, as compared to use of combined hormonal contraception (CHC; pill, patch, or ring) or non-hormonal/no contraception (control).

Methods: This study is a secondary analysis of data collected from the Contraceptive CHOICE Project. 2931 women who had a LNG-IUS inserted were stratified into three pre-insertion method groups: DMPA (N=190), CHC (N=731), and non-hormonal/control (N=2010). Differences in baseline demographics, method use, and bleeding patterns and amenorrhea at 3-month and 6-month follow-up were statistically compared.

Results: Preliminary analysis shows that, before insertion, more prior DMPA users had had no period in the last 12 months (29.5%) than prior CHC (1.2%) or control (2.9%) users, with far more current (at time of insertion) DMPA users reporting amenorrhea (42.4%). At 3-month and 6-month follow-up, more prior DMPA users reported no bleeding since insertion (18.9%, 29.9%) than prior CHC (9.2%, 20.2%) or control (6.4%, 15.3%) users.

Conclusions: Before achieving amenorrhea, irregular or frequent bleeding among new LNG-IUS users is a major reason for early LNG-IUS discontinuation. The DMPA dose-dependency of post-insertion bleeding patterns should be characterized in order to determine whether pre-insertion priming with DMPA can significantly improve LNG-IUS bleeding.

044 Coddington, Nathaniel

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Division: Center for Innovation in Neuroscience and Technology
Mentor: Eric C Leuthardt, MD

Phase-power coupling in complex partial neocortical seizures

Coddington N; Leuthardt EC

Introduction: Though long the object of study, the physiology of epilepsy remains incompletely understood. Modern advances in computers have allowed us to study the brain with unprecedented mathematical rigor, resulting in novel concepts for explaining normal and pathological brain states. Among those is phase-amplitude coupling, broadly defined as a phenomenon by which the phase of one frequency band modulates the amplitude in another. Changes in PAC have been associated with memory encoding (Tort et al., 2008) and changes in consciousness during anesthesia (Breshears et. al, 2010).

Methods: We took electrocorticography data from pre-operative epilepsy patients and compared PAC between ictal and interictal periods. The recordings were collected at the behest of the clinical team for pre-surgical seizure localization and functional assessment, and later released for our use. The analysis was performed in Matlab using a modified version of the code from Voytek et al., 2010.

Results: Overall, we found a marked increase in coupling between gamma (70-100 Hz) and low frequency bands (1 - 20 Hz), particularly theta (4-7 Hz), during seizure and persisting for several minutes after. Although there was a significant amount of intersubject variation, this is consistent with the subjects' varying subjective experiences.

Conclusions: Normally, PAC has been suggested as a potential means by which perceptions can be bound and experience can be gated. PAC allows spatial disparate ensembles of neurons to oscillate together. This synchronization of input followed by Hebbian synaptic modification would allow for information transfer and storage. While the exact triggering mechanism may differ, seizures may be conceived of as a derangement of this process, a hypersynchronization with associated changes in consciousness. This paper suggests a route of research that should be pursued more thoroughly with larger data sets.

067 Cole, Lyndsey

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Division: Child and Adolescent Psychiatry
Mentors: Natasha Marrus, MD, PhD; John Constantino, MD

Changes in reciprocal social behavior between 18 and 24 months

Cole LD; Marrus N; Constantino JN

Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and restricted, repetitive behaviors. The video-referenced measure of reciprocal social behavior (vrRSB) is a novel screening tool aimed at promoting early detection of ASD by measuring autistic traits in toddlers. Here, we classified distinct patterns of performance and explored quantitative change over time in vrRSB scores in a normative twin sample with the goal of identifying sub-groups within this typically developing population that could indicate risk for delay.

Methods: Parents of 162 typically developing toddler twins from the Missouri Family Register completed the vrRSB and an age-appropriate version of the MacArthur-Bates Communicative Development Inventory (MCDI) for their children at 18 and 24 months of age. We divided children into four groups of differing levels of social function based on their vrRSB scores and investigated whether these groups had different profiles of change in social and language development between 18 and 24 months. In a parallel quantitative analysis, we examined whether baseline vrRSB scores correlated with change in these domains over time.

Results: Profiles of change in social and language development differed across the four groups. Baseline vrRSB score significantly contributed to the amount of change in vrRSB score over time. Language ability was correlated with social function level.

Conclusions: In this normative population, children's social and language development differed as a function of their social function at 18 months. In the future, additional subjects can help confirm these differences cannot alternatively be explained by the mathematically expected variation of a normal distribution. Language ability correlation with the vrRSB supports an association between the development of social function and language.

062 **Cross, Kevin**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Mentors: David Gutmann, MD, PhD; Joseph Toonen, PhD

Met-RANTES exacerbates retinal Pathology in a Mouse Model of NF1 Optic Pathway Glioma

Cross K; Toonen J; Solga A; Gutmann DH

Introduction: Neurofibromatosis 1 (NF1) is an autosomal dominant-inherited tumor predisposition syndrome with an incidence of 1 in 3500. Recent research has shed light on the influence of the microenvironment on growth and development of NF1-associated gliomas. Microglia contribute heavily to tumor development in the context of NF1, and also express high levels of chemokines. The purpose of this study is to examine the effects of a CCL5-derived chemokine antagonist on the retinas of mice with optic pathway gliomas.

Methods: Nf1flox/-; GFAP-Cre genetically engineered mice were injected with 0.5 mg/kg, 1 mg/kg, or 2mg/kg doses of met-RANTES, or PBS, for 2 weeks post birth. After sacrifice, eyes were dissected and fixed. Retinas were examined using immunohistochemistry and immunofluorescence, and analyzed for markers of retinal damage associated with optic pathway glioma.

Results: Met-RANTES did not spare the retinas of treated mice from damage, but instead exacerbated the damage. No statistically significant differences were observed between control mice and mice treated with 0.5 mg/kg or 1 mg/kg met-RANTES. Mice treated with 2mg/kg met-RANTES exhibited thinning of the retinal nerve fiber layer, as well as reduction in the number of retinal ganglion cells.

Conclusions: Met-RANTES has previously been shown to reduce inflammation in the colon, kidney and lung of mice. These effects were attributed to its antagonism of chemokine function through binding of CCR1 and CCR5. This study, however, finds that met-RANTES is not an antagonist in the context of NF1 OPGs. It is hypothesized that, in this case, it functioned as a partial agonist. Met-RANTES, therefore, does not show promise as a treatment for optic pathway gliomas. However, evidence still suggests that microglia-targeted therapies can be successful in the future.

098 **Duong, Jennifer**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Infectious Diseases
Mentors: Robyn Klein, MD, PhD; Douglas Durrant, PhD

M1 and M2 microglial activation in West Nile viral encephalitis

Duong JT; Durrant DM; Klein RS

Introduction: Microglia are believed to exist in two activation states, exhibiting both inflammatory (M1) and immune resolving effects (M2). While polarization of M1 and M2 microglia has been studied in diseases such as Alzheimer's and multiple sclerosis, it has not been extensively studied in viral CNS pathologies. In this study, we examined the expression of M1 and M2 microglia and macrophages over the course of West Nile viral encephalitis. Characterizing the phenotypes of these cells at the different stages of disease would be valuable in developing therapeutics for viral encephalitis and other CNS pathologies.

Methods: Eight-week-old wild-type C57BL/6J mice were infected with WNV-E218A 2nt virus. Brains of infected mice were collected on day 8 and 20 post-infection for evaluation of M1 (TNFα, IFNγ, IL-1β, CD86, CD68) and M2 (dectin-1, IL-4, arginase-1, CD206) markers via flow cytometry and qRT-PCR.

Results: The number of Ly6C+ inflammatory macrophages was highest at peak disease at day 8 and declined by disease resolution at day 20, suggesting that M1 macrophages contribute to initiation of disease. M1 expression in macrophages was at high levels at day 8, and declined by day 20. This pattern of M1 expression was also seen in microglia, but to a lesser degree. By day 20, the number of Ly6C+ macrophages had declined, highlighting the disappearance of M1 macrophages. Because the M1 macrophages were not replaced by M2 macrophages, M2 microglia are likely responsible for promoting the resolution of infection. Accordingly, microglia expressing M2 markers had increased by day 20.

Conclusions: M1 macrophages were primarily responsible for the inflammation seen at the peak of the WNV encephalitis. As the infection cleared, the number of total macrophages declined, and we detected increased M2 expression in the microglial population, suggesting that M2 microglia may be responsible for promoting healing and repair. However, it is unclear whether M2 microglia seen at immune resolution resulted from the differentiation of M1 microglia or from infiltrating macrophages. An experiment involving the adoptive transfer of Ccr2RFP/+ and Cx3cr1GFP/+ macrophages into the CNS of WNV infected mice could resolve this question.

049 **Guniganti, Ridhima**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentors: Gregory Zipfel, MD; Henry Han, PhD

HSPG-mediated Aβ uptake in rat vascular endothelial cells

Mollman M; Guniganti R; Han H; Zipfel GJ

Introduction: Deposition of amyloid beta (Aβ) peptide in the cerebral vessels, a condition known as cerebral amyloid angiopathy (CAA), can be found in the brains of most Alzheimer's patients. CAA is associated with an increased risk of infarcts and thus contributes greatly to the progression of Alzheimer's dementia. Heparin sulfate proteoglycans (HSPG) have been suggested as a possible mediator of Aβ's deleterious effects on the cerebral vasculature.

Methods: We hypothesize that HSPG mediate Aβ uptake into vascular endothelial cells and thereby induce various intracellular changes associated with Aβ exposure. This was evaluated by measuring levels of reactive oxygen species (ROS) after Aβ exposure and determining whether the rise in ROS was attenuated in cells pre-treated with heparinase. To determine whether Aβ affected release of vasodilators from endothelial cells, nitric oxide production was measured in cells exposed to Aβ40 alone and in cells exposed to Aβ after pre-treatment with acetylcholine or bradykinin.

