



Washington University in St. Louis

SCHOOL OF MEDICINE

*10th Annual*

Research Training Symposium  
and Poster Session

October 22, 2015

Showcasing Basic, Clinical, and Translational research projects by junior faculty, fellows, residents, and training program students.

**Washington University in St. Louis School of Medicine**  
**Tenth Annual Research Training Symposium & Poster Session**  
**October 22, 2015**  
**Farrell Learning and Teaching Center**

**12:30 – 12:45 pm** Connor Auditorium

Welcome and Opening Remarks

**Alison J. Whelan, MD**

Professor of Medicine

Senior Associate Dean for Education

Washington University in St. Louis School of Medicine

**12:45 – 1:45 pm** Connor Auditorium

Keynote Address

**Anthony J. Windebank, MD**

Professor of Neurology

Director, Clinical and Translational Science Program

Mayo Clinic

**1:45 – 3:00 pm** Connor Auditorium

Oral Presentations

1:45 – 2:00 pm

Alejandro Siller

2:00 – 2:15 pm

Lauren Roland, MD

2:15 – 2:30 pm

Jun Yoshino, MD, PhD

2:30 – 2:45 pm

Foluso Ademuyiwa, MD, MPH

2:45 – 3:00 pm

Brian Fuller, MD, MSCI

**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>**

### **American Academy of Neurology (AAN)**

The scholarship program offers members of SIGN a summer stipend of \$3,000 to conduct a project in either an institutional, clinical, or laboratory setting where there are ongoing programs of research, service or training, or a private practice. Only applicants from schools with established SIGN chapters are eligible to apply. The AAN will award up to 20 scholarships to medical students with little to no research experience who have a supporting preceptor and a project with clearly defined goals. The project is to be conducted through a U.S. or Canadian institution of the student's choice and jointly designed by the student and sponsoring institution.

**Website: <http://tools.aan.com/science/awards/?fuseaction=home.info&id=58>**

### **American Association of Thoracic Surgery (AATS)**

The Summer Intern Scholarship program was established in 2007 to introduce the field of cardiothoracic surgery to first and second year medical students in a North American medical school with the goal of broadening their educational experience by providing an opportunity to spend eight weeks during the summer (June thru September) working in an AATS member's, cardiothoracic surgery department. The Scholarship is funded and administered by the AATS Graham Foundation and provides a grant of \$2,500 to the successful applicants for their living expenses during the eight weeks of training at the selected host institution. Additionally, successful applicants receive complimentary registration to the 96th AATS Annual Meeting taking place May 14 – 18, 2016 in Baltimore, MD.

**Website: <http://aats.org/research/Grants/Summer-Intern-Scholarship.cgi>**

### **American Society of Hematology (ASH)**

The American Society of Hematology (ASH) selects medical students to participate in the Minority Medical Student Award Program (MMSAP). The MMSAP is an 8- to 12-week research experience for students from the United States and Canada in their early years of medical school. As part of this experience, students collaborate with an ASH member who serves as their research mentor. Program participants are also paired with an ASH member who serves as a career-development mentor throughout the participants' medical schooling and residency.

**Website: <http://www.hematology.org/Awards/Medical-Student/383.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>**

### **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**

**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://mdstudentresearch.wustl.edu/find-a-project/programs/summer-research/>**

**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: Gary Weil, MD; Cynthia Wichelman, 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>**

**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: Vijay Sharma, PhD**

**Website: <https://www.mir.wustl.edu/research/summer-research-program>**

**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://mdstudentresearch.wustl.edu/find-a-project/programs/year-long-research/>**

### **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: Gammon Earhart, PT, PhD**

**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.rkp.wustl.edu/NIDA\\_T32.html](http://www.rkp.wustl.edu/NIDA_T32.html)**

### **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://oto.wustl.edu/Education/ResidentEducation/PhysicianScientistProgram.aspx>**

### **Radiology Society of North American (RSNA)**

To increase the opportunities for medical students to have a research experience in medical imaging and to encourage them to consider academic radiology as an important option for their future. Recipients will gain experience in defining objectives, developing research skills and testing hypotheses before making their final choices for residency training programs. Students are expected to undertake a research project requiring full time efforts for at least 10 weeks under the guidance of a scientific advisor during personal/vacation time or during a research elective approved by their medical school.

**Website:** [http://rsna.org/Research\\_Medical\\_Student\\_Grant.aspx](http://rsna.org/Research_Medical_Student_Grant.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

**Website:** <http://www.ot.wustl.edu/education/phd-in-rehabilitation-and-participation-science/application-process-and-requirements-207>

### **Siteman Cancer Center Leah Menshouse Springer Summer Opportunities 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:** Jaclyn McGuire

**Website:** <http://www.siteman.wustl.edu/summerprogram.aspx>

### **Summer Medical Education Research Fellowship (SMERF)**

The Summer Medical Education Research Fellowship supports medical students to conduct summer research in medical education.

**Program Contact:** Koong-Nah Chung, PhD

### **Summer Research Program in Global Health**

The Summer Research Program in Global Health (SRPGH), from the Global Health Center at the Institute for Public Health offers students (from undergraduates to medical students) the opportunity to work closely with outstanding faculty mentors focusing on global health. The goal of the program is to expose young investigators to research in a lab or field-based setting and further their interest in global health. The program includes regular seminars and opportunities to establish a career-building network.

**Program Contact:** Jacaranda Van Rheenen, PhD

**Website:** <http://publichealth.wustl.edu/resources/summer-research-programs/>

### **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://mdstudentresearch.wustl.edu/find-a-project/programs/summer-research/>**

**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://mdstudentresearch.wustl.edu/find-a-project/programs/summer-research/>**

**Washington University in St. Louis, Office of the Provost**

Washington University in St. Louis, Office of the Provost helps train Meharry Medical College students in the Washington University in St. Louis School of Medicine's (WUSM) Summer Research Program. 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 Contact: Koong-Nah Chung, PhD**

## Abstracts for Oral Presentations

*In the Order Presented*

### Siller, Alejandro F

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Radiology

Mentors: Tamara Hershey, PhD; Ana Maria Arbelaez, MD, MSCI

#### **Brain structure in newly diagnosed youth with type 1 diabetes**

Siller AF; Rutlin J; Lugar H; Semenkovich K; White NH; Shimony J; Arbelaez AM; Hershey T

**Introduction:** Studies of youth with type 1 diabetes (T1DM) have found associations between brain structural differences and greater exposure to glycemic extremes. However, the cause of these differences and when they emerge remains unclear. Knowledge of a root cause could greatly influence treatment strategies aimed at prevention of neurological deficits. Therefore, our primary aim was to determine if the presence of Diabetic Ketoacidosis (DKA), severity of DKA, or HbA1c at time of T1DM diagnosis in youth is related to brain structural differences evident at three months post-diagnosis. We hypothesized that a more severe presentation of T1DM would be associated with greater brain structural differences seen on MRI.

**Methods:** We performed MRI scans in T1DM patients (n=68) within 3 months of diagnosis and used their non-diabetic siblings (n=35) as healthy controls, and collected T1-, T2-, and diffusion-weighted imaging scans for analysis. MRI data were analyzed using FreeSurfer to derive volumes of subcortical structures (T1DM n=42; Controls n=26), and Tract- Based Spatial Statistics was used to assess white matter structural integrity across the entire brain (T1DM n=44; Controls n=24). Clinical information was collected at the time of diagnosis, including HbA1c, HCO<sub>3</sub>, osmolarity, and serum pH, and Diabetes Control and Complications Trial (DCCT) criteria were used to determine DKA status at diagnosis post hoc.

**Results:** DKA at presentation was associated with lower axial and radial diffusivity (AD and RD) in diffuse regions across the brain in T1DM patients who presented in DKA when compared to those who did not present in DKA (p<0.05), with the greatest effects seen in and around the corpus callosum. A higher HbA1c at diagnosis was related to lower hippocampal and thalamic volumes (p = 0.032, p = 0.006, respectively). An area of significant negative correlation between cortical thickness and HbA1c (p<0.01) in the right superior parietal lobe was also observed, along with an area of significant positive correlation between cortical thickness and HbA1c (p<0.01) in the right occipital lobe.

**Conclusions:** These data suggest that the severity of T1DM at diagnosis, as measured by DKA status and HbA1c, may determine brain structural outcomes in youth with T1DM. Early detection of T1DM may help avoid these severe metabolic states and optimize brain outcomes.

### Roland, Lauren, MD

T32 Otolaryngology Advanced Physician Scholars Program

Washington University in St. Louis School of Medicine

Department: Otolaryngology-Head and Neck Surgery

Mentors: Jonathan E Peelle, PhD; Jay F Piccirillo, MD, FACS

#### **Effects of mindfulness-based stress reduction therapy on subjective bother and neural connectivity in chronic tinnitus**

Roland LT; Lenze EJ; Mei-Hardin F; Kallogjeri D; Nicklaus J; Wineland A; Fendell G; Peelle JE; Piccirillo JF

**Introduction:** Chronic tinnitus is a common problem in otolaryngology with approximately one-third of tinnitus patients presenting with bothersome symptoms. 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). MBSR appears to be a promising intervention for chronic tinnitus with the potential for lasting therapeutic effects. 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:** This was an open-label interventional pilot study of 13 participants with a median age of 55 years, suffering from subjective, non-pulsatile bothersome tinnitus for at least 6 months. An 8-week MBSR program was conducted by a trained MBSR instructor. The program consisted of eight 2-hour classes and one 3-hour retreat as well as daily homework assignments and CD-guided activities. 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- and post-MBSR. Participants underwent pre- and post-MBSR functional connectivity MRI to serve as a neuroimaging biomarker of critical 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  $\Delta THI$  of -16 and median  $\Delta TFI$  of -14.8 between baseline and 4-week follow-up scores. There was also a statistically significant change in depression. 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.

**Yoshino, Jun, MD, PhD**

CRTC KL2 Career Development Awards

Washington University in St. Louis

Department: Center for Human Nutrition

Mentors: Samuel Klein, MD; Nada Abumrad, PhD

**Identification of adipose tissue biomarkers of obesity-induced insulin resistance**

Yoshino J; Kelly SC; Klein S

**Introduction:** Obesity-induced insulin resistance is an important risk factor for type 2 diabetes, cardiovascular disease, cancer and Alzheimer's disease. The complex mechanisms responsible for obesity-induced insulin resistance are not clear, but likely involve the alterations in adipose tissue secreted bioactive proteins, such as pro-inflammatory cytokines and adipokines, that can affect insulin action in key metabolic organs such as liver and skeletal muscle. The purpose of this study is to identify adipose tissue biomarkers of insulin resistance in people who are obese.

**Methods:** We conducted completed a microarray analysis of adipose tissue from insulin-sensitive metabolically-normal obese (MNO) and insulin-resistant metabolically-abnormal obese (MAO) people who have already been carefully characterized by evaluating insulin sensitivity using the hyperinsulinemic-euglycemic clamp procedure in conjunction with stable isotopically labeled tracer infusion.

**Results:** We identified several novel adipose tissue biomarkers that were significantly increased in MAO people compared with MNO people. These biomarkers include CTGF (connective tissue growth factor), TNMD (tenomodulin) and SEMA3C (semaphorin 3C) and adipose tissue expression of these genes was strongly associated with skeletal muscle insulin sensitivity.

**Conclusions:** The proteins encoded by CTGF, TNMD and SEMA3C are known to be secreted into the systemic circulation. The outcome of this study could provide novel blood biomarkers and mathematical models of obesity-induced insulin resistance. Moreover, the results from these studies might provide new mechanistic and therapeutic insights into the pathogenesis of obesity-induced insulin resistance.

**Ademuyiwa, Foluso O, MD, MPH**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology; CRTC MSC1 Degree Program

Department: Internal Medicine

Division: Oncology

Mentors: Kathy Weilbaeher, MD; Cynthia Ma, MD, PhD

**A triple negative breast cancer co-clinical trial with genomic discovery analysis**

Ademuyiwa FO; Ma C; Li S; Weilbaeher K; Ellis M

**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 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/m<sup>2</sup> q3 wks x 6, followed by surgery. Tissue collection for xenografting and correlative studies will occur at baseline, cycle 1 day 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 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. 15 patients have been enrolled and have had baseline tissue collection. Nine patients have completed protocol therapy; 3 (33%) achieved a PCR. Three patients have tissue at all 3 time points (=9 samples). Whole genome sequencing on those 9 samples to identify genomic lesions that predict for resistance is underway.

**Conclusions:** Achieving a higher PCR rate with this drug combination in patients with TNBC will translate to improved long-term clinical outcomes. Our planned discovery analysis may identify molecular markers of resistance that may be targeted in patients with chemotherapy resistant disease.

**Fuller, Brian, MD, MSCI**

CRTC KL2 Career Development Awards

Washington University in St. Louis

Department: Anesthesiology and Emergency Medicine

Division: Critical Care Medicine

Mentors: Marin H Kollef, MD; Richard S Hotchkiss, MD

**The implementation of lung-protective ventilation in the emergency department**

Fuller BM; Stephens RJ; Briscoe CA; Hotchkiss RS; Kollef MH

**Introduction:** A lung-protective ventilation (LPV) strategy, aimed at limiting tidal volume and alveolar distending pressure, improves outcome in patients with, and at risk for, acute respiratory distress syndrome (ARDS). Most patients with ARDS in the intensive care unit (ICU) receive initial care in the emergency department (ED).

Our previous work has shown that: 1) mechanical ventilation and ARDS have been studied little in the ED; 2) the current practice of mechanical ventilation in the ED can promote ventilator-associated lung injury; and 3) ED-based mechanical ventilation is associated with ARDS development. We therefore instituted a default LPV protocol in 2014 to prevent complications in this vulnerable cohort. We aim to investigate the effect of LPV in the ED on the incidence of ARDS and ventilator-associated conditions (VAC).

**Methods:** Quasi-experimental before (2009-2013)-after (2015-2016) investigation. The intervention consisted of the institution of LPV in the ED as the default approach unless contraindicated (2014). For the purposes of this analysis, descriptive statistics, chi-square, and t-test were used to compare the two groups.

**Results:** The before group consisted of 1,717 patients, and 3,599 ED ventilator settings; the study is ongoing and the after group currently includes 264 patients and 423 ventilator settings. When comparing the before vs. after group, the intervention was associated with a significant decrease in tidal volume, 8.1mL/kg predicted body weight (7.3-9.1) vs. 6.3 (6.0-6.6), increase in PEEP, 5cm H<sub>2</sub>O (5-5) vs. 5 (5-8), and decrease in F<sub>i</sub>O<sub>2</sub>, 80% (50-100) vs. 40% (40-60). Head of bed elevation increased from 39.0% to 89.1%. These are all significant at p<0.0001.

**Conclusions:** The LPV protocol targets ventilation practices that our prior work has shown could contribute to lung injury. These include: 1) high tidal volume; 2) universal PEEP setting at 5cm H<sub>2</sub>O; 3) prolonged administration of high levels of oxygen; and 4) low adherence to head-of-bed elevation. We have seen significant changes in mechanical ventilation practices in the ED, and protocol adherence has been excellent. The trial is ongoing and the effect of these changes on clinical outcomes is pending.

## Abstracts for Poster Session

*Alphabetically by Training Program and Author*

### American Academy of Neurology (AAN)

039

**Powell, Dylan**

American Academy of Neurology (AAN); Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurology

Division: Pediatric Neurology

Mentor: Liu Lin Thio, MD, PhD

**Predictive factors in the efficacy of the ketogenic diet for childhood epilepsy**

Powell DR; Thio LL

**Introduction:** The ketogenic diet is a high fat, low carb, adequate protein diet that has been shown to be effective in treating a range of drug-resistant epilepsies. However, it is highly time and effort-intensive, so it would be valuable to identify factors that predict the likelihood of a positive response. The purpose of this study was to compare the efficacy of the ketogenic diet with a number of potentially predictive factors.

**Methods:** A retrospective chart review was completed including all 183 patients treated with a ketogenic diet at St. Louis Children's Hospital from January 2006-April 2015. Efficacy was measured by the change in seizure frequency while on the diet. Seizure types and subtypes were obtained from physician histories. MRI data were obtained from MRI notes. Chi square tests were then performed to compare the effects of the potential predictors on treatment efficacy.

**Results:** Both seizure type and MRI findings were found to be statistically significant predictors. Of children who had normal MRI findings, 37.5% achieved a >90% seizure reduction, compared with 18.7% of children who had an abnormality thought to be causative of epilepsy ( $p<0.05$ ). In looking at seizure type, children who had a history of infantile spasms fared the worst, with 65.8% of children who had a history of infantile spasms achieving a <50% reduction in seizure frequency, and only 13.2% achieving a >90% reduction, compared to 39.2% and 30%, respectively, in children who did not have a history of infantile spasms ( $p<0.05$ ).

**Conclusions:** The importance of MRI findings and seizure type in predicting patient response indicates that these factors should play a greater role in determining the candidacy of a given patient for a ketogenic diet.

## American Association for Thoracic Surgery (AATS)

022

**Huang, Lingling, PhD**

American Association for Thoracic Surgery (AATS); Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Surgery, Duke University

Division: Cardiothoracic Surgery

Mentors: Mark Onaitis, MD; Daniel Kreisel, MD, PhD

**Comparative evaluation for anatomic lung resection by robotic-assisted vs video-assisted thoracoscopic surgery**

Huang L; Onaitis M

**Introduction:** Robotic-assisted lung resection has been offered increasingly to patients, but comparative studies evaluating its safety, complication profile and effectiveness are limited. Previous studies do not control for institution or surgeon expertise. Therefore, we performed this retrospective analysis to compare short-term and long-term outcomes for patients undergoing anatomic lung resection by robot or video-assisted thoracoscopic surgery (VATS) from a single surgeon experienced in both approaches.

**Methods:** A retrospective analysis of consecutive anatomic lung resections by robot or VATS was performed to compare perioperative characteristics and long-term survival outcomes.

**Results:** 61 patients underwent robotic surgery from 12/2010 to 06/2015, and 58 patients underwent VATS lung resection from 12/2012 to 06/2015. No statistically significant differences were found in patient demographics. The robotic group had a higher rate of prolonged air leak  $\geq 7$  d than VATS (14.75% vs 0.0%,  $p=0.0029$ ), and consistently a longer chest tube duration (median of 2.0 days vs median of 1.0 day,  $p=0.0175$ ). In addition, the robotic group had a longer length of hospital stay (median of 4.0 days vs median of 3.0 days,  $p=0.0110$ ). Other postoperative complications, mortality, nodal upstaging and conversion rate were similar in both groups. In patients undergoing either surgery from 12/2012 to 06/2015, disease-free survival was similar in both groups (median survival: 646.0 days in robotic and 595.0 days in VATS,  $p=0.4318$ ). However, the robotic group appeared to have slightly better overall survival than VATS (survival proportion: 100% vs 80.987%,  $p=0.0441$ ).

**Conclusions:** Our study found that robotic lung resection at its early stage of adoption is associated with a higher rate of prolonged air leak ( $\geq 7$  d), and slightly longer chest tube duration and hospital stay than VATS. Within the same follow-up period, disease-free survival was similar in both groups, while the robotic group had slightly better overall survival. Other perioperative characteristics, mortality and nodal upstaging, were similar in both groups. A multi-institution randomized trial should be considered before any one approach is deemed superior.

## American Society of Hematology (ASH)

097

### Konstantinoff, Katerina

American Society of Hematology (ASH)

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Internal Medicine

Division: Oncology

Mentor: Daniel Link, MD

#### **The role of megakaryocytes in G-CSF induced HSC mobilization**

Konstantinoff KS; Anthony BA; Link DC

**Introduction:** Granulocyte colony stimulating factor (G-CSF) is routinely used in the clinic to mobilize hematopoietic stem cells (HSCs) from the bone marrow to the blood for transplant. HSCs reside in specialized environments in the bone marrow where signals from surrounding stromal cells regulate HSC maintenance. It is known that G-CSF treatment decreases bone marrow CXCL12, a stromal cell factor key in HSC quiescence, and the loss of CXCL12 signaling through its receptor on HSCs results in their mobilization, but the details of how G-CSF suppresses CXCL12 are not yet fully understood. Fibroblast Growth Factors (FGFs) suppress CXCL12 in vitro and in vivo, and megakaryocytes are a major source of FGF1 in the bone marrow. GSEA of G-CSF-treated bone marrow shows a slight increase in FGFR1 signaling. Thus, we hypothesize that G-CSF alters megakaryocyte production of FGFs and that in turn suppresses CXCL12 production from stromal cells.

**Methods:** To determine if G-CSF regulates FGF expression in megakaryocytes, we grew megakaryocytes in culture, administered G-CSF, then looked at expression of FGF1, FGF2, and G-CSF receptor by qRT-PCR. We then treated WT mice with G-CSF to determine the effect on megakaryocytes during G-CSF-induced HSC mobilization. We measured changes in platelet number by CBC and changes in megakaryocyte number and morphology by IHC and flow cytometry at 1, 3, and 5 days of treatment. We also analyzed total bone marrow expression of FGF1 and FGF2 at these time points.

**Results:** We found that megakaryocytes express the G-CSF receptor, that G-CSF treatment results in mild thrombocytopenia by day 5 of treatment, and a loss of mature megakaryocytes in the bone marrow. Both in culture and in the G-CSF treated mice, we observed a decrease in FGF1 and FGF2 expression.

**Conclusions:** We determined that G-CSF can regulate FGF expression in megakaryocytes, and this project provides the groundwork for future experiments to further determine what role megakaryocyte FGFs play in HSC mobilization by G-CSF. We also wish to resolve if FGFR1 and FGFR2 signaling in bone marrow stromal cells contributes to HSC mobilization by G-CSF through postnatal deletion of FGFR1 and 2 in bone marrow stromal cells in vivo.

## Clinical Research Training Center (CRTC) KL2 Career Development Awards

- No Poster** **Ahmad, Fahd, MD, MSCI**  
CRTC KL2 Career Development Awards  
Washington University in St. Louis  
Department: Pediatrics  
Division: Pediatric Emergency Medicine  
Mentors: Tom Bailey, MD; Donna Jeffe, PhD; Chris Carpenter, MD, MSc  
**Developing a pediatric cervical spine injury risk assessment tool: methods for collecting paired observations from prehospital and ED providers**  
Ahmad FA; Browne LR; Schwartz H; Lassa-Claxton S; Wallendorf M; Leonard JC  
**Introduction:** Cervical spine injuries (CSIs) after blunt trauma in children are rare but cause significant morbidity. Emergency medical services (EMS) and emergency department (ED) providers utilize immobilization to prevent further injury and radiographs for CSI evaluation. However these practices may be harmful. An evidence-based guideline for CSI evaluation is needed. Creating such as tool requires prospective data collection from EMS and ED providers at the time of initial evaluation.  
**Methods:** This study is being conducted at four children's hospitals as a requisite for a planned larger study. We created a web-based, branch-logic questionnaire administered via an iPad to ED providers during their evaluation of children with blunt trauma, and to EMS personnel who provided scene response care. We collected information we determined a priori to be plausibly associated with CSI in children. Eligible children presented to the ED after blunt trauma and were spinal immobilized for scene transport, underwent trauma team evaluation, or received cervical spine imaging. Enrolled children were followed for 28 days to determine primary outcome of CSI by imaging review, or phone follow-up for those without imaging.  
**Results:** During RC hours, we prospectively screened 4983 children and enrolled 1736. 927 arrived by EMS scene response. EMS completed the survey for 60.2% (558/927) of enrolled patients, refused participation for 24 (2.6%), and were missed for 344 (37.1%). Of 626 missed eligible children, 276 (44.1%) were missed during RC hours. The capture rate for ED providers during RC hours was 86.3% (1736/2012). Of those missed during RC hours, 75 (27.1%) arrived by scene response EMS in spinal precautions. We enrolled 69% (29/42) of children with CSIs; of those missed, 84.6% (11/13) presented outside of RC hours.  
**Conclusions:** Our method demonstrates the ability to prospectively capture paired observations from EMS and ED personnel. The data will be used to create a risk assessment tool for CSI. It can be used to implement and evaluate this tool and as a model for studies requiring similar prospective data collection.
- No Poster** **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; Jeffrey F Peipert, MD, PhD  
**The incidence of post-partum infections at delivery, emergency department visit, and six week readmission in three large states**  
Bommarito KM; Fraser VJ; Olsen MA  
**Introduction:** To determine incidence of surgical site infection (SSI), endometritis (EMM), septicemia, urinary tract infection (UTI), and pelvic abscess during delivery admission, Emergency Department (ED) visit, and 6-week readmission stratified by delivery method in California, New York, and Florida.  
**Methods:** We used 2005-2011 HCUP CA, 2006-2012 NY, and 2005-2013 FL State Inpatient and ED Databases to determine the incidence of postpartum infections in women following vaginal and cesarean delivery. Infections were identified by ICD-9-CM diagnosis codes. Univariate analyses were performed, stratified by type of delivery.  
**Results:** A total of 5,502,603 deliveries (34.5% cesarean) were identified. Overall 186,555 (3.39%) of deliveries were coded for one or more of the following post-partum infections; SSI, EMM, septicemia, UTI, or pelvic abscess. In the cesarean delivery population, the postpartum infections identified in order of frequency were UTI (n=45,133), SSI (n=43,549), EMM (n=23,240), septicemia (n=3503), and pelvic abscess (n=2251). SSIs were most commonly first identified during an ED visit (44.7%), while EMM, septicemia, and UTI were most often first identified during the delivery hospitalization (76.1, 70.0, and 56%, respectively). In the vaginal delivery population, the postpartum infections identified in order of frequency were UTI (n=62,486), EMM (n=12,306), septicemia (n=3033), and pelvic abscess (n=2209). Pelvic abscess and septicemia were most commonly first identified during the delivery hospitalization (73.0 and 68.9% respectively), UTIs were first identified at delivery (50.0%) and at ED visit (41.4%), and EMM was most often identified at delivery (48.0%) and at readmission (42.0%).  
**Conclusions:** The proportion of patients diagnosed at delivery versus readmission or ED visit varied by type of postpartum infection. A higher proportion of septicemia and pelvic abscess cases were coded at delivery after cesarean and vaginal delivery. After vaginal delivery, a higher proportion of EMM cases were coded during a readmission and after cesarean most were coded at delivery. A higher proportion of UTI and SSI cases were diagnosed at ED visit compared to other infections. Surveillance should focus on identification of these infections before discharge from the delivery hospitalization.



**No** **Dhar, Rajat, MD**

**Poster** CRTCL2 Career Development Awards; CRTCL2 MSCI Degree Program

Washington University in St. Louis

Department: Neurology

Division: Neurocritical Care

Mentors: Jin-Moo Lee, MD, PhD; Carlos Cruchaga, PhD

**CSF volumetric analysis predicts malignant edema by 24-hours after large hemispheric infarction**

Dhar R; Yuan K; Kulik T; Ford A; Heitsch L; Chen Y; An H; Lee JM

**Introduction:** Malignant cerebral edema (MCE) is the leading cause of early death and neurologic deterioration after hemispheric infarction, but who is at highest risk is not well predicted by baseline clinical and radiographic variables. MRI estimation of infarct volume may provide an estimate of risk, but has limited widespread applicability. We propose that measuring change in cerebrospinal fluid ( $\Delta$ CSF) volume from baseline to follow-up (FU) CT scan at around 24 hours can predict MCE better than established variables.

**Methods:** We studied 33 stroke patients with baseline NIHSS (stroke scale)  $\geq 8$ , initial CT <6 hours of onset and FU CT at approx. 24 hours (median 18 hours, IQR 14-30). We outlined all CSF spaces (IL & CL sulci and ventricles) on both scans to quantify  $\Delta$ CSF, as well as volume of infarct-related hypodensity. We measured midline shift (MLS) on later CT with peak edema (n=20). We defined MCE as need for hemicraniectomy, osmotics, or deterioration/death with  $MLS \geq 5$ mm.

**Results:** 10 of 33 (30%) developed MCE. Baseline NIHSS did not differ (19 vs. 16,  $p=0.27$ ) but 24-hour NIHSS was higher in those with MCE (22 vs. 15,  $p=0.04$ ). CSF volume fell by 32 ml (22-54), a reduction of 32% from baseline.  $\Delta$ CSF was greater in those with MCE (41 vs. 28%,  $p=0.04$ ) and remained a predictor after adjusting for baseline & 24-hour  $\Delta$ NIHSS. Discriminative value was greatest for reduction in IL sulci volume (80 vs. 46%,  $p<0.001$ ), which also correlated strongly with peak MLS ( $r = -0.72$ ,  $p=0.003$ ). Hypodensity volume was greater in those with MCE (211 vs. 81 ml,  $p<0.001$ ) but only weakly correlated with peak MLS ( $r = 0.62$ ).  $\Delta$ CSF remained correlated with MLS after adjusting for infarct volume ( $p=0.025$  for IL sulci).

**Conclusions:**  $\Delta$ CSF measured on CT scan at 24-hours is a readily-accessible marker that was able to identify those at high-risk for MCE better than clinical variables.

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

**Poster** CRTCL2 Career Development Awards; CRTCL2 MSCI Degree Program

Washington University in St. Louis

Department: Neurology

Division: Neurocritical Care

Mentor: David Brody, MD, PhD

**Radiological biomarkers of early brain injury and neurobehavioral outcome in subarachnoid hemorrhage**

Kummer TT; Kim JH; Benetatos JJ; Milner E; Zipfel GJ; Brody DL

**Introduction:** Subarachnoid hemorrhage (SAH) is a deadly variant of hemorrhagic brain injury, carrying a 1-month mortality rate of approximately 40%. The most devastating consequences for survivors of SAH are neurocognitive, social, and emotional impairments. The causes of these deficits are unknown and invisible to clinical imaging tests. We recently found that SAH induces radiological and pathological axonal injury similar to that seen after trauma. As traumatic brain injury is also characterized by debilitating neurocognitive impairment, we sought to employ a mouse SAH model with paired histological and radiological analysis to determine whether axonal injury and other key early brain injury pathways are significant correlates of long-term neurobehavioral outcomes.

**Methods:** We examined the spatial and temporal evolution of three early brain injury pathways following SAH: axonal injury, microthrombosis, and ischemia. We furthermore developed a SAH induction and post-SAH screening protocol to model SAH-induced neurobehavioral deficits. Lastly, we developed advanced diffusion MRI approaches including diffusion kurtosis and generalized q-sampling imaging to define radiological biomarkers of early brain injury pathways, and to correlate these biomarkers with neurobehavioral outcomes.

**Results:** Quantitative histological approaches demonstrate unique gray and white matter distribution of studied injury pathways. Post-screening allowed measurement of neurobehavioral deficits in memory and cognition, in depression- and anxiety-related behaviors, and in social behavior. These impairments parallel those reported by patients after SAH. Advanced diffusion approaches provide superior signal-to-noise compared to diffusion tensor imaging, especially in gray matter, and provide unique contrast.

**Conclusions:** These results lay the groundwork for correlative and mechanistic analysis of these outcomes using clinically translatable radiological biomarkers. Defining the key injury sites and pathways underlying neurobehavioral impairments using this approach should facilitate development of precision treatments and parallel testing of injury-outcome correlations in patients.

040

**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

**Effect of sleep deprivation and sodium oxybate on CSF A $\beta$ 40 and A $\beta$ 42**

Lucey BP; Hicks TJ; McLeland J; Toedebusch C; Boyd J; Mawuenyega KW; Ovod V; Kasten T; Morris JC; Bateman RJ

**Introduction:** Studies in both transgenic mice that develop amyloid deposition and humans found that the concentration of amyloid- $\beta$  (A $\beta$ ), a key protein in the pathogenesis of Alzheimer's disease, fluctuates with the sleep-wake cycle as a diurnal pattern. A $\beta$  increases with sleep deprivation and decreases with administration of a sleep-inducing medication. Animal studies suggest that A $\beta$  concentration and deposition may be modifiable through manipulation of the sleep-wake cycle. The purpose of this study is to determine if A $\beta$  concentrations in the human central nervous system are modifiable through manipulation of sleep.

**Methods:** To determine if sleep manipulation affects A $\beta$  concentrations in the human central nervous system, we collected serial cerebrospinal fluid (CSF) samples via intrathecal lumbar catheter every 2 hours for 36 hours in 25 adults 18-60 years old during behavioral sleep deprivation (N=8), pharmacologic sleep induction with sodium oxybate (N=9), and control (N=8). A $\beta$ 40 and A $\beta$ 42 isoforms were quantitated by mass spectrometry. Sleep-wake activity was monitored with polysomnography.

**Results:** We found that concentrations of A $\beta$ 40 and A $\beta$ 42 increased 35-50% over 36 hours of sleep deprivation compared to control. This increase occurred during the sleep period, hours 18-24 or 01:00-07:00. Participants treated with sodium oxybate have not shown a significant change in A $\beta$  concentration compared to control, although study recruitment is on-going.

**Conclusions:** Sleep is hypothesized to be the primary driver of the A $\beta$  diurnal pattern and these data suggest that manipulation of this pattern may alter A $\beta$  concentrations in human CSF. Since changes in A $\beta$  concentration of 25-40% have been associated with causing or preventing Alzheimer's disease, manipulation of sleep has potential as a preventive therapy. Although the sleep induction group has not significantly decreased A $\beta$  concentrations compared to controls, our participants were screened to eliminate sleep disorders and individuals with poor sleep quality. Future investigations will be needed to assess if A $\beta$  concentrations are increased in individuals with poor sleep quality compared to controls and if this increase can be normalized with a sleep-inducing medication.

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, MS; Sarah Gehlert, PhD

**Hospital discharge summary receipt by community health centers: a chart review study**

Nagasako EM; Schenk E; Stoermer A

**Introduction:** The handoff from hospital providers to providers in the community is the foundation for safe transitions of care for patients traversing the inpatient and outpatient settings. However, results from a 2014 survey of St. Louis region community health center (CHC) primary care providers suggest that providers inconsistently receive transitions of care communication from inpatient providers. To better characterize the receipt of discharge summaries by community health center providers, we are auditing the current rates of discharge summary transmission to specific community health centers using chart review.