Results: While we were able to validate the protocol with a positive control, the other results of these experiments were not statistically significant, and the work is still ongoing. We expect that Aβ40 will induce a rise in ROS greater than that induced by Aβ42 and that this rise will be attenuated in cells pre-treated with heparinase. We further expect that Aβ40 will lower NO production below baseline and that cells treated with Aβ40 and a vasodilator (acetylcholine or bradykinin) will have lower concentrations of NO than those treated with a vasodilator alone.

Conclusions: Elucidation of the mechanism by which Aβ affects cerebral arterioles is necessary to understand the pathogenesis of CAA and will allow exploration of possible treatments to reduce CAA-associated vascular pathology and thus hopefully alleviate Alzheimer's dementia.

138 **Howdeshell, Seth**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Emergency Medicine
Mentor: Angela Lumba-Brown, MD

Discrepancy between head CT and acute brain MRI following closed head injury in children: a case series

Howdeshell SH; Lumba-Brown AK

Introduction: About one-half of children assessed for head trauma in North American emergency departments (EDs) undergo head computed tomography (CT) imaging. Head CT remains the gold standard ED diagnostic to evaluate for acute traumatic intracranial pathology. The absence of evidence of pathology in a child on CT scans following closed head injury is often reassuring to ED physicians, and children with a chief complaint of head injury are often diagnosed with mild traumatic brain injury (TBI) in the absence of findings on acute CT imaging. Brain magnetic resonance imaging (MRI) is the most sensitive modality in the demonstration of brain injuries; however, acute MRI is not routinely employed in children. In this case series, we describe six children who underwent both CT and MRI scans within 96 hours of closed head injury. In all cases, the CT scans revealed no intracranial abnormalities, but the following MRIs had positive findings.

Methods: A retrospective chart review was conducted for children 0-18 years of age seen between 2005 and 2014 at a large tertiary care ED with discharge diagnoses including ICD-9 codes for mild traumatic brain injury, concussion, and unspecified head injury, and who had an acute brain MRI within five days following closed head injury.

Results: The review identified 40 records of children who fit these criteria. Most children had a CT scan prior to the MRI. Of these 40 patients, six had no abnormal findings on acute CT imaging, but then proceeded to have positive findings on acute brain MRI. Five cases were consistent with a traumatic brain injury, and the sixth had an intracranial malformation. All children were ultimately discharged from the hospital with a diagnosis of mild traumatic brain injury or unspecified head injury, with stays ranging from two to twenty-four days and requiring subspecialty follow up.

Conclusions: This series raises the question of whether head CT imaging is the best predictor of injury severity in children with mild-moderate traumatic brain injuries. Brain MRI imaging represents a necessary imaging option in children with significant symptomatology and negative initial head CT imaging to characterize potential brain injury in the acute setting.

051 **Lalezari, Ramin**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurosurgery
Mentor: Albert Kim, MD, PhD

Predisposing factors to postoperative hemorrhage after meningioma resection

Lalezari R; Joshi N; Zohny Z; Kim A

Introduction: Intracranial meningioma, the most common primary brain tumor in adults, carries a variable risk of hemorrhage post surgery, which can lead to reoperation, longer hospital stays, and neurological injury. This paper will identify specific clinical characteristics of the patient, including patient demographics and coagulation status, as well as of the tumor, including location and histopathology, that correlate with the occurrence of post-operative hemorrhage following meningioma resection.

Methods: 726 patients who underwent resection for the presence of a meningioma at the Department of Neurosurgery at Washington University School of Medicine were retrospectively analyzed. Binary logistic regression was fitted to the data.

Results: Results are pending. Post operative hemorrhage can occur as a result of multiple different physiological processes. We expect patient coagulation status to be a major player in whether or not a hemorrhage occurs. We also anticipate tumor location to play a factor in the primary outcome, as tumor location predisposes longer surgeries and more difficult surgical technique. Extra surgical maneuver, such as placement of lumbar drain or use of brain retractor, also preliminarily has appeared to correlate with post operative hemorrhage.

Conclusions: Conclusions are pending. Factors that predispose to a conditionally and financially costly post operative hemorrhage can prove invaluable to a surgeon before resection of a meningioma. Proper precaution can be taken in the event of a patient with a risky profile predisposing to hemorrhage. If extra surgical maneuvers are shown to correlate with higher risk of hemorrhage, steps can be taken to minimize their use.

134 **Liu, Carol**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Newborn Medicine
Mentors: Jennifer Wambach, MD, MS; F Sessions Cole, MD

The heritability of respiratory distress syndrome in late pre-term and term infants

Liu CW; Meyer J; Cole FS; Wambach JA

Introduction: Respiratory distress syndrome (RDS) among newborn infants results from a deficiency of pulmonary surfactant, a phospholipid-protein complex which reduces surface tension and maintains alveolar expansion at end expiration. Traditionally, RDS has been attributed to a developmentally-regulated deficiency of surfactant, with an inverse correlation between RDS incidence and gestational age. However, twin studies suggest a genetic contribution to risk for RDS among premature infants, with heritability estimated at approximately 0.29-0.67. Estimates of heritability among premature infants may be confounded by increased risk of developmental disruption of surfactant production.

Methods: To reduce confounding by prematurity-associated risk of RDS, we estimated heritability in a large cohort (N=528) of late preterm and term infants by comparing the concordance rates for RDS among monozygotic and dizygotic twins >32 weeks gestation.

Results: Our preliminary data shows that monozygotic twins are more concordant for the phenotype than dizygotic twins, and suggests that RDS among term and late preterm infants is heritable.

Conclusions: Identification of genes that contribute to disease heritability would improve disease prediction models and lead to potential therapeutic targets for reducing morbidity and mortality of neonatal RDS.

087 **Marinshaw, Jeffrey**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Dermatology
Mentor: Shadmehr Demehri, MD, PhD

Characterizing the immune microenvironment along progression to skin cancer

Marinshaw JM; Demehri S; Cunningham TJ; Yokoyama WM

Introduction: Current therapies for squamous cell skin cancer and its precursor actinic keratosis (AK) rely on traditional models of cytotoxicity and have significant side effects. We are running a clinical trial to evaluate use of a cytotoxic agent together with a vitamin D analog to provoke a more robust immune response to treat AK. In addition to evaluating efficacy and side effects, we need to characterize the changes in the local immune environment induced by the treatment.

Methods: 4 mm punch biopsies were obtained with informed consent from healthy skin and sites of actinic keratosis before and after 4 days of twice daily topical application of either 5-fluorouracil (5-FU) or 5-FU plus calcipotriol. Biopsies were flash frozen in O.C.T. embedding medium prior to sectioning. Primary antibodies for immunofluorescence (IF) were verified on human tonsil before being used for overnight IF on biopsy samples from two patients with distinct reactions to the treatment.

Results: H&E staining revealed noticeably greater presence of inflammatory infiltrate deep to sites of actinic keratosis before and after treatment compared to healthy skin. IF data indicated that a large portion of this infiltrate is CD3+CD4+. TSLP expression appeared to be patterned differently in the two patient samples of treated actinic keratosis; we cannot confirm that the two samples are representative of different treatment arms until completion of sample collection. Future steps include the validation and use of other IF antibodies to more fully characterize the local immune environment before and after therapy. Based on previous lab findings in mouse models, we anticipate that the combination therapy triggers a Th2-mediated microenvironment and that protein and RNA levels will reveal greater TSLP expression in samples treated with calcipotriol.

Conclusions: Findings from this study will determine the use of topical calcipotriol to treat and prevent skin cancers and may have application in other solid cancers. The general concept that combined use of a cytotoxic agent and an immunomodulatory drug can have a synergistic effect against cancer, if proven, may have wide-reaching implications for cancer therapies in the skin and elsewhere.

081 **Moseley, Emily**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Emergency Medicine
Mentor: Lawrence M Lewis, MD

Preliminary analysis of insurance status and other factors as predictive characteristics of frequent utilization of emergency department services

Moseley ED; Luangruangrong L; O'Neil R; Lewis LM

Introduction: In the United States, the top 1% of healthcare users are responsible for nearly 25% of healthcare expenditures, and this usage correlates with emergency department (ED) use. There is limited information regarding what demographic and clinical characteristics are associated with these "super users", though insurance status has been shown to play a role. The purpose of our study is to characterize super users in the St. Louis Metro area with regards to insurance status and other demographic and clinical factors, and develop a predictive model for identifying those patients that are likely to become super users in the future.

Methods: This was a retrospective, case-control study. Subjects consisted of all patients that had visited the Barnes-Jewish ED at least once during the study years of 2010 or 2011. Electronic medical records from all 13 hospital EDs in the BJC System in Missouri and Illinois were reviewed. Patients were categorized and matched into "super users" (10+ ED visits in each of two consecutive years), "moderate users" (5-9 visits), and "infrequent users" (1 visit in 2010 or 2011).

Results: This study is ongoing. Preliminary results show a significantly greater proportion of black patients and patients with Medicare/Medicaid in the super/moderate users group compared to the infrequent users. We have hypothesized that certain clinical characteristics, in particular the presence of substance abuse, mental illness, and chronic pain will be more common among super-users, and the presence of these clinical diagnoses will increase the likelihood of being a super-user. We predict that even after matching on demographic criteria, patients with Medicare or Medicaid will have an increased likelihood of being a super user. We also expect to see some differences between the moderate and infrequent users, specifically in terms of chronic conditions.

Conclusions: The results of this study will help us to identify patients who are likely to become and remain super users, so that we can develop targeted intervention strategies that will have the greatest impact in reducing ED visits and better managing these patients' chronic conditions.

089 **Pizzorno, Galen**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: General Medical Sciences
Mentors: Bradley Evanoff, MD, MPH; Jaime Strickland, MA

Worksite influences on obesogenic behaviors in low-wage workers

Strickland JR; Pizzorno GU; Kinghorn A; Evanoff BA

Introduction: Obesity affects over one-third of US adults. Workplace programs to reduce obesity and improve overall health are common, but not available or accessible by all workers, particularly low-wage workers who have a higher burden of obesity. This study seeks to assess the determinants of two key obesogenic behaviors, diet and fitness, and participation in workplace health programs (WHPs) in two low-wage groups, hospital workers and retail workers. This will facilitate development of interventions targeted to these populations.

Methods: Using a self-reported questionnaire, we examined obesity, obesogenic behaviors, workplace factors, and WHP use in two groups of low-wage workers: hospital workers and retail workers.

Results: Over 40% of workers were obese and another 26% were overweight; hospital workers were more likely to be obese than retail workers. In general, both groups had poor diets (frequent consumption of sugary and high fat foods) and did little physical activity (only 30.9% meet recommended physical activity guidelines). Compared to retail workers, hospital workers were more likely to have access to and participate in workplace health programs. We identified several individual factors and modifiable workplace factors that were associated with diet, exercise, or WHP participation. While these factors varied by group, how participants obtained food for lunch was a strong predictor of diet. In particular, bringing lunch from home was associated with healthier diet.

Conclusions: This study illustrates the high prevalence of obesity and obesogenic behaviors in two low-wage worker groups. The differences between work groups indicate that each group has unique facilitators and barriers to healthy eating and exercise. It is important to understand how socioeconomic, demographic, and work-related factors influence health in order to identify high-risk populations for intervention and to design tailored interventions that are relevant to the intended audiences. Future work will use results from this study to modify existing wellness programs and test for changes in health status.

060 **Porcelli, Bree**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Division: Pediatrics
Mentors: Kimberly Johnson, PhD; David Gutmann, MD, PhD

Brain tumors and atopy in neurofibromatosis type 1

Porcelli BA; Johnson KJ; Gutmann D

Introduction: NF1 is one of the most common cancer predisposition syndromes. Cancer is the leading cause of death in the NF1 population, resulting in a reduced life expectancy. In the general population, there is a negative association between brain tumors in adults and children and allergic conditions. The purpose of this study is to examine whether this negative association is observed in the population of individuals with NF1.

Methods: A retrospective review of individuals with a diagnosis of NF1 seen at Washington University Medical Center from July 1997 to June 2014 was performed. The odds ratios and 95% confidence intervals were obtained for brain tumor diagnosis in individuals with asthma, allergies, or eczema.

Results: Pediatric patients with allergies were significantly more likely to have a brain tumor diagnosis (OR=2.142, CI95%= 1.293-3.550). The overall NF1 patient population did not show a statistically significant positive association (OR=1.301, CI95%= .890-1.901). Eczema was associated with a reduced odds ratio of a diagnosis of a brain tumor both overall and in pediatric patients (OR=.435, CI95%= .129-1.466; OR=.425, CI95%= .123-1.470). No significant inverse association was found between brain tumors and asthma. Race was also found to be a significant predictor of outcome in patients with NF1 (p=.002).

Conclusions: The results of this study suggest a possible protective effect of atopic conditions like asthma and eczema against brain tumor development in patients with NF1. There is also a possible positive association between allergy diagnosis and brain tumor diagnosis in pediatric patients with NF1. Finally, it appears that race is a significant predictor of brain tumor outcome.

030 **Rivera, Ana**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentor: Mary Politi, PhD

Adapting a health literacy intervention for informed consent for cancer clinical trials and comparing it to usual care in a randomized experiment

Rivera AG; Perkins HE; Politi MC

Introduction: Cancer patients deciding to enter a clinical trial can feel overwhelmed, uninformed or unsure of how to broach the subject, resulting in low participation. As a preference-sensitive decision, there is no clear benefit to either choice. Instead, it depends on personal preferences. A decision aid elicits these preferences, educates and offers advice on how to initiate discussion. We developed a decision aid for cancer clinical trials after eliciting feedback from stakeholders. We began a randomized trial to compare our intervention to standard care in terms of patient knowledge, self-efficacy for communicating, attitudes about cancer clinical trials, willingness to participate and satisfaction with informed consent procedures.

Methods: Feedback was gathered to improve the decision aid by surveying 30 stakeholders. We assessed feasibility, acceptability, and sustainability. Newly diagnosed cancer patients who have never participated in a cancer treatment trial are eligible for the randomized trial. Participants in the intervention condition are instructed to review the decision aid while those in the control view the Siteman Cancer Center clinical trial webpage. Participants then complete our outcome measures.

Results: The results showed positive feedback and a majority of suggestions were used to make the decision aid accurate and institutionally consistent. 108 out of 180 participants have been recruited and data collection is ongoing. Analyzing the demographic data of 86 participants has led the team to diversify participant pool based on gender and race. We anticipate the results will show that implementing the decision aid in addition to usual care will increase knowledge, increase patients' ability to communicate, and increase willingness to participate.

Conclusions: Involving cancer survivors, community partners and institutional stakeholders helped to improve the decision aid. As data collection is still ongoing for the randomized controlled trial, results for this aim are not yet available. Further work should include longitudinal studies to track if the decision aid increases enrollment rates in clinical trials.

073 **Schelble, Allison**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Anesthesiology
Division: Cardiothoracic Anesthesiology
Mentor: Michael Avidan, MBBCh

Assessment of preoperative falls

Schelble AP; Tang RD; Avidan MS; Ben Abdallah A; Wildes TS

Introduction: Falls are the third leading cause of deaths from accidental or unintentional injuries in the US and represent a major public health problem for all age groups. The purpose of this study was to examine the relationship between the occurrence of fall in the past year and patient health characteristics. A specific aim was to explore how fall history was related to measures of morbidity and quality of life among patients presenting for surgery.

Methods: 2,883 elective surgical patients at the Center for Preoperative Assessment and Planning at Barnes-Jewish Hospital completed a brief baseline survey that included information on fall history and quality of life. Descriptive statistics, chi-squared tests and t-tests were used in statistical analyses.

Results: Overall, 27.53% of participants reported one or more falls during the past year. A history of one or more falls was significantly more likely in patients with worse self-reported health status and in patients with higher ASA classifications ($p<0.0001$; $p=0.0010$). Fallers also had worse quality of life by self-reported physical and mental health than non-fallers ($p<0.0001$). Quality of life was lower in patients with ASA levels of 3 and 4 as compared to patients with ASA levels of 1 and 2 ($p<0.0001$).

Conclusions: The results of this study demonstrate that patients who reported one or more falls in the past year had worse quality of life than those who reported no falls. Moreover, fall history provided nearly equivalent information about quality of life as ASA classification did. Since ASA score requires sophisticated patient history and a certain level of provider expertise, fall history may be a simpler, more efficient way to assess patient health. In the future, consideration should be given to including fall history as part of routine preoperative assessment. Additional research regarding the ability of fall history to predict postoperative complications and outcomes is warranted and would make these findings more compelling.

082 **Scott-Wittenborn, Nicholas**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Emergency Medicine
Mentor: Christopher Holthaus, MD

Sepsis in the emergency department: an over looked diagnosis

Scott-Wittenborn N; Holthaus C

Introduction: In 1991, the Society of Critical Care Medicine Consensus Conference attempted to standardize the definitions of sepsis, severe sepsis, and septic shock. In spite of this meeting, the definitions of sepsis and is sequelae are still not well standardized in the medical community. This study aims to assess whether the diagnosis of sepsis, septic shock and severe sepsis are being applied correctly to patients in the Barnes-Jewish Emergency Department.

Methods: An electronic screening tool was used to alert researchers to the presence of a possibly septic patient in the Emergency Department of Barnes-Jewish Hospital. Researchers then confirmed the septic status of patients who had been screened by assessing the subject's vital signs and lab results. After a subject was determined to have sepsis, severe sepsis, or septic shock, the subject's physician was alerted to the presence of sepsis in the subject. Researchers then conducted a retrospective chart review of patients who they had determined to have sepsis in order to assess whether a correct diagnosis of sepsis, severe sepsis, and septic shock was made

Results: The results of this study are still pending as one of the primary outcomes, thirty day mortality is not available at this time for all patients.

Conclusions: The research team found that sepsis, severe sepsis, and septic shock were all under diagnosed in the Emergency Department. What is troubling about this study is that each of these providers were informed of the patients' sepsis status, and still did not diagnose sepsis in the patient. This trend demonstrates a hesitancy to diagnose sepsis which could occur for a multitude of reasons, such as a widespread lack of understanding the definition of sepsis, discomfort in specifying the diagnosis for medical or legal reasons, or a dissatisfaction with the current standards of diagnosis.

026 **Shen, Tony**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Plastic and Reconstructive Surgery
Mentors: Susan Mackinnon, MD; Matthew Wood, PhD; Amy Moore, MD

Effect of nerve allografts supplemented with temporally controlled GDNF-expressing Schwann cells on functional recovery after peripheral nerve injury

Shen TS; Wu-Fienberg Y; Ee X; Yan Y; Hunter D; Sakiyama-Elbert S; Mackinnon SE; Wood M; Moore A

Introduction: Options for treating peripheral nerve injuries with large gaps remain limited. Glial-derived neurotrophic factor (GDNF) holds promise in increasing regenerative potential. However, direct injection of GDNF into a nerve graft results in entrapment. The purpose of this study is to determine if modulation of GDNF expression can enhance nerve regeneration while avoiding entrapment.

Methods: 40 Lewis rats underwent sciatic nerve transection followed by graft placement. Experimental grafts were injected with Schwann cells modified to decrease GDNF expression.