**Methods:** Observational, retrospective chart review. Data will be abstracted from both hospital and community health center electronic health records. Fields abstracted will include the date and time of discharge, date and time of the initial signature, date and time of finalization by attending, whether the summary was received and, if received, the date and time the summary was received. The primary outcome measure will be the number of summaries received by the health center within 24 hours of patient discharge divided by the number of eligible CHC patient discharges. Secondary measures will include the number of discharge summaries received by the health center at various time intervals after discharge, and stratification of results by CHC affiliation and by whether a health center physician was listed as a referring physician or family MD in the physician discharge summary.

**Results:** We anticipate that results will help better characterize the degree to which discharge summary information is available to community health center providers and provide preliminary information on the factors that may affect discharge summary transmission to these providers.

**Conclusions:** A better understanding of discharge summary transmission to community health center providers and the factors contributing to receipt of these summaries by providers will help direct quality improvement activities by highlighting areas where the risk of adverse post-discharge outcomes can be reduced through improved hospital-provider communication.

060

**Palanca, Ben, MD, PhD, MSCI**

CRTC KL2 Career Development Awards

Washington University in St. Louis

Department: Anesthesiology

Division: Clinical and Translational Research

Mentors: Marcus Raichle, MD; Michael Avidan, MBBCh; Joseph Culver, PhD

**Resting-state functional magnetic resonance imaging correlates of sevoflurane-induced unconsciousness**

Palanca BJ; Mitra A; Larson-Prior L; Snyder AZ; Avidan MS; Raichle ME

**Introduction:** The mechanisms whereby anesthetic agents induce profound derangements of consciousness and cognition remain incompletely understood. Blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI) has been used to study the effects of anesthetic agents on correlated intrinsic neural activity. Previous studies have focused primarily on intravenous agents. The authors studied the effects of sevoflurane, an inhaled anesthetic.

**Methods:** Resting-state BOLD fMRI was acquired from 10 subjects before sedation and from 9 subjects rendered unresponsive by 1.2% sevoflurane. The fMRI data were analyzed taking particular care to minimize the impact of artifact generated by head motion.

**Results:** BOLD correlations were specifically weaker within the default mode network and ventral attention network during sevoflurane-induced unconsciousness, especially between anterior and posterior midline regions. Reduced functional connectivity between these same networks and the thalamus was also spatially localized to the midline frontal regions. The amplitude of BOLD signal fluctuations was substantially reduced across all brain regions. The importance of censoring epochs contaminated by head motion was demonstrated by comparative analyses.

**Conclusions:** Sevoflurane-induced unconsciousness is associated with both globally reduced BOLD signal amplitudes and selectively reduced functional connectivity within cortical networks associated with consciousness (default mode network) and orienting to salient external stimuli (ventral attention network). Scrupulous attention to minimizing the impact of head motion artifact is critical in fMRI studies using anesthetic agents.

084

**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

**Pharmacoepidemiology of cytomegalovirus prophylaxis in a large retrospective cohort of kidney transplant recipients with Medicare Part D coverage**

Santos CAQ; Brennan DC; Saeed MJ; Fraser VJ; Olsen MA

**Introduction:** Cytomegalovirus (CMV) prophylaxis or preemptive treatment are recommended for seronegative recipients of kidneys from seropositive donors (D+/R-) and seropositive patients (R+), but not D-/R- patients. Real-world use of CMV prophylaxis for US kidney transplant recipients has never been examined using prescription drug claims data.

**Methods:** We assembled a cohort of 21,117 kidney transplant patients from July 2006 to June 2011 with Medicare Part D coverage using US Renal Database System (USRDS) data to determine prescription of CMV prophylaxis, defined as daily oral valganciclovir ( $\leq 900$  mg), ganciclovir ( $\leq 3$  g) or valacyclovir (6-8 g) prescribed within 7 days of transplant hospitalization discharge. Non-nested multilevel logistic regression analyses were performed to determine factors associated with CMV prophylaxis.

**Results:** CMV prophylaxis (96% valganciclovir) was prescribed to 71% of kidney transplant recipients (median duration, 89 days); 83% of D+/R- patients; 74% of R+ patients; 71% of patients with unknown serostatus; and 40% of D-/R- patients. Variability in prophylaxis prescription among transplant centers was greater than variability within transplant centers. Eighteen percent of transplant centers prescribed CMV prophylaxis to  $> 80\%$  of their D-/R- patients. CMV donor/recipient serostatus, lymphocyte-depleting agents for induction and mycophenolate for maintenance immunosuppression were associated with the prescription of CMV prophylaxis.

**Conclusions:** CMV prophylaxis was commonly used among kidney transplant recipients. Routine prescription of CMV prophylaxis to D-/R- patients may have occurred in some transplant centers. Limiting unnecessary use of CMV prophylaxis may decrease healthcare costs and drug-related harms.

- No Poster** **Smith, Gordon, PhD**  
CRTC KL2 Career Development Awards  
Washington University in St. Louis  
Department: Center for Human Nutrition  
Division: Geriatrics and Nutritional Sciences  
Mentors: Bettina Mittendorfer, PhD; Brian Finck, PhD  
**The muscle anabolic and function enhancing effects of n-3 PUFA treatment appear to be, at least in part, transcriptionally regulated**  
Smith GI; Yoshino J; Stromsdorfer KL; Kelly SC; Julliard S; Reeds DN; Mittendorfer B  
**Introduction:** Dietary fish oil-derived n-3 PUFA supplementation can increase muscle mass, reduce oxygen demand during physical activity and improve physical function (including muscle strength and power, and endurance). Results from studies conducted in vitro and in vivo in animals suggest that the anabolic and performance-enhancing effects of n-3 PUFA are at least in part transcriptionally regulated. The effect of n-3 PUFA therapy on the muscle transcriptome in people is unknown. Accordingly, the goal of our study was to test the hypothesis that fish oil-derived n-3 PUFA therapy increases the expression of genes involved in mitochondrial function and anabolic and regenerative pathways and decreases the expression of genes involved in autophagy and atrophy in muscle.  
**Methods:** We evaluated: 1) the expression of multiple gene set pathways known to be involved in regulating mitochondrial function, cell growth, and structural support by using the microarray technique and 2) the gene expression of MYOD1, MSTN, FST (muscle anabolism/hypertrophy), TIMP1, MMP14, MEGF10 (regeneration), GBARAP, LC3, ATOH8 (autophagy), and FOXO3, MAFBX, MURF1 (atrophy) by using quantitative RT-PCR in skeletal muscle biopsies of older adults who participated in a 6-month long double-blind, randomized controlled trial (RCT) that evaluated the effect of n-3 PUFA therapy on muscle volume and strength (Smith et al., Am J Clin Nutr, 102, 115-22, 2015).  
**Results:** We found that although the expression of a few select genes (assessed by RT-PCR) known to be involved in muscle hypertrophy (MYOD1, MSTN, FST), regeneration (TIMP1, MMP14, MEGF10), atrophy (FOXO3, MAFBX, MURF1), and autophagy (GBARAP, LC3, ATOH8) was not affected by n-3 PUFA therapy, several gene set pathways involved in regulating mitochondrial function and extracellular matrix organization were increased (Z-scores ranging from 1.96 to 4.26;  $P < 0.05$ ) and pathways related to calpain- and ubiquitin-mediated proteolysis and inhibition of the key anabolic regulator mTOR (Z-scores ranging from -2.13 to -3.48;  $P < 0.05$ ) were decreased by n-3 PUFA therapy.  
**Conclusions:** The beneficial effects of n-3 PUFA on muscle mass and function in older adults are, at least in part, transcriptionally regulated.
- 122** **Vesoulis, Zachary, MD**  
CRTC KL2 Career Development Awards; CRTC MSCI Degree Program  
Washington University in St. Louis  
Department: Pediatrics  
Division: Newborn Medicine  
Mentors: Amit Mathur, MD; Joseph Culver, PhD  
**Empirical estimation of the normative blood pressure in infants <28 weeks gestation using a massive data approach**  
Vesoulis ZA; El Ters N; Wallendorf M; Mathur AM  
**Introduction:** Determining the target blood pressure range in very preterm infants (<28 weeks gestation) has been the subject of debate for several decades. Description of a normative set of blood pressure values in very preterm infants is confounded by varied methodology, heterogeneous patient populations used in prior studies, substantial changes in strategies for hemodynamic support and monitoring methodology, and survival rates among preterm infants. The specific aim was to determine the expected systolic, mean and diastolic blood pressures at birth and respective rates of change during the first 72 hours of life in infants born <28 weeks estimated gestational age (EGA) with a favorable short-term outcome, defined as survival to 14 days with grade II or less IVH.  
**Methods:** Systolic, mean and diastolic blood pressures were continuously sampled at 0.5 Hz via umbilical artery catheter from birth through 72 hours. The raw data were aligned by postnatal hour and underwent error correction. For each infant, the mean values of systolic, mean and diastolic blood pressure were calculated for each postnatal hour. The slope and intercept of best-fit line for each of the three blood pressure parameters was then calculated. Infants that received inotropic medications, died in the first 14 days of life, or had IVH grade III or IV were excluded.  
**Results:** Using 11.9 million valid data points from 35 infants (mean EGA =  $25.7 \pm 1.5$  weeks, mean birth weight =  $865 \pm 201$  grams), we found independent associations of African-American race ( $p < 0.01$ ) and a complete course of antenatal steroids ( $p < 0.01$ ) with higher blood pressures at birth and a slower rate of increase. Acute chorioamnionitis was independently associated ( $p = 0.02$ ) with lower blood pressures at birth and a faster rate of increase. EGA and birth weight were not independently predictive of blood pressure parameters.  
**Conclusions:** We found that (i) the estimated mean blood pressure at birth is approximately 33 mmHg in a cohort of very preterm infants (ii) blood pressure gradually increases with postnatal age (iii) systolic blood pressure increases at a faster rate than diastolic blood pressure, (iv) race, antenatal steroid exposure, and chorioamnionitis are independent modulators of blood pressure while EGA and birth weight are not. These results suggest a normative blood pressure higher than previously suggested.

**Vouri, Scott, PharmD, MSCI**

CRTC KL2 Career Development Awards

St. Louis College of Pharmacy

Department: Pharmacy Practice

Mentors: Margaret Olsen, PhD, MPH; Mario Schootman, PhD

**Harms of antimuscarinics for the treatment of overactive bladder in older adults: a systematic review and meta-analysis**

Vouri SM; Kebodeaux CD; Stranges PM; Teshome B

**Introduction:** Overactive bladder (OAB) is a condition that negatively impacts 25% of the older adult population. Antimuscarinics, a treatment option for OAB, should be used with caution in older adults due to the potential for adverse drug events (ADEs) including dry mouth, blurry vision, and constipation. Studies have also shown an association between ADEs and high discontinuation rates. Systematic reviews and meta-analyses (SMRAs) have analyzed efficacy and safety; however, these did not differentiate based on age. We performed an exploratory SRMA to evaluate harms (ADEs and treatment discontinuations) in adults 65 or older taking antimuscarinics for OAB.

**Methods:** We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement for reporting this review. Randomized controlled trials (RCTs) along with sub-analyses and pooled analyses of parent RCTs that compared antimuscarinics (oxybutynin, tolterodine, trospium, solifenacin, darifenacin, fesoterodine) to placebo or another antimuscarinic were included. We searched MEDLINE, EMBASE, SCOPUS, and Cochrane Central Register for Controlled Trials. Duplicates and non-relevant studies were removed by the primary investigator. Full-text articles were screened and extracted by two separate authors. Jadad Criteria and McHarm Tool were used to assess the quality of the included and parent studies.

**Results:** A total of 16 of the 26,166 studies that were reviewed met the inclusion criteria. An additional 16 parent studies of pooled and sub-analysis studies were also reviewed to assess the Jadad Criteria and McHarm Tool. Eighty adverse events and 27 reasons for treatment discontinuation were noted. Adverse events and anticholinergic ADEs were more common in antimuscarinics compared to placebo. There were also significantly higher rates of dizziness (Number Need to Harm, (NNH)=70), dyspepsia (NNH=48), and urinary retention (NNH=66) with fesoterodine, headache (NNH=73) with darifenacin, and urinary tract infection (NNH=35) with solifenacin.

**Conclusions:** This exploratory SRMA confirmed the risk of anticholinergic ADEs in older adults. Less well-known ADEs were also identified and can be further explored using observational data.

## Clinical Research Training Center (CRTC) K12 Paul Calabresi Career Development Awards for Clinical Oncology

- 074**      **Campian, Jian, MD, PhD**  
CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Oncology  
Mentors: John F DiPersio, MD, PhD; Gerald Linette, MD, PhD  
**Lymphopenia in elderly patients with glioblastoma treated with radiation and temozolomide**  
Mendez J; Govindan A; Huang J; Campian JL  
**Introduction:** Management of elderly patients with high grade glioma often includes radiation therapy (RT) +/- temozolomide (TMZ). A previous report showed that standard RT/TMZ resulted in severe lymphopenia in 40% of patients (median age of 57) with an associated shorter survival (Grossman, 2011). Similar findings were described in patients with head and neck, non-small cell lung, and pancreatic cancer. This study is designed to evaluate whether elderly patients (age >65) with glioblastoma (GBM) develop severe treatment-related lymphopenia after RT/TMZ and whether treatment-related lymphopenia is associated with reduced survival.  
**Methods:** Elderly patients (age >=65) newly diagnosed with GBM and followed-up at Washington University (2000-2013) were eligible. Radiation parameters and serial total lymphocyte counts (TLC) were collected.  
**Results:** Seventy-two patients were eligible: median KPS 70, median age 71 years (range 65 – 86) with 56% of patients >70 years, 53% female, 32% received RT <6 weeks, 44% had a baseline TLC <1000 cells/mm<sup>3</sup> with 84% taking glucocorticoids. Baseline median TLC prior to treatment was 1100 cells/mm<sup>3</sup> with a fall by 45% at 2 months (median 600 cells/mm<sup>3</sup>, range 100-2500 cells/mm<sup>3</sup>). At 2 months, 21% of patients had a drop in TLC to <500 cells/mm<sup>3</sup> (median 400 cells/mm<sup>3</sup>, range 100-400 cells/mm<sup>3</sup>). Patients with TLC <500 cells/mm<sup>3</sup> at 2 months had a shorter survival than those with TLC >=500 cells/mm<sup>3</sup> with a median overall survival of 6.9 vs 10.1 months, respectively. Multivariate analysis revealed a significant association between treatment related lymphopenia and survival (HR 2.36, 95%CI 1.13-4.93, p=0.023).  
**Conclusions:** Chemoradiation induced lymphopenia is frequent, severe, and an independent predictor for survival in elderly patients with GBM. These findings add to the body of evidence that immunosuppression induced by chemoradiation is associated with inferior clinical outcomes.
- 076**      **Shirai, Cara, PhD**  
CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Oncology  
Mentors: Matthew J Walter, MD; Daniel C Link, MD  
**Preclinical activity of splicing modulators in U2AF1 mutant MDS/AML**  
Shirai CL; Tripathi M; Ley JN; Ndonwi M; White BS; Tapia R; Kim S; Webb TR; Graubert TA; Matthew JW  
**Introduction:** Myelodysplastic syndromes (MDS) are the most common myeloid malignancies in adults. Spliceosome gene mutations are detectable in ~50% of MDS patients, making this the most commonly mutated cellular pathway in MDS and providing a novel therapeutic target. Our group and others identified recurrent heterozygous missense mutations in the splicing factor gene U2AF1 in 11% of MDS patients. We previously reported that in vivo expression of mutant U2AF1 in transgenic mice resulted in expansion of hematopoietic progenitor cells and leukopenia, both phenotypes seen in MDS patients. We also identified mutant U2AF1-specific alterations in pre-mRNA splicing in transgenic mouse cells and primary human MDS and acute myeloid leukemia (AML) patient samples. We hypothesize that cells harboring spliceosome gene mutations have increased sensitivity to pharmacological perturbation of the spliceosome by splicing modulator drugs, providing a new treatment approach for patients with U2AF1 mutations.  
**Methods:** For our studies, we use sudemycin compounds that bind the SF3B1 spliceosome protein and modulate pre-mRNA splicing. We performed in vitro and in vivo studies to examine the sensitivity of cells expressing mutant U2AF1 to sudemycin.  
**Results:** Primary human MDS/AML cells with U2AF1 mutations display increased sensitivity to sudemycin compared to non-mutant controls in a cell cycle (EdU incorporation) assay (n=3); treatment with daunorubicin showed no specificity for mutant U2AF1(S34F) samples compared to non-mutant controls. Primary mouse bone marrow cells transduced with a retrovirus expressing mutant U2AF1 display an increase in apoptosis (by Annexin V+) in response to increasing concentrations of sudemycin compared to controls (p<0.001, n=3-5). In addition, in vivo treatment of mutant U2AF1 transgenic mice with sudemycin resulted in attenuation of hematopoietic progenitor cell expansion by colony forming unit (CFU-C) assay (p<0.01, n=6-11) and by flow cytometry for lineage-, c-Kit+, Sca-1+ (KLS) cells (p<0.001, n=6-11).  
**Conclusions:** Together, these data suggest that we may be able to specifically treat hematological cancers with U2AF1 mutations using pre-mRNA splicing modulators such as sudemycin.

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**Verdoni, Angela, PhD**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Oncology  
Mentor: Tim Ley, MD

**Specific patterns of accurate DNA remethylation in the bone marrow cells of Dnmt3a deficient mice with induced expression of wild type human DNMT3A**

Verdoni AM; Ketkar S; Helton NM; Cole CB; Venezia CS; Fronick C; O'Laughlin M; Fulton RS; Spencer DH; Ley TJ

**Introduction:** We previously identified recurrent mutations in the de novo DNA methyltransferase DNMT3A in patients with acute myeloid leukemia (AML). The most common DNMT3A mutation in AML (R882H) creates a dominant negative protein that reduces DNA methylation activity by ~80% in AML cells, and causes canonical patterns of DNA hypomethylation in the AML genome. Approaches to restore DNMT3A activity in these AML genomes may be therapeutically relevant, but only if patterns of remethylation are accurate, restoring these genomes to their native methylation state. To begin to address whether DNA methylation can be restored in hematopoietic cells that are deficient for Dnmt3a, we performed an "add-back" experiment using a transgenic mouse model system.

**Methods:** We carried out whole genome bisulphite sequencing (WGBS) on DNA derived from the bone marrow cells of wild type mice, mice with a deletion in Dnmt3a, and mice with this deletion as well as expression of a wild type human DNMT3A transgene at various timepoints.

**Results:** Total bone marrow cells from Dnmt3a<sup>-/-</sup> mice show a canonical pattern of DNA hypomethylation at specific CpG residues and regions in the genome. Differential methylation analysis was performed on 2kb tiled windows across the whole genome, revealing 108,797 differentially methylated regions (DMRs) that were virtually all hypomethylated. After two weeks of human DNMT3A transgene expression, 59% of these DMRs were remethylated, increasing to 83% remethylation by week 9. Most CpGs are remethylated after only 2 weeks of DNMT3A expression, but some lag, and are remethylated later. A small subset of these CpGs remethylate very slowly, if at all. Inspection of specific regions of the genome showed that regions that are normally unmethylated in the bone marrow cells of WT mice are rarely methylated by adding back human DNMT3A in this system, showing that remethylation is highly specific and accurate.

**Conclusions:** Although the mechanisms involved in specifying remethylation are not yet clear, these data may have important implications for therapeutically restoring DNMT3A activity in AML patients with DNMT3A mutations that reduce its activity.

**No  
Poster**

**Waqar, Saiama, MBBS, MSCI**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology  
Washington University in St. Louis  
Department: Internal Medicine  
Division: 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.

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**White, Brian, PhD**

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

**Meta-analysis increases power and reduces false discoveries in detecting alternative splicing**

White BS; Shirai CL; Ley JN; Ndonwi M; Okeyo-Owuor T; Kim S; Graubert TA; Walter MJ

**Introduction:** Published RNA-seq studies of the effects of cancer-associated spliceosome mutations, such as in U2AF1, have failed to consistently nominate common alternative splicing (AS) events. This study aims to determine whether study sample size is a likely contributor to this effect and how it can be mitigated.

**Methods:** We analyzed an RNA-seq study of transgenic mouse common myeloid progenitor (CMP) cells expressing an S34F U2AF1 mutation (n=3) or U2AF1 (WT; n=3). We used Fisher's method to combine the mouse results with results from a data set of primary human CD34+ hematopoietic cells transfected with WT or S34F U2AF1 and from The Cancer Genome Atlas (TCGA) acute myeloid leukemia (AML) data set of patient samples with S34F U2AF1 mutations or without splicing factor mutations.

**Results:** We performed six leave-out-one (LOO) analyses of the CMP data, in which each of the six samples was excluded from analysis, with AS events detected in the subset compared to those detected in full data set. A typical analysis showed that the LOO data set achieved low power (~50-70%) and high eFDR (~40-50%) relative to the full data set. These poor results suggest that analysis of the full data set is highly dependent on sample size. Meta-analysis using Fisher's method to combine the mouse CMP data set with the CD34+ and AML data sets, as in our published results, dramatically improved power (> 80%) and eFDR (< 20%). Meta-analysis resulted in a set of 555 concordantly dysregulated junctions, including in genes associated with cancer (GNAS, PICALM, BCOR, DIS3, KDM6A) or involved in stem cell biology (H2AFY, MED24). Additionally, the set has a highly statistically significant enrichment for spliceosome genes (p-value:  $5 \times 10^{-8}$ ). These results suggest, but do not guarantee, that meta-analysis mitigates the sensitivity of analysis to small sample sizes.

**Conclusions:** Our leave-out-one (LOO) analyses suggest that typical RNA-seq splicing data set sizes (n=3) are unable to differentiate biologically-relevant AS from noise. This effect can be mitigated by meta-analysis, which increases power to detect true AS events and reduces false discovery of AS events.

No  
Poster

**Wildes, Tanya M, MD, MSCI**

CRTC K12 Paul Calabresi Career Development Awards for Clinical Oncology  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Medical Oncology  
Mentors: Graham Colditz, DrPH, MD, MPH; Nancy Morrow-Howell, PhD

**Geriatric assessment predicts survival after hospitalization in older adults with cancer**

Wildes TM; Jonna S; Chiang L; Liu J

**Introduction:** Improved prediction of survival among older adults with cancer is necessary to facilitate decision-making and advance care planning.

**Methods:** We undertook a retrospective cohort study of 803 individuals who were admitted to the Acute Care for Elders-Oncology unit at Barnes-Jewish Hospital 2000-2008. Geriatric assessment was performed as routine clinical care. Overall survival was defined as time from index admission to death, censored at last follow-up. Survival analysis using Cox proportional hazard modeling was performed.

**Results:** Median age was 73.4 (range 40-96); 51.8% male; 77% white, 21% black, 2% other race/ethnicity. Most (56.4%) had stage IV or metastatic cancer, and only 23.7% were receiving treatment with curative intent; 8.1% were discharged with hospice services. The median length of stay was 6 days (range 1-117); 253 (31.4%) were readmitted within 30 days of discharge. Geriatric syndromes were extremely common. Over 80% had comorbidities using the ACE-27 comorbidity index (47.5% mild, 23.5% moderate, 10.6% severe). The median number of medications on admission and discharge was 6 (range 0-24) and 7 (0-36) respectively. Nearly one-third of patients (30%) were on one or more medication considered inappropriate in older adults by Beers criteria. Over half of patients (50.4%) were dependent in one or more activities of daily living (ADLs); 74% were dependent in at least one instrumental activity of daily living (IADLs). 43% either screened positive for cognitive impairment by the Short Blessed Test, the Clock Construction test or a diagnosis of dementia. On multivariate analysis, factors associated with survival included male gender [HR1.23 (CI1.03-1.46)], type of cancer [1.66 (1.38-1.99)], reason for admission [1.29 (1.08-1.54)], readmission after index hospitalization [1.49 (1.23-1.80)], discharge with hospice [3.64 (2.58-5.15)], IADL dependence [1.33 (1.11-1.60)], and cognitive impairment [1.23 (1.02-1.47)].

**Conclusion:** We identified factors independently associated with shorter survival following a hospitalization in older adults with cancer which may aid patients, clinicians and families with decision-making about cancer treatment.



## Clinical Research Training Center (CRTC) Master of Science in Clinical Investigation (MSCI) Degree Program

- 073 Alahmari, Bader, MBBS**  
CRTC MSCI Degree Program  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Oncology  
Mentors: John DiPersio, MD, PhD; Jaebok Choi, PhD  
**Targeting  $\alpha 4$  Integrin (CD49d) to Reduce GvHD**  
Alahmari BA; Choi J; Cooper ML; Vij K; Ritchey J; DiPersio JF  
**Introduction:** Acute graft versus host disease (aGvHD) is a life-threatening condition that complicates allogeneic hematopoietic cell transplantation (allo-HCT). Donor T cells recognize the recipient's tissues as foreign causing GvHD. In this study, we examined if inhibition of  $\alpha 4$  integrin subunit, which is required for transendothelial migration and access to GvHD target organs, could reduce GvHD.  
**Methods:** To genetically eliminate  $\alpha 4$  from allogeneic donor T cells, we generated Tie-2 cre+  $\alpha 4^{fl/fl}$  mice (B6, H-2b, CD45.2+). Splenic pan T cells were isolated from these mice and T cell-depleted bone marrow cells (TCD BM) isolated from congenic B6 mice (CD45.1+).  $5 \times 10^6$  TCD BM and  $5 \times 10^5$  splenic pan T cells were transplanted into lethally irradiated (900 cGy) allogeneic Balb/c recipient mice (H-2d, CD45.2+).  
**Results:** We found that  $\alpha 4^{-/-}$  T cells significantly reduced GvHD compared to Tie-2 cre+ control T cells. In addition, recipients transplanted with  $\alpha 4^{-/-}$  T cells had significantly lower histopathology score (median score 3 vs.6;  $p=0.0263$ ). To test whether  $\alpha 4^{-/-}$  T cells maintain GvL we performed bioluminescence imaging (BLI) using a systemic leukemia mouse model. CBRluc-expressing A20 leukemia cells (Balb/c-derived) were transplanted intravenously ( $1 \times 10^5$  cells) along with TCD BM (B6) into Balb/c recipients at day 0. Pan T cells either from Tie-2 cre+ or  $\alpha 4^{-/-}$  mice were infused at day 11. After weekly BLI, we found  $\alpha 4^{-/-}$  T cells were able to control leukemia cells as effectively as Tie-2 cre+ T cells. In addition, we performed BLI to track CBRluc-transduced pan T cells ( $2 \times 10^6$  cells) after allo-HCT in vivo. We found a significant difference in the percentage of BLI signal intensity between control and  $\alpha 4^{-/-}$  T cells in spleen and gut at day 14 and 21 post allo-HCT. In addition,  $\alpha 4^{-/-}$  T cells significantly upregulate CTLA-4 and GZMB compared to control T cells.  
**Conclusions:** These data suggest that not only altered T cell trafficking to GvHD target organs but also altered T cell functions might be the reason for the reduced GvHD. We propose that  $\alpha 4$  represents a promising therapeutic target for future efforts to mitigate GvHD after allo-HCT.
- 059 Cavallone, Laura Francesca, MD**  
CRTC MSCI Degree Program  
Washington University in St. Louis  
Department: Anesthesiology  
Division: Clinical and Pain  
Mentors: Robert Gereau, PhD; Evan Kharasch, MD, PhD  
**Pharmacokinetics and anti-hyperalgesic efficacy of the mglu5 antagonist fenobam**  
Cavallone LF; Montana MC; Frey K; Kharasch ED; Gereau RW  
**Introduction:** G-protein coupled metabotropic glutamate receptor 5 (mGlu5) has been demonstrated to modulate nociception in rodents. The investigational compound fenobam [N-(3-chlorophenyl)-N'-(4,5-dihydro-1-methyl-4-oxo-1H-imidazole-2-yl)urea] is a selective antagonist of mGlu5. Preclinical data suggest that fenobam is analgesic via an mGlu5 specific mechanism in rodents, and no analgesic tolerance or significant side effects develop with repeated dosing. With the aim of translating these promising preclinical results in humans, our current study investigates the pharmacokinetics and side effects profile of three doses (50 mg, 100 mg, and 150 mg) of orally administered fenobam, and tests the hypothesis that fenobam will reduce measures of hyperalgesia in a model of central sensitization in healthy human volunteers compared to placebo.  
**Methods:** After IRB approval 32 healthy, 18-50 year-old volunteers, received either 50, 100, or 150 mg of oral fenobam or placebo in a double blinded fashion. Plasma samples were then collected at multiple time points to measure fenobam concentration. Subjects were also assessed for side effects. The effects of fenobam on central sensitization were evaluated in a randomized, double-blinded, two-way, cross-over trial with 32 additional volunteers who received either 150 mg fenobam or placebo and were then exposed to the heat capsaicin model of cutaneous sensitization in two consecutive sessions, one week apart.  
**Results:** Fenobam reaches peak plasma concentration between 2 and 5 hours after oral administration with pronounced inter-individual differences. No significant side effects were detected. Skin sensitization with the heat capsaicin model was obtained and verified in our conditions, and we hypothesize we will observe an effect of fenobam on measures of sensitization.  
**Conclusions:** Oral fenobam administration in human subjects demonstrates variable, but dose dependent plasma concentrations without significant clinical side effects. Measurable effects of fenobam in a human model of central sensitization would strengthen the evidence supporting the analgesic potential of negative modulation of mGlu5 in pathological pain in humans.

## Clinical Research Training Center (CRTC) TL1 Predoctoral Interdisciplinary Clinical Research Training Program

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### Boozalis, Amanda

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

Mentor: Jeffrey F Peipert, MD, PhD

#### Changes in libido with hormonal contraception

Boozalis AL; Tutlam NT; Chrisman Robbins C; Peipert JF

**Introduction:** Six-month discontinuation rates for contraceptives are high, and unintended pregnancy often follows contraceptive discontinuation. Side effects are cited as the most common reason for stopping contraceptive use, and sexual side effects specifically are commonly reported by contraceptive users. At present, there are conflicting data on whether there exists a link between hormonal contraceptives and libido. Oral contraceptives have been studied extensively in this regard and have been found not to affect libido in a majority of women. However, the effects of other forms of hormonal contraception on libido have not been studied as comprehensively as oral contraceptives. The purpose of this analysis was to examine differences in libido across women using different forms of contraception.

**Methods:** We analyzed data from 1,938 participants enrolled in the Contraceptive CHOICE Project, a prospective cohort study of women who were offered no-cost reversible contraception. Our primary objective was to compare rates of loss of libido between women using different contraceptive methods. We collected data about loss of sexual desire from questionnaires administered six months after enrollment in the CHOICE Project. We used logistic regression to assess the association between contraceptive method and loss of sex drive, controlling for potential confounding factors.

**Results:** Loss of libido was reported by 23.9% of women in our cohort. Reported decreased libido is more prevalent in women who are young (<18 years: adjusted odds ratio (ORadj)=2.04, 18-20: ORadj =1.55), black (ORadj =1.78), and married or living with a partner (ORadj =1.82). We observed a significant reduction of libido in participants who used the subdermal contraceptive implant (ORadj =1.60, 95% confidence interval (CI)=1.03-2.49), depot medroxyprogesterone (DMPA) injection (ORadj =2.61, 95% CI=1.47-4.61), and contraceptive vaginal ring (ORadj =2.53, 95% CI=1.37-4.69).

**Conclusions:** We found a significant reduction of libido in women who used the contraceptive implant, DMPA injection, and vaginal ring. We found no significant association between other FDA-approved reversible contraceptive methods, including the copper and hormonal IUDs, oral contraceptive pill, and contraceptive patch, and reduction of libido. Future research should confirm these findings and explore the physiological basis of these results, as changes in sex drive are an important factor in women's satisfaction with and continuation of their contraceptive method.

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### Britt, Daniel

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

Current Doctoral Program of Study: Pharmacy

St. Louis College of Pharmacy

Department: Neurology

Division: Knight Alzheimer's Disease Research Center (ADRC)

Mentors: John Morris, MD; Gregory Day, MD

#### Evaluating the cognitive impact of medications in Alzheimer disease

Britt DMI; Morris J

**Introduction:** Alzheimer disease (AD) is the most common cause of dementia for individuals over the age of 65. In addition to AD, advancing age brings other chronic illnesses that require multiple prescriptions to reduce morbidity and mortality. Bupropion, oxybutynin, and furosemide are all common medications that have been found to cause cognitive impairment in cognitively normal adults >65. Will these same medications cause a greater cognitive decline in preclinical AD compared to cognitively normal individuals? Will these same medications cause a greater cognitive decline in AD compared to cognitively normal individuals? The aim of this study will be to calculate the magnitude of effect of these offending medications on participants with normal cognition, preclinical AD, and symptomatic AD.

**Methods:** This study is a retrospective cohort study utilizing the Knight Alzheimer Disease Research Center (ADRC) database. Participants will be divided into four different cohorts depending on cognitive impairment - no AD, preclinical AD stage 1, preclinical AD stage 2, and symptomatic AD. After dividing participants into their respective cohorts, they will further be divided into cohorts consisting of prescribed and not prescribed offending medication. The non-parametric Wilcoxon rank-sum test will allow comparison of cognitive performance and functional impairment within each cohort and between cohorts.

**Results:** This research is currently ongoing with hopes to finish it within the academic year. The anticipated results include seeing a greater decline in cognitive performance in both preclinical AD and symptomatic AD compared to cognitively normal participants. Furthermore, participants with symptomatic AD will show a greater cognitive decline when compared to participants with preclinical AD.