Results: At the time of writing, harvested tissues are being analyzed by histomorphometry. This analysis will measure axon counts coming from the proximal stump, at mid-graft, and at the distal stump. If reduction of GDNF expression allows axons to grow through the graft, this would suggest that nerve entrapment may be overcome by modulating GDNF levels.

Conclusions: Further conclusions may be made pending histomorphometry results.

063 **Standlee, Jordan**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology; Pathology and Immunology
Mentors: John Morris, MD; Nigel Cairns, PhD, FRCPath; Jason Hassenstab, PhD

Neurofibrillary burden is the neuropathological correlate of subjective cognitive decline

Standlee JT; Morris JC; Cairns NJ; Hassenstab J

Introduction: Community-dwelling, cognitively normal older adults commonly report subjective cognitive decline (SCD). However, the etiology and significance of SCD in cognitively normal individuals is not well understood. To help elucidate this issue, we aimed to find a neuropathological correlate to SCD in this population.

Methods: Archival data was retrospectively analyzed from 94 cognitively normal older adults involved in the Memory and Aging Project at the Knight Alzheimer Disease Research Center (ADRC). All participants had undergone annual clinical evaluations and brain autopsy at death. SCD status was assessed at each evaluation, and at autopsy, brains were examined for the regional distribution of neurofibrillary tangles using Braak staging. Logistic regression models tested whether Braak stages were associated with SCD status after controlling for relevant covariates.

Results: Participants with SCD had higher Braak stages than participants without SCD. In multiple logistic regression models controlling for age, sex, education, family history of dementia, APOE status, and depression, participants with higher Braak stages at death were more likely to complain of cognitive decline during life. Participants with a Braak stage of V or VI had a 10.7 times increased risk of SCD compared to participants with Braak stages 0, I, or II.

Conclusions: Patients with SCD may have underlying tau neuropathology even in the absence of objective cognitive deficits.

135 **Sung, Abby**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Newborn Medicine
Mentors: Hillary Heins; Daniel J Wegner, MS; F Sessions Cole, MD

Cellular and secreted phospholipid profiles of A549 and differentiated human fetal alveolar type II cells

Sung AT; Heins H; Yang P; Wegner DJ; Patterson BW; Hsu F; Cole FS

Introduction: Human alveolar type II epithelial cells are the sole producers of lung surfactant, which is essential for normal fetal-neonatal pulmonary transition. Genetic disruption of surfactant-associated genes ABCA3 and VPS13D is associated with dysfunctional surfactant, abnormal surfactant lipidomic signatures, and neonatal respiratory distress syndrome (RDS). However, the study of the mechanisms involved in genetic disruption of surfactant phospholipids has been limited by lack of availability of alveolar type II cells and difficulty maintaining these cells in culture. A549 cells, a human, pulmonary, carcinoma-derived epithelial cell line, have been used to investigate surfactant-associated gene changes. This study seeks to compare the lipidomic profiles of human alveolar type II and A549 cells.

Methods: Using a modified Bligh and Dyer protocol for extraction of phospholipids and electrospray ionization/tandem mass spectrometry and gas chromatography/mass spectrometry, we compared phospholipid profiles in secretagogue-induced cell lysates and media from A549 cells and human alveolar type II cells. For preliminary evaluation of the effects of genes known to disrupt surfactant production and function, we compared surfactant-associated phospholipid profiles in A549 cells and human alveolar type II cells after shRNA-mediated silencing of ABCA3 and VPS13D.

Results: The surfactant-associated PC species signature (especially PC32:0) in A549 cells is different from the PC signature in alveolar type II cells. A549 cells appear to secrete more phospholipid, especially longer-chain phosphatidylcholine (PC) species, than human alveolar type II cells. Human alveolar type II cells contain and secrete more shorter-chain PC species which are critical for surfactant function. Silencing of ABCA3 and VPS13D resulted in difficult to interpret differences in surfactant phospholipid profiles.

Conclusions: The surfactant-associated PC profile of A549 cells and human alveolar type II cells are different, a finding that suggests that A549 cells are not a good model for investigation of genetic disruption of surfactant production and function.

064 **Tang, Mengxuan**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Mentors: Randall Bateman, MD; Davis Ryman, MD, PhD

Phenotypic variability in autosomal dominant Alzheimer's disease

Tang M; Ryman DC; Jasielec MS; Bateman RJ

Introduction: While the remarkable degree of phenotypic variation seen in autosomal dominant Alzheimer's disease (ADAD) is well-established in literature, the pathophysiologic mechanisms that may explain this diversity are not well understood. This study's purpose is to systematically examine the associations between mutation type, symptoms, pathology, and atypical biomarker or imaging characteristics, in order to gain insight into the biological mechanisms that lead to the appearance of atypical clinical presentations.

Methods: A mixed model was fitted to clinical data gathered from 1150 carriers of a known dominantly-inherited Alzheimer's disease mutation gathered from published literature from 1994-2014, in addition to records from 70 participants from the DIAN Observational Study. Ward's method of hierarchical clustering was used to identify clusters of mutations that share similar presentations as well as symptoms that tend to appear together in the same individual. Biomarker and imaging data from the DIAN Observation Study will be incorporated into this analysis once our data request is granted.

Results: Of the individuals included in our analysis, 908 carried a mutation in PS1, 56 in PS2, and 256 in APP. Overall, PS1 mutation carriers are significantly more likely to report myoclonus, spasticity, and corticobulbar deficits, while hemorrhagic and ischemic stroke are more prevalent in APP mutation carriers. The reported rates of seizures, apraxia, visual agnosia, behavioral and psychiatric symptoms, and hallucinations are similar among the three groups. We anticipate that, with the addition of pathological, biomarker, and imaging data, distinct sub-groups will emerge highlighting correlations between clinical presentation and pathophysiological change.

Conclusions: The results of this study highlight the diversity in disease presentation of PS1, PS2, and APP mutation carriers, likely correlated to the distinct biological roles played by the products of these genes. These differences suggest the existence of subtypes within the overarching ADAD diagnosis. Further analysis of the physiological correlates of atypical presentation will be valuable to investigators examining disease mechanisms in AD and to clinicians and affected families in determining prognosis.

032 **Vakkalagadda, Chetan**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentor: Graham Colditz, MD, DrPH

Integrating a health risk assessment mobile app into a federally qualified health center setting – a pilot project

Vakkalagadda CV; Stoll CR; Colditz GA

Introduction: Chronic diseases are the leading cause of death in the United States today, making prevention of such diseases an important public health endeavor. The power of mobile technologies has recently been harnessed for disease prevention purposes, and Washington University researchers and collaborators have contributed to the growing number of health management apps with the development of the Zuum health risk assessment tool. Zuum is an iPad app that administers a health status questionnaire to patients and sends them daily text messages based on their responses. We are piloting Zuum in Grace Hill Clinic, a Federally Qualified Health Center in north St. Louis. The purpose of this study is to assess how well Zuum is implemented into the FQHC setting and whether it improves patient outcomes or health knowledge.

Methods: 150 patients attending Grace Hill for a primary care appointment who are willing and able to receive daily text messages will be given both a health knowledge pre-intervention questionnaire and the Zuum questionnaire to complete prior to their doctor appointments. After reviewing their Zuum results with their physicians, patients will then receive daily text messages about prevention, tailored to their Zuum responses, for a period of three months. Patients have the opportunity to stop receiving texts at any time. Following the three-month text message period, a post-intervention survey will be administered to participants by phone assessing their knowledge of health behaviors and whether they liked Zuum or found it helpful.

Results: This is an ongoing pilot project so there are no concrete results to report at this time. Anticipated results are that Zuum improves knowledge of health behaviors in participants receiving text messages and that it is a useful tool for patients and providers.

Conclusions: Successful implementation of Zuum would indicate a novel, cost-effective method of chronic disease prevention that could reduce chronic disease morbidity and mortality as well as improve health disparities associated with these diseases.

065 **Zhang, Lily**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Neurology
Mentor: Randall Bateman, MD

Amyloid-beta stable-isotope labeling kinetics in iPSC-derived neurons

Zhang L; Kasten T; Mawuenyega K; Karch CM; Ovod V; Bateman RJ

Introduction: Autosomal-dominant Alzheimer's disease (ADAD) is conferred by mutations in the genes associated with the amyloid precursor protein processing pathway and has offered significant insight into the pathophysiology of all Alzheimer's disease (AD) cases. A feature of AD is the presence of amyloid plaques in the brain, due to either an overproduction or under-clearance of the amyloid-beta peptides that comprise the plaques. Previous studies using stable-isotope labeling kinetics (SILK) show an overproduction of the disease-associated isoform, Abeta-42, in ADAD. Here, we show that a similar Abeta kinetics assay can be accomplished with induced pluripotent stem cell (iPSC)-derived neurons from an AD mutation carrier and non-carrier relative.
Methods: We generated iPSC-derived neurons from a presenilin-1 (PSEN1) mutation carrier and a non-carrier relative. Using stable isotope labeling kinetics (SILK) combined with mass spectrometry analysis, we characterized the kinetics of amyloid-beta isoforms in these neuron cultures.
Results: In initial experiments, we see an overproduction of amyloid-beta isoforms in the mutation-carrier compared with that of the non-carrier relative. Further analysis and replications with other ADAD mutations is ongoing.
Conclusions: Understanding the pathophysiology of AD in humans has always been a challenge. Human iPSC-derived neurons are a flexible and powerful system for providing greater understanding of AD and in developing treatments.

086 **Zuckerman, Aaron**

T35 NIH NHLBI Training Grant
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Gastroenterology
Mentor: Matthew Ciorba, MD

The probiotic LGG does not reduce tumor radiosensitivity in syngeneic tumor model

Zuckerman A; Zou J; Colonna M; Ciorba M

Introduction: In patients receiving radiation for pelvic tumors, bowel toxicity leading to diarrhea is the biggest obstacle to complete and aggressive therapy. Probiotic bacteria including *Lactobacillus rhamnosus* GG (LGG) have been shown to have radioprotective effects in the small intestine by selectively protecting normal intestinal cells. For clinical application of this agent, it needs to be determined whether LGG can protect the normal epithelium without shielding tumor cells. In this study we sought to examine the effect of LGG administration on both tumor growth and total mouse weight between both irradiated and non-irradiated mice.
Methods: 3-month-old female BALB/c mice were injected in the lower extremity with CT26 cancer cells and assigned to receive LGG or vehicle (control) treatment and irradiation or no irradiation. LGG/vehicle was administered by gavage prior to irradiation. Tumor volume was measured daily in both experiments, while daily weight was measured only in Experiment 2.
Results: In both experiments, LGG- and vehicle-receiving mice showed no difference in mean tumor volume, fold change, or weight when controlling for irradiation. As expected, irradiated mice showed overall lower tumor volumes than non-irradiated mice, with this difference being about twofold in Experiment 1 and about five-fold in Experiment 2. Mouse weight in Experiment 2 also predictably depended on irradiation alone, with irradiated groups losing on average 20% of their starting body mass.
Conclusions: Treatment with LGG is no more tumor-protective than vehicle treatment when controlling for irradiation. These findings support the use of LGG as a supplemental therapy for patients receiving radiation therapy for pelvic tumors as a means by which to preserve normal intestinal epithelia and reduce radiation enteropathy.

T35 NIH NIDDK Short-Term Training Program

137 **Ben Abdallah, Miriam**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Emergency Medicine
Mentors: Mark Manary, MD; Indi Trehan, MD, MPH, DTM&H

Evaluating the effectiveness of a post-recovery intervention for pediatric moderate acute malnutrition

Ben Abdallah MR; Manary M; Trehan I

Introduction: 7.5 million children under the age of 5 die each year in developing countries and 35% of those deaths can be attributed to malnutrition. In Malawi, Dr. Manary's work has been shown to alleviate Moderate Acute Malnutrition (MAM) by helping children attain a healthy weight and reduce their risk of morbidity and mortality. However, current research indicates that after initial recovery from MAM using ready-to-use therapeutic food and chiponde formulas, nearly 25% of children relapse into malnutrition and 4% of these children will die. This study is a cluster randomized control trial of two post-recovery nutritional and health interventions to prevent relapse for children who have recovered from MAM. Primary outcome measures include recurrent state of MAM, parasite acquisition and immune response through complement measurement. By determining an effective measure to reduce relapse rates, treatment and follow up care can be optimized to truly improve and, in some cases save, the lives of these children.

Methods: This cluster randomized control clinical effectiveness trial will follow 1332 children who have recovered from MAM from 18 clinics in Malawi who will be randomized into two groups - one receiving standard of care and one receiving the study intervention. The intervention incorporates nutritional supplements in addition to parasitic prophylaxis and treatment, a zinc regimen and a bed-net. In addition, 100 children from each group will be selected to have their blood drawn upon enrollment in the study and again at 1, 2, 3, 6, and 12 months during the study to determine serum C3 (complement component) levels as a measure of immune response.

Results: The results of the study are pending. This summer we were able to enroll 216 of the 1322 needed for the study to have significant power. The study will continue to enroll children as they graduate from the MAM program. A difference in outcome will be observed between the Standard of Care Group and the Study Intervention group in the proportion and rate of relapse.

Conclusions: No conclusions can be made at this time. This study should impact the way children are treated after recovering from moderate pediatric malnutrition.

066 **Cole, Jordan**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Psychiatry
Division: Child and Adolescent Psychiatry
Mentor: Kelly Botteron, MD

Thickness of the anterior cingulate cortex in preschool-onset major depressive disorder and its relationship to emotional regulation skills

Cole JJ; Botteron KN; Marrus N; Nishino T

Introduction: The anterior cingulate cortex (ACC) is a region responsible for emotional appraisal, expression, and regulation, and structural alterations in the ACC are observed in major depressive disorder. We examined cortical thickness in the ACC in children with preschool-onset depression (PO-MDD), and investigated whether emotional regulation ability and cortical thickness of the ACC are related.

Methods: Participants, taken from a larger sample of subjects enrolled in a longitudinal study of PO-MDD, participated in brain imaging between ages 7 to 12 years old. Cortical thickness of the ACC was compared in children with and without PO-MDD. Emotional regulation was measured using Children's Emotional Management Scales (CEMS) questionnaires, and scores were compared between children with and without a PO-MDD history. The relationship between CEMS scores and cortical thickness of the ACC was then examined.

Results: The right subcallosal anterior cingulate cortex (ACC) is significantly thinner in children with PO-MDD compared to all other subjects. PO-MDD subjects also had significantly lower Anger Coping scores than all other subjects. Thickness of the left and right rostral ACC significantly correlate with increased Sadness Dysregulation scores.

Conclusions: The results further support the involvement of the ACC in MDD in this previously unexplored population of preschool-onset subjects. Emotional regulation differences and thinner right subcallosal ACC seen in children with PO-MDD indicate possible causes and/or effects of MDD in this population. Longitudinal studies will be required to determine how these differences may lead to or evolve as a result of MDD. Additionally, correlations of the thickness of the rostral ACC with Sadness Dysregulation scores support the previously proposed function of the rostral ACC as a regulator of emotion.

028 **Fan, Jessica**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentor: Kimberly Kaphingst, ScD

Predictors of intentional and unintentional medication nonadherence in patients with type 2 diabetes

Fan JH; Goodman MS; Blanchard MS; Kaphingst KA

Introduction: Type 2 diabetes affects 26 million adults in the United States and 285 million adults worldwide, and diabetes outcomes such as glycemic control, obesity, and self-reported health status remain poor. Medication adherence has been associated with improved diabetes outcomes, but predictors of medication adherence remain unclear. In this study, we investigate predictors of overall medication adherence, unintentional medication adherence, and intentional medication adherence.

Methods: Patients were recruited from a primary care clinic in St. Louis, MO. Patients completed a survey including demographic information, health literacy and medication adherence. Information regarding insurance status, medication regimen, and depression was obtained from patient medical records. Bivariate and multiple regression analysis were performed to assess predictors of overall medication adherence, unintentional medication nonadherence and intentional medication nonadherence.

Results: In multivariable models, age and income were associated with overall medication adherence. Uninsured patients were less likely to be unintentionally nonadherent than patients with private insurance. Patients with incomes less than $20,000 were more likely to be intentionally nonadherent than patients with incomes greater than $20,000.

Conclusions: Results suggest differences in factors affecting intentional and unintentional nonadherence. These differences may contribute to the inconsistent results for predictors of overall medication adherence in prior studies. Further investigation into the predictors of different types of medication nonadherence may prove beneficial to health practitioners in developing interventions to improve adherence.

141 **Gartland, Rachel**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Research
Mentor: David Rudnick, MD, PhD

Investigating the mechanisms that regulate liver regeneration

Gartland RL; Huang J; Rudnick DA

Introduction: Recovery from all liver injuries depends on the liver's ability to regenerate. Thus, liver regeneration is studied using models like rodent partial hepatectomy (PH) with hope for development of regenerative treatments for human liver diseases. Our lab showed that zinc-dependent histone deacetylases (Zn-HDACs) are regulated during and important for liver regeneration. Based on these data, we began characterizing the liver histone acetylome throughout regeneration, using acetyl-histone chromatin immunoprecipitation combined with next generation DNA sequencing (acetyl histone ChIP-Seq) and validating interesting ChIP-Seq findings using ChIP-qPCR. Our data show that early (12 hours) after PH, pro-regenerative changes in histone acetylation can be identified. Based on these data, I hypothesized that early regenerative patterns of histone acetylation are reversed at later time points after regenerative recovery of the liver is complete, and proposed the following aim: to compare patterns of histone acetylation in liver 72 hours after PH or sham surgery to results of our completed analyses of the 12-hour time point.

Methods: Surgery was performed on 2-month old mice. Liver tissue was harvested 72 hours after surgery and immunoprecipitated (IP'd) using an anti-acetyl-histone antibody. ChIP-qPCR was conducted on IP'd DNA for specific genes identified as differentially acetylated 12 hours after PH and IP'd DNA was submitted to WU GTAC for next-generation sequencing (ChIP-Seq).

Results: ChIP-qPCR analysis of liver harvested 72 hours after PH showed reversal of PH-induced changes in histone acetylation identified 12 hours after PH in anti-proliferative genes Foxo3 and Cebpa. Genome-wide ChIP-Seq results are pending.

Conclusions: Gene-specific patterns of change in liver histone acetylation during early liver regeneration are reversed at later times, implicating dynamic epigenetic regulation of pro-regenerative and anti-proliferative genes in the control of liver regeneration. The 72-hour ChIP-Seq data will further assess the genome-wide breadth of such regulation.

083 **Geisman, Taylor**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Gastroenterology
Mentors: Srinivas Gaddam, MD, MPH; Steven Edmundowicz, MD

Efficacy of wide field endoscopic mucosal resection in the treatment of high grade dysplasia and intramucosal adenocarcinoma in patients with Barrett's Esophagus: results from a tertiary care referral center

Geisman T; Gaddam S; Edmundowicz SA

Introduction: High-grade dysplasia (HGD) and intramucosal adenocarcinoma (IMC) arising in the background of Barrett's esophagus (BE) can be effectively treated by endoscopic mucosal resection. A novel approach, wide field endoscopic mucosal resection (wfEMR), can increase the success rate of complete eradication (CE) in a single setting. The aim of this study is to evaluate the safety and efficacy of wfEMR in the therapy of HGD and IMC in a large tertiary care referral center.