**Conclusions:** This research could provide a broad report on common medications, in a variety of classes known to cause impairment in normal individuals, in participants with preclinical and symptomatic AD. The results from this study will provide clinical recommendations to physicians and pharmacists to reassess prescribing and dispensing practices. Acknowledging situations when these medications may be necessary, the results could provide information on when to avoid offending medications and when to appropriately use alternatives. This study can lead to a greater positive impact in the lives of individuals with cognitive deficits.

048

**Chacko, Ravi**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

Current Doctoral Program of Study: MD/PhD

Washington University in St. Louis

Department: Neurosurgery

Mentors: Eric Leuthardt, MD; ShiNung Ching, PhD; Maurizio Corbetta, MD

**Predicting lateralized spatial attention and reaction time with Electrocoercography**

Chacko R; Ching S; Corbetta M; Leuthardt E

**Introduction:** Spatial attention is a cognitive selection mechanism that is disrupted in Hemispatial Neglect (HN). The purpose of this study is to characterize the Electrocoercographical (ECoG) correlates of spatial attention. The long term goal is to design a neurofeedback rehabilitation paradigm for HN. We hypothesize that band limited alpha and gamma power correlates with left and right shifts in covert spatial attention. We expect that directionally tuned ECoG activity will exist in parieto-occipital cortices. Additionally, we predict lower frequencies (delta, theta) modulate higher frequencies (alpha, gamma) to influence reaction time.

**Methods:** All subjects are patients with intractable epilepsy that underwent surgery at Barnes Jewish Hospital in St. Louis for implantation of intracranial electrodes to map seizure foci using electrocoercography (ECoG). Subjects are requested to maintain fixation on a central fixation cross throughout the entire task. A left or right cue appears for 500 ms to indicate which side the target stimuli is most likely to appear. The target appears in the specified area 80% of the time (valid) and on the opposite side of the screen 20% or the time (invalid). The target is a rotated letter 'L' or 'T' presented 7 degrees off center. Subjects are asked to respond using a two-button mouse as rapidly as possible to identify the target letter. ECoG Recordings: Recordings were made using the BCI2000 platform. ECoG data was recorded from platinum 2.3 mm diameter electrodes in grids (8x8) and strips (1x4,1x6) spaced 1cm apart (PMT Corporation, Chanhassen, MN).

**Results:** We hypothesized that band-limited power predicts left vs right shifts in covert spatial attention. Correct trials with the highest 90% of reaction times were used for classification. The classifier had 73% accuracy at classifying the location of targets. Phase-amplitude coupling (PAC) refers to the ability of low frequency phase to modulate high frequency amplitude. PAC was calculated using the Modulation Index (MI). MIs for beta and gamma coupling to delta phase are negatively correlated with reaction time.

**Conclusions:** This study characterizes band-limited power correlates of lateralized covert spatial attention. Additionally, it reveals correlations between MI and reaction time. We predict that these signals can be used in an EEG-neurofeedback paradigm to rehabilitate HN. Our future work will involve recording EEG signals from HN patients and building an off-line algorithm that predicts the locus of attention and reaction time.

008

**Dardas, Agnes**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Division: Hand & Upper Extremity

Mentor: Ryan P Calfee, MD, MSc

**Preferences for shared decision making in older adult patients with orthopedic hand conditions**

Dardas AZ; Stockburger C; Calfee RP

**Introduction:** The practice of medicine is increasingly shifting from a paternalistic doctor-patient relationship to a model in which the patient and doctor collaborate to decide the optimal course of treatment. The goal of this study was to determine if the older orthopedic population desires a shared decision making (SDM) approach to their care and to identify predictors for the type of SDM approach offered. These data were to be used in the creation of decision aids for older adults with symptomatic hand conditions.

**Methods:** This cross-sectional investigation enrolled 100 patients, greater than 65 years old, presenting to the Peterson Hand Clinic from March-June 2015. All patients completed the control-preference scale (CPS), a validated system of determining patient preferences for SDM. Chi-square test and Kruskal-Wallis statistical analyses assessed correlations between demographics, clinic encounter variables, and the primary outcome of CPS preferences.

**Results:** Eighty one percent of older adult patients reported they would prefer a more active role in decision making, with 51% citing a collaborative approach as their most preferred model of decision making and 67% citing the most passive approach as their least preferred model of decision making. Forty nine percent reported that spending more time with their physician to address questions and explain the diagnosis would be the most useful in making a health care decision and 73% preferred additional informational material in written form. Familiarity with the provider and treatment for a fracture were correlated with being more likely to prefer a collaborative approach, whereas a watch-and-wait treatment decision was correlated with a more passive preference.

**Conclusions:** Older adult patients with symptomatic hand conditions are interested in more active roles during clinic visits and desire a SDM model when it comes to making treatment decisions with their provider. Given the limited amount of reliable information being obtained outside of the office visit, our data suggest that written decision aids may be most helpful when determining the course of treatment provided to the older orthopedic patient.

068

**Denny, George**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Internal Medicine

Division: Dermatology

Mentors: Milan Anadkat, MD; Jay Piccirillo, MD, FACS

**Patient factors associated with positive response to first line medical therapy in Hidradenitis Suppurativa**

Denny GO; Anadkat MJ

**Introduction:** HS (hidradenitis suppurativa) is a debilitating cutaneous condition of unknown etiology characterized by recurrent painful nodules, abscesses, sinus tracts, and scarring. It is estimated to occur in up to 4% of the general population, is associated with many predisposing factors and diseases, and the treatment is often empiric and inadequate. The purpose of this study was to determine which patient factors are associated with a positive response to first-line medical therapy.

**Methods:** A retrospective chart review was conducted of all HS patients seen at our institution between 1/1/1992 and 10/1/2014. For inclusion, all patients must have had a dermatologist confirmed diagnosis of HS, been treated with first-line medical therapy at their initial visit, and been seen for follow-up within 6 months. A multivariate binary logistic regression model was built examining the interplay of age, race, sex, BMI, smoking status, medical comorbidities, family history, disease severity, and therapy initiated.

**Results:** 945 patients with HS were seen during this time period, 246 meet inclusion criteria, with 198 patients included in the final model. After controlling for all variables in the model, non-smokers (OR=2.614, 95%CI=1.297-5.267), those with no previous diagnosis of HS (OR=2.118, 95%CI=1.080-4.152), and older individuals (OR=1.046 for each additional year, 95%CI=1.021-1.072) were much more likely to have noted improvement at follow-up. Additionally, current smokers were significantly more likely to be older, non-Caucasian, have a history of an autoimmune condition, have inframammary HS disease, and less likely to have a positive family history of HS.

**Conclusions:** The results of this study suggest that we may be able to more accurately predict which patients with HS will respond to first-line medical therapy, and which patients may require therapy escalation to biologic medications or surgery. Additionally, this study provides further evidence that smoking, a modifiable factor, is associated with a poorer response to treatment. Overall, the results of this study could prove to be highly important for both patient education and guiding treatment.

110

**Ferguson, Ian**

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: Ophthalmology and Visual Sciences

Mentor: Gregory Van Stavern, MD

**Risk factors for radiation optic neuropathy: a case-control study**

Ferguson I; Huang J; Van Stavern G

**Introduction:** Radiation optic neuropathy is a rare, late complication of radiation therapy to the optic pathway marked by acute, painless, irreversible vision loss. Various predisposing factors appear to increase the risk of radiation optic neuropathy. This study aims to identify risk factors for developing radiation optic neuropathy in cases where the maximum point dose of radiation to the optic pathway falls below accepted tissue-tolerance thresholds.

**Methods:** This study applies a case-control study design to interrogate patient characteristics and treatment parameters as potential risk factors for radiation optic neuropathy. Cases and controls were identified from Barnes Jewish radiation oncology records and frequency matched on the basis of maximum point dose to the optic pathway for a ratio of controls to cases equaling 10. The association of attributes with the outcome of interest was analyzed by logistic regression.

**Results and Conclusions:** Current radiation treatment planning protocols limit maximum points doses to the optic pathway to 50.4 Gy in 1.9 Gy fractions in order to minimize the occurrence of radiation optic neuropathy despite that doses in the range of 60 to 70 Gy are often needed to establish local tumor control. Identifying risk factors for radiation optic neuropathy may help inform treatment planning for certain patients. Patients at high risk may require lower cumulative doses of radiation, or may no longer be appropriate candidates for radiation therapy. Patients at low risk may safely tolerate higher cumulative doses of radiation and so establish better local tumor control.

**No Poster**     **Goldring, Annie**  
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program  
Current Doctoral Program of Study: Medicine  
Drexel University  
Department: Orthopaedic Surgery  
Mentor: Devyani Hunt, MD  
**Changes in hip range of motion in adolescent female soccer players over a 3-year period**  
Goldring A, Hunt D  
**Introduction:** Previous evaluation of asymptomatic female soccer players revealed differences in passive hip range of motion (including hip flexion, internal rotation and external rotation) based on age and competitive level of play. The purpose of this study was to examine longitudinal changes in hip range of motion in the adolescent subset of our study population over a three-year period. Our goal was to test the hypothesis that decreased range of motion at the hip would be observed over the course of this period.  
**Methods:** Asymptomatic female soccer players from a competitive youth club were assessed on measures of hip range of motion over a consecutive three-year period. Data from each of the three time points was compared within the grade school and middle school group, as well as within the high school athletes, by repeated measures ANOVA and post hoc Tukey tests.  
**Results:** Twenty-seven athletes with a mean age of  $12.6 \pm 1.8$  (range 10-17) participated. Analysis revealed statistically significant changes in right-sided hip flexion, left-sided internal rotation and external rotation of both hips in the grade school/middle school group.  
**Conclusions:** Further analysis of this dataset will examine provocative test results and rates of injury in this population over the three-year period. In order to better characterize the female soccer player and her risk for problems related to the hip, future studies with long-term tracking are needed to capture physical changes that occur over time and compare them to the normal population.

**035**     **Groenendyk, Jacob**  
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: Surgery  
Division: Urologic Surgery  
Mentor: Seth A Strope, MD, MPH  
**Assessing the compliance of an Enhanced Recovery After Surgery (ERAS) protocol for radical cystectomy**  
Groenendyk JW; Vetter J; Strope SA  
**Introduction:** Enhanced Recovery After Surgery (ERAS) protocols can improve patient outcomes after complex surgery. However, there is no published data on compliance with ERAS protocols in urology. Here we present compliance data for 111 patients that underwent a novel ERAS protocol for radical cystectomy between March 2014 and June 2015 at our center. We describe where gaps in compliance occurred and assess variables associated with noncompliance.  
**Methods:** The ERAS bundle included elements of preoperative, perioperative, and postoperative care. Key elements included preoperative teaching visits, maintenance of normothermia, timely delivery of a number of preoperative and postoperative drugs (including alvimopan), implementation of a clean closure protocol, and minimization of operating room traffic. Compliance with each element was assessed through documentation of regular clinical care, or assessed with prospective data entry for elements of the bundle that were outside usual clinical care. Elements were collapsed into categories to create a 12 point scale of compliance. Compliance was assessed both overall and by chronological quartile.  
**Results:** Compliance varied considerably, both by protocol element and by quartile. Compliance within categories varied from 28.4% (appropriate timing of preoperative antibiotics) to 98.1% (holding area compliance). However, compliance by overall phase of surgery (preoperative, perioperative, and postoperative) and total compliance for the entire bundle were significantly lower. Only four patients were considered compliant with every element of the protocol. Only 1 of the 12 categories reached 100% compliance by the end of the study period. Despite the inconsistent compliance with the protocol elements, length of stay decreased from over 8 days before stating the standardized care pathway to 5.5 days with the pathway.  
**Conclusions:** ERAS protocols help improve clinical outcomes for patients, but not all of the interventions may be needed. Adoption of these protocols with simultaneous quality assurance investigations provides an effective means for improving cystectomy care.

047

**Habiyaremye, Gakwaya**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program

Current Doctoral Program of Study: Medicine

Meharry Medical College

Department: Neurosurgery

Division: Pediatric Neurosurgery

Mentors: David D Limbrick, MD, PhD; Jay F Piccirillo, MD, FACS

**Biomarkers of neuroinflammation in post-hemorrhagic hydrocephalus of prematurity**

Habiyaremye G; Morales DM; Morgan CD; McAllister JP; Mercer D; Limbrick DD

**Introduction:** The role of neuroinflammation in post-hemorrhagic hydrocephalus (PHH) is not well understood. Therefore, a profile of cerebrospinal fluid (CSF) inflammatory biomarkers would further knowledge on the pathogenesis of PHH. The objective of this clinical study was to measure the CSF content of major cytokines (IL-1 $\alpha$ , IL-10, TNF- $\alpha$ , TGF-b1), chemokines CCL-3, CXCL-12, CX3CL-1) and of P-selectin in neonatal PHH.

**Methods:** Study groups consisted of PHH (n= 12) and preterm controls (n= 11). CSF samples were collected during spinal tap perinatally and ELISA was used to quantify CSF biomarker concentrations. Basic descriptive and inferential statistics were used to analyze the results.

**Results:** CCL-3 (p $\leq$ 0.003; md: 0.09 $\pm$ 0.028 ng; 95% CI: 0.15 to 0.03), and P-Selectin (p $\leq$ 0.03; md: 2.17 $\pm$ 0.98 ng; 95% CI: 4.17 to 0.17) were selectively increased in PHH while IL-1 $\alpha$  (p $\leq$ 0.0001; md: 0.09 $\pm$ 0.01 ng; 95% CI: 0.06 to 0.11) and TNF-  $\alpha$  (p $\leq$ 0.0003; md: 0.14 $\pm$ 0.04 ng; 95% CI: 0.08 to 0.22) were decreased. No significant differences were detected in CXCL-12, CX3CL-1, IL-10 and TGF-b1.

**Conclusions:** These results suggest that CSF increases in CCL-3 and P-Selectin (both of which are potent acute inflammatory biomarkers) may be implicated in the PHH inflammatory process. IL-1 $\alpha$ , and TNF- $\alpha$  decrease in PHH indicates that these biomarkers may not be involved in the PHH inflammatory process. Furthermore, it appears that XCL-1, CXCL-12, CX3CL-1 and TGF- b1 may not be involved in PHH pathophysiology. Importantly, CCL-3 and P-Selectin may be considered as critical therapeutic targets in an effort to prevent PHH development or progression.

118

**Jain, Radhika**

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

Mentors: Katie Plax, MD; Gaurav Kaushik, MPH

**Using a comprehensive medical home model to increase access to contraception for youth in foster care**

Jain R; Kaushik G; Plax K

**Introduction:** Teenage pregnancy amongst American adolescents has decreased in the last two decades; recent studies estimate, however, that young women in foster care are up to two times more likely to have a pregnancy than their counterparts outside the child welfare system. Because youth in foster care have extensive trauma histories and lack access to consistent health care, eliminating unplanned pregnancy takes on particular urgency. In our study we evaluate the efficacy of a comprehensive medical home environment at reducing teenage pregnancy for youth in foster care, by supporting access to and use of contraception.

**Methods:** The Creating Options and Choosing Health (COACH) clinic is a medical home for youth in foster care created by the SPOT youth center in St. Louis, Missouri. A retrospective chart review was conducted on all patients entering COACH between Nov. 2011 and May 2015. Descriptive statistics were used to determine how many sexually active female patients received contraception at the clinic as well as the proportion of young women given contraception who returned for reproductive health visits.

**Results:** 72.5% (n=79) of female COACH patients reported sexual activity; 17.7% (n=14) of sexually active females had a pregnancy before or during COACH service. 51.9% (n=41) of sexually active females had used a hormonal contraceptive method prior to COACH; 82.3% (n=65) received hormonal contraception at COACH. 69.2% (n=45) of these young women returned for subsequent visits related to contraception. Depo-Provera (n=40) was the most popular hormonal method, followed by combined oral contraceptive pills (n=32) and Implanon/Nexplanon (n=21). 98.5% of sexually active females receiving contraception also utilized dental, psychiatric, immunization, and/or case management services.

**Conclusions:** The results of this study suggest that the COACH comprehensive model increases access to hormonal contraception for young women in foster care and encourages them to return for multiple visits related to reproductive health. Utilization of medical and social services in a single, drop-in location could improve broader health outcomes that also contribute to safe sex behavior.

105

**Mejia, Manuela**

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: Clinical Research  
Mentor: Jeffrey F Peipert, MD, PhD

**Effect of baseline bleeding on amenorrhea with levonorgestrel intrauterine system use**

Mejia M; McNicholas CP; Madden T; Peipert JF

**Introduction:** The levonorgestrel-releasing intrauterine system (LNG-IUS) is among the most effective long-acting reversible contraceptive methods. LNG-IUS use alters endometrial histology and bleeding patterns; approximately 20% of women become amenorrheic within one year of insertion, which is generally viewed as a beneficial side effect. This analysis aims to evaluate the effect of baseline bleeding pattern on the onset of amenorrhea in LNG-IUS users. We hypothesized that participants with shorter and lighter menstrual bleeding would be more likely to experience amenorrhea at 12 months.

**Methods:** In this secondary analysis of the Contraceptive CHOICE Project, we included participants who had a LNG-IUS inserted within one month of enrollment. Based on survey data at 12 months, amenorrhea was defined as no bleeding or spotting during the prior 6 months. We used chi-square and multivariable logistic regression to assess the association of bleeding pattern with amenorrhea at 12 months while controlling for confounding variables.

**Results:** Of 2361 participants, 14.5% reported amenorrhea at 12 months. Participants with light bleeding were more likely to become amenorrheic at 12 months than those with moderate bleeding (adjusted odd ratio (aOR): 1.34; 95% confidence interval (CI) 1.01-1.78), while those with heavy bleeding were less likely to report amenorrhea (aOR, 0.34; 95% CI, 0.17-0.68). Women with short duration of flow were more likely to become amenorrheic than those with average duration (aOR, 1.36; 95% CI, 0.99-1.88), while those with longer flow were less likely (aOR, 0.69; CI, 0.46-1.04). However, these latter two findings were not statistically significant in our final adjusted model.

**Conclusions:** This study suggests that women with lighter menstrual bleeding are more likely than women with normal bleeding to become amenorrheic at 12 months. These results could impact patient anticipatory counseling, improve LNG-IUS continuation and satisfaction and ultimately reduce unintended pregnancies.

043

**Mendiola-Pla, Michelle**

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  
Mentors: Joel Perlmutter, MD; Scott Norris, MD

**Electrode lead localization in the brain by co-registration of magnetic resonance images with optical images**

Mendiola-Pla MA; Norris SA; Milchenko M; Yablonskiy D; Wen J; Perlmutter JS

**Introduction:** Deep brain stimulation surgery is used to treat the movement dysfunction symptoms of Parkinson Disease (PD). However, its mechanism of action and how it translates to clinical effect is unknown. An obstacle to being able to do so comes from the inability to accurately and consistently define the location of where the electrode leads lie relative to brain landmarks. This purpose of this study is to define a protocol for verifying the location of an electrode lead by using magnetic resonance imaging (MRI) and optical images of ex vivo, gross histological anatomy and their co-registration to localize and define a burn lesion induced through a lead.

**Methods:** 3D brain volumes will be constructed of the MRI data and of the optical image data for every subject, of which there are currently six. These will then be co-registered with one another digitally and discrepancies between them in subject-specific atlas space will be measured, the optical image volume being used as the standard.

**Results:** The project to date is not yet finalized. We have been able to qualitatively identify the location of the burn lesion in MRIs thanks to the optimized sequence and image processing techniques we applied to the images to highlight tissue contrast in fixed, ex vivo brain tissue. The current limiting factor is the amount of time required to cryoprotect whole brains for histological sectioning, which requires anywhere between 3-4 months. We anticipate that the burn lesion will be distinguishable from the unlesioned brain tissue and can be captured in a sequence of images through the volume of the brain. Ultimately, we anticipate that the co-registration of these two image modalities will show minimal discrepancy between them, verifying the accuracy of MRI to localize a lead in the brain against other imaging modalities, such as functional MRI or positron electron tomography.

**Conclusions:** The results of this study will largely impact science by establishing the "golden standard" of magnetic resonance imaging in research to localize leads on electrode implants by comparing it directly to gross histopathological sections of the same brain tissue. This will especially be important for future studies using functional brain imaging to identify and describe how stimulation at specific coordinates eliminates motor dysfunction in Parkinson Disease patients. Clinically, the findings could go on to improve how deep brain stimulation is applied and personalized by patient to treat diseases.

052

**Moore, Shawn**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program

Current Doctoral Program of Study: Medicine

Saint Louis University

Department: Neurosurgery

Mentor: Michael Chicoine, MD

**Parameters influencing outcomes of Microsurgery followed by Gamma Knife of Vestibular Schwannomas**

Moore SM; Chicoine MR

**Introduction:** Management of large vestibular schwannomas presents with the challenges of stabilizing tumor growth while preserving nearby nerves and structures. The standard method for treating larger vestibular schwannomas is the use microsurgical (MS) resection; which also has an increased risk of facial nerve injury. Gamma knife radiosurgery is a less invasive option, but it has an increased failure rate of growth control in larger vestibular schwannomas. A proposed method of subtotal microsurgical resection followed by gamma knife radiosurgery of the remnant vestibular schwannomas is believed to offer optimal tumor growth control while preserving facial nerve function. In this study, an examination of parameters effecting tumor reduction and facial nerve function was performed.

**Methods:** A retrospective review of 27 patients that received a combined subtotal microsurgical resection followed by gamma knife radiosurgery was performed. Data analysis was performed using SPSS v. 22.

**Results:** Average age at time of MS was 44.4 (range 21-77) and at time of GKS was 46.5 (range 21-78); Mean pre-operative maximum tumor diameter at the CPA was 3.2 (range 1.0-5.0). Mean time elapsed between procedures was 60 months (range 7-283). On average, tumor size was reduced by 42.3% (range -20 to 82.1). Mean follow up time for physical exams was 82.1 months and for MRI was 93.3 months. Variables with a p-value<0.5 for tumor regression were pre-operative tumor size, MRI appearance, and surgical approach and for facial nerve function was Age, preoperative tumor size, radiation dose, number of targets, time elapsed between procedures and duration of follow up for physical exam.

**Conclusions:** Parameters that influence tumor regression following MS+GKS includes pre-operative tumor size, MRI appearance, and surgical approach and for facial nerve function includes age, preoperative tumor size, radiation dose, number of targets, time elapsed between procedures and duration of follow up for physical exam.

002

**Nemanich, Samuel**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSC1 Degree Program

Current Doctoral Program of Study: Movement Science

Washington University in St. Louis

Department: Physical Therapy

Mentor: Gammon Earhart, PhD, PT

**Automaticity of two motor tasks in Parkinson disease**

Nemanich ST; Earhart GM

**Introduction:** Motor automaticity, or the ability to perform movement with little attention, is impaired in Parkinson disease (PD) and underlies much of the motor dysfunction observed in PD (e.g. handwriting, walking, hypomimia). It is unclear if automaticity is impaired across the motor system, or if it only affects certain movements. Therefore, we wished to further explore automaticity of two movements, reaching and saccades (eye movements), using a commonly employed anti-saccade paradigm to compare across movement types.

**Methods:** Individuals with idiopathic PD and healthy age-matched controls took part in the study. Participants completed saccades and reaches to (pro-) or away (anti-) from visual targets under single- and dual-task conditions. We defined pro-trials as "automatic" and anti-trials as "non-automatic". Measures of latency, error rates, peak velocity, and gain were compared across groups and movement types.

**Results:** The PD group was slower and committed more errors during anti-saccades trials compared to controls. No differences in velocity or gain were noted. All measures were similar across groups for pro-saccade trials. For anti-saccades, all participants were slower and committed more errors during dual-task compared to single-task conditions. Analysis of group data on reaching movements is underway.

**Conclusions:** Movement automaticity does not appear to be impaired in PD when making saccades toward visual targets. Further analyses will include comparisons between those with and without freezing of gait, a common gait disturbance, to investigate the effect of freezing on non-gait automaticity. Characterization of motor impairment is important for continual management of motor symptoms and development of appropriate movement training.



045

**Newton, Brandon**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Neurology  
Mentor: Alexandre Carter, MD, PhD

**Connectivity and plasticity in human brain networks**

Newton B; Hong X; Zinn K; Carter A

**Introduction:** Stroke is the second most common cause of mortality worldwide after coronary heart disease and in the United States it remains the leading cause of disability among adults. As far as health care services, medications, and productivity loss stroke costs the United States \$34 billion dollars each year. The goal of this project is to assess the utility of Transcranial Magnetic Stimulation and Prism Adaptation therapy in the treatment of stroke patients who have Hemispatial Neglect due to right parietal lesions.

**Methods:** We plan to examine patients who have received Transcranial Magnetic Stimulation treatment, Prism Adaptation therapy, or both in comparison to no intervention. Subjects with right hemisphere injury due to ischemic or hemorrhagic stroke and left-sided spatial neglect will be recruited based on clinical judgment and initial testing. Subjects must be within 2 months of their initial stroke in order to minimize confounding results due to minor spontaneous recovery. Patients were excluded from the study based on prior history of brain comorbidities such as epilepsy, head trauma, major psychiatric disorders, cognitive impairment as well as substance abuse. We will assess patients using the Posner attention test as well as by changes in the Functional Connectivity Matrix through fMRI and Mesulam Cancellation test.

**Results:** The results for subjects receiving both Prism Adaptation Therapy and Transcranial Magnetic Stimulation show that there was indeed a change in brain connectivity. The Functional Connectivity Matrix showed higher synchronized firing among neurons of both the Dorsal Attention Network and the Motor Network. There was a decrease in the reaction time for the Posner attention test from the first to last session in response to stimuli on the right as well as a decrease in the number misses for stimuli on the left. In addition the center of cancellation from the mesulam test showed a decrease in right bias from the first to last session. We still are in the process of gathering results for each intervention alone as to compare to no intervention. One of the major difficulties in data collection has been the slow recruitment process for stroke patients who demonstrate hemispatial neglect.

**Conclusions:** Although this research project is still in progress the results gathered within this time frame have shown that these interventions are highly beneficial to patients dealing with hemispatial neglect and may eventually serve to increase quality of life as well as cut down on the financial burden stroke patients are faced with.

062

**Sadiq, Furqaan**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program  
Current Doctoral Program of Study: Medicine  
University of Missouri - Kansas City  
Department: Anesthesiology  
Mentors: Michael Avidan, MBBCh; Arbi Ben Abdallah, PhD

**Identifying frailty among surgical patients**

Sadiq F; Abdallah AB; Avidan MS

**Introduction:** Frailty is a process of declining physical, cognitive, and social functioning and is linked to adverse surgical outcomes. Nearly four in every 10 people presenting for surgery are frail. Compared to non-frail patients, frail ones are twice as likely to suffer post-operative complications and spend more time in the hospital after surgery. Current assessment tools are cumbersome and rely on scaled scores, which inherently neglect the nuances of frailty. So, there's a gap in the field regarding the optimal pre-operative screening approach for frailty. Also unclear are the specific factors that contribute to frailty and how they relate to adverse outcomes in surgery.

**Methods:** As an exploratory, retrospective study, data was merged from two sources, yielding a sample of 2,828 patients with complete information: the peri-operative electronic medical record and the pre-operative survey data collected from patients undergoing elective surgery. These baseline surveys are a part of the SATISFY-SOS project operated by the Department of Anesthesiology at Washington University in St. Louis. 1: Factor Analysis (FA) identified most contributive factors to frailty. Factors with loadings > 0.50 were indicative of high contributor to frailty. Step 2: Item Response Theory (IRT) determined which factors are discriminatory and can tell frail patients apart. Step 3: Latent Class Analysis (LCA) grouped similar patterns of frailty into classes. One factor's probability should be > 0.8 in order to be a strong member of that class.

**Results:** Factor Analysis yielded 21 out of 43 factors (0.40 - 0.80 loadings) covering physical, emotional, and social domains of frailty, as well as disease burden. IRT further reduced the factors to 14 items, where the most discriminative were patient-centered outcomes. LCA identified 3 classes of patients with distinct frailty patterns.

**Conclusions:** Physical factors play a more influential role in frailty than psychological factors or one's burden of disease. Most highly contributive frailty factors include patient-reported outcomes of quality of life and a change in physical health & exhaustion.

**No Poster** **Savarese, Erica**  
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Psychiatry  
Mentor: Laura Bierut, MD

**Combustible cigarettes, electronic cigarettes, and carbon monoxide levels among smokers**

Savarese ES; Bierut LJ

**Introduction:** Smoking combustible cigarettes leads to multiple health problems, and is associated with an increased level of carbon monoxide (CO) in the lungs. Electronic cigarettes, though largely unstudied, have been considered a method in harm reduction strategies for smokers. This study aims to identify a possible correlation between carbon monoxide levels and the use of electronic cigarettes among smokers. Participants were interviewed about their smoking habits and consequently given a score based on the Fagerstrom Test for Nicotine Dependence. The CO levels were then analyzed for smokers grouped based on their scores, as well as whether or not they used electronic cigarettes.

**Methods:** The recruitment process involved active street recruitment. Participants who completed the interview process were compensated \$25 for their time. Current smokers were screened before participating - they must have smoked at least 15 out of the past 30 days, been between the ages of 25-44, and blown two carbon monoxide levels of 7 or greater prior to conducting the interview. Select questions from the interview were analyzed for the participants, which were separated into two groups: those who used electronic cigarettes and those who reported never using one. The average CO levels of both groups overall, and then for each FTND (Fagerstrom Test for Nicotine Dependence) score were found. Independent samples t-tests were performed on data from 1006 participants between the ages of 25-44.

**Results:** Overall, the average carbon monoxide reading among smokers who used electronic cigarettes was  $21.6 \pm 12.5$ , and the average among those who did not use electronic cigarettes was  $20.5 \pm 11.22$  measured in ppm. Averages between the groups stratified based on FTND scores were compared using an independent samples t-test with a value of .48. The results of this study suggest that smokers having reported using an electronic cigarette have no significant difference in carbon monoxide levels when compared to smokers who report not using an electronic cigarette.

**Conclusions:** The length of the study this summer ranged from June 8 through July 31, but is a continuation of the study conducted last year. Last year's study enrolled a total of 1006 participants, while the goal for this summer was to enroll 500. This study does not include information on the extent of electronic cigarette use, simply whether or not the participant reports having ever used one. A limitation of this study is the degree to which the participants use E-cigarettes; the data only show a positive or negative response to having smoked an e-cig, not the frequency or nicotine levels. In order to have a more complete understanding of the effect of electronic cigarette use as a harm reduction strategy, a study should be conducted that accurately measures the degree to which participants use electronic cigarettes. The nature of this study does not raise any immediate ethically questionable concerns. The sole issue with investigating further is the lack of FDA approval of an electronic cigarette with which to conduct research. The fact that this topic is not widely studied provides an ethical argument for performing this research, which could lead to improvements in health outcomes.

**No Poster** **Schmidt, Eric**  
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program  
Current Doctoral Program of Study: Physical Therapy  
Washington University in St. Louis  
Department: Physical Therapy  
Mentors: Gretchen B Salsich, PhD, PT; Marcie Harris-Hayes, DPT

**Hip adduction in those with dynamic knee valgus is greater in people with prearthritic hip disorder compared to people with patellofemoral pain**

Schmidt E; Salsich GB; Harris-Hayes M

**Introduction:** Prearthritic hip disease (PAHD) and patellofemoral pain (PFP) are both prevalent musculoskeletal pain problems which can lead to loss of function. Dynamic knee valgus (DKV), an excessive medial collapse of the knee during weight-bearing, is associated with both PAHD and PFP. It's possible that differences in lower extremity motion during DKV may help explain why some people with DKV develop hip pain, while others develop knee pain. The purpose of this study is to determine if lower extremity kinematics differ between those with PFP and PAHD who demonstrate a DKV, as well as to determine if lower extremity kinematics within these two groups are related to pain and function.

**Methods:** We compared hip and knee kinematics in the frontal and transverse planes as captured by 3-dimensional motion analysis between 20 women with PFP, and 14 women with PAHD, who demonstrate DKV during single leg squats. An independent t-test was used to compare kinematic data between groups, and functional measures (Anterior Knee Pain Scale and Modified Harris Hip Score) as well as pain scales (Visual Analog Scale and 11-point verbal numeric scale) were correlated to the kinematic data using Pearson correlation coefficients.

**Results:** At peak knee flexion, hip adduction was greater in the PAHD group ( $23.6 \pm 4.8^\circ$  vs.  $14.3 \pm 5.7^\circ$ ,  $p < 0.001$ ) compared to the PFP group. Femoral adduction was positively correlated to average pain intensity over the past week ( $r = .60$ ,  $p = 0.022$ ) in the PAHD group.

**Conclusions:** Excessive hip adduction may contribute to PAHD in those with DKV. Reducing hip adduction may therefore be important in decreasing pain and improving function in this population.

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**Skillington, S Andrew**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Otolaryngology

Mentors: Jay F Piccirillo, MD, FACS; Dorina Kallogjeri, MD, MPH; Jeffrey F Peipert, MD, PhD

**The prognostic value of p16 and the role of adjuvant chemotherapy in p16-positive oropharyngeal squamous cell carcinoma**

Skillington SA; Kallogjeri D; Lewis JS; Piccirillo JF

**Introduction:** The incidence of human papilloma virus (HPV)-positive oropharyngeal squamous cell carcinoma (OPSCC) has risen dramatically in recent years. HPV-positive OPSCC has a good prognosis; but the HPV marker, p16, has not been validated as an independent prognosticator. For patients with p16-positive OPSCC, the role of adjuvant chemotherapy has not been determined. The objectives of this study were to define the prognostic value of p16 in OPSCC and to evaluate the efficacy of adjuvant chemotherapy for p16-positive OPSCC patients treated with surgery and adjuvant radiotherapy.

**Methods:** The Oncology Data Services tumor registry was searched to identify 300 consecutive OPSCC patients who were diagnosed and treated at Barnes Jewish Hospital from 1996 to 2010. Supplementary clinicopathological data were gathered from the electronic medical record, and p16 immunohistochemical staining was conducted retrospectively by a single pathologist. Kaplan-Meier curves were constructed and Cox proportional hazards analyses were performed to quantify the prognostic value of p16. Among p16-positive patients, the comparative effects of different treatments on overall survival were evaluated in an inverse probability-weighted multivariate Cox proportional hazards model.

**Results:** In univariate analysis, p16-negative status was associated with increased risk of death from any cause (HR, 4.2 [95% CI, 2.9 to 6.0]). After controlling for age, gender, race, comorbidity, smoking, clinical stage, and treatment, p16-negative status remained significant (HR, 2.1 [95% CI, 1.4 to 3.4]). Among p16-positive patients treated with primary surgery and adjuvant radiotherapy, the addition of chemotherapy conferred no additional survival benefit after controlling for all other variables (HR, 1.5 [95% CI, 0.9 to 2.3]).

**Conclusions:** Currently, OPSCC is treated with combination surgery, radiotherapy, and chemotherapy without consideration for HPV/p16 status. Adjuvant chemotherapy may be unnecessary for p16-positive OPSCC patients who receive surgery and adjuvant radiotherapy.

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**Stephens, Robert**

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: Emergency Medicine

Mentor: Brian Fuller, MD, MSCI

**The Impact of a standardized lung-protective mechanical ventilator protocol in the Emergency Department on the incidence of ventilator-associated conditions**

Stephens RJ; Fuller BM

**Introduction:** Mechanical ventilation exposes patients to risk of complications, such as Ventilator-Associated Conditions (VAC). Lung-protective mechanical ventilation is effective in treating VAC. Intervention trials have been conducted in the intensive care unit (ICU) and operating room with little evidence existing from the Emergency Department (ED). Ventilator-Associated Lung Injury occurs over a short period of time following initiation of mechanical ventilation. Due to the poor prognosis of individuals suffering from VAC and the few treatment options, prevention of the lung injury leading to VAC may be a better option. Preliminary data show that the mechanical ventilation strategy provided in the ED is commonly non-protective. ED utilization and boarding time trends have increased the number of patients receiving mechanical ventilation in the ED for prolonged periods. As such, the potential for VAC in the ED is high. This study has been designed to determine if using lung-protective ventilation in the ED can prevent VAC. We hypothesized that utilization of a standardized lung-protective ventilation protocol in the ED at BJH would result in reduced incidence of VAC when compared to historic controls. This study evaluates the impact of established therapy in a novel location, which will provide further insight into VAC prevention.

**Methods:** Our study is a single-center before-after quasi-experimental study evaluating the effect of a lung-protective ventilator protocol in the ED on the incidence of VAC that develop after admission to the ICU compared to historic controls. In addition, we evaluated the two cohorts for differences in length of admission, duration of ventilation, and mortality to discharge.

**Results:** Raw data collection for the retrospective cohort is complete, but we are still waiting on information vital for conclusions. Data collection for the prospective study should be complete in February 2016 and at this point does not have enough participants to make preliminary conclusions.

**Conclusions:** At this point in time we are unable to make any conclusions due to continued data collection and the small sample size of the prospective cohort.

**No Poster** **Strutz, Patricia, MS**  
CRTCL1 Predoctoral Interdisciplinary Clinical Research Training Program  
Current Doctoral Program of Study: Medicine  
University of Illinois at Chicago  
Department: Anesthesiology  
Mentor: Michael Avidan, MBBCh

**The nose knows: impaired olfaction and postoperative delirium**

Strutz PK; Avidan MS

**Introduction:** Postoperative delirium is one of the most common complications observed in the geriatric population undergoing major surgery with general anesthesia; for patients older than 60, up to 70% may be affected. With little known about the cause of postoperative delirium, we hope to investigate the relationship between impaired olfaction and postoperative delirium in the geriatric population. Recently, impaired olfaction has been associated with a greater adjusted risk of postoperative delirium for cardiac surgery patients. In an effort to further investigate these findings, we hypothesize that patients who have impaired olfaction will have a higher incidence of postoperative delirium; thus potentially demonstrating impaired olfaction as a feasible measurement of risk for postoperative delirium.

**Methods:** Adults 60 years and older undergoing major elective surgery are assessed pre- and post-surgery for impaired olfaction and delirium. Impaired olfaction is determined using the Alcohol Sniff Test, which measures olfaction threshold. Delirium is evaluated postoperatively through day 5 with the Confusion Assessment Method (CAM). Final analysis will include multivariate logistic regression to determine the efficacy of impaired olfaction as a risk factor compared to established risk factors of postoperative delirium.

**Results:** This research is still ongoing. However, based off previous findings, we hypothesize that patients who have impaired olfaction will have a higher incidence of postoperative delirium. Overall, we predict a 25% incidence of delirium within our study population.

**Conclusions:** Since postoperative delirium is associated with substantial implications including additional healthcare costs, longer stays in the hospital, and increased postoperative mortality, a quick, reliable test for risk of postoperative delirium in the geriatric community would be significant. The potential of identifying at-risk patients would provide critical information to a patient's health care team, allowing for improved patient care. This research will also help characterize postoperative delirium, allowing further investigation of possible mechanisms involved with this illness.

**No Poster** **Syed, Ali**  
CRTCL1 Predoctoral Interdisciplinary Clinical Research Training Program  
Current Doctoral Program of Study: Medicine  
University of Illinois at Chicago  
Department: Orthopaedic Surgery  
Mentors: Mathew Dobbs, MD; Christina Gurnett, MD, PhD

**Generalized joint hypermobility as a prognostic tool for predicting curve severity in adolescent idiopathic scoliosis**

Syed AA; Dobbs M; Gurnett C

**Introduction:** Adolescent Idiopathic scoliosis (AIS), which affects approximately 2%-3% of the population, is considered to be a torsional deformity of the spine, which combines a rotation and translation of a variable number of vertebrae, causing a change in the 3D geometry of the spine. It is evident that idiopathic scoliosis has a heritable component, but as of yet the cause remains unknown. The association of conditions such as Marfan syndrome, which are caused by collagen fiber defects, with idiopathic scoliosis have led researchers to investigate the connective tissues in scoliosis. The connection to connective tissues is further supported by studies showing an increased prevalence of generalized joint hypermobility in patients with IS. Scoliosis in patients can range from mild or moderate to severe and as of yet there isn't a way to predict which category of scoliosis the patients will ultimately end up having. The aim of this study is to develop a diagnostic tool which predicts the progression of scoliosis in patients. As such, one aspect of our study focused the predictive power of the relationship between generalized joint hypermobility and the maximal angle of curvature achieved by the spine.

**Methods:** 550 subjects were recruited from the spine clinics located at Shriners Children's Hospital and St. Louis Children's Hospital that presented with concerns for scoliosis. Those whose spinal deformity was Cobb angle > 15 were recruited to the study provided that they consented and had no other medical conditions that may have been associated to their scoliosis. Once recruited they were asked to participate in the Beighton test and their performance was recorded. The subjects were then retrospectively followed to monitor their curve progression, if they progressed to surgery the maximal curve before the surgery was recorded.

**Results:** Overall the generalized joint hypermobility as defined by the Beighton test was not statistically significant in predicting maximal curve progression in patients with adolescent idiopathic scoliosis with a p value of 0.719. However, three criterion of the test (overextension of right and left elbow and the ability to place your palm to the floor as defined by the test) were significant. Each of the three were significant on their own but the overall significance when the three criterion was a p value of > 0.0001. If a patient possessed the three criterion then on average the maximal curve achieved by the patient was on average eight degrees less than control group which had no predictors of hypermobility (as defined by a score of zero on the Beighton test).

**Conclusions:** In conclusion analyzing each component of the Beighton score revealed that there were three criterion which were significant for predicting the maximal Cobb's angle even though the overall score was not. Though current research shows that you are more likely to get scoliosis if you have hypermobility, this study shows that once you have scoliosis hypermobility is protective against curve progression, so much so, that if you have a hypermobile spine then it decreases your overall angle by ~8-10 degrees. This information provides a relatively simple and inexpensive test for clinicians to judge the progression of scoliosis in severe cases.

009

**Tian, Andrea**

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  
Division: Hand and Upper Extremity Surgery  
Mentor: Daniel Osei, MD

**Long-term outcomes of proximal row carpectomy vs. four-corner arthrodesis for treatment of SLAC wrist**

Tian AC; Rebehn KA; Osei DA

**Introduction:** Proximal row carpectomy (PRC) and 4-corner arthrodesis (FCA) are two commonly used motion-preserving salvage procedures for treatment of scapholunate advanced collapse (SLAC) wrist. The only comparative studies that have been completed assess the short or mid-range outcomes of both procedures, with mean follow-up periods of less than 6 years. The purpose of our study is to increase knowledge regarding the long-term durability of these two procedures with a mean follow-up of 14 years.

**Methods:** Twelve patients who received surgery at Barnes Jewish Hospital between 1997 and 2003 participated in our study. Patients' wrists were assessed for objective outcomes (Range-of-motion (ROM) and strength), and subjective outcomes (pain and functionality).

**Results:** PRC allowed for greater ulnar deviation ( $p=0.004$ ). All other measures were not statistically significant. There were no significant differences in other aspects of ROM, strength, pain levels, or overall functionality.

**Conclusions:** The results of this study suggest that while PRC may allow for slightly greater ROM, most of the outcomes following either procedure do not differ significantly in the long run. These findings are similar to those of short or mid-range comparative studies. Further investigation should expand on the present study with a larger sample size.

**No  
Poster**

**Toner, Kaitlyn**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; CRTC MSCI Degree Program  
Current Doctoral Program of Study: Audiology  
Washington University in St. Louis  
Department: Audiology and Communication Sciences  
Mentors: Lisa S Davidson, PhD, CCC-A; Rosalie M Uchanski, PhD

**Segmental and suprasegmental speech perception in children with hearing aids**

Toner KA; Davidson LS; Uchanski RM

**Introduction:** An infant's ability to parse continuous speech into words is critical for speech and language development. Suprasegmental perception (perception of "how something is said" and "who says it") is assumed to be the basis of this parsing ability. Children with hearing loss have difficulty parsing and perceiving speech due to their poorer hearing. Clinicians focus on the relationship between acoustic hearing thresholds and segmental perception (perception of "what is said"). To date, the relationship between acoustic hearing thresholds and suprasegmental perception is unknown. Understanding the relationship between acoustic hearing thresholds and suprasegmental perception will guide clinicians' recommendations for hearing devices for children as they develop spoken language.

**Methods:** Twenty children, ages 4-11 years, participated in the study. Participants were recruited from pediatric clinic populations, oral schools for the deaf and mainstream educational schools. Segmental (open-set word recognition) and suprasegmental (syllable-stress discrimination, talker discrimination) speech perception, word segmentation (a test of parsing words) and receptive language (vocabulary) skills were assessed. Correlations were calculated to examine the effect of audibility (aided and unaided thresholds and a spectral modulation detection test of frequency resolution) on outcome measures. Regression analyses were calculated to assess developmental age effects.

**Results:** Measures of audibility and segmental speech perception are not correlated, likely due to audibility being maximized (the participants' hearing aids were fit well). Low frequency PTA (unaided) is correlated with suprasegmental speech perception; this was expected because suprasegmental acoustic properties primarily have low frequency content. Several of our measures are highly correlated with age, suggestive of developmental effects.

**Conclusions:** These results may be very important for helping clinicians decide how much hearing is needed, for children with more severe hearing loss, who may be candidates for one or two cochlear implant devices, for maximizing speech and language development.

**No Poster** **Uzamere, Theodor**  
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Pediatrics  
Division: Pediatric Hematology and Oncology  
Mentors: Allison King, MD, PhD, MPH; Ashley Houston, OTD, MSCI, MPA; Regina Abel, PhD

**The development of a sickle cell inheritance educational tool**

Uzamere TU; Houston AJ; Abel RA; King AA

**Introduction:** Sickle Cell Disease (SCD) is a group of autosomal recessive red blood cell disorders. These disorders lead to the production of abnormal hemoglobin. Red blood cells become hard and sticky with a crescent or sickle shape. These characteristics of the red blood cells lead to vasoocclusion which causes pain episodes, organ damage, infection, acute chest syndrome, and stroke. One hundred thousand individuals in the United States have SCD with a majority of those individuals being African American. SCD occurs in 1 in 500 African American births and approximately 1 in 12 African Americans have Sickle Cell Trait (SCT). Due to breakthroughs in technology and treatment, life expectancy for individuals with SCD has risen from 20 years of age in 1970 to approximately 50 years of age in 2014. Although states in the U.S. screen for sickle cell in newborns, the frequency of the allele has not decreased in the African American population. Little evidence exists showing the success of screening programs in African American communities, thus a gap exists between newborn screening and ensuring that couples have knowledge about their status. Our objective is to validate a tool which will assess the expected knowledge base of an individual after genetic counseling with their primary care provider.

**Methods:** A comprehensive set of knowledge questions within eight domains was created by a panel of experts to serve as a pre-assessment and a post-assessment. A free, publicly available, educational video from St. Jude Children's Research Hospital was chosen as an educational medium. Eighty people from the Center for Advanced Medicine at Barnes Jewish Hospital and Washington University School of Medicine's campus participated. Upon consent, participants completed the pre-assessment followed by the educational video and completion of the post-assessment. Each participant received a \$25 Target gift card. A paired samples T-test was used to make appropriate comparisons.

**Results:** Overall the rate of correct answers from pretest to posttest increased from 50.4% to 62.7% ( $p < 0.001$ ). Participants improved their understanding of inheritance (52.5% vs. 67.9%,  $p < 0.001$ ), the importance of knowing their status (29.3% vs. 48.4%,  $p < 0.001$ ), and the definition of SCD (19.4% vs. 61.9%,  $p < 0.001$ ). No significant impact on participant knowledge occurred for knowledge on clinical manifestations (72.5% vs. 61.2%,  $p = 0.06$ ), distinguishing SCD from SCT (51.8% vs. 56.8%,  $p = 0.08$ ), understanding testing (80.8% vs. 85%,  $p = 0.114$ ), SCD complications (68.8% vs. 72.5%,  $p = 0.48$ ), or SCD incidence (35% vs. 42.5%,  $p = 0.08$ ).

**Conclusions:** Overall, results indicated patients' knowledge of SCD improved significantly after the intervention with statistically significant increases in knowledge of inheritance patterns, the definition of SCD, and importance of knowing SCT status. These domains were the most specific in regards to the participants' decision making capacity leading us to believe that these particular questions may, in fact, reduce the gap between SCD screening and the knowledge individuals have on the disease. This could possibly lead to a reduction in SCD pain episodes, hospitalizations and deaths in African American communities. We will continue to recruit participants until  $n = 200$  to complete factor analysis for validation.

**091** **Wagan, Samiullah**  
CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program  
Current Doctoral Program of Study: Medicine  
Saint Louis University  
Department: Internal Medicine  
Mentor: Bradley Evanoff, MD, MPH

**Are construction workers' health risk perceptions congruent with their health risks?**

Wagan S; Strickland J; Evanoff B

**Introduction:** Construction workers are often exposed to dangerous working conditions resulting in higher rates of injuries and fatalities compared to most other occupations; however, personal health behaviors such as smoking, high alcohol consumption, not wearing seatbelts and being overweight, also place construction workers at higher risk of morbidity and premature mortality. Construction workers continue to have a higher prevalence of smoking (Ham et al. 2011), as well as alcohol use (Barnes and Zimmerman 2013) than those employed in professional and related occupations. The aim of this study was to further evaluate health attitudes among construction workers and assess their health behaviors and perceptions of risks from work related and non-work related health hazards.

**Methods:** In our prospective study, 1636 construction workers completed a health behavior survey distributed at training classes and union meetings. In the survey we assessed pertinent health issues including BMI, tobacco use, alcohol use, seatbelt use, and degree of concern for health related to different injuries, diseases, and exposures. Concern for health was measured on a six point scale (1= not at all concerned 6 = very concerned), which in analysis was dichotomized to "not concerned" (<3) and "concerned" (>4). The results of our survey were also compared to national data from the Behavioral Risk Factor Surveillance System (BRFSS) survey conducted by the Center of Disease Control (CDC), to assess health practice among a similar national dataset. We also examined workplace perception of smoking among smokers and non-smokers, and assessed whether the construction workers believed that smoking should be allowed at worksites, if smoking hurt job performance, and if smoking reduced site safety.

**Results:** Construction workers were more likely to smoke (35.1%) compared to other white males in Missouri (24.4%). In addition, construction workers drank alcohol more frequently nearly every day/every other day (21.4% vs 11.9%), in more quantity of 20 or more drinks per week (14.1% vs 5.6%), and were more like to have heavy alcohol use (5+ binge drinking days in the past 30) (31.4% vs 5.5%). Construction workers were also less likely to wear seatbelt (15.6% vs 8.6%), and finally had more overweight people (46.2% vs 39.2%) but fewer obese (24.7% vs 27.2%) and morbidly obese (1.9% vs 3.1%). For certain health issues, there was not appropriate correspondence between health concerns and health states or behaviors. Finally, there was a difference in belief as to whether smoking should not be allowed at worksites among non-smokers and smokers (57.6% vs 17.5%), or whether they preferred to be on sites without smoking (65.7% vs 11.5%). Among the non-smokers, 55.5% thought that smoking hurt job performance some/a lot, while only 19.8% of the smokers believed the same, and more non-smokers believed smoking reduced worksite safety by some/a lot compared to smokers (39% vs 14.4%).

**Conclusions:** Our findings illustrated that the health behaviors in this group were dramatically different than other white males in Missouri. Concern about health issues did not always correspond with health risks related to behaviors. We also demonstrated that the relationship between work-related health risks and personal behaviors was not concordant among construction workers. Finally we showed that there was a disconnect among construction workers themselves on the impact of smoking at the worksite.

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**Wagner, Julia**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; MA/MD Degree Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Internal Medicine

Division: Oncology

Mentor: Todd Fehniger, MD, PhD

**Natural killer cell memory in cancer therapy**

Wagner JA; Berrien-Elliott MM; Rosario M; Jewell BA; Schappe T; Leong JW; Romee R; Fehniger TA

**Introduction:** Natural killer (NK) cells are innate lymphoid cells with potent effector function against cancer. Cytokine preactivation elicits innate immunologic memory in human NK cells. Cytokine-induced memory-like (CIML) NK cells display enhanced effector function against leukemia and may improve NK cell-based cancer therapies. Therefore, a first-in-human phase I clinical trial of CIML NK cells in relapsed or refractory (rel/ref) acute myeloid leukemia (AML) patients has been initiated with the following objectives: Aim 1: To determine the safety and maximal tolerated dose (MTD) of CIML NK cells. Aim 2: To elucidate the number, phenotype, and functional activity of CIML NK cells in rel/ref AML patients.

**Methods:** Adult patients with rel/ref AML receive chemotherapy to deplete lymphocytes followed by infusion of haploidentical donor CIML NK cells. Interleukin (IL)-2 injections are administered every other day for two weeks post-infusion to promote donor CIML NK cell function and proliferation. A standard 3(+3) phase 1 dose escalation design will test the tolerability of increasing doses of CIML NK cells.

**Results:** Two patients have been enrolled to date with no dose-limiting toxicities (DLT) observed. Donor CIML NK cells were detectable in patient blood and bone marrow from 3-28 days post-infusion. Further, donor CIML NK cells responded more robustly to ex vivo restimulation with tumor targets than naive recipient NK cells. Enrollment continues with the goal of defining the MTD and analyzing CIML NK cells in vivo.

**Conclusions:** Patients with rel/ref AML have limited treatment options and a poor prognosis. If CIML NK cells prove to be safe and effective against AML, they could represent an alternative, non-toxic immunotherapy for AML and other malignancies.

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**Yates, Tari-Ann, MHS**

CRTC TL1 Predoctoral Interdisciplinary Clinical Research Training Program; Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Meharry Medical College

Department: Otolaryngology

Mentor: Jay Piccirillo, MD, FACS

**Exploring risk factors for the diagnosis of acute invasive fungal sinusitis in patients with leukemia: a nested case control study**

Yates TE; Roland L; Kallogjeri D; Piccirillo J

**Introduction:** Acute Invasive fungal sinusitis (AIFS) is an aggressive and often fatal disease. AIFS develops most commonly with inhalation and deposition of Aspergillus and Mucor species, in the moist paranasal sinuses. The aggressive nature of the disease allows a rapid hematogenous spread to nearby structures such as the brain and orbits. Immunocompromised patients, such as leukemic patients, are at the highest risk for AIFS infections.

**Methods:** This nested case control study is part of a larger retrospective cohort study of 5,881 leukemia patients admitted to the Barnes Jewish Hospital from 2004-2014. There were 13 patients diagnosed with AIFS from the larger cohort. The control population was matched to the cases, 2:1, by their year of birth and whether they had new or relapsed leukemia. Patients' charts were reviewed and data was collected on demographic characteristics, clinical and vital sign data, pathology reports, as well as laboratory values. Bivariate analysis was used to explore the association of potential risk factors with presence of AIFS in leukemic patients.

**Results:** Of the 13 patients with AIFS, 4 (31%) experienced mortality. The median length of stay in the hospital was significantly longer in cases as compared to controls (delta 13 days (95% CI 4 to 21) days). The number of days being neutropenic, was 8 days longer (95% CI 6 to 16 days) in cases than controls. There was no significant difference in the number of days before the first neutropenia as well as the number of days before discharge not neutropenic. The number of days until recovery from neutropenia was 9 days longer (95% CI 2 to 19 days) in cases than controls.

**Conclusions:** Prolonged neutropenia before AIFS diagnosis, and a later neutropenia recovery day are associated with the diagnosis of AIFS and may be considered risk factors for this condition.

## Dames Fellowship

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### Jiang, Diana

Dames Fellowship; Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Genetics

Mentors: Josh Jang; Ting Wang, PhD

#### **Conditional Bi-allelic knockout via CRISPR-Cas9 in zebrafish**

Jiang D; Jang J; Wang T

**Introduction:** With emergence of the CRISPR-Cas9 systems for genome editing, zebrafish models for studying gene function have become even more simple and robust than previously. However, due to genome duplication in zebrafish, complete knock-out of a single gene remains difficult and limited. By utilizing multiple sgRNA to target a single gene, we hope to attain greatly improved mutagenesis and gene disruption rates.

**Methods:** The method we describe utilizes PCR extension for straightforward addition of sgRNA sequences to U6 promoters, which can then be Gibson assembled into a plasmid. The resulting plasmid can be validated using both restriction enzyme digest and PCR amplification for the desired regions. We inject a Tol2 transposase containing GFP along with our confirmed plasmid to transfer the designed plasmid into the zebrafish genome. By using genetically engineered zebrafish, we are able to induce expression of Cas9 following heat-shock, allowing conditional control of the CRISPR-Cas9 knockout pathway. To validate that our multiplex single-gene knockout method is more effective, we compare it to a single sgRNA knockout using 1) FACS sort, 2) DNA/RNA extraction and qPCR, 3) T7 endonuclease mismatch, 4) MiSeq sequencing, and 5) phenotypic quantification of the F1 population.

**Results:** We anticipate that validation will show that using four sgRNA to target multiple loci in a single genome will result in greater bi-allelic knockout and mutagenesis frequency of the targeted gene as the mutagenesis frequency of in-frame in-del mutations theoretically reduces from one in three to one in eighty-one.

**Conclusions:** The simplicity and cost-effectiveness of designing DNA targets with the CRISPR-Cas9 target model and the tight control of heritable gene knockout provided by our method should enable a vast number of Zebrafish gene function studies that can be done with greater precision and efficiency. These Zebrafish genetic models can then be used to understand genetic function in humans and thereby transform medical research and our ability to develop therapies for disease.



## David F. Silbert Summer Fellowship

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### Liang, Brooke

David F. Silbert Summer Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Medical Oncology  
Mentor: Russell Pachynski, MD

#### Evaluation of the leukocyte chemoattractant receptor CMKLR1 on T cells

Liang B; Crowder RJ; Pachynski RK

**Introduction:** Chemokine-like receptor 1 (CMKLR1; ChemR23) is the G-protein coupled receptor (GPCR) for the novel leukocyte chemoattractant protein, chemerin, that mediates chemotaxis. CMKLR1 expression is found to be expressed on innate immune cell subsets but has not been shown on T cells. Here, we explored whether CMKLR1 can be induced on T cells using factors abundant in the tumor microenvironment.

**Methods:** T cells were cultured in tumor-conditioned media, or with the cytokines IL-1, IL-10, TGF- $\beta$ , TNF- $\alpha$ , or VEGF. In addition, T cells isolated from tumor-bearing mice were examined. Quantitative real-time PCR (qPCR) and flow cytometry were used to evaluate expression of CMKLR1 on T cells.

**Results:** We preliminarily show the upregulation of CMKLR1 on T cells in an NK-depleted splenocyte culture exposed to VEGF. Interestingly, NK-containing splenocyte culture identically exposed to VEGF did not show this upregulation, suggesting a role for NK cells in the regulation of CMKLR1 on T cells.

**Conclusions:** It would be clinically significant if CMKLR1 could be expressed on T cells, as CMKLR1-expressing T cells in conjunction with therapeutics that activate T cells could be the basis for novel cancer treatments.

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### Toland, Angus

David F. Silbert Summer Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Biology  
Mentor: Douglas Chalker, PhD

#### A conserved amino acid motif in Lia3 is required for binding to G Quadruplex DNA

Toland AM; Chalker DL

**Introduction:** Tetrahymena thermophila, a free-living ciliate, is a model organism used to study the regulation of eukaryotic genomes. Ciliates use a germline micronucleus as a template to generate a somatic, polyploid, junk DNA-free macronucleus. A recently discovered protein, Lia3, has been shown to be important in targeting the elimination of DNA flanked by 5'-A5-G5-3' sequences. These 5'-A5-G5-3' sequences have the capacity to form G quadruplex structures in vitro and have been shown to be bound by telomerase in vivo. The goal of this project was to produce mutations in amino acid sequences within a region of ~100 amino acids conserved amongst Lia3 and functional homologs (Lia3-like or LTL proteins) also expressed in T. thermophila and observe effects on G quadruplex binding.

**Methods:** DNA oligomers containing mutant sequences coding for GRG310-312AAA or IYI315-317AYA were used in PCR to produce two mutant strains of Lia3 fused to maltose binding protein (Lia3-MBP) in a pMAL plasmid expressed in 10G strain Escherichia coli. The mutant proteins were then expressed in BL21 strain E. coli and induced with isopropyl  $\beta$ -D-1-thiogalactopyranoside. The Lia3-MBP was then isolated from induced culture via maltose elution. Purified protein was then incubated with radiolabeled G quadruplex DNA and separated by electrophoresis through a 4.5% polyacrylamide gel.

**Results:** The IYI315-317AYA mutant demonstrated successful G quadruplex DNA binding while the GRG310-312AAA mutant did not, indicating the amino acid sequence of the former mutation does not disrupt binding while that of the latter does. This data indicates that some, but not all, of the highly-conserved amino acids of Lia3 are critical for binding of G quadruplex DNA.

**Conclusions:** During this study, we demonstrated that some of the highly-conserved amino acid sequences of Lia3 are critical for G quadruplex binding. Because these sequences are found in the LTL family, which do not bind G-quadruplex DNA, it is not likely that these sequences are directly responsible for G quadruplex binding, but rather play a role in accessory binding or functional Lia3 and LTL formation (e.g. protein folding, dimerization, etc.). Additional studies will address these questions as well as determine the effect of these mutations on in vivo Lia3 function.

## Dean's Fellowship

025

### CreveCoeur, Travis

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Surgery, Johns Hopkins University

Division: General Pediatric Surgery

Mentors: David Hackam, MD, PhD; CP Sodhi, PhD; Diego Nino, MD, PhD

#### **The Role of Microglial Activation in the Development of Premature Brain Injury Associated with Necrotizing Enterocolitis**

CreveCoeur TS; Nino D; Sodhi CP; Hackam DJ

**Introduction:** Necrotizing Enterocolitis (NEC) is the most frequent gastrointestinal emergency that affects premature infants. It is characterized by high mortality (20 – 50%) and among those that survive there is high incidence of neurodevelopmental impairment compared to non-affected infants of similar gestational age. Neurological deficits in NEC survivors have been attributed to CNS white matter abnormalities, but the underlying mechanisms remain unexplored. We hypothesize that systemic inflammation, as observed in NEC, leads to activation of the innate immune cells of the brain (microglia), which subsequently may play a detrimental role in brain development. Utilizing a well-established rodent model of NEC we aim to determine the role of microglia in the development of premature brain injury associated with this disease.

**Methods:** Necrotizing enterocolitis will be induced in neonatal (7 – 12 day old) C57BL6 mice by gavage-feeding formula supplemented with bacteria isolated from human NEC five times/day. In addition, mice will be exposed to hypoxia (5%O<sub>2</sub>, 95%N<sub>2</sub>) for 10 min in a hypoxic chamber twice daily for 4 days. Microglial activation, in isolated brains, will be determined by measuring the expression of ionized calcium-binding adapter molecule 1 (Iba-1) both by immunohistochemistry and Western blotting. In addition, expression of other markers of neuroinflammation will be evaluated by quantitative RT-PCR and Western blotting.

**Results:** We anticipate that systemic inflammation in the context of NEC will induce microglial activation, which will be evident both by immunohistochemistry as well as gene expression.

**Conclusions:** We observed significant changes in microglial activation and myelination when comparing the NEC-induced pups. When given a drug D-NAC, these effects appeared to be somewhat mitigated.

007

### Cusworth, Brian

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Division: Foot & Ankle

Mentors: Jeremy McCormick, MD; Sandra Klein, MD; Jeffrey Johnson, MD

#### **Outcomes of revision ankle arthroscopy**

Cusworth BM; Johnson JE; Klein SE; McCormick JJ

**Introduction:** There is very little research on the efficacy of revision ankle arthroscopy. This study aims to evaluate whether it proves to be a beneficial procedure for the patient.

**Methods:** A retrospective chart review was performed of the 611 arthroscopic ankle procedures by three foot and ankle surgeons at our institution between 1997 and 2015. 96 of these were revision procedures. Patient outcomes were assessed using phone calls and a mailed Foot and Ankle Ability Measure (FAAM) compared with FAAM from initial visit.

**Results:** Patients were divided into two categories by variation of procedure: 1) osteochondral defect (OCD) debridement and microfracture, and 2) arthroscopic procedure with limited or extensive debridement without OCD. Arthroscopic fusions, debridement of septic arthritis, and procedures that were explorations antecedent of more extensive ones were all removed from the study. Once these exceptions were removed, there were 26 in the OCD group and 16 in the non-OCD group. The OCD group showed a minor reduction in the visual analog pain scale from 5.4 to 3.8 in those with no other surgery since. The OCD group also showed an increase in FAAM score in activities of daily living from 65.7 to 78.7 and a satisfaction of 7.3 out of 10. 3 of 11 who responded had undergone further surgery to the indicated ankle. The non-OCD group showed a similar, yet larger reduction in pain scale from 6.5 to 1.8 in those with no further surgery. Only one non-OCD patient had returned the FAAM at the time of this writing, but those who responded to phone questions and had no further surgery indicated a satisfaction of 9 out of 10. 3 of 8 had undergone further surgery. The study was ongoing at the time of submission, and no statistical analysis had been performed yet.

**Conclusions:** Preliminary data suggests a reduction in pain, an improvement in activity level, a high level of patient satisfaction and no further surgery following repeat ankle arthroscopy in the majority of patients. Further analysis will look for correlation between preoperative indicators and outcomes.

010

**Dalton, Jonathan**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Mentor: Michael Kelly, MD, MSc

**Persistent pain and dissatisfaction with self-appearance determine poor outcomes in adult spinal deformity (ASD) surgery: evaluation of 229 Patients with two-year follow-up**

Dalton JF; Kelly MP

**Introduction:** Patient reported reasons for poor outcomes following adult spinal deformity (ASD) surgery are poorly defined. The purpose of this study is to evaluate the prevalence of health-related quality of life (HRQOL) failure following ASD surgery and identify HRQOL components that contribute most to poor outcomes.

**Methods:** The data for this project was derived from evaluation of a multicenter ASD registry. Inclusion criteria for this project were surgery for ASD and  $\geq 2$  year follow up. We evaluated demographic, operative, radiographic, and HRQOL data (SF-36, ODI, SRS-22r, NRS-BACK, NRS-LEG). Classical test theory was used to calculate minimum detectable change (MDC) for SRS-22r. Surgical failures (FAILURE) were defined as patients failing to improve beyond the MDC for SRS-22r total or worsening scores. Pre- and post-operative data were compared between FAILURE and Non-failure (NF) groups using non-parametric methods. Recursive partitioning was used to identify postoperative HRQOL associations with surgical failure.

**Results:** Of 369 patients, 229 patients met inclusion criteria of which 16% (n=37) met failure criteria; 9% (n=21) were unchanged (SRS-22r total did not improve or worsened  $\leq$  MDC) and 7% (n=16) had decline in SRS-22r total  $\geq$  MDC. Baseline demographics, ODI, SF36, and SRS-22r scores were similar between NF and FAILURE. Recursive partitioning identified pain (threshold SRS-22r Pain  $< 2.33$ ; OR 10.8, 95% CI) most predictive for surgical failure. FAILURE patients reporting pain scores below threshold values demonstrated worse NRS-BACK (6.8 vs. 3.0) and NRS-LEG pain (4.4 vs. 2.2) than NF ( $p < 0.05$ ). Poor self-appearance SRS-22r score (score  $< 3.5$ ; OR: 205.1; 44.5-946.5) was most predictive of poor outcomes for patients that met FAILURE criteria without substantial pain complaints.