Methods: We retrospectively collected data of all patients treated for BE at Barnes-Jewish Hospital between 2000 and 2014 and entered them into a Microsoft Access database. Demographics, procedure details including the highest histology, and adjunctive therapies were recorded. Only patients who had at least 50% of their circumferential BE (C) and 50% of their maximal BE (M) resected by EMR in one sitting were considered to have undergone wfEMR. Only patients with at least 3 months of endoscopic follow-up were included in this study.

Results: Sixty patients underwent wfEMR and fit the inclusion criteria (male (90%), Caucasian (98%) and mean age (SD) = 64.6 + 9.2 years). Nineteen underwent wfEMR for IMC (31.7%), 31 for HGD (51.7%), 8 for low grade dysplasia (13.3%), 1 for indefinite dysplasia (1.7%), and 1 for nondysplastic BE (1.7%). Steroids were given to 29 patients (48.3%). The mean follow-up period was 1.54 (1.2) years. CE of all dysplasia was achieved in 56 patients (94.9%) and CE of all BE was achieved in 50 patients (83.3%). Three patients returned with recurrent IMC and one with low grade dysplasia. Overall, 33 patients (55%) were reported as having a stricture and 30 (50%) required esophageal dilation. Other complications included bleeding (12%) and one delayed perforation (1.9%). All patients were managed successfully by endoscopic therapy.

Conclusions: This study shows that wfEMR for endoscopic eradication therapy is safe and effective. wfEMR has an efficacy of 95% in the endoscopic therapy of dysplastic BE. Although it is associated with a high stricture rate, these can be effectively managed with repeat endoscopic esophageal dilations. Other complications of this procedure were rare.

127 **Gokhale, Arjun**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pathology and Immunology
Division: Anatomic and Molecular Pathology
Mentor: Joseph Gaut, MD, PhD

Investigation of MIOX as a potential biomarker for acute kidney injury

Gokhale A; Gaut J

Introduction: Patients undergoing a cardiopulmonary bypass (CPB) are at a heightened risk for Acute Kidney Injury (AKI). Finding ways to predict the onset of AKI is an area of active ongoing research that could yield many therapeutic benefits as interventions can be started earlier to preserve kidney function. Serum creatinine has proven to be an unreliable biomarker that leaves clinicians with insufficient time to prevent kidney injury. The purpose of this study was to evaluate MIOX as a potential biomarker for AKI in patients undergoing a CPB.

Methods: Blood plasma and urine samples from patients eventually undergoing a cardiopulmonary bypass were collected prior to the bypass and at 0, 3, 6, 12, 18 and 24 hours after the bypass. The blood plasma samples were then analyzed for MIOX concentration using an ELISA assay. After a sufficient number of patient samples have been analyzed, then the researchers will associate the MIOX values with the specific patients and perform a chart review to see which patients suffered from an AKI in the period following a CPB.

Results: Samples from over 50 patients have been analyzed for MIOX activity. Currently we are waiting on collecting more samples before associating specific values with patients and the existence of an AKI. We anticipate a statistically significant detectable rise in MIOX levels in patients prior to acquiring an AKI. We predict that these levels will rise in a clinically significant period of time prior to any rise in currently used biomarkers such as creatinine. Future studies will analyze other procedures associated with an elevated risk of AKI to discern whether these cause a rise in MIOX preceding the onset of an AKI.

Conclusions: If MIOX proves to be a valuable biomarker for AKI, patients undergoing procedures at risk for AKI as a resulting complication will have access to more timely intervention and have better outcomes.

094 **Jacquez, Jordan**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Rheumatology
Mentors: Chyi Hsieh, MD, PhD; Sunaina Khandelwal

Improving the stool collection process for microbiota research studies—a case study in patient enrollment

Jacquez JM; Khandelwal S; Hsieh CS

Introduction: Scientists have long-known about the presence and utility of commensal bacteria that inhabit the human gut, but advancements in sequencing technologies have sparked a mini-revolution in the field of bacterial genomic analysis. A prevailing notion is specific strains or consortia of bacteria might be directly involved as pathogenic agents in inflammatory diseases. Unfortunately, there is currently no easy or precise way to collect a large amount of stools for human research. The purpose of examining our 10 week case study of consenting patients and acquiring stool samples is to elucidate the shortcomings of current approaches while suggesting possible new avenues for more successful research.

Methods: We interrogated the utility of CIDER, an electronic biomedical database and traditional physician assisted patient identification for patient recruitment into stool studies. We also compare the efficacy of patient recruitment in the inpatient vs. the outpatient setting.

Results: We found that only about 15% of our search results from CIDER resulted in patients that had the inflammatory disease we were looking for. We also noticed that consenting patients in the hospital proved to be very difficult and that a disproportionate amount of time was spent checking patient eligibility when an attending physician was not present. On the other hand, we consented 22/24 of the patients from about 15 days in the outpatient clinic setting.

Conclusions: Therefore the best model of enrolling patients in stool studies is in an outpatient, physician assisted setting. However, this model is unsustainable; mining through large patient populations by individually looking up each person with a physician is not practical. The current electronic databases need upgrades that make searching for study participants more adaptive, specific, and reliable.

029 **Kronen, Alyssa**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Division: Public Health Sciences
Mentors: Graham Colditz, MD, DrPH; Ebony Carter, MD

Identifying barriers to care and unmet needs of women with gestational diabetes through patient perspectives

Kronen A; Carter E; Colditz G

Introduction: We sought to identify unmet needs and barriers to care of patients with gestational diabetes (GDM) in an urban clinic caring for underserved women. Specifically, our aims were (1) to give women with GDM a voice to identify barriers to care and unmet needs through a CBPR method known as Photovoice, (2) to gather qualitative data on patient perspectives of gaps in care and desired improvements to care through a written survey, and (3) to refine and clarify community perspectives collected through the two methods above during a culminating focus group with study participants.

Methods: We invited 44 of the women attending clinic to complete a short survey while they waited for their visit. They were also given the option to participate in Photovoice, a type of community-based participatory research in which participants take photographs representing their experiences with GDM. Photovoice participants discussed and developed narratives for their photographs in a focus group.

Results: 48 patients were approached to participate in the study. Of these, 32 (66.7%) completed the survey and 10 (20.8%) completed both Photovoice and the survey. The most commonly cited barriers to receiving care were transportation, time, and money (38.1% each). Although most respondents rated care received at the clinic as very good or excellent (84.4%), almost a third (32.2%) rated their ability to manage diabetes as poor or fair. The majority of participants indicated interest in group prenatal care (58.1%) and thought it would be helpful to hear about the experiences of other patients at the clinic (69%). Additionally, the Photovoice participants indicated that their day-to-day lives were strongly affected by having GDM, especially with regard to difficulty making food choices.

Conclusions: Patients experience significant barriers to care and many do not feel confident in their ability to manage GDM. Efforts to address barriers to care and improve support for patients, such as group prenatal care, may lead to improved outcomes in women with GDM.

080 **Lin, Angela**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Internal Medicine
Division: Emergency Medicine
Mentor: Christopher Carpenter, MD, MSc

Predicting one-month ED returns in undifferentiated geriatric patients: Derivation of a clinical decision rule

Lin AH; Carpenter CR

Introduction: Geriatric patients in the emergency department (ED) are at higher risk than younger patients for avoidable short-term, post-discharge adverse outcomes such as return visits to the ED. Rapid identification of susceptible sub-populations could target preventative resources to these individuals. We aimed to derive a prognostic instrument that identifies community-dwelling older patients in the ED who are at increased risk of ED returns within 30 days of discharge.

Methods: This was a secondary data analysis of a prospectively collected cohort of community-dwelling patients aged 65 and older presenting to one urban academic ED. Research assistants evaluated subjects in the ED using standardized assessment instruments including the Charlson Comorbidity Index (CCI) and Older American Resources and Services Activities of Daily Living (OARS-ADL). Patients were asked if they had presented to the ED during the previous 12 months. Diagnoses at ED discharge were registered from hospital records. A research assistant blinded to the baseline results obtained hospital records of ED returns at 30 after discharge. Recursive partitioning using the rpart package for R was used to identify predictor variables associated with ED returns at 30 days.

Results: Among 301 enrolled subjects, 59 (19.6%) returned to the ED within 30 days of discharge. Enrolled patients were 45.8% male and 52.5% African-American, with mean age 74.8. We developed five candidate prognostic instruments consisting of ED presentation in the previous 12 months, pulmonary component to ED diagnosis, hypertension as part of ED diagnosis, CCI, OARS-ADL, and age. Patients defined as high-risk by these prognostic instruments were significantly more likely to require subsequent ED use at 30 days than the lower-risk cohort.

Conclusions: The instruments developed in this study identify older ED patients that are at higher risk for 30-day ED returns. The predictive factors identified in these instruments do not have sufficient predictive value to recommend them for clinical use, but in conjunction with additional factors, they may be able to identify higher-risk geriatric patients in the ED.

119 **Meyer, Melissa**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Reproductive Endocrinology and Infertility
Mentor: Emily Jungheim, MD, MSCI

BMI and cumulative live birth rates after IVF

Meyer MF; Leung M; Jungheim ES

Introduction: With obesity affecting more than one third of adults in the United States, it is important to understand the impact of increased weight on reproductive outcomes. Increased BMI has been associated with decreased pregnancy and live birth rates following in vitro fertilization (IVF). While per-cycle outcomes have been studied, the impact of increased BMI on cumulative outcomes is not fully understood. In this study we followed women for up to four cycles, to determine if differences in BMI affected IVF outcomes throughout a woman's course of treatment.

Methods: Data was retrospectively analyzed from 2270 women beginning IVF treatment between January 1, 2001 and December 31, 2010. Patients were stratified by BMI at the start of treatment. Cumulative success rate of IVF will be determined by statistical analysis.

Results: Analysis of the data is currently being performed, but our anticipated results include Cox Regression Analyses of BMI versus cumulative pregnancy and live birth rates, while controlling for relevant covariates.

Conclusions: We expect our results to show an association between increased BMI and decreased clinical pregnancy rate and live birth rate. However, we believe this association will be diminished with increasing age. Clinically, this is important because few studies have looked at cumulative live birth rate when most patients undergo more than one cycle of IVF. These results will help in appropriately counseling women, potentially allowing us to identify women who would benefit from weight loss prior to initiating treatment versus those who would not, helping to ensure that each woman undergoing IVF has the best chance of having a child.

130 **Schoer, Morgan**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Endocrinology, Metabolism, and Lipid Research
Mentors: Abby Hollander, MD; Jennifer Heeley, MD

Declining rate of clitoroplasty in females with CAH: a retrospective chart review

Schoer MB; Heeley JM; Hollander AS

Introduction: Prior to the 1990's, most 46,XX infant girls with clitoromegaly secondary to congenital adrenal hyperplasia (CAH) were treated with feminizing genitoplasty to make their cosmetic appearance congruent with their genotypic sex. In the mid 1990's, adult females who were unsatisfied with the results of their infant genitoplasties campaigned for change in the surgical management of virilized female infants. A 2006 consensus statement on the management of intersex disorders accepted input from patient advocates and did not support purely cosmetic surgery for clitoromegaly. This study examines the extent to which the desired change was implemented in practice.

Methods: Retrospective chart review was performed on the 60 female CAH patients treated by endocrinology, gynecology, and/or urology at Washington University Medical Center from 1995 to the present. All females with documented CAH and at least one correspondence in the medical record were included. The variables collected for each patient included birthdate, length of follow up at Washington University, degree and kind of virilization, and whether or not the patient underwent genitoplasty. Furthermore, if applicable, age at surgery, kind of procedure, need for additional surgeries, and complications were all examined.

Results: Of the 45 patients who were virilized, 40 of them had clitoromegaly and 39 had a UG sinus or posterior labial fusion. 27 patients (67.5%) underwent clitoroplasty and 33 (84.6%) underwent perineoplasty. We observed a linear decline in the rates of clitoroplasty for patients born from 1979 to 2013. Four out of four infants (100%) with clitoromegaly born between 1979-85 received surgery, while only three of seven (43%) born from 2007-2013 did.

Conclusions: The percentage of virilized female infants with CAH who received clitoroplasty declined steadily between 1979 and 2013. This change demonstrates the adoption of updated clinical practice recommendations which were developed with input from former patients. Our data represents an early example of the influence of patient advocacy to improve clinical practice.

139 **Tanakit, Alisa**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Pediatrics
Division: Pediatric Emergency Medicine
Mentor: Mark Manary, MD

Learning from the St. Louis Nutrition Project in Malawi summer of 2014

Tanakit A; Manary M

Introduction: I went to Malawi from May 31st – July 30th to participate in the St. Louis Nutrition Project and the current two studies that were happening there at that time were: 1. A comparison study between therapeutic food based on whey vs. one based on soy. 2. A study that followed recovered children for 12 months to determine whether interventions helped reduced relapse rates. The reason study 1 is pertinent is to reduce costs. The reason study 2 is important is to help kids STAY healthy. I also went to Malawi to get a picture of clinical research and foreign aid administration.

Methods: A cluster randomized (by site), controlled clinical effectiveness trial assessing a combined nutrition and health intervention will be performed. Eligible subjects are children 6-62 months of age and determined to have recently recovered from MAM (recovery is defined as 12.5cm or above in MUAC in 12 weeks). These children are from the group that participated in the whey permeate trial. The trial will be 12 weeks with follow ups occurring at three, six, and 12 months. We will also take blood samples to assess fat content at first enrollment and then six or eight weeks later. The whey study was randomized and included children who were diagnosed with MAM - defined by having an arm circumference between 11.5cm and 12.5 cm.

Results: The anticipated results are that the interventions will reduce relapse rates in children recently recovered from MAM. The anticipated results for the whey study are that there will be a less than 3% difference in outcomes from the different therapeutic study foods.

Conclusions: Because of this research there will be in place a better platform to treat malnourished children in third world countries where delivery and cost are big issues. Personally I got a much better view of how clinical research is done and it changed what I thought about foreign aid. If in the future I continue to help in foreign aid I will utilize this knowledge to make a model I think will be most effective.

125 **Vryhof, Nicholas**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Ophthalmology and Visual Sciences
Division: Ophthalmology
Mentors: Carla J Siegfried, MD; Jason Rupp, MD, PhD

Minimally invasive glaucoma surgery: ab interno trabeculotomy vs. endoscopic cyclophotocoagulation

Vryhof NW; Siegfried CJ; Rupp J

Introduction: Cataracts affect 24.4 million Americans over the age of 40, while glaucoma affects 2.7 million. Combined surgery for both of these conditions has traditionally been trabeculectomy with phacoemulsification, but ophthalmologists are increasingly turning to combining phacoemulsification with minimally invasive glaucoma surgeries (MIGS) that have less surgical risk. The purpose of this study was to compare the safety and efficacy of two of these MIGS: ab interno trabeculotomy (Trabectome) and endoscopic diode cyclophotocoagulation (ECP).

Methods: This retrospective chart review looks at 64 eyes undergoing Trabectome with phacoemulsification and 62 eyes undergoing ECP and phacoemulsification. Previous retrospective studies evaluating these new glaucoma procedures combined with phacoemulsification rarely include a comparison group. Because cataract surgery alone is associated with intraocular pressure (IOP) reduction, the relative contribution of the glaucoma procedure in lowering IOP cannot be determined in these studies. This study aims to compare outcomes against a cataract surgery alone control group.

Results: The results of this study are ongoing. Preliminary results show that, at 24 months, ECP and phacoemulsification and Trabectome and phacoemulsification reduced IOP, on average, by 2.1 mm Hg and 2.8 mm Hg, respectively. They also reduced the number of medications, on average, by 0.61 and 0.68, respectively. Trabectome with phacoemulsification was associated with a greater risk of hyphema, hypotony, and IOP spike, while ECP with phacoemulsification was associated with a greater risk of persistent inflammation at 3 months and macular edema.

Conclusions: Both ECP with phacoemulsification and Trabectome with phacoemulsification reduce IOP and number of glaucoma medications. However, until the control data are collected, the relative contribution of the glaucoma procedure in lowering IOP compared to phacoemulsification alone cannot be determined. Preliminary data suggest both surgeries achieve mild to moderate gains in IOP reduction, but with less surgical risk than trabeculectomy.

043 **Wang, Robert**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Surgery
Mentor: Michael Awad, MD, PhD

The effect of patient obesity on minimally invasive surgeon's muscle fatigue

Wang R; Liang Z; Awad M

Introduction: Laparoscopy has become the treatment of choice for many abdominal diseases requiring surgical intervention. The laparoscopic approach has been associated with significant reductions in morbidity and mortality for a wide range of procedures, including ventral hernia repairs, paraesophageal hernia repairs, bariatric surgeries, and cholecystectomies. However, the benefits to the patient may come at a cost to the surgeon, as this type of surgery creates unique ergonomic challenges with the potential to cause pain or injury, especially in the neck and upper arm region. As obesity rates have remained steadily high in the United States, we sought to quantify how patient BMI might influence these ergonomic stressors.

Methods: Using a Trigno Wireless EMG system, we recorded electrical activity in the biceps, triceps, deltoid, and trapezius muscle groups of five laparoscopic surgeons in a total of 32 abdominal surgeries. These recordings were then used to calculate average muscle activation during the surgery, normalized to a percentage of the maximum voltage of contraction (MVC). As a subjective measure of task difficulty, the subjects also completed the NASA Task Load Index (NASA-TLX or NTLX) survey after each case.

Results: Surprisingly, our initial analysis suggests that average muscle activation during surgery and subjective task difficulty are not correlated with patient BMI. These results suggest that laparoscopic surgery reduces or eliminates potential difficulties of operating on high-BMI patients, possibly though eliminating the need for gross manipulation of body mass by the surgeon.

Conclusions: The result of this study suggests that there is no significant association between patient obesity and surgeon's muscle fatigue. However, due potential confounding factors such as procedure type and the role of the attending surgeon versus the assisting resident, further detailed analysis should be conducted before any solid conclusions can be drawn.

118 **Yang, Michael**

T35 NIH NIDDK Short-Term Training Program
Summer Research Program
Current Doctoral Program of Study: Medicine
Washington University in St. Louis
Department: Obstetrics & Gynecology
Division: Maternal Fetal Medicine and Ultrasound
Mentor: Alison Cahill, MD, MSCI

Does baseline change influence neonatal outcomes

Yang M; Stout MJ; Colvin R; Macones GA; Cahill AG

Introduction: Abnormalities of the fetal baseline heart rate, though rare, have been associated with adverse outcomes. More commonly, fetal heart rate (FHR) baseline fluctuates within the normal range, though with presently unknown meaning. We aimed to estimate the association between changes in normal baseline FHR with acidemia and neonatal outcomes.

Methods: Within an ongoing prospective cohort study of all consecutive singleton, nonanomalous, term pregnancies, we included all women with continuous electronic fetal monitoring (EFM) in the last 2 hours of labor. To examine normal baselines, we excluded fetuses with any bradycardia or tachycardia. EFM patterns were extracted by trained obstetric research nurses blind to clinical and outcome data. We divided the last 2 hours into 10 minute periods and assigned one baseline FHR to each. Increase or decrease of ≥20 bpm from one period to any later period was considered baseline change. Change ≥30 bpm was also assessed. Risk of acidemia (umbilical cord arterial pH ≤7.10) and NICU admission in infants with baseline change was estimated with GEE adjusting for nulliparity, obesity, fever, delivery mode, and within patient change.