**Conclusions:** ASD patients reporting HRQOL failure following surgery demonstrated that persistent or worsening back and leg pain and dissatisfaction with self-appearance are the primary drivers of poor outcomes. Greater insight is needed to determine reasons for persistent pain and poor self-appearance to optimize surgical outcomes.

012

**Hall, Douglas**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Mentor: Michael Kelly, MD, MSc

**Surgical and nonsurgical outcomes for odontoid fractures in the elderly: a national retrospective analysis**

Hall DJ; Kelly MP

**Introduction:** Fractures of the dens are the most common cervical spine fracture in patients over 70 due to a high frequency of falls, car accidents, and osteopenia. Treatment of these fractures is traditionally performed with a halo-vest (HV), cervical orthosis (CO), or surgical fixation. Previous studies comparing clinical outcomes associated with these treatments have suggested that surgery may be a valid option even for elderly patients, however, these studies have been relatively small. We aim to compile and analyze information from the National Trauma Data Bank in order to create a large pool of data and thoroughly analyze clinical outcomes of the various odontoid fracture treatment options.

**Methods:** Data was pulled from the National Trauma Data Bank for patients 65 years of age or older who were treated for type II odontoid fracture. Patients with an ISS greater than 15, with other cervical injuries, or with disseminated cancer were excluded from analysis leaving 2220 subjects. Inverse probability weighting was used to control confounding variables and a logistic regression analysis determined the influence treatment strategy had on major complication rates, minor complication rates, days spent in intensive care, and other relevant clinical markers.

**Results:** At this time complete results separated by type of operative or nonoperative treatment are pending; however, preliminary findings have shown that the operative treatment group had higher rates of major and minor complications (OR of 3.4 and 2.3 respectively). They also spent a significantly longer amount of time in the Intensive Care Unit (ICU), on a ventilator, and in the hospital.

**Conclusions:** These results suggest that conservative treatment may be the better course of action in elderly patients with odontoid fractures. However, full analysis is not yet complete and more thorough results may lead to alternate conclusions. Therefore we will continue to analyze data based on more specific treatment groups.

051

**Jo, Sally**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurosurgery

Mentors: Wilson Z Ray, MD; Matthew MacEwan, MD, PhD

**Utilizing allogeneic amniotic membrane tissue to repair peripheral nerve injuries**

Jo S; MacEwan M; Ray W

**Introduction:** Tubulization, or the implantation of a hollow conduit at a nerve injury site, is utilized for bridging gaps in peripheral nerves that have undergone a complete transection and cannot be reconnected in a tensionless manner. Various biomaterials have been incorporated into such conduits. Amniotic membrane tissue, which is rich with extracellular membrane components and exhibits low immunogenicity, may be an ideal material with which to build guidance conduits for peripheral nerve repair. The current study assessed whether amniotic membrane grafts enhance functional and morphological outcomes after peripheral nerve injury. Also examined were the effects of the biomaterial on reducing inflammation and scarring at the injury site.

**Methods:** Conduits made of allogeneic amniotic membrane tissue, type 1 collagen, or silicone were microsurgically implanted in a rat model of sciatic nerve gap injuries. Conduits were also wrapped around cut-and-repaired sciatic nerves. Terminal outcomes were assessed via evoked muscle force measurements and histomorphometric analysis of the regenerated nerve.

**Results:** The amniotic membrane tissue was overly pliable in situ, hindering the formation of the material into cylindrical form. Thus, the material may be more suitable for supplementing end-to-end coaptation repairs. The study awaits additional results on how amniotic membrane grafts affect the functional and morphological outcomes of peripheral nerve injuries.

**Conclusions:** We anticipate that the results of this study will indicate whether the amniotic membrane is a suitable biomaterial for nerve repair. We hope that further development of novel biomaterials will enable safe and efficacious clinical management of peripheral nerve injuries.

028

**Li, Kevin**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Surgery

Division: Plastic and Reconstructive Surgery

Mentor: Fox Ida, MD

**Management of concomitant vascular and nerve trauma to the upper extremity: a 15 year review**

Li KZ; Fox IK

**Introduction:** Penetrating trauma to the upper extremity can result in life and limb-threatening vascular injury of the brachial artery and disability associated with concomitant injury to the surrounding nerves. In some cases, treatment of peripheral nerve injuries is completed at least two weeks post-injury to allow for declaration of the extent of nerve tissue damage. In contrast, immediate management of the associated injuries allows for a single stage surgical procedure and a rapid transition to recovery and rehabilitation. The purpose of this study was to identify and compare the patient populations who received either immediate or delayed nerve repair.

**Methods:** 15-year retrospective chart review of patients seen within the BJC network for vascular and peripheral nerve injuries to the upper extremity.

**Results:** Of the twenty patients who satisfied the criteria of vascular and nerve injury to the upper extremity, eleven received immediate repair, four received delayed repair, and five did not receive nerve repair even though they had received a diagnosis of nerve injury. Total surgical time was significantly greater in the delayed repair group than either the immediate and no repair groups, both of which were not significantly different from each other. Among the five patients who had not received nerve repair, four had nerve injury diagnoses that were postoperative.

**Conclusions:** The observation that 20% of patients receive a postoperative diagnosis of nerve injury, yet none received nerve surgery, points to the need for early identification of nerve injury during the pre and intra operative period. In addition, longer surgical times place greater demands on the patient undergoing the procedures and additional burdens on hospital operations.

006

**Lingam, Deepak**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery, University of California San Francisco

Division: Biomechanical Testing Facility

Mentor: Safa Herfat, PhD

**Creating a testing machine for arm flexion studies**

Lingam D; Herfat S

**Introduction:** Researchers are slowly understanding the macroscopic and microscopic effects of osteoporosis. The purpose of the study was to see if it is feasible to create a cadaver shoulder simulator of arm flexion at the glenohumeral joint. This simulator would help compare the forces required for flexion between non-diseased joints and diseased joints.

**Methods:** The simulator was created using a cadaver specimen with all the musculature and skeletal elements from the C8 vertebra to the T9 vertebra. Additionally, a pulley-cable system previously used for cadaver spine studies was re-purposed to control various muscles that cross the glenohumeral joint. The rotator cuff muscles are engaged using free hanging weights. Finally, control is provided through the uses of motors and feedback via strain gauges.

**Results:** Initial testing showed that using solely the anterior deltoid muscle fibers led to a lack of flexion due to all of the energy being used to generate a shrugging motion. Engagement of the infrapinatus, supraspinatus and upper trapezius muscle fibers helped reduce the magnitude of the shrug, it still was not enough to produce the flexion motion. The anticipated results are proper flexion with negligible shrugging or rotation.

**Conclusions:** From the preliminary studies it is shown that manipulating solely the anterior deltoid muscle fibers while stabilizing the glenohumeral joint through the rotator cuff muscles is insufficient to create flexion of the joint. Further tests are already being planned to start including other muscles such as the pectoralis major to see what the minimum number of muscles is to produce the desired motion. The successful creation of the simulator can lead to validation of finite element muscle models. It can also be used to do load testing on cadaver specimen comparison tests between osteoporotic and non-osteoporotic glenohumeral joints. Further refinement of the simulator can lead to its usage in various other motions including abduction, extension and rotation. The goal is to create a simulator capable of controlling a shoulder joint throughout its entire range of motion.

029

**Masserano, Benjamin**

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: Kamlesh Patel, MD; Gary Skolnick, MS

**Temporal expansion in unilateral coronal craniosynostosis: a comparison between endoscopic and open repair and an analysis of long-term repair result**

Masserano B; Skolnick GB; Naidoo SD; Woo AS; Smyth MD; Proctor MR; Patel KB

**Introduction:** Previous studies demonstrate that fronto-orbital advancement is ineffective in correcting temporal hollowing in patients with unilateral coronal craniosynostosis (UCS). We aim to compare post-operative temporal expansion in patients treated by either fronto-orbital advancement or endoscopic-assisted craniectomy with orthotic therapy. Additionally, the long-term efficacy of surgical correction for UCS is assessed by comparing 5-year post-operative patients to individuals with untreated UCS.

**Methods:** This is a retrospective, cohort study of patients with UCS. Pre-operative and post-operative craniometric dimensions were obtained from computed tomographic (CT) scans. Nonsynostotic and synostotic side measures included: (1) posterior temporal width, (2) anterior temporal width, (3) orbital width and (4) anterior cranial fossa area.

**Results:** The study included 55 UCS patients after fronto-orbital advancement or endoscopic repair, 10 age-matched controls, 5 patients with 5-year post-operative CT scans, and 5 untreated UCS patients. Both treatments showed symmetric improvement in orbital width and anterior cranial fossa area ( $p < 0.001$ ), but no significant improvement was observed in the temporal region ( $0.008 \leq p \leq 0.621$ ). Linear regression revealed no difference between the two methods of treatment ( $0.013 \leq p \leq 0.809$ ).

**Conclusions:** Fronto-orbital advancement and endoscopic-assisted craniectomy with orthotic therapy showed equivalent outcomes 1-year post-operatively with regard to cranial width and anterior cranial fossa area. Orbital width and anterior cranial fossa area were the only measurements to show consistent symmetric improvement, but persistent osseous asymmetry remains in all measured regions and Sub-analysis revealed that age at surgery did not affect symmetric improvement.

- 096**      **Mejias, Christopher**  
Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Otolaryngology  
Mentors: Randal Paniello, MD, PhD; Neel Bhatt, MD  
**Laser tissue welding to repair complete nerve transection**  
Mejias CA; Bhatt N; Paniello RC  
**Introduction:** Surgical damage to the Recurrent Laryngeal Nerve (RLN) is the principal cause of vocal fold paralysis. Transection of the RLN during surgery is conventionally repaired using micro-suture reanastomosis. Laser nerve welding (LNW) – using a laser to spot-weld the epineurium of the two transected nerve endings – has been shown in animal models to be a novel alternative to micro-suture repair. LNW has not been described in the setting of RLN injury. We used a rat model to compare two types of laser welding techniques, CO2 and KTP, to micro-suture repair to determine which repair promoted the best nerve recovery.  
**Methods:** Rat posterior tibial nerves were surgically transected and then repaired using micro-suture repair (n=15), CO2 laser weld (n=15) and KTP laser weld (n=15). Functional recovery was assessed using footprint analysis. Histological analysis will be used to determine the degree of nerve regeneration.  
**Results:** In each of the three experimental groups, there was a significant recovery in print length from the poster operative walking track to week 6 (P < 0.001). At week 6, the recovery index of the KTP group was greater than that of the CO2 group (P < 0.05). There was no significant difference between the recovery index of the micro-suture group and either the CO2 group or the KTP group. KTP laser repair (5.5 minutes) and CO2 laser repair (6.4 minutes) were significantly faster than micro-suture repair (18.2 minutes).  
**Conclusions:** KTP laser nerve welding of the rat posterior tibial nerve produced better functional recovery than CO2 laser. Neither of the laser welding groups produced significant differences in functional recovery compared to micro-suture repair. Given the functional recovery and the decrease in operative time compared to micro-suture repair, LNW may be a superior method for RLN repair.
- 069**      **Otchere, Elaine**  
Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Dermatology  
Mentors: William H McCoy IV, MD, PhD; Caroline M Mann, MD  
**Granulomatous dermatitis as a post-herpetic isotopic response in immunosuppressed patients: a report of 5 cases**  
Otchere ES; McCoy WH; Musiek A; Anadkat M  
**Introduction:** Wolf's isotopic response is the phenomenon of a new skin disease presenting at the same site of a healed, unrelated skin disease. The most commonly observed inciting cutaneous lesions prior to a Wolf's isotopic response are those caused by herpes viruses, while the most common secondary post-herpetic lesion reported is granulomatous dermatitis (PHIR-GD).  
**Methods:** We conducted a retrospective study of 5 immunocompromised patients diagnosed with PHIR-GD in our department. We also reviewed and summarized clinical and histological findings from previously reported cases of PHIR-GD in the literature.  
**Results:** Isotopic granuloma annulare cases have been predominantly observed in immunocompromised patients (57%) and chronic lymphocytic leukemia (CLL) is the most common cause of immunosuppression in these patients (50%).  
**Conclusions:** These observations suggest immunosuppression both generally and specifically that are associated with CLL are distinct risk factors for PHIR-GD. These cases and summary of the immunocompromised PHIR-GD literature will hopefully spark investigations into this phenomenon to both inform on both general granulomatous dermatitis and, specifically, PHIR-GD.

055

**Page, Joshua**

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: John Constantino, MD

**Quantitative autistic trait measurements index background genetic risk for ASD in Hispanic families**

Page JB; Constantino JN; Zhang Y; Abbacchi AM; Zambrana KA; Martin ER; Tunc I; Messinger DS

**Introduction:** Recent studies have indicated that quantitative autistic traits (QATs) of parents reflect inherited liabilities that may index background genetic risk for clinical autism spectrum disorder (ASD) in their offspring. Moreover, preferential mating for QAT has been observed as a potential factor in concentrating autistic liabilities in families across generations. Heretofore intergenerational studies of QAT have focused almost exclusively on Caucasian populations—the present study explored these phenomena in a well-characterized Hispanic population.

**Methods:** The present study examined QAT scores in siblings and parents of 83 Hispanic probands meeting research diagnostic criteria for ASD, and 64 non-ASD controls, using the Social Responsiveness Scale-2 (SRS-2). Ancestry of the probands was characterized by genotype, using information from 541,929 single nucleotide polymorphic markers.

**Results:** Across the entire sample, significant quantitative trait correlations between siblings (on the order of 0.35), between children and their parents (on the order of 0.20), and between spouses (on the order of 0.55) were observed. Analysis of ancestry-informative genetic markers among probands in this sample was consistent with observations for Hispanic populations in the Genetic Origins and Admixtures of Latinos (GOAL) study.

**Conclusions:** Quantitative autistic traits represent measurable indices of inherited liability to ASD in Hispanic families, and aggregations of these traits can be observed within and across generations among Hispanic families affected by ASD. The occurrence of preferential mating for QAT—the magnitude of which may vary across cultures—constitutes a mechanism by which background genetic liability for ASD might accumulate across generations, especially when as pronounced as observed in this sample.

016

**Rizzo, Michael**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Mentors: Robert Brophy, MD; Charles Goldfarb, MD

**Complications associated with orthopedic ambulatory surgery centers and their associated risk factors: a literature review**

Rizzo MG; Weiner EJ; Bansal A; Brophy R

**Introduction:** An increasing portion of orthopedic surgeries are performed at ambulatory surgical centers (ASCs) as opposed to hospitals. For example, there was a 272% population-adjusted rise in outpatient rotator cuff repairs from 1996 to 2006 with a corresponding 67% decline in inpatient surgeries. Outpatient surgery is more convenient for patients and their families and more cost effective (20-70%) for the health care system. Despite these trends, there is limited outcomes data regarding ASC-based orthopedic surgeries.

**Methods:** A literature search of PubMed and JAAOS was conducted. Studies that examined surgical outcomes and risk factors at Ambulatory Surgery Centers were included. Outcomes included unanticipated hospital readmission rates, infection rates, and complication rates.

**Results:** The rate of complications and adverse events (including direct hospital admission), following orthopedic surgeries at ASCs is described as ranging widely from 0.05%-10.6%. The most common complications are pain and nausea, followed by infection, impaired healing, and bleeding. There is variability in the reported complications rates as well as some correlation with surgical and patient risk factors. The most important surgical factors are operative time, type of anesthesia, and site of operation, while antibiotic prophylaxis does not appear to affect outcomes. Similarly, significantly associated patient comorbidities include diabetes, smoking status, and BMI.

**Conclusions:** As the utilization of ASCs continues to rise, an understanding of outcomes and risk factors becomes increasingly important to guide indications for and management of orthopedic surgery patients in the outpatient setting.

071

**Rosenberg, Abby**

Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Dermatology  
Mentor: Lynn Cornelius, MD

**Pilot study to determine quality of life in melanoma patients**

Rosenberg AR; Weston S; Deshields TL; Cornelius LA

**Introduction:** Quality of life (QOL) has been studied in patients with many types of cancer, but there is a lack of research examining how QOL is affected in melanoma patients. QOL in cancer patients is associated with time since diagnosis, stage of disease, and treatment type. Personality traits and their influence on health behaviors may also play a role in the impact of melanoma on QOL. This study assesses QOL in melanoma patients at all stages of disease in order to identify physical, social, emotional, and functional concerns.

**Methods:** Melanoma patients within 2 years of diagnosis completed 3 surveys at a dermatology, oncology, and surgery clinic. The Functional Assessment of Cancer Therapy–Melanoma (FACT-M) measures QOL specifically in melanoma patients. The revised Synthetic Aperture Personality Assessment (SAPA) assesses personality traits that predict health behaviors and outcomes. A behavior checklist appraises smoking, exercise, sun protection, and drug compliance. Age, sex, date of diagnosis, stage, location and treatment were recorded from patient charts. Hierarchical linear modeling will be used to predict QOL associated with these factors as well as personality traits.

**Results:** At this time, data is available for 45 of the anticipated 100 participants. Early trends show that patients with stage III or IV disease reported lower QOL than patients with stage 0, I, or II disease. Patients with advanced disease reported particularly diminished physical and functional well-being. Patients with localized disease reported feeling equally nervous despite their favorable prognosis. Female participants reported lower emotional well-being and were more concerned about surgical scars. Complete analysis is expected to confirm that QOL also varies with age, time since diagnosis, treatment, and personality factors.

**Conclusions:** If the anticipated results are confirmed, then this study will allow healthcare providers to recognize QOL issues that specifically affect melanoma patients. By considering how QOL is affected depending on age, sex, time since diagnosis, stage, treatment, and personality, providers can identify patients at particularly high risk for poor QOL in order to provide them with counseling and other resources.

065

**Schloemann, Derek**

Dean's Fellowship  
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

**The utility of serum biomarkers in the diagnosis of mild traumatic brain injury**

Schloemann DT; Lindburg M; Fucetola RP; Welch RD; Lewis LM

**Introduction:** There is currently no single accepted criterion standard for diagnosing mild traumatic brain injury (mTBI). An objective and reproducible diagnostic test with a high sensitivity for mTBI could greatly improve its diagnosis. Little is known about the diagnostic properties of glial fibrillary acidic protein (GFAP), and ubiquitin carboxyl-terminal hydrolase L1 (UCHL1) in concussion. The purpose of this study was to determine if the initial serum GFAP and UCHL1 concentrations were significantly higher in patients with a "definite" concussion than those with an "unlikely" concussion. Our secondary objective was to determine whether there are lower threshold values of UCHL1 and GFAP that will reliably exclude concussion.

**Methods:** This study included 250 adults aged 18-80 with a Glasgow coma score of 9-15 who underwent a computed tomography scan of the head after presenting to one of seven hospital emergency departments. All subjects experienced a blunt closed head injury and had potential mild to moderate traumatic brain injury. Serum levels of GFAP and UCHL1 were assessed using an ELISA assay. Sensitivity and specificity of both biomarkers for the diagnosis of concussion were determined, and change point analysis was used to determine significant changes in the receiver operating characteristic (ROC) curves.

**Results:** Overall, 191 of the 250 eligible patients were determined to have "definite" concussion. The median GFAP concentration was higher in the "definite" concussion group than in the "unlikely" concussion group (median 14.20 pg/mL vs. 5.59 pg/mL,  $p < 0.0001$ ). The median UCHL1 concentration was higher in the "definite" concussion group than in the "unlikely" concussion group (median 75.94 pg/mL vs. 43.36 pg/mL,  $p < 0.0001$ ). The biomarkers were able to differentiate between patients with "definite" and "unlikely" concussion with areas under the ROC curves of 0.7036 for GFAP and 0.6596 for UCHL1. The highest sensitivity change point in the ROC curve for GFAP (7.71 pg/mL) gave a sensitivity of 0.780 with a specificity of 0.407. The highest sensitivity change point in the ROC curve for UCHL1 (15.63 pg/mL) gave a sensitivity of 0.921 with a specificity of 0.254.

**Conclusions:** This study suggests that both UCHL1 and GFAP are able to identify patients with concussion after head injury with high sensitivity and reasonable specificity. Future work should focus on confirming the diagnostic capabilities of GFAP and UCHL1 in a larger cohort of patients and identifying the temporal trends in serum levels of these biomarkers following head injury.



119

**Stanley, Katherine**

Dean's Fellowship; Pathology  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Pediatrics  
Division: Infectious Disease  
Mentor: Gregory Storch, MD

**Resurgence of rare rotavirus genotype G12 in St. Louis during the 2014-2015 rotavirus season**

Stanley KM; Storch G

**Introduction:** Rotaviruses are a leading cause of gastroenteritis in infants in industrialized and resource-deprived nations. The introduction of rotavirus vaccines dramatically reduced rotavirus occurrence, however we have noticed mild to moderate recurrences in the St. Louis area biennially. In 2013, following another surge of rotavirus cases, we found rotavirus genotype G12 to be the dominant strain in St. Louis. During the 2014 – 2015 rotavirus season we genotyped positive rotavirus samples to monitor the course of rotavirus trends.

**Methods:** Samples were collected at the St. Louis Children's Hospital Microbiology Laboratory and positive samples were determined through a rapid antigen test. We used reverse transcriptase-polymerase chain reaction (RT-PCR) to determine genotype and determined rotavirus immunization records when available.

**Results:** Out of 30 typed viruses, 29 were confirmed to be G12 (97%). Vaccination histories were available from 16 patients, all of which had the G12 genotype. Out of these 16 patients, 4 were vaccinated, 3 received incomplete dosages, and 9 were not vaccinated.

**Conclusions:** G12 re-emerged as the prevailing genotype in 2015, comprising a higher percentage of cases than in 2013. Once again, the majority of patients with G12 and available vaccination histories were unvaccinated; however, this slight increase in incomplete dosages and fully vaccinated patients who still acquired complicated rotavirus infections demonstrates the continued need for surveillance of rare rotavirus genotypes not covered by available vaccines.

085

**Tooba, Rubabin**

Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Infectious Disease  
Mentors: Rupa Patel, MD, MPH, DTM&H; Aimee James, PhD MPH

**Pre-exposure prophylaxis for HIV (PrEP) knowledge, acceptability, and messaging preferences among young adult men who have sex with men in the Midwest**

Patel R; Tooba R; Caburnay C; Proctor E; James A

**Introduction:** Pre-exposure prophylaxis for HIV (PrEP) has been included in national HIV prevention guidelines for high-risk men who have sex with men (MSM). There is little data to guide implementation efforts in the Midwest. We sought to understand PrEP 1) knowledge, 2) acceptability and 3) dissemination messaging preferences in order to aid programming in St. Louis.

**Methods:** We interviewed 31 participants from July 2014 to July 2015. Study inclusion criteria was age 18-35 years, MSM, and having anal sex in the past 6 months. Recruitment included social app ads. The pre-interview survey included demographics and risk behaviors. The interview guide included 1) current PrEP knowledge, 2) PrEP acceptability, and 3) preferred PrEP messaging content (effectiveness and taglines). PrEP acceptability was defined as someone who was willing to try PrEP and PrEP knowledge was defined as having heard of PrEP before study participation. Two raters coded the transcripts, 20% of transcripts were double-coded. Codes were inductively developed using a grounded theory approach.

**Results:** Participant median age was 29 years (IQR 25-32), 52% (n=16) were non-white and 32% (n=10) had graduated college. Many had not heard of PrEP but the majority reported PrEP was a good idea and that they were willing to try it. Motivators to take PrEP included it was highly effective and had low self-perceived risk while the main barrier was inaccessibility due to lack of insurance and high medication costs. Few knew of medication cost assistance plans. Some reported first learning about PrEP on "About Me" sections of potential sexual partners on social apps. Racial differences in preferred PrEP spokespersons included whites preferred a medical professional whereas non-whites preferred peers and community leaders. Preferred PrEP messaging would address high medication costs with words like "affordable" or "almost free" and include upper limit, efficacy percentages such as "92% effective" versus paraphrases like "highly effective."

**Conclusions:** Knowledge of PrEP among MSM is relatively low in STL compared to larger US cities where acceptability is high. PrEP implementation should include initial messaging that addresses high medication costs to overcome perceived barriers to use.

016

**Weiner, Eric**

Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Orthopaedic Surgery  
Mentors: Robert Brophy, MD; Charles Goldfarb, MD

**Complications associated with orthopedic ambulatory surgery centers and their associated risk factors: a literature review**

Rizzo MG; Weiner EJ; Bansal A; Brophy R

**Introduction:** An increasing portion of orthopedic surgeries are performed at ambulatory surgical centers (ASCs) as opposed to hospitals. For example, there was a 272% population-adjusted rise in outpatient rotator cuff repairs from 1996 to 2006 with a corresponding 67% decline in inpatient surgeries. Outpatient surgery is more convenient for patients and their families and more cost effective (20-70%) for the health care system. Despite these trends, there is limited outcomes data regarding ASC-based orthopedic surgeries.

**Methods:** A literature search of PubMed and JAAOS was conducted. Studies that examined surgical outcomes and risk factors at Ambulatory Surgery Centers were included. Outcomes included unanticipated hospital readmission rates, infection rates, and complication rates.

**Results:** The rate of complications and adverse events (including direct hospital admission), following orthopedic surgeries at ASCs is described as ranging widely from 0.05%-10.6%. The most common complications are pain and nausea, followed by infection, impaired healing, and bleeding. There is variability in the reported complications rates as well as some correlation with surgical and patient risk factors. The most important surgical factors are operative time, type of anesthesia, and site of operation, while antibiotic prophylaxis does not appear to affect outcomes. Similarly, significantly associated patient comorbidities include diabetes, smoking status, and BMI.

**Conclusions:** As the utilization of ASCs continues to rise, an understanding of outcomes and risk factors becomes increasingly important to guide indications for and management of orthopedic surgery patients in the outpatient setting.

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**Wong-Siegel, Jeannette, MPH**

Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Pediatrics  
Division: Hematology and Oncology  
Mentors: Kimberly Johnson, PhD; Todd Druley, MD PhD

**A retrospective analysis of pediatric oncology patients and congenital anomalies**

Wong-Siegel JR; Johnson KJ; Gettinger K; Druley TE

**Introduction:** Congenital anomalies are the leading cause of infant death and contribute to disability and pediatric hospitalizations. Studies have provided substantial evidence of an association between congenital anomalies and cancer risk in children. While variable, these associations hint at potential underlying cancer-predisposing conditions due to abnormal human development. This study investigates the relationship between congenital anomalies and tumor subtypes in the St. Louis Children's Hospital (SLCH) pediatric oncology patient population.

**Methods:** Electronic medical records of pediatric oncology patients diagnosed at SLCH from January 1, 2004 to August 30, 2008 were reviewed. Congenital anomalies were extracted from text in the charts and verified with ICD-9 codes found in hospitalization summaries when available. Bivariate analyses compared demographic characteristics between patients with and without a congenital anomaly indication. We then used the Kaplan-Meier method to compare survival rates following tumor diagnosis.

**Results:** Out of 560 SLCH pediatric oncology patients reviewed, 85 (15%) patients were identified with a congenital anomaly. Among those with a congenital anomaly, there were significantly more males compared to those without a congenital anomaly ( $p=0.02$ ). In addition, there was a significant excess of CNS tumors compared to other tumors among those with a congenital anomaly ( $p=0.01$ ). There were no significant differences in distribution by tumor type but a potential trend in the relationship between neurological anomalies and excess in males developing tumors ( $p=0.06$ ). There were also no significant differences among those with or without a congenital anomaly indication by age at diagnosis or survival.

**Conclusions:** This study provides new and additional evidence on the relationship between congenital anomalies and pediatric cancer development. Moreover, it contributes additional important prognostic and surveillance information to families with children affected with congenital anomalies that may guide new screening policies, and supports the need for additional research investigating the mechanisms underlying tumor predisposition in children with congenital anomalies.

**Zárate Rodriguez, Jorge**

Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Surgery

Division: Pediatric Surgery

Mentors: Adam Vogel, MD; Lauren Muckleroy, MD

**Extracorporeal life support outcomes in neonatal and pediatric cardiac patients**

Zárate Rodriguez JG; Muckleroy L; Vogel AM

**Introduction:** Systemic anticoagulation is a necessary component in the management of critically ill patients receiving extracorporeal life support (ECLS) for reversible respiratory and cardiac failure. Bleeding (BC) and thromboembolic complications (TEC) are common and result in significant morbidity and mortality. The goal of this study is to assess the impact of current anticoagulation practices on BC, TEC and mortality in neonatal and pediatric cardiac patients that received ECLS.

**Methods:** Neonatal and pediatric patients receiving ECLS at St. Louis Children's Hospital during 2012 were reviewed. Demographic, clinical, and outcome data (BC, TEC, ECLS duration, and mortality) was collected. BC and TEC were categorized by clinical severity: major, intermediate, and minor hemorrhage; major and minor patient thromboembolic; major and minor circuit thromboembolic. Cardiac patients were compared to non-cardiac patients. Descriptive statistical analysis was performed.

**Results:** A total of 31 patients were reviewed, 22 of which were cardiac. The mean age for cardiac and non-cardiac patients was 34.8 and 47.1 months respectively. Mean ECLS duration was 5.8 days for cardiac patients and 7.7 for non-cardiac. 59% of cardiac patients had either a BC or TEC, compared to 44% in non-cardiac patients. In cardiac patients: 11 had BC only, 1 had TEC only, and 1 had both types. Of the BC in cardiac patients, 73% were major, 18% were intermediate, and 9% were minor hemorrhages. The 1 patient that had a TEC suffered major thrombosis; while the 1 patient with both types of complications faced a major hemorrhagic event and major embolism. All of the complications (4) in the non-cardiac cohort were major hemorrhagic events. Mortality in the cardiac group was 50% compared to 22% in the non-cardiac cohort.

**Conclusions:** Neonatal and pediatric cardiac patients receiving ECLS have an increased rate of BC and TEC with a high mortality. Given the complexity of these patients and the presence of multiple confounding variables, the significance of this relationship is unclear. Prospective studies are needed to assess the impact of systemic anticoagulation practice on morbidity and mortality in these critically ill patients.

## DeNardo Education and Research Foundation Grant

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**Robb, Caroline**

DeNardo Education and Research Foundation Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Radiology

Division: Cardiothoracic Imaging

Mentor: Constantine Raptis, MD

**Impact of pre-transplantation computed tomography on organ donation in patients who have suffered terminal events**

Robb CL; Raptis CA

**Introduction:** Radiologic imaging is routinely used to evaluate potential living organ donors, however, this method of assessment is rarely used to determine the viability of organs from deceased donors. In 2010, Mid-America Transplant Services (MTS), an organ procurement facility in St. Louis, MO, installed a computed tomography (CT) scanner at its facility. Since then, CTs have been performed on any patients who have suffered terminal events who had not received a CT scan prior to arrival at MTS, to determine whether they are viable organ donors. The CT results, in conjunction with evaluative protocols, were then used to direct donation decisions and assist in procurement procedures.

**Methods:** A retrospective analysis of data from 373 cases, dated from January 2010 through May 2015, was systematically collected from the MTS online database and analyzed. This data included patient medical histories, biopsy results, operative findings, and CT results for liver and lung transplants.

**Results and Conclusions:** CT findings resulted in the rejection of 25% rejected livers and 16.3% of the rejected lungs, with the leading cause of findings of vasculature calcification and emphysema, respectively. CT results regarding liver steatosis and emphysematous changes in the lungs correlated highly with biopsy results. Every liver found by CT evaluation to be cirrhotic was rejected for transplant. CT findings of variant hepatic arterial anatomy agreed with operative findings in 75.8% of cases that received contrast ( $p < 0.0001$ ). CT-determined liver weights were found to be statistically accurate when compared to operative findings ( $t = 10.124$ ,  $p < 0.0001$ ).

053

**Shah, Amar**

DeNardo Education and Research Foundation Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurosurgery

Mentor: Gavin Dunn, MD, PhD

**The use of intraoperative MRI in glioblastoma multiforme and other prognostic factors: a single institution study**

Shah A; Sylvester PT; Evans JA; Chicoine MR; Dunn GP

**Introduction:** Intraoperative MRI (iMRI), the use of high-field magnetic resonance imaging in the surgical suite, was adopted at Washington University School of Medicine (WUSM) in 2008. Studies evaluating iMRI use at large studies have been few in number until recently. Here, we report the effects of iMRI use on surgical outcomes, including overall-survival (OS) and progression-free survival (PFS), in glioblastoma multiforme (GBM) patients at our institution. Age at time of surgery, pre-operative risk assessment scores, and genetic marker statuses are known baseline factors of prognostic significance that will be included in outcomes analysis.

**Methods:** WHO Grade IV Gliomas treated at WUSM were selected from the I-MIND 2.0 database, yielding 670 cases. Kaplan-Meier analyses were performed to determine univariate factors upon overall survival and progression-free survival. iMRI use, age (defined by decade), ASA physical classification score, MGMT promoter methylation were included. Multivariate analysis via Cox-regression modelling is pending.

**Results:** Median OS for the study population was 13 months (95% CI 11.931, 14.069). Patients who received an iMRI had longer OS than those who did not. In 594 primary GBMs, median OS increased from 12 months (95% CI 10.647, 13.353) to 17 months (95% CI 14.765, 19.23) with use of iMRI ( $n = 159$ ; log-rank  $p = 0.001$ ), though additional resection of tumor did not significantly increase survival within this subgroup ( $n = 90$ ; log-rank  $p = 0.342$ ). Age (younger), ASA score (lower), and MGMT status (positive) were statistically significant predictors of greater OS (log-rank  $p = 0.000$ ).

**Conclusions:** This study shows that patients who receive iMRI have better outcomes than those who do not at WUSM. Younger patients with better physical status have better surgical outcomes. It is clear that MGMT promoter methylation status is clinically relevant and is an important addition to the GBM workflow. Analysis of the effect of other genetic factors is hampered by incomplete data; as these tests become more common, it may be possible to further validate prognostic relevance. Multivariate analysis of significant factors, pending, is the logical continuation of this research.

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**Wesevich, Victoria**

DeNardo Education and Research Foundation Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Neurology  
Division: Pediatric Neurology  
Mentor: Nico Dosenbach MD, PhD

**A novel system for real-time head motion monitoring and feedback during functional MRI**

Wesevich V; Koller J; Greene D; Dosenbach NUF

**Introduction:** Magnetic Resonance Imaging (MRI) research is stunted by data loss due to head motion, especially in children and patient populations. Head movement during MRI scanning distorts the blood-oxygenation level dependent (BOLD) signal that serves as the basis for resting-state functional connectivity MRI (rs-fcMRI). The purpose of this study is to test a novel system for fMRI Integrated Real-time Motion Monitoring (FIRMM), developed to monitor BOLD data quality during collection and to implement real-time motion feedback that trains pediatric participants to suppress unwanted head movement.

**Methods:** Nineteen of twenty-seven children, ages 5-15, have undergone testing using FIRMM and its feedback paradigm to suppress head motion. Participants received visual feedback if their head movement exceeded a certain frame-wise displacement (FD) threshold on the previous data acquisition frame.

**Results:** Data collection will be completed by 9/1/15. Results are anticipated to show decreased rs-fcMRI data loss from head motion due to visual feedback during scanning, especially in older children (11-15yr olds). Additionally, we plan to compare two feedback paradigm types, one with a standard rs-fcMRI display using a gaze-centering fixation-cross, and one presenting movie clips. Results are anticipated to show an overall reduction of head movement during movies, independent of feedback. We expect this effect to be greatest in younger children (5-10 years old).

**Conclusions:** We expect this study to support implementation of our novel FIRMM system into current and future rs-fcMRI studies. The improvements in rs-fcMRI data quality and amount will reduce the costs of rs-fcMRI studies, expediting higher-quality results and progressing the field of pediatric neurology and neuroimaging research.

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**Wood, Ian**

DeNardo Education and Research Education Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Plastic and Reconstructive Surgery  
Mentors: Amy Moore, MD; Susan Mackinnon, MD

**The effect of a proximal crush on neuroma formation and pain marker expression in rats**

Wood IS; Hong TS; Hunter DA; Ee X; Yan Y; Mackinnon SE; Wood MD; Moore AM

**Introduction:** Following traumatic injury, regenerating nerves may form a painful swelling at the severed end. The development of painful neuromas is associated with significant pain in the distribution of the affected nerve, which in some cases can be more debilitating to the patient than other more prominent symptoms such as loss of motor function or sensation. A multitude of treatment modalities have been attempted but met with only limited success. It has been hypothesized that a proximal nerve crush may have therapeutic benefits. We thus aim to study the effect of a proximal nerve crush on the sciatic nerve in rats, using the expression of pain markers in the L4/L5 dorsal root ganglia as an indicator of pain.

**Methods:** All surgeries were performed on the right sciatic nerve in male Lewis rats. Injuries were performed about 5mm proximal to the trifurcation, and for groups that also received a crush, a 30 second proximal crush was performed 5-10mm proximal to the site of injury. The rats were divided into six experimental groups: 1) sham surgery where the nerve was simply exposed and freed, 2) sham surgery followed by proximal crush, 3) total sciatic transection involving complete transection with the distal stump ligated and embedded in muscle (simulating an amputation injury), 4) total sciatic transection followed by a proximal crush, 5) Bennet's chronic constriction injury model involving four 5-0 chromic gut sutures tied loosely around the sciatic nerve, each about 1mm apart, and 6) Bennet's chronic constriction injury model followed by a proximal crush. The rats were sacrificed at 2 weeks and the nerves and L4/L5 dorsal root ganglia preserved for histomorphometry and rtPCR respectively. Histomorphometry was used to qualitatively and quantitatively analyze axonal regrowth and neuroma formation while rtPCR of the DRGs quantitatively measured the expression of pain markers.

**Results:** Results are pending analysis, but it is anticipated that a proximal crush will alleviate pain marker expression.

**Conclusions:** Conclusions are pending analysis, but should the results be as anticipated, the research would translate into studies on higher animals or into clinical trials.

**Zhang, Shiyang**

DeNardo Education and Research Foundation Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Radiation Oncology

Mentors: Christina Tsien, MD; Mikhail Milchenko, PhD

**Physiologic MR imaging parameters in detecting non-enhancing tumor and predicting outcome in glioblastoma multiforme (GBM)**

Zhang S; Tsien C; Milchenko M

**Introduction:** Glioblastoma is the most common primary brain tumor and remains associated with poor outcomes. Treatment is confounded by the highly invasive nature of GBM, with neoplastic cells commonly found at significant distances from the primary tumor site. These 'non-enhancing' tumors are often invisible to current contrasting agent-based MRI techniques, which visualize tumor anatomy. We predict that multi-parametric MR imaging techniques that investigate brain physiology in combination with traditional MRIs will be a better predictor at identifying those tumors that are non-responsive than any one biomarker alone.

**Methods:** MR imaging data from pre-operative, post-treatment, and follow-up scans will be segmented into regions of interest and registered to the common atlas using UPenn's Glioma Image Segmentation and Registration (GLISTR) protocol. Instance of tumor recurrence will be identified and characterized by location and signal in coregistered T1, T1ce, T2, FLAIR, DTI, and DSC. Disease progression will be evaluated similarly in following scans. Its location in the atlas will be used to trace the location of non-enhancing tumor in preceding scans. Within these regions of interest (ROI), we will evaluate whether fluid-attenuated inversion recovery (FLAIR)/apparent diffusion coefficient (ADC) mismatch, as indicated by LaViolette et al., is predictive of neoplastic growth. We will perform relative cerebral blood flow (rCBF), relative cerebral blood volume (rCBV), and fractional anisotropy (FA) as potential signposts for recurrence.

**Results:** Final results have not yet been developed. MRIs from 8 patients' pre-operative scans were segmented into regions of interest by GLISTR. To confirm the segmentations produced by the protocol, we compared the results with pathological reports taken from biopsies at various sites within and surrounding the patients' tumor. Initial findings show only mild correlation between the tissue fraction estimations produced by our segmentation protocol and the pathology, indicating need for finer tuning. This has been a challenging process due to the complexity of GLISTR's algorithms and the uncertainty of what defines a robust segmentation. Once we are confident that GLISTR produces tissue segmentations with high fidelity, the protocol will be applied to post-treatment and follow up scans. Coregistration of these scans will then allow us to analyze physiologic parameters from preoperative scans at the location of future tumors.

**Conclusions:** No conclusions can be made from the data at this time.

## Forum for International Health and Tropical Medicine (FIHTM)

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### Davis, Emily

Forum for International Health and Tropical Medicine (FIHTM); Dean's Fellowship  
Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Research Affiliation: Philani Maternal, Child Health and Nutrition Project, Zithulele, South Africa

Mentors: Karl le Roux, MD; Indi Trehan, MD, MPH, DTM&H

#### **Challenges mothers and babies face in a rural South African setting**

Davis EC, le Roux K

**Introduction:** Zithulele Hospital is located in a rural portion of the Eastern Cape of South Africa where mothers and infants face poverty, a lack of resources, and limited infrastructure. To gain a better understanding of maternal and early childhood health, the Zithulele births follow up study (ZIBFUS) was created to examine a wide range of health topics such as access to healthcare and immunizations, feeding practices, HIV status and care, social support, maternal health, and more.

**Methods:** All mothers in the area who gave birth in the Zithulele catchment area between January and April 2013 and their newborn babies were recruited to participate in this study. Data collectors visited participants in their homes to administer interview-style surveys at birth, 3, 6, 9, 12, and 24 month intervals and recorded the information on mobile phones that also captured GPS data.

**Results:** 470 mothers and 479 newborn babies were recruited into the study at birth, and at the one year follow up 92.3% of participants were retained. Although data has yet to be completely analyzed, initial surveys showed that: 99% of study participants received antenatal care; 63% of the babies born to study participants were not planned; 80% of participants were unemployed at the time they gave birth, 16% were in school, and only 4% were employed; 29% of mothers are HIV-positive; 92% of participants were receiving government grants (mostly child support grants for previous children) at the time of birth; and while 59% planned to exclusively breastfeed at the time of birth, only 22% were exclusively breastfeeding their babies at the time of their 3-month surveys.

**Conclusions:** Health workers in rural areas of South Africa have long acknowledged a lack of reliable information about what challenges and decisions their patients face outside the hospital gates. This study provides important insight for medical and public health workers concerned with maternal and infant health outcomes. Knowledge of the resources, beliefs, and practices of mothers in Zithulele will hopefully provide a more solid foundation to guide future maternal and child health interventions.

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### Kolodziej, Julia

Forum for International Health and Tropical Medicine (FIHTM); Dean's Fellowship  
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

#### **The effect of interventions on the relapse rate of Malawian children recovered from moderate acute malnutrition**

Kolodziej J; Manary M; Trehan I

**Introduction:** The global prevalence of moderate acute malnutrition (MAM) in children under age 5 is estimated to be 7.7 percent which carries an increased risk for morbidity and mortality. Ready-to-use supplementary food (RUSF) is used to treat children with MAM in Malawi and has been shown to be an effective therapy. However, relapse rates have been determined to be 27 percent, with 4 percent of children dying within a year of successful treatment of MAM. This study seeks to address the issue of high relapse rates by providing interventions that might prevent children from becoming malnourished after recovery. These interventions include mosquito nets, additional nutritional supplements, and parasitic prophylaxis. The primary outcome is the children's nutritional status during post-recovery follow-up visits. It is expected that these results may alter the treatment that children receive for MAM to prevent subsequent relapse.

**Methods:** Clinic sites in rural villages across southern Malawi were randomized to be intervention or control sites. At these sites, about 1500 children are being followed after recovery from MAM for 12 months, during which their mid-upper arm circumference (MUAC) is measured at 1, 3, 6, and 12 months as well as three visits during the malaria season. The children at intervention sites received zinc supplements, albendazole as a parasitic prophylaxis, bed nets, and a lipid-dense nutritional supplement (LNS). In both groups, as children relapse, they are placed back on RUSF until recovery. Also as part of this study, local health workers conduct home visits to complete a survey on household food insecurity, 24 hour dietary recall, and their experiences with the malnutrition treatment program. In addition to this survey, a 10-question household food insecurity survey is conducted at each follow-up appointment.

**Results:** Enrollments were completed in June 2015; however, the results of this study are pending completion of data collection in summer of 2016.

**Conclusions:** No conclusions can be drawn at this time; however, the findings of this study may impact the care of children recovering from moderate acute malnutrition.

**Maidl, Elizabeth**

Forum for International Health and Tropical Medicine (FIHTM); Dean's Fellowship  
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

**Assessing the efficacy of post-recovery interventions for pediatric moderate acute malnutrition in southern Malawi**

Maidl EM; Manary M

**Introduction:** It has been estimated that malnutrition plays a role in the deaths of upwards of 3 million children each year, primarily in developing countries. Moderate acute malnutrition (MAM), defined as having a mid-upper-arm-circumference (MUAC) of 11.5-12.5 cm, affects 11% of children under the age of five. Children with MAM are 3x more likely to die than well-nourished children, in addition to having higher risk of infections and developmental delays. Current studies indicate that 37% of children who recover from MAM following treatment with ready-to-use supplementary food (RUSF) will relapse into malnutrition. This study aims to assess the efficacy of post-recovery interventions in the health of children with MAM in Southern Malawi. Primary outcome measures include recurrence of and severity and length of relapse into malnutrition. By assessing such measures for prevention of post-recovery relapse, a definitive standard-of-care treatment can be determined that will improve the lives of malnourished children across the globe.

**Methods:** This study is a cluster randomized (by site) control clinical effectiveness trial that will follow approximately 1600 children for 12 months after their recovery from MAM. Upon their graduation from the feeding program and subsequent enrollment into the study, participants are randomized into two groups – a control group receiving the current standard-of-care and a treatment group receiving the study interventions: parasitic prophylaxis with albendazole, zinc supplementation, and a bed net.

**Results:** The results of this study are pending. Enrollment for the study was completed on July 1, 2015. The study will continue to follow all children for 1 year, with return visits at 1, 3, 6, and 12 months. Outcomes for children involved in the control program versus those receiving interventions will be assessed for differences at the completion of follow ups.

**Conclusions:** No conclusions can be made at this time. The results of this study should improve the understanding of how to treat pediatric moderate acute malnutrition in order to prevent post-recovery relapse.



## Movement Science Program

001

**Bittel, Daniel, PT, DPT**

Movement Science Program (MSP)

Current Doctoral Program of Study: Movement Science

Washington University in St. Louis

Department: Physical Therapy

Mentor: David Sinacore, PT, PhD, FAPTA

**Leg muscle quality and performance in diabetes-induced sarcopenic physical frailty**

Bittel DC; Bittel AJ; Sinacore DR

**Introduction:** Sarcopenia, an age-related loss of skeletal muscle mass, leads to diminished strength and physical function. Diabetes (the combination of type 2 diabetes (T2DM) and obesity) may accelerate sarcopenia and physical frailty. This study examines the relationship between diabetes and underlying sarcopenic contributors in the leg (eg intermuscular adipose tissue- IMAT), and how these factors may confer physical frailty.

**Methods:** 43 subjects were recruited - 12 T2DM, 21 T2DM with peripheral neuropathy (T2DMPN), and 10 age, sex, and BMI-matched controls. IMAT volumes (a measure of muscle quality) were quantified using T1-weighted MRI. Plantarflexor (PF) power was measured via isokinetic dynamometry. A 9-item physical performance test (PPT) was administered to classify physical frailty (PPT score <29). Sarcopenic indices were calculated via DXA and the Skeletal Muscle Index. Chi-square analysis determined group differences in frailty classification. Group differences in IMAT and muscle performance were assessed using one-way ANOVAs. Multiple regression was used to predict frailty from group status, leg IMAT, and PF power.

**Results:** 80% of those with diabetes, and 60% of controls were sarcopenic. T2DMPN was more likely to be classified as frail ( $p=.033$ ), have higher IMAT ( $p=.013$ ), and lower ankle PF power ( $p=.027$ ) than controls or T2DM. Frail individuals had higher IMAT volume, and lower leg muscle power than non-frail participants (both  $p<.05$ ). Total calf IMAT was inversely correlated with PF power ( $p=.03$ ) and PPT score ( $p<.001$ ). T2DMPN is associated with a more precipitous decline in PPT score than T2DM or controls ( $p=.01$ ); for every 1 point increase in leg IMAT, there is a .1 point reduction in PPT score ( $p=.004$ ).

**Conclusions:** Obese individuals with T2DM are more likely to be sarcopenic than their non-diabetic counterparts. As diabetes progresses, these individuals may exhibit frailty and reduced muscle quality (via excess IMAT accumulation). Individuals with diabetes may be particularly susceptible to accelerated sarcopenic decline and frailty. Interventions designed to reduce IMAT and improve muscle performance in this population requires further study.

## Otolaryngology NIH T32 Physician Scientist Program (PSP)

094

### Goldberg, Rachel

Otolaryngology NIH T32 Physician Scientist Program (PSP); Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Otolaryngology  
Mentor: Jay Piccirillo, MD, FACS

#### **Ecological Momentary Assessment (EMA) of tinnitus, a reliable instrument to assess and understand tinnitus**

Goldberg RL; Kallogjeri D; Spitznagel Jr EL; Piccirillo M; Nicklaus J; Skillington SA; Piccirillo JF

**Introduction:** Tinnitus is the perceived sensation of sound without stimulation. Existing tinnitus assessment tools are flawed by summarizing and recall biases. In contrast, Ecological Momentary Assessment (EMA) allows for repeated measures about the current moment. EMA questions about various aspects of tinnitus could be used to define an underlying latent variable to capture true tinnitus severity. The aims of this study were: (1) Evaluate the test-retest reliability of EMA of tinnitus; (2) Determine if EMA questions can define a latent variable tied to an underlying vulnerability to tinnitus; (3) Explore if the latent variable is predictive of tinnitus severity.

**Methods:** A test-retest trial using EMA of patients with chronic non-pulsatile tinnitus was performed in an outpatient academic medical center. Participants received EMAs about tinnitus loudness, environment noise, stress, tinnitus bother, and overall feeling, 4 times per day for 2 weeks (study part 1); this was repeated (study part 2) after a 2-week break. Standard descriptive statistics were used to define the study population. Paired t-test, Pearson's correlation tests, and interclass correlation coefficient were used to assess EMA reliability. A latent factor analysis and linear regression analysis were used to explore an underlying vulnerability to tinnitus and to predict tinnitus severity, respectively.

**Results:** There was significant inter/intra-patient variability in EMA responses. The responses in study parts 1 and 2 were highly correlated and there was no statistically significant difference between them. A tinnitus vulnerability latent variable, including four of the EMA questions, was created; the model demonstrated excellent fit. The latent variable significantly predicted greater baseline severity, as per a linear regression model.

**Conclusions:** Based on a paired t-test and Spearman correlations comparing Part 1 and Part 2 of the study, EMA is a reliable method for capturing information about tinnitus severity. Four EMA questions loaded well onto one tinnitus latent factor, which can be used to comprehensively describe the tinnitus experience, including moment-to-moment variability. EMA and the "Tinnitus Latent Factor" that it can measure, together, provide a deeper understanding of the tinnitus patient population.

093

### McCarley, Saudia

Otolaryngology NIH T32 Physician Scientist Program (PSP); Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Otolaryngology  
Mentors: John Chi, MD; Jay Piccirillo, MD, FACS

#### **Quality-of-life instruments following post-Mohs facial reconstruction**

McCarley SM; Chi J; Piccirillo JF

**Introduction:** Following Mohs surgery, facial reconstruction is performed to correct the resulting defect. Given the myriad of options for facial reconstruction, the initial pre-reconstruction consultation with the reconstructive surgeon is a vitally important encounter. A critical part of this encounter is an honest discussion of the patient's questions, concerns and limitations in their peri-operative care. Currently, no quality of life instrument exists specifically for post-Mohs facial reconstruction patients. Developing such an instrument would be invaluable in establishing the most appropriate reconstructive plan for post-Mohs patients. Prior post-Mohs facial reconstruction patients will be key to the development of a post-Mohs facial reconstruction quality of life instrument.

**Methods:** This is a prospective and retrospective study in which a quality of life instrument is developed regarding patient expectations and concerns relating to Post-Mohs reconstructive surgery. Medical records were used to identify patients who had or would be receiving post-Mohs facial reconstructive surgery. Identified patients were questioned regarding their physical problems, functional limitations, and emotional consequences of their surgery and their disease-specific quality of life. Patients were interviewed on what they felt was important regarding quality of life expectations and concerns with facial reconstruction. These expectations were analyzed and categorized into physical, functional, and emotional expectations. A questionnaire was built with these expectations. The questionnaire was distributed to prior post-Mohs facial reconstructive patients and compared with how their surgical site appeared in relation to their quality-of-life. Through actual patient use, the number of items on the questionnaire will be reduced to those most influential and pertinent with quality of life.

**Results:** It is anticipated that patients will reveal their specific questions and concerns through the survey. This can be utilized to provide better care for each individual patient making their overall surgery outcome better suited for him or her.

**Conclusions:** The project is undergoing IRB approval at this time. Upon approval, patients may then be interviewed so that the questionnaire development will be completed. This will be tested on prior post-Mohs reconstruction patients first. It is anticipated that the responses of these patients will help in our understanding of the best approach to modifying the quality-of-life instrument for patients who will undergo post-Mohs reconstructive surgery in the future.

**Thompson-Harvey, Adam**

Otolaryngology NIH T32 Physician Scientist Program (PSP)

Current Doctoral Program of Study: Medicine

Saint Louis University

Department: Otolaryngology

Division: Otology/Neuro-otology

Mentors: Joel A Goebel, MD, FACS; Belinda Sinks, AuD

**Validation of optimal target size during gaze stabilization testing**

Thompson-Harvey AC; Sinks BC; Goebel JA

**Introduction:** The Gaze Stabilization Test (GST) is a reliable, functional assessment of the vestibulo-ocular reflex (VOR). The GST measures the maximum head velocity a patient can elicit while maintaining their visual acuity on a presented target (optotype). The GST protocol requires an optotype size a few lines above a patient's static visual acuity (SVA), for which there is no consensus of expert opinion. In this study, we studied the optimal target size to be presented during the GST.

**Methods:** 20 healthy control participants completed three randomized GST trials for each of two established optotype sizes: two sizes above SVA and three sizes above SVA.

**Results:** Results revealed a significant difference between optotypes two and three sizes above SVA ( $p = .020$ ). Intraclass coefficients (ICC) and standard error of measurement (SEM) measured between and within-subject variability for two and three sizes above SVA (ICC = .836 and .900, respectively; SEM = 18.50 and 15.35, respectively). While both GST optotypes maintained excellent consistency between subjects, within-subject variability increased when using the optotype two sizes above SVA.

**Conclusions:** This study suggests that healthy participants are able to maintain gaze stabilization at higher head velocities in GST with a larger optotype. Even more, using an optotype of three sizes above SVA may yield more reliable GST scores. Next, we will test patients with vestibular disease to evaluate which optotype better differentiates healthy participants from those with vestibular disease.

## Radiological Society of North America (RSNA)

019

### Chang, Randy

Radiological Society of North America (RSNA); Dean's Fellowship  
Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Radiology, University of California, Los Angeles

Mentors: Whitney B Pope, MD, PhD; Jesse G Jones, MD

#### **Melanin as a MRI tracking agent in intracerebral cell delivery for stroke**

Chang RO; Jones JG; Pope WB

**Introduction:** Current treatments for ischemic stroke are directed towards restoring blood flow but do not directly treat the long-term disability effects. Embryonic stem neural precursor cells (ES-NPC) have been shown to improve neurological function in animal stroke models, but translating ES-NPCs into a viable therapy necessitates post-delivery monitoring. Melanin is a positive contrast agent whose signal intensity correlates well with cell number and can be produced in a controlled manner via transgene expression of tyrosinase. The purpose of this study is to demonstrate the feasibility of expressing tyrosinase in human embryonic kidney (293-HEK) and the use of embryonic stem neural precursor (ES-NPC) cells as MRI tracking agents in the stroked mouse brain.

**Methods:** 15 mice underwent photothrombosis-induced (PT) ischemic stroke. Non-transfected 293-HEKs, transfected 293-HEKs, and transduced ES-NPCs were intracerebrally injected into 5 mice each. All cohorts and controls underwent T1-weighted, T2-weighted, and T1 mapping by MRI following transplantation. Mice brain coronal slices were immunohistochemically stained for human nuclear antigen (HuNu) and imaged via confocal laser scanning microscopy (CLSM). A Wilcoxon rank-sum test was performed to test the significance of T1 relaxation time between controls and cohorts.

**Results:** T1 shortening was present in all mice injected with transfected 293-HEK cells. Mean T1 relaxation time in the region of interest around the injection sites was 960.2 ms, compared to 1392.8 ms for nontransfected 293-HEK cells ( $p = .008$ ). Complete data for transduced ES-NPCs is still being collected but expected to be significant. Specimens through PT stroke demonstrated a sharply demarcated border between the infarct and normal neuronal cells. Slices through all cell injections were HuNu positive. These regions colocalize with dark melanic pigment under light microscopy.

**Conclusions:** Preliminary data support the purpose of the study. Repeated MRI and CLSM data collection on subsequent post-stroke days will allow for tracking of ES-NPC distribution and migration over time and will lend further insight into the effectiveness of this novel imaging protocol.

## Rehabilitation and Participation Science (RAPS) Doctoral Program

003

### Baune, Nathan

Rehabilitation and Participation Science (RAPS) Doctoral Program  
Current Doctoral Program of Study: Occupational Therapy  
Washington University in St. Louis  
Department: Occupational Therapy  
Mentor: Scott H Frey, PhD

#### **Localization of touch on a replanted or transplanted hand: evidence for late-occurring improvements that may reflect central adaptations**

Baune NA; Philip BA; Kaufman C; Kutz J; Frey SH

**Introduction:** Following sensory nerve transection and repair, peripheral nerve regeneration is estimated to proceed at a rate of up to 2mm per day. However, patients that undergo surgical nerve repairs of the arm or hand show persistent difficulties in localization of touch without vision long after nerve regeneration is thought to be complete. This may reflect chronic disorganization of finger maps within the primary somatosensory cortex (S1). Prior fMRI results show that hand transplant patients recover the former cortical territory devoted to processing sensory information. We tested the hypothesis that central adaptations associated with extended experience can mitigate these functional limitations in former amputees that have had they injured hands replanted (heterotopic hand replants), or received transplantations of donor hands (allogeneic hand transplants).

**Methods:** We adapted the locognosia method developed by Noordenbos to measure the ability to localize light touch (100mN) without vision on the ventral surface of the hand and digits in 22 healthy adults, 4 heterotopic hand replant patients and 4 allogeneic hand transplant patients.

**Results:** Compared to the mean accuracy of healthy controls hand transplant patients had a much greater difficulty in localizing touch on their hand and digits. There was a moderate correlation ( $r = -.62$ ) between the years since surgery in transplant patients and performance. For two of the transplant patients multiple measures were taken over time and for both locognosia performance improved at each subsequent session.

**Conclusions:** Patients' functional ability to localize touch appears to improve with time post surgery. Localization improves even after nerve regeneration has completed which suggests that central mechanisms could be affecting recovery. A future avenue may be to test whether neural modulation methods can be used to enhance recovery in patients post nerve regeneration.

004

### Boone, Anna, MSOT, OTR/L

Rehabilitation and Participation Science (RAPS) Doctoral Program  
Current Doctoral Program of Study: Occupational Therapy  
Washington University in St. Louis  
Department: Occupational Therapy  
Mentor: Jack Engsberg, PhD

#### **Development of a quantitative portable assessment of spasticity**

Boone AB; Foreman MH; Standeven J; Wang TY; Wu CY; Sutton OM

**Introduction:** Spasticity is a velocity dependent, abnormal increase in muscle tone present during passive movement that results from an alpha motor neuron lesion. Accurate and repeatable measurement is essential for treatment decisions. Many assessments exist and fall short of rigorous psychometric properties, but predominantly the Modified Ashworth Scale (MAS) is used clinically. The MAS is limited by subjectivity and ordinal level ranking. Engsberg created an objective, quantitative measure of spasticity that utilized range of motion, velocity, and resistance of force to establish a single spasticity number spasticity quantification. Its sole limitation was cost and space required to gather the biomechanical information. Therefore the purpose of this work was to apply current technology to create a valid, reliable, quantitative measure of spasticity that is clinically feasible in cost and size.

**Methods:** Trial and error methods were used to determine the appropriate technology to be used according to sensitivity and clinical utility requirements. Hardware consisting of a flexible metal cuff and gripping handle coupled with software consisting of Arduino, an accelerometer, a force sensing resistor, a Bluetooth module, and a smart phone were integrated for a working prototype.

**Results:** A prototype of a tool including hardware and software was developed that is able to measure each component of spasticity including range of motion, velocity, and resistive force. Each of these measurements may then be mathematically combined. The slope of the work versus velocity graph then represents the magnitude of the spasticity in accordance with the Engsberg method.

**Conclusions:** The end result is a prototype of a quantitative assessment of spasticity that has been developed that accurately measures range of motion, resistive force, and velocity and seamlessly integrates them into the force-work curve. The force sensor is accurate to .2 N and the accelerometer to 0.0153 g. Velocity is indirectly obtained and tested to have an error rate <2.5%. Additional iterations of design are required for minimizing size of the device and determining the validity and reliability.

005

**Hu, Yi-Ling, MS**

Rehabilitation and Participation Science (RAPS) Doctoral Program

Current Doctoral Program of Study: Rehabilitation and Participation Science

Washington University in St. Louis

Department: Occupational Therapy

Mentor: Susan Stark, PhD, OTR/L, FAOTA

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

Hu Y

**Introduction:** The need for effective fall prevention programs tailored to medically underserved older adults is urgent. Home modifications and Life Style and Functional Prevention Program (LiFE) are two effective programs that reduce falls among older adults in Australia. Medically underserved older adults were not the target for these programs, but they may benefit from these home-delivered fall prevention interventions. To successfully implement these programs, a better understanding of the perceptions and concerns of medically underserved older adults toward fall prevention is needed.

**Methods:** Focus groups were used to explore local older adults' perception about the two fall prevention programs in order to culturally adapt the programs. Three focus groups were conducted 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 identified potential barriers to implementation. Trust, autonomy and cost were the main concerns participants identified for the home modification program. Using plain language, using photographic images that represent the participant's race in the manual, tailoring, and group support would enhance motivation for LiFE.

**Conclusions:** Medically underserved older adults do acknowledge the values of the fall prevention programs, but modifications to the fall prevention programs are the key to initiate acceptance of the programs.

## Siteman Cancer Center Leah Menshouse Springer Summer Student Program

117

### Lapidus, Jodi

Siteman Cancer Center Leah Menshouse Springer Summer Student Program; Dean's Fellowship  
Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Pediatrics

Division: Hematology & Oncology

Mentor: Joshua Rubin, MD, PhD

#### **Molecular signatures of angiogenesis in high grade glioma**

Lapidus JB; Rubin JB

**Introduction:** High-grade glioma (HGG) is among the most deadly cancers, and prognosis has remained largely unchanged despite advancements in treatment. There is currently no standard of care for recurrent HGG, but anti-angiogenics are often used as adjuvant therapy. Bevacizumab (Avastin, Genentech/Roche) is a monoclonal antibody against VEGF, a highly potent stimulator of angiogenesis. The purpose of this study is to examine the variations in protein expression in HGGs and to define a molecular subtype of response to bevacizumab therapy.

**Methods:** Lysates of pediatric (n=8) and adult (n=11) biopsies were analyzed using the Human Angiogenesis Antibody Array (R&D Systems). Quantification was done by fluorescent imaging and integrated density measurement.

**Results:** To describe angiogenic potential, an index value was calculated by comparing expression levels of pro- and anti-angiogenic proteins. The index values ranged from -366.92 to 534.63 (mean: 32.2, SD: 225.3). When comparing the index to progression free survival (PFS), two distinct groups emerged. Non-linear regression showed group 1 (n=7) to have a negative correlation between PFS and index ( $R_{sq} = 0.96$ ), and group 2 (n=6) to have a positive correlation ( $R_{sq} = 0.99$ ).

**Conclusions:** The results of this study suggest that there are large differences in protein expression levels across HGGs. Comparison of PFS to index value allowed stratification of the samples into two groups of opposite relationships, indicating that there indeed might be different subtypes that can prospectively predict response. Future research is needed to clarify the factors that drive the index, which proteins are most important in each patient subgroup, and the ways in which expression levels change after treatment.

083

### Pruett, Cliff

Siteman Cancer Center Leah Menshouse Springer Summer Student Program; Dean's Fellowship  
Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Internal Medicine

Division: Hematology & Oncology

Mentors: John DiPersio, MD, PhD; Michael Rettig, PhD

#### **Characterization of a set of novel peptide CXCR4 antagonists**

Pruett CH; Rettig MP; DiPersio JF

**Introduction:** Disruption of the interaction between CXCR4 and SDF-1 $\alpha$  (CXCL12) induces hematopoietic stem and progenitor cell (HSPC) mobilization into the peripheral blood and sensitizes leukemia cells to cytotoxic therapy. In 2008, the small molecule plerixafor (AMD3100, Mozobil) was approved as an HSPC mobilizing agent when administered in combination with G-CSF for non-Hodgkin's lymphoma and multiple myeloma patients undergoing autologous stem cell transplantation. However, there remains a significant proportion of patients who fail to mobilize enough HSPCs to proceed to transplant and plerixafor exhibits significant cardiotoxicity. As such, we seek to develop safer and more effective CXCR4 antagonists for normal HSPC mobilization and leukemic cell mobilization and chemosensitization.

**Methods:** We tested a novel series of small peptide CXCR4 antagonists in vitro by direct SDF-1 binding experiments and calcium flux and apoptosis assays. We also assessed HSPC mobilization in mice and assayed peptide stability via peptide binding experiments in the presence of mouse plasma.

**Results:** Two peptides (CMD-144 and -148) were identified that inhibited the binding of SDF-1 to CXCR4 similar to plerixafor. Similar to plerixafor, CMD-144 and -148 inhibited the binding of CXCR4 antibody clone 12G5 but not clone 1D9 to cells and did not directly stimulate Ca<sup>2+</sup> flux in an ALL cell line. While one previously published peptide CXCR4 antagonist (BKT-140) directly inhibited leukemia cell growth in vitro, plerixafor, CMD-144 and -148 did not. Unfortunately, the peptides failed to mobilize murine white blood cells (WBCs) and HSPCs in vivo.

**Conclusions:** CMD-144 and -148 exhibit greater binding affinity than plerixafor to CXCR4. These appear to function by preventing the binding of SDF-1, but do not possess any agonist activity themselves. CMD-144 and -148 did not exhibit any HSPC mobilization in vivo and preliminary data suggest that the peptides fail to function due to their rapid degradation by plasma proteases. If successful, this project will lead to peptide-based CXCR4 antagonists with desirable in vivo normal and leukemic cell mobilization and leukemic cell chemosensitization profiles.

## Summer Medical Education Research Fellowship (SMERF)

042

### Margolis, Mathew

Summer Medical Education Research Fellowship (SMERF); Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Neurology  
Mentor: Douglas Larsen, MD

#### **The effects of varying spaced repetition methods in preparation for preclinical board examinations**

Margolis MS; Larsen DP

**Introduction:** Studies in cognitive psychology laboratories and medical education settings have shown that repeated testing of information, which requires learners to actively process and retrieve information compared to passive learning methods such as reading, produces significantly better long-term retention. Despite this, the majority of medical programs rely on passive learning methods, possibly in part due a lack of research on optimized or even standardized methods for employing study retrieval practice, also known as test-enhanced learning. Due to the rising medical student use of self-testing, especially in preparation for preclinical board examinations, it has become critical to evaluate these methodologies. This study aims to evaluate various currently practiced methodologies of preparation for preclinical board examinations using the spaced repetition test-enhanced learning platform Anki.