Results: Of 3,021 women with continuous EFM and normal baseline throughout the last 2 hours of labor, 272 (9.0%) had change ≥30 bpm, and 1267 (41.9%) ≥20 bpm. Baseline change was not associated with acidemia at ≥20 bpm or ≥30 bpm in any direction. NICU admission was not significantly more likely with baseline increase ≥20 bpm or change in any direction ≥30 bpm. Decrease ≥20 bpm (adjusted odds ratio [aOR] 2.98; 95% confidence [CI] 1.21 – 7.33) and any change ≥20 bpm (aOR 4.19; 95% CI 1.52–11.56) were associated with NICU admission, but poor predictors of outcome (respectively, sensitivity 40%, 75%; specificity 18%, 42%; positive predictive value 1.4%, 1.2%; negative predictive value 0.4%, 0.2%).

Conclusions: Changes of normal baseline heart rate are common in term labor and are poor predictors of morbidity, regardless of direction or magnitude.

Additional Training Programs

050 **Janjua, M Burhan, MD**
Washington University in St. Louis
Department: Neurosurgery
Mentor: Wilson Zack Ray, MD

Patient demographics, insurance status, and race predict morbidity and mortality after spinal cord injury

Janjua MB; Yarbrough YK; Zhang A; Tang M; Ghenbot R; Hawasli AH; Gamble PG; Kelly M; Ray WZ

Introduction: Health-care disparities among preventable diseases have been an ongoing public health problem. Since trauma does not rely on the same infrastructure observed for preventable diseases, less disparity based on demographics and socioeconomic status may result. In this study, we reviewed all spinal cord injury (SCI) admissions to a large level I tertiary referral center over 11 years to analyze factors affecting outcome from SCI.

Methods: A retrospective review of 795 all SCI patients between 2003 and 2013 was performed. Diagnosis, patient demographics, race, insurance status, comorbidities, complications, outcomes, and readmissions were collected. The effects of insurance status and race on readmission were evaluated with univariate and multivariate analysis while linear regression was used to analyze length of stay (LOS), ICU-LOS, age and BMI with respect to 30 day and 1 year readmission rates.

Results: 248 women (32%) and 511 men (68%) with an average age of 40.9 years and an average BMI of 26.7 were diagnosed with SCI. Payor status did not affect LOS, ICU-LOS, or perioperative complications. However, payor status was a significant predictor of readmission within 30 days of discharge ($p<0.005$). Medicare (17.4%) and Medicaid (24.5%) showed higher rates of readmission than commercial insurance (13%), self-funded (7.8%), workers compensation (4.7%), and military patients (0%). Medicaid versus other payors shows a significant higher rate of readmission (Odds ratio: 2.1, 95% confidence interval 1.32-3.34). Univariate analysis identified the following significant predictors for 30 day readmission: race, LOS, ICU-LOS, and diabetes. 22.8% of African-Americans were readmitted, versus 12.3% of other patients (Odds ratio: 2.2, 95% confidence interval 1.36-3.27, $p<0.001$). Correcting for payor status lessened but did not eliminate the effect of race on readmission. Age, gender, tobacco use, and BMI did not affect readmission in this patient population.

Conclusions: Payor status does not affect in-hospital parameters of patient care during initial management of SCI. After discharge, patients with Medicaid and Medicare show higher rates of 30 day readmission, as do African-Americans. These data may result from the effect of payor status on post-hospitalization rehabilitation and home care. The effect of race on readmission is multifactorial, and is explained by the increased rate of Medicaid coverage in African-Americans in our institutions catchment area.

No Poster **Janjua, M Burhan, MD**
Washington University in St. Louis
Department: Neurosurgery
Mentor: Wilson Zack Ray, MD

Weekend admission and operations do not adversely affect patient outcomes in treatment of spinal cord injury

Janjua MB; Yarbrough YK; Zhang A; Tang M; Ghenbot R; Hawasli AH; Gamble PG; Kelly M; Ray WZ

Introduction: Weekend admissions have been associated with worsened clinical outcomes for multiple acute adverse events. This data has been used in some settings to delay transfer of patients to tertiary centers and to justify scheduling treatment of acute spinal conditions in semi-elective fashion. In this study, we reviewed all spinal cord injury admissions to a large level I tertiary referral center from the past 11 years.

Methods: A retrospective review of all spinal cord injury patients admitted between 2003 and 2013 was performed. 795 patients were identified, 163 of whom underwent surgery on the weekend. Patient demographics, race, insurance status, comorbidities, complications, outcomes, and readmissions were collected. We utilized linear regression to analyze length of stay, ICU length of stay, 30 day, and 1 year readmission rates.

Results: 192 of 795 patients (25.7%) were admitted on the weekend, and 163 of 795 patients (22.3%) required surgery on the weekend. Neither weekend admission nor weekend operation affected length of stay, ICU length of stay, or readmission by 30 days. Patients undergoing weekend surgical treatment had lower perioperative complication rates when compared with patients undergoing surgical treatment on a weekday (2.2% vs. 6.5%, $p<0.01$). 119 of 795 patients (15.9%) were discharged on the weekend. Discharge on the weekend was associated with a significantly lower rate of readmission by 30 days (OR: 0.07, 95% confidence interval 0.009-0.525, $p<0.005$).

Conclusions: In our study, weekend admission and operations did not adversely affect patient outcomes. On the contrary, perioperative complications were lower in patients undergoing surgical treatment on the weekend. While this data is reflective of only a single institution with a large volume of spinal cord injury, it refutes other reports suggesting that weekend treatment of spinal trauma is deleterious. Thus, we support efficient and effective surgical intervention regardless of whether a patient arrives during the "work week."

039 **Moore, Katelynn**

Student Intern: Lab of Dr. Scott Mason
Washington University in St. Louis
Department: Surgery
Division: Urology
Mentors: Paul Austin, MD; Scott Manson, PhD

Injury to the developing kidney leads to impaired maturation but not inflammation or fibrosis

Moore KH; Geminiani JJ; Vricella GJ; Guo Q; Manson SR; Austin PF

Introduction: Inflammation and fibrosis are widely accepted as the key processes driving the progression of renal injuries to kidney disease in the mature kidney. However, congenital defects are the leading cause of pediatric kidney disease and the pathogenesis of renal injury in the developing kidney remains poorly understood. In this study, we provide the first direct comparison of injury responses during each of the critical stages of kidney development.

Methods: Disease progression was examined in chronic and reversible murine models of unilateral ureteral obstruction (UUO) at several developmental time points: (1) P1, during nephrogenesis/nephron maturation, (2) P14, during proliferative growth, and (3) P60, in the mature kidney. Renal pathology was assessed by immunostaining for molecular markers of key processes in kidney development and the pathogenesis of renal injury.

Results: UUO at either P1 or P14 in the developing kidney leads to decreased kidney growth, reduced proliferative expansion of nephrons, increased apoptosis in progenitor cells, and impaired nephron differentiation. There is also a notable absence of fibroblast and macrophage recruitment, inflammation, and fibrosis in the developing kidney. This contrasts the mature kidney where there is a marked increase in reparative proliferation, inflammation, and fibrosis. [All results are n=5, $p<0.05$]

Conclusions: This study reveals that developmental context has a significant impact on the pathogenesis of renal injuries. In contrast to the mature kidney, injury in the developing kidney is characterized by profound developmental deficits and a distinct absence of inflammation and fibrosis. This suggests that treatment strategies for pediatric kidney disease can be optimized by stimulating proliferation and minimizing apoptosis at early stages of development while inhibiting inflammation and fibrosis at later stag

054 **Reyes, Arith Ruth**

Summer Research Program
Current Doctoral Program of Study: Medicine
Department: Pharmacology and Physiology, Drexel University College of Medicine
Mentor: Elisabeth Van Bockstaele, PhD

Amyloid beta and norepinephrine are co-localized in the rat prefrontal cortex

Reyes AR; Ross J; Van Bockstaele E

Introduction: Alzheimer's disease is a neurodegenerative disorder marked by aggregates of amyloid beta (Aβ) plaques. One of the brain regions affected with neuronal loss in Alzheimer's disease is the locus coeruleus, the primary site of synthesis for norepinephrine that sends projections to almost all levels of the neuraxis. The purpose of this study is to examine the interactions between amyloid beta and norepinephrine. Specifically, localization of amyloid beta and norepinephrine will be examined in the rat prefrontal cortex.

Methods: Light microscopy was used to examine the distribution of Aβ in the rat prefrontal cortex. Confocal microscopy was used to examine the localization of Aβ and dopamine beta hydroxylase (DβH), an enzyme that catalyzes formation of norepinephrine from dopamine. Electron microscopy was used to examine the subcellular localization of Aβ and DβH.

Results: Light microscopy indicated that Aβ-immunoreactive processes are present in the rat prefrontal cortex. Confocal microscopy revealed that processes immunoreactive for Aβ also express DβH. Electron microscopy showed that Aβ is localized to norepinephrine-containing axon terminals as well as to dendritic processes postsynaptic to norepinephrine-containing axon terminals.

Conclusions: The results of this study suggest that there may be an interaction between Aβ and norepinephrine. This interaction may serve as a cellular substrate contributing to the aggregation of Aβ plaques in Alzheimer's disease.

Abstracts and Posters

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CRTC K12 Paul Calabresi Career Development Awards For Clinical Oncology

CRTC Postdoctoral Mentored Training Program in Clinical Investigation (MTPCI)

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program (cont.)

Dames Fellowship

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Dean's Fellowship (cont.)

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T35 NIH NIDDK Short-Term Training Program

Additional Training Programs

Abstract Authors

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