**Methods:** Differences between spaced interval test-enhanced learning methodologies including given vs. self-generated materials, re-reading at intervals, mentally recalling at intervals (standard flashcard format), and type-to-recall at interval methods were evaluated for a six-group within-subject study of rising second-year medical students using digital platform Anki. Results will be assessed by means of an ANOVA with planned post-hoc t-tests, with descriptive statistic analysis of collected user metrics.

**Results:** On taking our final assessment 30 days after study onset, 15 students assessed scored on average 49.6% on material related to cards they had been given vs. 37.8% on material related to self-composed cards. Participants scored an average of 31.8% on material related to cards that they re-read at intervals, 47.8% on material related to cards that they recalled at intervals, and 51.3% on material related to cards that they typed to recall at intervals. All students surveyed said they would continue to use Anki in the future, with 96% wishing to receive pre-made cards in the future. Further analysis via means of an ANOVA with planned post-hoc t-tests, with descriptive statistic analysis of collected user metrics is underway to determine clinical significance and confidence intervals of this data.

**Conclusions:** While at this point in time further analysis is required to determine clinical significance and confidence intervals of this data, this study has shown us the value of spaced-interval test enhanced learning in the setting of preclinical medical education with recall methods providing up to twice the retention value of repeated readings. Participants' strong performance on given cards coupled with an overwhelming desire to receive materials in the identical form in the future suggest that implementing such methodologies into pre-clinical coursework would be both well received, and yield promising results in terms of retention.

088

### Ye, Yuting

Summer Medical Education Research Fellowship (SMERF); Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Medical Education  
Mentor: Sabrina Nunez, PhD

#### **A review for USMLE Step 1 Biochemistry**

Ye Y; Nunez S

**Introduction:** Students at Washington University School of Medicine (WUSM) start first year with the biochemistry course – Molecular Foundation of Medicine. However, it is hard for students to appreciate the clinical perspectives of biochemistry so early in medical school. The goal of my research project is to produce a biochemistry review with a clinical perspective and a focus on USMLE Step 1.

**Methods:** I reviewed a number of mainstream biochemistry textbooks and board review books for biochemistry. I also worked through the biochemistry questions in USMLE Step 1 Qmax question bank.

**Results:** I wrote a total of 15 biochemistry review supplements, covering most of the high-yield USMLE Step 1 biochemistry topics.

**Conclusions:** This review emphasized two clinical perspectives. The whole body perspective--various organs (for instance liver, adipose tissues, muscles) are always working together in both healthy and pathological states. The various pathways are interconnected and metabolic intermediates are constantly shuttled between different pathways, depending on the metabolic states (for instance fed state, fasting state and starvation state) and the level of major hormone signals (insulin, glucagon etc.). However, this whole body concept is frequently not emphasized enough in basic biochemistry textbooks. The diagnostic perspective – in a clinical setting, physicians use patient demographic information, clinical presentations and laboratory test results to reach a clinical diagnosis. Thus, when studying clinical biochemistry it is essential to be aware of the typical patient demographics, clinical manifestations, and laboratory test results associated with each disease, and these are not emphasized sufficiently in a typical basic biochemistry textbook. I try to emphasize these two perspective in my review, and hopefully this review can assist WUSM students in reviewing clinical biochemistry.



## Summer Research Program in Global Health (SRPGH)

102

### Daniels, Elizabeth

Summer Research Program in Global Health (SRPGH); Dean's Fellowship

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Molecular Microbiology

Mentors: Jacqueline Kimmey; Christina Stallings, PhD

#### **Investigating the effect of autophagy on neutrophil differentiation**

Daniels EA; Kimmey JM; Stallings CL

**Introduction:** Recent in vitro experiments have suggested that defects in autophagy, a mechanism by which cells degrade cytoplasmic components, may increase the rate of murine neutrophil proliferation and differentiation. Neutrophils are a key component of the immune system, and changes in neutrophil proliferation could affect the body's ability to control infection. Past experiments have demonstrated that neutrophils deficient in ATG5, a factor essential for autophagy, proliferate and differentiate more quickly than wild-type neutrophils. However, ATG5 can function independently of autophagy, and it is unknown whether other autophagy factors affect neutrophil proliferation or maturation.

**Methods:** To test whether ATG5 increases the rate of neutrophil differentiation due to its role in autophagy, we compared the rate of differentiation of neutrophils separately knocked-down for three factors essential for autophagy, ATG5, ATG7, and ATG16, to that of controls. Genetic knockdown was achieved via stable expression of shRNA in neutrophil precursors, and defects in autophagy were confirmed by western blotting for LC3-lipidation and p62 accumulation. Cells were allowed to mature for 3, 4, or 5 days, and differentiation was monitored based on cellular morphology.

**Results:** If autophagy plays a role during neutrophil differentiation, we predict that cell lines deficient in either ATG5, ATG7 or ATG16L1 will each mature faster in vitro than controls. However, if cells deficient in ATG5 display faster maturation than both controls and those deficient in ATG7 and ATG16L1, this would suggest an autophagy-independent role for ATG5.

**Conclusions:** Our experiments will help define the role of autophagy and autophagy-essential factors in neutrophil maturation and, more broadly, the control of infection.

## T35 NIH NHLBI Training Grant

116

### **Berg, Julia**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Pediatrics

Division: Hematology & Oncology

Mentor: Shalini Shenoy, MD

#### **Reduced-intensity conditioning for hematopoietic stem cell transplantation using mismatched bone marrow or cord blood in children with non-malignant hematological diseases**

Berg JM; Murray L; Shenoy S

**Introduction:** Hematopoietic stem cell transplantation (HSCT) has the potential to cure several hematologic diseases, but its use is limited by the morbidity and mortality associated with transplant and the availability of suitable donors. Since patients with non-malignant disease do not require complete elimination of the host bone marrow, transplantation with a less intensive, less toxic regimen may still be curative. In this study, we aim to determine whether a reduced-intensity conditioning regimen with alemtuzumab, fludarabine, thiotepea, and melphalan will have favorable outcomes with regard to mortality, graft rejection, graft-versus-host-disease (GVHD), and infections in children receiving mismatched bone marrow or cord blood transplants.

**Methods:** Patients with indications for transplant for a non-malignant disease but lacking a fully matched related or unrelated donor were eligible for the trial. This was a multicenter trial with participating centers in the US and Canada. Data was collected from Case Report Forms and medical records and compiled into an Excel database to prepare for analysis and publication. Missing data was collected from participating centers.

**Results:** Overall, 23 patients were included in the analysis: 13 in the mismatched bone marrow (BM) cohort and 10 in the cord blood (CB) cohort. Overall survival was 77% (BM) and 80% (CB). Causes of death included sepsis and acute GVHD. Of those patients who survived without graft rejection, none had disease recurrence. Graft rejection was 8% (BM) and 10% (CB) due to osteopetrosis and sickle cell, comparable to myeloablative regimens. Acute GVHD occurred in 62% (BM) and 50% (CB) of patients. The median number of infections in the first year was 3 (BM) and 4.5 (CB).

**Conclusions:** These results suggest that this reduced-intensity conditioning regimen has a high rate of engraftment and successful immune reconstitution. The principal barrier to expanding the use of this regimen is the mortality rate. Improved acute GVHD prevention has the potential to reduce mortality and thereby enhance the acceptability of transplant as a curative option for these patients. A recent amendment to the trial added abatacept to the GVHD prophylaxis regimen for eligible patients.

067

### **Briscoe, Cristopher, JD**

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: Brian Fuller, MD, MSCI

#### **Lung-protective ventilation and the prevention of ventilator-associated conditions in the emergency department**

Briscoe CC; Fuller B

**Introduction:** Mechanical ventilation is commonly employed in hospital emergency departments, and it has been hypothesized that ventilator use may in some cases lead to certain ventilator-associated conditions (VACs), including acute respiratory distress syndrome (ARDS). Studies have demonstrated that lung-protective ventilation may reduce the incidence of progression to VACs in at-risk patients. We seek to investigate whether initiation of lung-protective ventilation in the emergency department leads to a corresponding decrease of VACs in patients later admitted to the intensive care unit (ICU).

**Methods:** Prospective observational study comparing development of VACs in mechanically-ventilated patients in the emergency department at Barnes Jewish Hospital (BJH). Data from these patients will be analyzed and compared with a historical control group of mechanically-ventilated patients in the BJH emergency department who were not ventilated under the lung-protective ventilator protocol.

**Results:** Study is ongoing. We are currently obtaining data from the prospective cohort and analyzing data from the historical control group.

**Conclusions:** Study is ongoing and we cannot yet draw any conclusions. We hypothesize that the use of lung-protective ventilation in the BJH emergency department will be associated with a decrease in ARDS and other VACs as compared to the historical control group.

100

**Burdis, Nora**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Molecular Microbiology  
Mentor: Scott Hultgren, PhD

**Type 1 pili and motility in uropathogenic Escherichia coli**

Burdis NC; Schreiber HL; Hultgren S

**Introduction:** Uropathogenic Escherichia coli (UPEC) are responsible for the majority of urinary tract infections (UTIs) and are phylogenetically and genetically diverse. UTIs occur when bacteria from the GI system are introduced to the urethra and travel to the bladder. Attachment to host tissues and swimming motility are critical to UPEC colonization during UTIs and are mediated by flagella and type 1 pili, respectively. Previous research has indicated that regulation of motility and type 1 pili production are inversely correlated; however, these studies focused extensively on B2 clade E. coli strains and largely neglected other clades (A, B1, D, and E).

**Methods:** To better define the regulation of these virulence-associated phenotypes in diverse UPEC, we determined swimming motility and type 1 pili production for 66 E. coli strains isolated from the urine of 28 female patients with UTIs.

**Results:** Neither type 1 pili nor motility correlated with infection recurrence or E. coli clade. Additionally, high type 1 pili levels did not lead to low motility.

**Conclusions:** The correlation found previously between high type 1 pili production and low motility existed for B2 clade E.coli but not for E. coli in other clades (A, B1, D, and E). Additionally, type 1 pili production can't be used to explain why some UPEC strains cause recurrent infections while others do not. However, the conclusions that can be drawn for this study are limited due to the nature of urine E. coli samples.

020

**Coley, Avril**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Division of Cardiothoracic Surgery  
Mentor: Traves Crabtree, MD

**Adherence to lymph node sampling guidelines in non-small cell lung cancer patients**

Coley AK; Ray S; Crabtree TD

**Introduction:** Though treatment guidelines for non-small cell lung cancer (NSCLC) include systematic lymph node dissection as a necessary component of adequate staging, lymph node sampling practices are often suboptimal. The aims of this study are to evaluate nodal sampling practices in the Washington University Department of Thoracic Surgery, and to implement an intervention to improve adherence to national guidelines. While our center performs well in terms of patient outcomes, our goal is to implement a quality initiative to continue improving our performance and to increase accountability for delivering exceptional care to our patients.

**Methods:** Institutional data from NSCLC lung resections that took place between January 2013 and December 2014 were analyzed. The number of lymph nodes collected and the number of N2 nodal stations sampled per case were analyzed for the department overall, by type of resection, and by individual surgeon. We developed and implemented an intervention to educate members of the operating room faculty and staff about the importance of nodal sampling in the surgical work flow.

**Results:** Overall, adherence to the guideline of 3 N2 stations sampled per case was 32.2% and the average number of nodes collected per case was 10.8 (s=7.8). The group of surgeons' median adherence was 30.2% (range, 9.7% - 59.5%). For the mean number of stations sampled per case, the median of the group was 1.68 (range, 1.3 - 2.56). When evaluated by procedure type, the highest rate of adherence and the highest number of stations sampled per case were during lobectomies. As the number of N2 stations sampled increased from 0 to 3, the percentage of patients pathologically upstaged increased from 7.14% to 15.15%.

**Conclusions:** Consistent with findings in the literature, nodal sampling practices at this institution were suboptimal. After re-educating the surgical team, we hope to see an increase in adherence to national guidelines. Increasing adherence will hopefully result in more accurate staging of NSCLC patients and an overall improvement in care delivery.

086

**Dandulakis, Mary**

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: John Constantino, MD; Azad Bonni, MD, PhD

**Induced pluripotent stem cell derived neuronal model of familial x-linked autism**

Dandulakis M; Constantino J

**Introduction:** Autism spectrum disorder (ASD) exhibits a male to female prevalence ratio of about 4:1 although ASD is primarily an autosomal linked disease. One hypothesis regarding the modulation of this ratio is that the X chromosome is influencing the phenotypic expression of ASD associated variants. The purpose of this study is to use induced pluripotent stem cells (iPSC) from a family of an unaffected mother carrying an X-linked MECP2 ASD associated mutation and an affected son with the same mutation to establish excitatory cortical neurons in order to determine structural, biochemical and electrical differences between mom and son.

**Methods:** iPSCs from patients were differentiated into neural progenitor cells (NPCs) following the Stem Cell Technologies protocol Stemdiff Neural System. NPCs were cultured in Neural Induction Medium and Neural Progenitor Medium (Stem Cell Technologies). The NPCs will be differentiated into neurons following a small molecule protocol. Eventually immunocytochemistry, synaptic electrical measurements, soma size measurements, and counting number of synapses will be completed to determine differences between mother and son's cells.

**Results:** Thus far the NPCs have been cultured and expanded. Immunocytochemistry demonstrated that both mother and son's NPCs expressed markers associated with neural progenitor cells. Interestingly the mother's cells differentiate much faster than the son's.

**Conclusions:** Further work will need to be conducted in order to determine the morphological as well as electrical differences between the mother and son's excitatory cortical neurons. In addition it will need to be determined which X chromosome is active in the mother's cells in order to differentiate mother's cells expressing mutant MECP2 versus cells expressing wild type MECP2. This study could help establish the differences between normal and ASD affected excitatory neurons, as well as potentially what is the mechanism responsible for the gender ratio in ASD.

049

**Del Valle, Michael**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurosurgery

Mentors: Eric Leuthardt, MD; David Bundy, PhD

**Beta-gamma phase-amplitude coupling differences between contralateral and ipsilateral arm movements**

Del Valle MB; Leuthardt E

**Introduction:** Cross-frequency coupling has been suggested to play a role in neural computation, communication, and learning. The strength of the phase-amplitude cross-frequency coupling has been demonstrated to change with sensory, motor, and cognitive events. Though decreases in phase-amplitude coupling have been demonstrated during motor movements, it is unknown how this differs in contralateral and ipsilateral tasks. Work may reveal the relationship between coupling and rhythms within cortical activity.

**Methods:** Previously collected electrocorticographic (ECoG) 2D and 3D center-out reaching task data in conjunction with visually-guided finger movement task data, both with contralateral and ipsilateral limb movement, was used to allow comparison of the phase-amplitude coupling that occurs during unilateral limb movements.

**Results:** Research is still ongoing, however, during contralateral limb movements, beta-gamma phase-amplitude coupling in the primary motor cortex is predicted to decrease relative to resting periods, while during ipsilateral limb movement, beta-gamma phase-amplitude coupling is predicted to persist.

**Conclusions:** Determining the manner in which phase-amplitude coupling differs during contralateral and ipsilateral limb movements may shed light on the relationship between coupling and rhythms within cortical activity as well as to further understand the role of the ipsilateral hemisphere during limb movements.

050

**Desai, Kshitij**

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

**Application of remote ischemic conditioning to subarachnoid hemorrhage**

Desai KA; Brent B; Zipfel G

**Introduction:** For over two decades, vascular conditioning has been effectively aiding patient recovery from myocardial ischemia/reperfusion-related injury in clinical settings, establishing a cardioprotective effect. More recently, clinical examination of ischemic conditioning's impact on physiological vasculature change, first focused in the fields of cardiology, nephrology, and pulmonology, has now expanded into neuroscience, spurring investigation of vascular conditioning's contribution to neuroprotection and its overall mechanism. In this paper, we explore the potential of adapting the principles of remote limb ischemic conditioning to improve patient recovery in subarachnoid hemorrhage (SAH), particularly in their ability to reduce the incidence of vasospasm and delayed cerebral ischemia (DCI).

**Methods:** We conducted a multi-database, general review of over 70 articles focusing on the use of ischemic conditioning in clinical and basic science settings. This included the impact of remote ischemic conditioning (RIC) impact on cardiac ischemia, ischemic strokes, early brain injury, and SAH. Presentation of conditioning agents and vascular conditioning was also performed. Finally, we elaborated upon the potential to apply condition-based therapy, capitalizing on endogenous mechanisms of RIC to SAH.

**Results:** Vascular conditioning has had a marked impact on improving surgical recovery in several fields, especially cardiology. Over two decades, this has progressed into the field of neurosurgery and given rise to the idea of vascular neuroprotection against DCI and vasospasm; clinical data on patients recovering from SAH has shown that conditioning aids in decreasing these fatal effects post-surgically. Due to the vascular pathologies associated with SAH, it is likely that remote ischemic limb conditioning can benefit patient recovery.

**Conclusions:** To date the Zipfel lab is conducting RIC experimentation on mice recovering from induced SAH. Preliminary results indicate that RIC does have a marked neuroprotective effect and can be successfully applied in clinical settings once its window of opportunity and dosage-response characteristics have been more fully explored.

109

**Erickson, Stephen**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Ophthalmology and Visual Sciences  
Mentor: Rajendra Apte, MD, PhD

**Diagnostic biomarkers in uveitis and intraocular lymphoma**

Erickson SP; Santeford A; Apte RS

**Introduction:** Distinguishing uveitis and intraocular lymphoma often poses a diagnostic challenge for clinicians. As a 'masquerade syndrome,' primary intraocular lymphoma often presents with signs and symptoms that mimic uveitis. Current diagnostic methods rely on flow cytometry and histopathology using small samples with very few cells, complicating diagnosis. Previous work in animal models has shown that autophagy is obstructed in macrophages during/leading to uveitis. Therefore, markers of autophagy such as p62 hold potential as biomarkers for the diagnosis of uveitis versus intraocular lymphoma. Accumulation of p62 reflects reduced autophagic flux and thus uveitis.

**Methods:** In this study p62 levels were quantified via ELISA in vitreous humour, plasma, and peripheral blood mononuclear cells (PBMC) from patients with diagnoses of uveitis, lymphoma, or non-inflammatory eye conditions.

**Results:** In vitreous humour samples, p62 levels were higher in patients with uveitis versus lymphoma and undetectable in those with non-inflammatory eye conditions. PBMC samples showed little difference in p62 levels between patients with uveitis and non-inflammatory eye conditions. In plasma samples, p62 was present at low levels, but levels were higher in patients with non-inflammatory eye conditions versus uveitis.

**Conclusions:** The use of autophagy proteins as diagnostic biomarkers to distinguish these conditions holds promise in vitreous humour samples and warrants further exploration. Although PBMC samples showed little difference in p62 levels, this may be due to differences in baseline expression of p62. Not unexpectedly, plasma samples showed very low p62 levels and should not be analyzed in future studies. In addition to p62, other markers of autophagic flux such as LC3 should be investigated.

082

**Guo, Mindy**

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

Mentors: David A Russler-Germain; Timothy J Ley, MD

**Molecular consequences of AML-associated mutations in DNMT3A**

Guo M; Russler-Germain DA; Ley TJ

**Introduction:** Mutations in DNMT3A, encoding a de novo DNA methyltransferases, are initiating events in the development of acute myeloid leukemia (AML). Wild-type (WT) DNMT3A functions as a tetramer; the highly recurrent R882H mutation decreases the catalytic activity of and alters oligomerization of DNMT3A in a dominant-negative fashion. We explored how DNMT3A oligomerization is influenced by several recurrent AML-associated DNMT3A mutations.

**Methods:** We developed a high-throughput assay using the Perkin-Elmer AlphaLISA technology to measure direct interactions between DNMT3A molecules from any allele combination of interest. We utilized lysates of HEK293T cells expressing C-terminal epitope (FLAG or V5) tagged wild-type or mutant (R635W, S714C, R736H, R882H, Q515\*, E616fs, and L723fs) DNMT3A. Mixing DNMT3A-FLAG and DNMT3A-V5 lysates with anti-FLAG "donor" and anti-V5 "acceptor" beads (akin to a FRET assay) provided a robust signal for investigation of interactions between DNMT3A molecules.

**Results:** Using the WT:WT DNMT3A interaction as a baseline, we investigated interactions between WT DNMT3A and seven mutant DNMT3A forms. The WT:R882H interaction was more favorable as well as more resistant to increased NaCl or KCl levels than the WT:WT interaction, whereas the WT:S714C interaction behaved equivalently to the WT:WT interaction. In contrast, WT DNMT3A was unable to interact with R635W, R736H, Q515\*, E616fs, or L723fs DNMT3A.

**Conclusions:** We found that several recurrent AML-associated DNMT3A mutations have distinct molecular consequences. Five mutant forms of DNMT3A (R635W, R736H, Q515\*, E616fs, and L723fs) fail to interact with WT DNMT3A, suggesting that they contribute to leukemogenesis through mechanisms other than direct dominant-negative effects on WT DNMT3A. In contrast, S714C DNMT3A and R882H DNMT3A retained their abilities to interact with WT DNMT3A. The WT:R882H interaction was favorable to and more stable than the WT:WT interaction, helping explain its potent dominant-negative effects. Future studies will be required to elucidate the unique contributions to leukemogenesis of the various DNMT3A mutations found in AML.

021

**Haque, Nowrin**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Cardiothoracic Surgery  
Mentor: Ralph J Damiano, Jr, MD

**Effectiveness of surgical ablation for atrial fibrillation in patients with hypertrophic obstructive cardiomyopathy**

Haque N; Labin J; Sinn L; Schuessler R; Damiano R

**Introduction:** In patients with hypertrophic obstructive cardiomyopathy (HOCM), atrial fibrillation (AF) is one of the most common arrhythmias with a twenty percent prevalence. However, the role of surgical ablation as a treatment for AF in patients with HOCM undergoing septal myectomies has yet to be defined. The purpose of this study is to evaluate the outcomes of surgical ablation in HOCM/AF patients undergoing concomitant septal myectomies in comparison to those of an AF patient population undergoing lone surgical ablations at Barnes-Jewish Hospital.

**Methods:** Two cohorts, HOCM/AF patients undergoing septal myectomies and concomitant surgical ablations and AF patients undergoing lone surgical ablations, were retrospectively reviewed from January 2002 through July 2015. Perioperative variables, demographics, freedom from atrial tachyarrhythmias (ATA), and freedom from antiarrhythmics (AAD) were evaluated at 3 month, 6 month, and 1-5 year intervals.

**Results:** While data analysis is currently ongoing for this study, preliminary results exist for the HOCM/AF patient cohort. Twenty-three patients were identified and reviewed, twenty-one of whom underwent a biatrial Cox-Maze procedure (CMP) as their surgical ablation. Preoperatively, 17/23 (74%) of patients were in NYHA Class 3/4 heart failure and 15/23 (65%) had paroxysmal AF while 7/23 (30%) had persistent AF. Post-operatively, median hospital length of stay was 11 days while median ICU length of stay was 5 days. Three-month survival was 96% (22/23) while three-year survival was 73% (11/15). Overall freedom from AF was 95%, 100%, 100%, 93%, and 88% at 3, 6, 12, 24, and 36-month time points, respectively. Freedom from AADs 30%, 68%, 60%, 93%, and 88% at 3, 6, 12, 24 and 36-month time points, respectively.

**Conclusions:** Surgical ablation for AF in patients receiving concomitant septal myectomies was very effective with a 100% freedom from ATAs even at 1 year. This suggests that contrary to popular belief and practice, concomitant surgical ablations should be considered in all HOCM patients with atrial fibrillation undergoing septal myectomy, particularly when it can be performed without adding significantly to morbidity or mortality.

027

**Hong, Thomas**

NIH T35 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: Amy Moore, MD; Matthew Wood, PhD; Susan Mackinnon, MD

**Prevention of neuromas using acellular nerve allografts**

Hong TS; Wood IS; Hunter DA; Ee X; Yan Y; Mackinnon SE; Wood MD; Moore AM

**Introduction:** A neuroma is a chaotic regrowth of axons on the proximal end of a severed peripheral nerve which can cause pain. Numerous methods have been used to prevent their formation but no consensus has been reached as to their effectiveness. As a result of combat casualties and peripheral vascular disease, the treatment of neuromas secondary to amputation is a current concern. Previous research using acellular nerve allografts (ANAs) to repair nerve gaps has shown an unintentional, controlled termination of axonal regrowth with increasing graft length. Applying these findings, this study aims to determine the parameters needed in an ANA in order to effectively “cap” an injured nerve and prevent neuroma formation.

**Methods:** In order to simulate the environment of an amputation, the sciatic nerves of 25 rats were transected and the distal nerve was ligated to remove any neurotrophic effects. The animals were then randomized into 5 groups (n=5/group) which received: 1) nerve transection alone, 2) 0.5cm closed end silicone conduit, 3) 0.5cm ANA, 4) 2.5cm ANA, or 5) 5.0cm ANA attached to the proximal nerve end. The rats were sacrificed at 5 weeks, and the nerves and dorsal root ganglia (DRG) were harvested for histomorphometry to analyze axonal regrowth and qRT-PCR to measure gene expression for a select panel of known pain markers, respectively.

**Results:** Gross examination findings showed axonal growth extending from the proximal stump of the transection group. The conduit group appeared to have no axonal regrowth within the conduits but an inflammatory response about the conduit. The 0.5cm ANA group had axonal growth extending from the distal end of the ANA. Axonal growth beyond the ANA in the 2.5 and 5.0cm ANA groups was not found. Histomorphologic and qRT-PCR data is pending.

**Conclusions:** Preliminary qualitative data support the use of long ANA caps to prevent neuroma formation. Histomorphological and pain marker gene expression data will be used to substantiate these findings. If long ANA grafts prevent neuroma formation, this would support their use in large animal studies to confirm their efficacy prior to human use.

046

**Javaherian, Kavon**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurology

Mentors: Brianne Disabato, MD; John Morris, MD; Josh Weng

**Examining the relationship between depressive symptoms and cognitive deficits in preclinical dementia of the Alzheimer type**

Javaherian KM; Disabato BM; Weng J; Hassenstab J; Morris JC

**Introduction:** Depression and Alzheimer’s disease (AD) are common, often comorbid conditions with overlapping psychiatric symptoms and complex etiologies. As a result, the relationship between depression and AD is not well understood, confounding timely diagnosis and research. This complexity also extends to psychotropic medications. Patients with preclinical AD, the neurodegenerative process prior to clinical manifestation, and concomitant depression can potentially exhibit poorer cognitive performance. The aims of this study were to examine the relationships between depression, preclinical AD, psychotropic medication use, and cognitive function in cognitively normal older adults.

**Methods:** ANCOVA analysis was conducted on 356 cognitively normal participants enrolled between 1997 and 2014 in longitudinal studies of memory and aging at the Knight Alzheimer’s Disease Research Center (KADRC) in order to assess the relationships between depression, preclinical AD, psychotropic medication use, and cognitive performance in multiple domains.

**Results:** The presence of depression or the use of psychotropic medications is not associated with cognitive performance in any domain. Regardless of depression status, cognitive performance was not affected by the presence of preclinical AD. No correlation exists between the use of psychotropic medications and preclinical AD with the exception of benzodiazepines, which showed a positive correlation between benzodiazepine use and preclinical AD markers.

**Conclusions:** Our results suggest that there is no relationship between depression, preclinical AD and cognitive performance, and a similar lack of association between many classes of antidepressants, preclinical AD and cognitive performance in nondemented older adults. The apparent absence of these relationships can add clarification to future research pertaining to depression and AD.

099

**Karlow, Nicholas**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Cardiology  
Mentor: Dana Abendschein, PhD

**Targeting the antithrombotic effect of human apyrase directly to the site of arterial thrombosis**

Karlow N; Abendschein D

**Introduction:** Antithrombotic treatment with dual antiplatelet (aspirin plus clopidogrel/ticagrelor) plus anticoagulant (heparin or bivalirudin) drugs is requisite for percutaneous coronary intervention (PCI) in patients with acute myocardial infarction. Despite giving these potent antithrombotics, however, myocardial reperfusion is inadequate, and reocclusion from recurrent thrombosis as well as dose-limiting bleeding occurs in a significant fraction of treated patients. We have previously shown in an animal model of coronary arterial injury that an optimized human apyrase (APT102), which degrades ATP (an activator of inflammation) and ADP (a potent activator of platelets), decreases recurrent thrombosis and reperfusion injury after fibrinolysis without causing bleeding. The purpose of this study is to determine if APT402, a novel fusion protein comprised of APT102 and Annexin V (ANV), a physiologic anticoagulant that binds phosphatidylserine, will not only attenuate platelet activation and coagulation, but moreover, target these effects specifically to thrombus and other sites of cell damage bound by ANV, thereby resulting in increased potency and efficacy as compared to APT102 alone and/or the current standards of care.

**Methods:** In an animal model of carotid thrombus, New Zealand White Rabbits received either IV saline as a control, ticagrelor by gavage, IV bivalirudin, or IV doses of APT402 30 minutes before electrical vascular injury. Complete vessel occlusions, cyclic flow variations, and thrombus weight at 2 h was measured to assess thrombosis attenuation. Bleeding time and blood loss was measured before and serially after agent administration to assess any changes.

**Results:** Pending confirmation by further study with larger sample sizes, APT402 has been shown to promote increased arterial patency and reduced thrombus weight compared to ticagrelor plus bivalirudin while inducing minimal increases in bleeding time and blood loss. Conversely, treatment with ticagrelor plus bivalirudin significantly increases bleeding time and blood loss while not preventing occlusive thrombosis.

**Conclusions:** This novel fusion protein, if proven effective by further study, may be a first step in breaking the link between antithrombotic potency and increased bleeding risk in PCI patients. This would have a significant impact on the standard-of-care therapeutics for PCI after myocardial infarction and other procedures that induce vascular injury.

056

**Kuang, Dalen**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Psychiatry  
Division: Child Psychiatry  
Mentor: Kelly Botteron, MD

**Longitudinal changes in the anterior cingulate cortical (ACC) thickness in children with preschool-onset major depressive disorder (MDD)**

Kuang DC; Nishino T; Marrus N; Botteron, K

**Introduction:** The ACC is involved in the neural circuitry underlying MDD, and other mood disorders. Adult and adolescent research has shown decreases in ACC volume and thickness in MDD populations when compared against healthy controls; however, limited data on PO-MDD exists. This study examines longitudinal changes in ACC thickness in PO-MDD.

**Methods:** Children enrolled in the 10-year longitudinal Preschool Depression Study were recruited and underwent brain imaging over three time points, spanning 2-5 years. Cortical thickness was measured and longitudinal changes were compared between the PO-MDD and the healthy control groups.

**Results:** Mean CT decreased over the course of the three visits in both PO-MDD and non PO-MDD groups. The mean CT found in PO-MDD subjects was lower, but the results were not statistically different when compared against the control group. There was a trending significance found in the right side of the ACC.

**Conclusions:** Mean CT thickness differences between PO-MDD and non PO-MDD groups showed trending differences in the right ACC, but not the left, which may be due to failure to accurately capture the segmentation on the left subcallosal region, or due to differences in the pathophysiology of PO-MDD and adolescent/adult onset MDD.



023

**Labin, Jonathan**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Cardiothoracic Surgery

Mentors: Ralph J Damiano, Jr, MD; Richard B Schuessler, PhD; Laurie Sinn, RN, BSN

**Rheumatic mitral valve disease is not associated with a lower success rate of the Cox-Maze IV procedure**

Labin JE; Haque NS; Sinn LA; Schuessler RB; Damiano RJ

**Introduction:** The Cox-Maze IV procedure (CMPIV) has been established as the gold standard for surgical ablation of atrial fibrillation (AF) associated with nonrheumatic mitral valve disease. However, the relative success of the CMPIV in patients with rheumatic mitral valve disease remains ill-defined. The aim of this study was to determine whether the underlying etiology of mitral valve disease (MVD), due to either rheumatic or degenerative processes, affects the long-term outcomes of the CMPIV.

**Methods:** Between February 2001 to July 2015, 245 patients received a CMPIV and concomitant mitral valve operation. Two cohorts were formed based on the underlying etiology of mitral valve disease, degenerative (n=153) and rheumatic (n=92). Patients were followed prospectively (mean follow up 3.28 years) and were monitored for AF via Holter monitoring, pacemaker interrogation, and interrogation of continuous cardiac loop recorders, EKG, and physician reports. Preoperative variables, perioperative variables, and long-term freedom from AF on and off anti-arrhythmic drugs (AADs) was assessed and analyzed retrospectively.

**Results:** The two groups differed in that patients with rheumatic MVD were younger, more predominantly female, had a larger preoperative left atrial diameter, and had a worse New York Heart Association class ( $P \leq 0.001$ ). While there was no difference in operative mortality or overall major complications between the groups, the median ICU length of stay was longer in the rheumatic cohort (4 vs 3 days,  $P=0.005$ ). Freedom from AF and AADs up through 5 years was similar when comparing the rheumatic to the degenerative MVD cohort (70% and 75% at 6 months; 75% and 80% at 1 year; 74% and 73% at 3 years; 52% to 70% at 5 years).

**Conclusions:** The long-term efficacy of the CMPIV and concomitant mitral valve procedure in treating AF was similar in patients with either rheumatic or degenerative mitral valve disease. Despite potentially representing a sicker patient population, patients with AF associated with rheumatic MVD equally benefit from the CMPIV compared to patients with degenerative MVD.

024

**Majumdar, Shamaita**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Cardiothoracic Surgery  
Mentor: Varun Puri, MD, MSCI

**Utility of preoperative biopsy for lung nodules suspicious for early stage lung cancer**

Majumdar S; Puri V; Rodgers A; Bell JM; Krupnick AS; Kreisel D; Meyers BF; Patterson A; Crabtree TD; Broderick S

**Introduction:** The objective was to study the utility of preoperative biopsy in patients with pulmonary nodules suspicious for clinical early stage lung cancer (ESLC). We hypothesized that such patients can be safely operated on using a single stage approach of intraoperative tissue diagnosis and immediate definitive resection.

**Methods:** Patients who underwent resection for clinical ESLC between 2008 and 2014 were identified and dichotomized by preoperative biopsy status. Lung lesions were characterized as central or peripheral. After univariate analysis of perioperative data, multivariable regression models were fitted to study factors determining preoperative biopsy.

**Results:** Of 1368 study patients, 575 (42%) received a preoperative biopsy. Patients with preoperative biopsy had larger tumors (3.6 vs 2.9 cm,  $p < 0.001$ ), higher clinical stage, and were more likely to have had prior thoracic operations. Patients in the biopsy group were more likely to have central tumors and receive workup in a community hospital setting. 813 (59.4%) patients had peripheral lesions. Of these patients, 278 (34.2%) underwent a preoperative biopsy. In univariate analysis of peripheral tumors only, patients with larger tumors, higher stage, greater comorbidity, prior thoracic operations, and initial workup in a community hospital setting were more likely to receive a biopsy. In a multivariate logistic regression model of peripheral tumors only, increasing tumor size (OR 1.394, 1.147-1.694) was associated with biopsy while workup at an academic center was protective against biopsy (OR 0.588, CI 0.388-0.801). In patients with peripheral tumors, operative times were longer in the biopsy group (3.44 vs 3.24 hours,  $p=0.014$ ). Benign resection was less likely in the biopsy group (12.6% vs. 27.5%,  $p < 0.001$ ). No difference was observed in postoperative complication rate, length of stay, 30-day readmission, or perioperative mortality in the biopsy vs. no biopsy groups.

**Conclusions:** Preoperative biopsies and their associated risks can be safely avoided in patients with peripheral lesions suspicious for ESLC without increasing operative times or perioperative morbidity.

063

**Mathur, Kunal**

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

Mentors: Aimee James, PhD, MPH; Graham Colditz, MD, DrPH, MPH

**Insurance “instability” and colorectal cancer screening utilization**

Mathur KM; Muthukrishnan M; Colditz GA; James AS

**Introduction:** Colorectal cancer (CRC) is a leading cause of cancer-related death in the United States. While CRC-specific mortality has been decreasing, significant disparities by race/ethnicity and socioeconomic factors persist. Unfortunately, less than 2/3 of age-eligible adults meet screening guidelines. While research often treats insurance status as a stable socioeconomic factor, many low income people cycle on and off insurance. Our goal in this analysis is to describe how patient demographic characteristics, specifically the varied experience of insurance, are associated with CRC screening rates.

**Methods:** This study utilized survey data from 289 patients in 4 urban federally qualified health centers. Surveys included items on socioeconomic factors, healthcare, and screening utilization. We analyzed select items with  $\chi^2$  associations against screening adherence. Patients were screening “up-to-date” if they received a fecal occult blood test in the past year and/or a flexible sigmoidoscopy or colonoscopy within the past 5 years.

**Results:** 115 (39.8%) of our patients met the up-to-date criteria. Initial results showed a number of statistically significant demographic differences by screening status ( $p < 0.05$ ). Screening up-to-date patients were significantly more likely to be currently insured (86.1% vs. 61.8%) and had different distributions of insurance type than not up-to-date patients. Moreover, stably insured patients were more likely to be up-to-date than both stably uninsured and insurance unstable patients (Bonferroni corrected  $\alpha = 0.0167$ ;  $p = 0.000, 0.005$ , respectively).

**Conclusions:** Less than 40% of age-eligible patients were screening up-to-date in our study. Our preliminary findings indicate that insurance stability might play a positive role in CRC screening adherence. Statistical modeling might better characterize the role of insurance and other demographic factors in screening. Researchers should consider the nuances of measuring insurance stability when studying the association between insurance status and healthcare utilization. In addition to guiding future research, these findings could drive future politico-structural improvements to health care policy.

120

**Merfeld, Emily**

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; Molly Stout, MD, MSCI; F Sessions Cole, MD

**Neonatal outcomes after spontaneous versus indicated preterm birth**

Merfeld EC; Wambach JA; Stout MJ; Cole FS

**Introduction:** Preterm birth is the most common cause of neonatal mortality and morbidity in the United States. Multiple, diverse maternal and fetal factors contribute to the common outcome of preterm birth. The underlying mechanisms that lead to preterm birth may impact neonatal outcomes. Our hypothesis is that neonatal mortality and morbidities including respiratory outcomes differ between infants born via spontaneous and indicated preterm births.

**Methods:** We performed a retrospective cohort study of maternal and neonatal records from consecutive live-born preterm (<37 weeks gestation) deliveries at Barnes-Jewish Hospital from 2004-2008. We defined ‘spontaneous’ preterm birth as delivery preceded by preterm labor and/or premature rupture of membranes and ‘indicated’ preterm birth as delivery precipitated by maternal or fetal indications. We collected clinical information including neonatal course and common complications of preterm birth. We will link information from the maternal and infant charts and use Chi square and regression analyses to compare outcomes between infants born after spontaneous and indicated delivery.

**Results:** We collected information for 1230 infants who met criteria for study inclusion. Many preterm infants required respiratory support: 351 (28%) infants were mechanically ventilated, 597 (49%) received non-invasive respiratory support, and 500 (41%) received nasal cannula. At 7 days of life, 352 (29%) of infants required oxygen. At 36 weeks corrected gestation (clinical definition of bronchopulmonary dysplasia), 163 (13%) infants required respiratory support. Preliminary data suggest that neonatal respiratory morbidities are more severe after indicated preterm birth compared to spontaneous preterm birth; analysis is ongoing.

**Conclusions:** Neonatal morbidities remain significant among preterm infants. Our next step will be to merge the maternal and infant data and compare clinical factors and neonatal outcomes for ‘spontaneous’ and ‘indicated’ births. Differences between the infant groups may provide information regarding the pathophysiology of preterm birth and may inform both antenatal and postnatal counseling of parents and strategies for prevention and management of preterm birth.

013

**Mokkarala, Mahati**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Orthopaedic Surgery

Mentors: Daniel Kang, MD; Jacob Buchowski, MD, MS

**Comparison of sacral alar-iliac screws (S2AI) vs iliac screw pelvic fixation outcomes and complications**

Mokkarala M; Kang DG; Buchowski JM

**Introduction:** Pelvic fixation is performed during spinal fusion surgery to improve fixation strength and rigidity at the lumbosacral junction. This project will conclusively verify, via large retrospective analysis, the outcomes and complications of sacral alar-iliac (S2AI) compared to traditional iliac screws pelvic fixation.

**Methods:** We analyzed the medical records of 421 pediatric and adult patients with either S2AI screw or traditional iliac screw pelvic fixation, from two-senior spine surgeons, at a single center. We extracted demographic, comorbidity and spinal instrumentation data from medical records. Preliminary statistical comparisons were generated using the Mann-Whitney U test (for continuous non-parametric), t-test (for continuous non-parametric), and chi-square with  $p < 0.05$  significance.

**Results:** Out of 421 patients, 270 had iliac screw pelvic fixation and 151 had S2AI pelvic fixation. S2AI patients had an older mean age (59.9 years) than traditional iliac screw patients (54.4 years). S2AI patients also have statistically significant higher mean ASA (2.37 v 2.26,  $p = .045$ ) and Charlson comorbidity index (2.30 v 1.95,  $p = 0.024$ ) compared to patients with traditional iliac screw pelvic fixation. S2AI pelvic fixation surgeries also had a larger number of mean instrumentation levels (11.1 v 9.01  $p < 0.001$ ) than surgeries with traditional iliac screw pelvic fixation. Surgeries with S2AI pelvic fixation had significantly less broken screws (0%) and iliac screw complications (2.2%) compared to traditional iliac screw pelvic fixation (4.1% and 13.3% respectively). Patients with iliac screw pelvic fixation required more re-operations (20.8%) than patients with S2AI pelvic fixation (7.50%,  $p = 0.001$ ). Finally patients with S2AI pelvic fixation operations had more neurological complications (8.20% v 2.20%,  $p = 0.007$ ) than patients with traditional iliac screw pelvic fixation surgeries.

**Conclusions:** The S2AI pelvic fixation technique, despite being used in more complicated spinal surgeries for patients with worse comorbidities, had significantly less complications including screw breakage, iliac screw pain and re-operation frequencies than traditional iliac screw pelvic fixation.

038

**Morris, Gabriela**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurology

Division: Knight Alzheimer's Disease Research Center

Mentor: John C Morris, MD

**Comparison of three dementia-screening approaches to predict neuropathological Alzheimer disease (AD)**

Morris GM; Weng H; Xiong C; Cairns NJ; Morris JC

**Introduction:** The objective of this study was to validate the Ascertain Dementia-8 item Questionnaire (AD8) using neuropathological confirmation of Alzheimer's disease (AD) and to compare the AD8 with two other screening measures for cognitive impairment, namely a Subjective Memory Complaint (SMC) and the Mini-Mental State Examination (MMSE), with the goal of determining which screening test can best be implemented during Annual Wellness Visits for Medicare recipients.

**Methods:** Using data from the Memory and Aging Project (MAP) of the Knight Alzheimer Disease Research Center from 2005 to 2015, individuals who received baseline clinical assessments and who later came to autopsy were examined. Logistical regression was used to correlate scores from AD8, SMC (determined by response to item 10 on the Geriatric Depression Scale [GDS]), and MMSE to neuropathological data obtained from autopsy. Multiple logistic regression was then used to compare each of the screening methods with each other.

**Results:** After adjusting for interval year, apolipoprotein E allele (APOE4) status, and age, logistic regression models revealed that positive scores from the AD8, SMC, and the MMSE screening tests were each associated with increased odds of neuropathologic AD in the future. The multiple logistic regression models revealed that there was no significant difference between AD8's predictive ability of neuropathological AD with those of SMC or MMSE. Multiple logistic regression models revealed there was also no significant difference between the predictive ability of item 8 from the AD8 questionnaire with those of SMC or MMSE. Adjusted odds ratios, 95% confidence intervals, and p-values were calculated for each of these models.

**Conclusions:** Our studies revealed that objective tests (MMSE), SMC (item 10), and informant-based interviews (AD8) are each able to predict future neuropathological AD. Since the short AD8 test and a single query about SMCs accomplish the same goal as longer tests, such as the MMSE, they may be preferable as screening tests to implement during Annual Wellness Visits. Future research can shed light on the neuropathological validation of the AD8 test at other institutions or with a bigger sample size.

030

**Murthy, Sindhoora**

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  
Mentor: Albert Woo, MD

**Long-term characterization of cranial defects after surgical correction for single-suture craniosynostosis**

Murthy S; Skolnick G; Huang Z; Woo A

**Introduction:** Craniosynostosis is defined as the premature fusion of the cranial sutures and is typically surgically corrected within the first year of life through cranial vault reconstruction. The procedure often leaves an open calvarial defect which is sometimes corrected with an additional surgical procedure, cranioplasty. A better understanding of the calvarial osseous healing process is needed. Our study aims to assess the long-term changes in defect size after cranial vault reconstruction.

**Methods:** One year post-operative and long-term computed tomography scans were retrieved from the Washington University in St. Louis School of Medicine Craniofacial Database. Analysis used custom software. All defects above the size of 1 cm<sup>2</sup> were analyzed and tracked.

**Results:** We analyzed a total of 74 defects. The average initial defect surface area was  $3.27 \pm 3.40$  cm<sup>2</sup> (range of 1.02 to 22.59). The average final defect surface area was  $1.71 \pm 2.54$  cm<sup>2</sup>. The average decrease in defect surface area was  $1.56 \pm 1.43$  cm<sup>2</sup>. The average percent decrease was  $55.06 \pm 28.99\%$ . We found that there was a significant difference in the percent decrease of defects in the parietal and fronto-parietal locations: 68.4% and 43.7% respectively ( $p = 0.001$ ). We also performed cluster analysis to compare the variance of percent decrease in area within patients and between patients and found a significant difference Chi-squared (1) = 8.7 ( $p = 0.003$ ).

**Conclusions:** We describe and make available a novel, validated method of measuring cranial defects. We found that parietal defects close more than fronto-parietal defects. The information from this study may aid physicians in decision-making and in minimizing additional procedures and radiation for patients.

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**Naylor, Adam**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Internal Medicine  
Division: Pulmonary and Critical Care  
Mentors: Steven Brody, MD, PhD; Allen Cole Burks, MD

**Status of autophagy in airway epithelial cells from asthmatic and non-asthmatic donors**

Naylor AD; Brody SL

**Introduction:** Autophagy is a conserved catabolic pathway characterized by the trafficking of double membrane autophagosomes to lysosomes for degradation. Numerous studies have reported a link between autophagy and the pathogenesis of asthma in various cell types. The goal of this study was to characterize the status of autophagy in human airway epithelial cells at baseline levels and in response to known activators of autophagy.

**Methods:** Human airway epithelial cells (hTEC) from asthmatic and non-asthmatic subjects were cultured and treated with IL-13 and spermidine, both known activators of autophagy. Western blot analysis was performed to quantify autophagy flux using a well-described assay employing chloroquine.

**Results:** There were no differences in basal autophagy flux rates between cells from asthmatic donors compared with non-asthmatic donors. This observation was true in differentiated and undifferentiated hTEC. IL-13 activates autophagy in differentiated hTEC in both sets of donors; however the response is blunted in cells from asthmatic donors. A lack of donors has precluded a proper statistical analysis. More experiments are ongoing.

**Conclusions:** Given previous findings in the literature, we hypothesized IL-13 to induce greater flux in hTEC from asthmatic donors. Our preliminary results do not support this hypothesis. We are currently gathering and analyzing more data. We plan to analyze autophagy with an alternate method in order to validate the chloroquine assay in our experiment. We will also determine mRNA expression of the mucin MUC5AC in the treatment protocols above and phenotype differentiated hTEC, or determine the relative percentage of ciliated and goblet cells.

014

**Newcomer, Kenneth**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Orthopaedic Surgery  
Mentor: Denis Nam, MD

**Short term survivorship of cemented and cementless total knee arthroplasty**

Newcomer KF; Nam D

**Introduction:** Cemented total knee arthroplasty (TKA) is the current standard surgical option for end-stage knee osteoarthritis; however, newer cementless designs may be more resistant to stress-induced aseptic loosening because they rely on a physiological bond at the bone-implant interface. Studies have shown that the amount of TKA procedures performed per year is increasing, and the mean age of patients is decreasing, suggesting a need for implants that can maintain their function in more active individuals. As such, it is important to evaluate the effectiveness of cementless TKA in comparison to traditional cemented designs.

**Methods:** Postoperative radiographs were taken from 6 weeks, 1 year, and 2 year follow-up of patients after cementless or cemented TKA at Barnes-Jewish Hospital. Radiographs were evaluated for radiolucency at the bone-implant interface (an indicator of separation) and measured for alignment.

**Results:** Preliminary results indicate that the short term (2-year) survivability of the cementless and cemented implants is identical in this patient population. The average separation at the bone-implant interface was less than 0.1 mm in both groups, and there was no difference between cementless and cemented patients. As additional patients follow up, and more data is available regarding patient pain and flexibility, the results will reflect a more complete assessment of clinical outcome.

**Conclusions:** The results are in accordance with other findings that cemented and cementless implants have identical clinical outcomes. Because it preserves more of the patients' bone and forms a physiological bond at the bone-implant interface, cementless TKA may be a better surgical option for younger, more active patients. Additional studies are required to evaluate the long-term clinical outcomes of patients who receive cementless TKA.

015

**Opara, Gregory**

T35 NIH NHLBI Training Grant  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Orthopaedic Surgery  
Mentors: Hua Shen, MD, PhD; Stavros Thomopoulos, PhD

**Enhanced flexor tendon healing via delivery of stem cell sheets to the repair site**

Opara G; Shen H

**Introduction:** Flexor tendon injuries to the hand are debilitating and heal poorly. Despite decades of work optimizing surgical repair techniques and rehabilitation strategies, approximately half of all repairs gap or rupture. This study had two aims, to determine if adipose-derived stem cells could be induced to undergo tenogenic differentiation by exposure to BMP12, and if they could be delivered to injury repair sites via collagen sheets.

**Methods:** Adipose-derived stem cells were exposed to BMP12 in solution, and via the collagen-based microspheres in order to induce tenogenic differentiation and then qPCR was performed on the cell cultures to determine whether the differentiation was successful.

**Results and Conclusions:** We expect to find that the adipose-derived stem cells have undergone tenogenic differentiation as evidenced by tenogenic mRNA expression. This should then translate to figuring out how to deliver these cells in a controlled, progressive manner utilizing the collagen sheets.

070

**Pokala, Naveen, MS**

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: Milan J Anadkat, MD

**Mortality in patients with graft-versus-host disease after hematopoietic stem cell transplant**

Pokala NK; Tripathi SV; Anadkat MJ

**Introduction:** Graft-versus-host disease (GVHD) is a prevalent negative outcome of hematopoietic stem cell transplant (HSCT). GVHD is known to be associated with significant morbidity and mortality. However, the symptoms of GVHD and survival time can vary widely between patients. The purpose of this study is to assess if there is an association between the time to develop GVHD and time to death post-transplant.

**Methods:** Patient data will be retrospectively collected from deceased patients with a history of GVHD post-HSCT seen at Washington University School of Medicine between 1994 and 2015. Multivariable regression models will be fitted to assess whether there is a temporal association between GVHD onset and either non-relapse or all-cause mortality. Additional models will be fitted to specifically assess cutaneous GVHD onset and gastrointestinal GVHD onset and their temporal associations with mortality.

**Results:** At the time of writing, the results of this study are still pending. Patient data is still being collected retrospectively from patient records.

**Conclusions:** No conclusions can be made at this time. The results of this study can help establish whether the time-course for the development of GVHD can serve as a predictor of patient mortality after hematopoietic stem cell transplant.

061

**Soares, Andrea**

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

**Intraoperative awareness with explicit recall: a sub-study of SATISFY-SOS**

Mathur S; Soares A; Wildes T; Sharma A; Avidan M

**Introduction:** Unintended intraoperative awareness with explicit recall (AWR) is a dreaded complication. Patients who experience AWR often report recollections of hearing things, of being unable to breathe, or of pain, paralysis, and panic. Because of recently implemented interventions at our institution, we hypothesize that i) the incidence of AWR would be significantly lower than 0.2%, and ii) AWR experiences would be associated with known risk factors.

**Methods:** We conducted a prospective cohort study including a modified Brice questionnaire and an additional structured interview to determine the incidence of AWR following our interventions. There were a total of 16,807 unique respondents for the study.

**Results:** 721 patients surveyed using the modified Brice interview reported having recollections of hearing, pain, paralysis, and/or distress. 282 patients with either pain, paralysis, and/or distress were contacted via telephone and given a structured interview. Of the 149 who participated, 117 had memories of their surgical experience, and 91 of these had memories during their surgery. Of these 91, 31 patients expected to be conscious and 80 had unexpected consciousness. 23 of these patients had received general anesthesia, and 11 of these cases were incidences of definite awareness, an incidence of 0.06%. When examining the anesthetic records of these patients, we found that in most instances, low anesthetic concentration was responsible for their consciousness.

**Conclusions:** The results of this study indicate that the intervention methods used to prevent AWR are not currently sufficient to lower the incidence of awareness. While the incidence of awareness was lower than the reported incidence, it was not lower by a significant order of magnitude. AWR was associated with the most common risk factor, low anesthetic concentration, something which could be prevented by using BIS and ETAC alerts to monitor patients' level of anesthetic and consciousness.

064

**Thomas, R Lucas**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Anesthesiology

Mentors: Michael Avidan, MBBCh; Ben Palanca, MD, PhD

**Power spectral density analysis of EEG and delirium in cardiac surgery patients**

Thomas RL; Geczi K; Avidan M

**Introduction:** Delirium is an acute fluctuating neurologic disorder that shows a change from baseline cognition. Its main features are inattention and disorganized thinking (DSM5 2013). It affects up to 70% of surgical patients over the age of 60. Most studies show an incidence of around 30 to 50%. Delirium can cost over \$60,000 per patient per year and was listed as one of the top concerns of 40% of 1,000 surveyed preoperative patients. Simply the occurrence of delirium as well as how long it is present can increase morbidity and mortality, length of hospital and intensive care unit stay, and the likelihood of functional and cognitive decline.

**Methods:** Patients already enrolled in the Systematic Assessment and Targeted Improvement of Services Following Yearly Surgical Outcomes Surveys (SATISFY-SOS) study have the option to also enroll in the Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES) study. These patients must also be undergoing major elective surgery with general anesthesia that requires at least 2 postoperative days of recovery in the hospital. Data Collection: This is a sub-study of the Electroencephalograph Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES) Study.

**Results:** Current and anticipated results are that postoperative delirium results in a shift to higher power in the lower frequency bands of a power spectral density graph. This should be somewhat evident in all electrode pairings, though F8-Fpz should show the greatest correlation to delirium. This shift is reversed, with a return to baseline power levels in the various frequency bands, after the delirium is no longer present.

**Conclusions:** EEG should be given a higher priority role in monitoring patient health during and after surgery. Replacement of the currently used BIS index with a more comprehensive analysis of brain activity could result in better surgical outcomes, with fewer episodes of delirium and lower readmission rates. Since postoperative mortality is also linked to delirium, preventing delirium could drastically improve the survival rates of cardiac surgery patients, where some operations have delirium rates as high as 30%.

054

**Veligati, Sirish**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurosurgery

Mentor: Eric Leuthardt, MD

**Capturing the "Aha!" moment: EEG examination of insight**

Veligati S; Leuthardt E

**Introduction:** The "Aha!" moment, or insight, is a sudden comprehension that can result in a re-interpretation of a situation in a different context and therefore present a solution to the given problem. Insight is present in a broad spectrum of cognitive processes, which makes it difficult to isolate in an experimental setting. Additionally, insight is characterized by solutions being computed unconsciously, and then later emerging suddenly into conscious awareness. Prior neuroimaging studies have isolated neural electrophysiological correlates of insight events, however findings vary greatly between studies. This variation may be accounted for by differences between how these studies elicit and define an insight event. Currently there are no standardized means of inducing or measuring an insight event.

**Methods:** EEG and audio data was collected from subjects while they solved compound-remote-associates (CRA) problems. In these problems, the subject is presented with 3 words (e.g. Swiss, cottage, cake) and instructed to think of a solution word (e.g. cheese) which forms a compound word or phrase with each of the 3 problem words. Classification of solutions as either insight or non-insight events was determined by subjects' trial-by-trial interpretation of their solving strategy.

**Results:** Data acquisition is ongoing. Anticipated results include high-frequency (gamma-band) burst of electrical activity preceding insight solutions as opposed to non-insight solutions.

**Conclusions:** The significance of this study is that it tests the efficacy of real-time statistical analysis of EEG data in determining the occurrence of an insight event.

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**Wentworth, Caroline**

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: Colleen McNicholas, DO, MSCI

**Levonorgestrel-releasing intrauterine system for emergency contraception**

Wentworth CJ; McNicholas CP; Peipert JF

**Introduction:** Nearly half of the pregnancies in the United States each year are unintended. Emergency contraception (EC), defined as methods used in the immediate post-coital period, can prevent pregnancy when used within 72-120 hours of unprotected sex. Despite the availability of a number of methods of EC, there has been no appreciable epidemiologic impact on unintended pregnancy. The purpose of this study is to evaluate the levonorgestrel-releasing intrauterine system (LNG-IUS), currently approved as a highly effective long-acting reversible contraceptive (LARC), for use as EC.

**Methods:** Eighty-five women ages 18-45 who had had unprotected sex within 120 hours of enrollment were randomized to receive either an LNG-IUS or oral EC (oral levonorgestrel or ulipristal acetate). Participants were assessed for EC failure 4-6 weeks after enrollment. Another survey at six months evaluated unintended pregnancies since enrollment and current contraceptive use and satisfaction.

**Results:** No EC failures occurred in either group. Within 6 months, women who had received an LNG-IUS were significantly less likely to experience an unintended pregnancy than women who received oral EC. They were also more likely to be using contraception, especially highly effective LARC methods. Participants randomized to use an LNG-IUS were more satisfied with their 6-month contraceptive method than were women who had used oral EC.

**Conclusions:** Our preliminary results suggest that the LNG-IUS may be an ideal method of EC, as it not only works to prevent pregnancy in the post-coital period, but is also highly effective and well-accepted contraception for continued use. Increasing LARC uptake by using the LNG-IUS as EC could produce a public health impact not yet seen with other EC methods. Further research is needed to confirm these preliminary results and develop strategies to overcome cost, access, and educational barriers to LNG-IUS EC use.

044

**Zheng, Lingjin**

T35 NIH NHLBI Training Grant

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurology

Mentor: Morvarid Karimi, MD

**Anatomical connectivity differences in isolated idiopathic focal dystonias**

Zheng LZ; Karimi M

**Introduction:** Dystonia is a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal and repetitive movements, postures, or both. The cause of dystonia is unknown, but most researchers agree that it has to do with a dysfunction of brain networks, particularly the basal ganglia and cerebellar networks. Alterations in functional connectivity and microstructure have been observed in dystonia. One way to examine microstructure is through Diffusion Tensor Imaging (DTI), which measures diffusion of water molecules to provide information about axon integrity. Previous DTI studies have found white matter aberrations in dystonia, but have had inconsistent findings with regards to which tracts are affected.

**Method:** This study aims to find anatomical connectivity differences in a larger sample size and using a higher powered 3T MRI scanner.

**Results:** After looking for Fractional Anisotropy (FA) and Mean Diffusivity (MD) differences in 23 previously defined regions of interest, including the right and left thalamus, putamen, caudate, and various areas of the cerebellum, we found decreased MD for dystonic patients in the right thalamus, bilateral anterior putamen, left caudate, and the right cerebellum lobe VI. There was also a decrease in FA values in the left and right posterior cerebellum in dystonic patients.

**Conclusions:** This suggests that dystonia patients have altered cellularity and axon integrity in certain regions. Future directions of this project will further examine tractography from these regions of interest to experimentally derived cortical areas.



## T35 NIH NIDDK Short-Term Training Program

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### Bauman, Tyler

T35 NIH NIDDK Short-Term Training Program  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Urologic Surgery

Mentors: R Sherburne Figenshau, MD; Aaron M Potretzke, MD

#### **Cerebrovascular disease and chronic obstructive pulmonary disease increase risk of complications during robotic partial nephrectomy**

Bauman TM; Potretzke AM; Vetter JM; Bhayani SB; Figenshau RS

**Introduction:** Metrics such as the RENAL nephrometry score and the Charlson comorbidity index (CCI) have incorporated tumor- and patient-specific factors to better predict the complexity and perioperative outcomes of partial nephrectomy (PN). The relative contribution of individual comorbidities within the CCI is still unknown. The purpose of this study was to identify specific comorbidities within the CCI that are associated with increased complication rates after robotic-assisted PN (RAPN).

**Methods:** After IRB approval, a consecutive series of 641 patients undergoing RAPN was retrospectively identified. Perioperative complications were defined and classified using the Clavien grading system. Fisher's exact test or chi square test was performed to evaluate the association of individual comorbidities with perioperative complications. Logistic regression was used for multivariable analysis to adjust for other non-CCI comorbidities and tumor-specific and patient-specific characteristics.

**Results:** Of the 641 patients undergoing RAPN, complications occurred in 67 patients (10.5%) within 30 days of surgery. Cerebrovascular disease [odds ratio 3.01 (95% CI 1.05-8.04)  $p=0.03$ ] and chronic pulmonary disease [3.12 (1.19-7.72)  $p=0.02$ ] predicted complications in multivariable analysis of clinico-pathological characteristics including all CCI and non-CCI comorbidities. In additional modeling including only CCI comorbidities, only cerebrovascular disease [2.93 (1.01-7.96)  $p=0.04$ ] and chronic pulmonary disease [2.69 (1.03-6.76)  $p=0.04$ ] predicted complications. No other variables reached statistical significance in either model, including nephrometry score or estimated blood loss ( $p>0.50$  for both).

**Conclusions:** Cerebrovascular disease and chronic pulmonary disease predict perioperative RAPN complications within 30 days of surgery. Identification of patients with these comorbidities preoperatively may afford improved counseling and risk stratification.

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### Chen, Howard

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  
Mentors: Rajendra Apte, MD, PhD; Jonathan Lin

#### **Role of microRNA-150 in macrophage aging and cholesterol homeostasis**

Chen HC; Lin JB; Apte RS

**Introduction:** Macrophages play an important role in lipid-induced inflammation processes that lead to age-related macular degeneration (AMD) and other age associated diseases such as atherosclerosis. MicroRNA-150 (miR-150) has been shown to be up-regulated in old macrophages compared to young (unpublished data from the Apte Lab). The purpose of this study is to determine how miR-150 affect cholesterol homeostasis in old macrophages.

**Methods:** Macrophages are extracted from young mice and transfected with miR-150 mimics or negative control oligonucleotides. Gene expression of M1 macrophage, M2 macrophage, and cholesterol markers are assessed through qPCR.

**Results:** Our results show no statistically significant differences in gene expressions of ABCA1, CCL2, ARG, ABCG1, IL-6, VEGFA, and MYB markers. PRKAA2 shows a significant decrease in gene expression with the 5nM ( $p < 0.05$ ) and 50nM ( $p < 0.01$ ) miR-150 mimic transfection.

**Conclusions:** This project is still ongoing but it will help us understand the role of miR-150 in macrophage aging, which can lead to potential development of novel therapeutic targets and biomarkers that can be used to assess severity and predict the progression of diseases that come with aging, such as age-related macular degeneration and atherosclerosis.

041

**Christenson, Eleanor**

T35 NIH NIDDK Short-Term Training Program

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Neurology

Mentors: Kimberly Johnson, MPH, PhD; David Gutmann, MD, PhD

**Prevalence of diabetes in individuals with neurofibromatosis type 1**

Christenson ER; Gutmann DH; Johnson KJ

**Introduction:** In two previous reports, inverse relationships between neurofibromatosis type 1 (NF1) and diabetes were noted. The purpose of this study was to determine the prevalence of diabetes in a cohort of individuals with NF1 and whether BMI, a primary Type II diabetes risk factor, may explain any differences in diabetes prevalence in individuals with NF1 compared to those without NF1.

**Methods:** We ascertained individuals (n = 733) with NF1 in the BJC and Washington University systems by querying the Clinical Investigation Data Exploration Repository (CIDER) database for NF ICD-9 codes. All subjects were subsequently validated for NF1 diagnostic criteria through chart review. We abstracted heights and weights and any relevant information to determine diabetes histories from the patient's charts. Diabetes diagnoses were separated into verified and possible based on the presence of the ICD-9-CM code for diabetes (250.00) in the patient's chart. The diabetes prevalence in the NF1 cohort was calculated and compared to the national prevalence. Prevalences of overweight (>25 kg/m<sup>2</sup>) and obese BMI (>30 kg/m<sup>2</sup>) were also calculated for the NF1 cohort and compared to national prevalence data.

**Results:** The type 2 diabetes prevalence of the NF1 cohort (1.2% total diabetes and 0.95% verified diabetes) was significantly lower than both national and Missouri type 2 diabetes prevalence estimates at 9.3 and 9.6%, respectively. The 2011 and 2012 prevalence of overweight and obese BMI for adults 20 years and older in the NF1 cohort was consistently lower, but not always significantly, than the 2011 and 2012 national prevalences for the same age groups reported in the National Health and Nutrition Examination Survey.

**Conclusions:** This study provides evidence that the prevalence of type 2 diabetes is lower in individuals with NF1 than in individuals without NF1. However, further work needs to be done to determine if the lower prevalence is a result of a lower BMI in individuals with NF1.

057

**Dib, Paolo**

T35 NIH NIDDK Short-Term Training Program

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Psychiatry

Mentor: Andrew C Heath, DPhil

**Predictors of discordance for obesity in dizygotic twin pairs**

Dib PT; Heath AC

**Introduction:** Obesity has been shown to be associated with altered gut microbial profiles. Obese individuals are characterized by lower diversity and abundance of bacterial phyla. These taxonomic differences reflect on the metabolic functions performed by the bacterial fauna, which in turn are associated with the obese/lean phenotype. Despite significant individual variability, gut microbial profiles are highly heritable, with the highest similarity being between twin pairs. For this reason, twin pairs provide an attractive model for the comparison of lean and obese individuals; they provide a natural case-control setup that eliminates confounders like genetic variation and early home environment. However, discordant twin pairs for obesity are rare. This scarcity points to the remarkable heritability of BMI in twins (around 75% in dizygotic pairs) and thus makes the development of discordance all the more intriguing and worthy of meticulous analysis.

**Methods:** We surveyed data collected from 21- to 32-year-old female twin pairs (n=1539) enrolled in the Missouri Adolescent Female Twin Study (MOAFTS). We included twin pairs stably discordant for obesity (n=15) and twin pairs stably concordant for leanness (n=107). Within each discordant pair, we compared the lean twin to the obese twin to identify any associated mental illnesses (depression, attention deficit disorder), or health behaviors (smoking and history of smoking). We also looked for any history of childhood sexual abuse and childbirth.

**Results:** We constructed 2x2 contingency tables, none of which reached statistical significance. However, depression and childbirth were nominally more common in obese twins. Then we compared concordant and discordant pairs to try to identify predictors of discordance. Both the father's BMI (Odds Ratio=1.36, p=0.001) and the number of years spent with the biological mother (O.R. = 2.59, p=0.0002) had significant effects on discordance.

**Conclusions:** It seems that paternal BMI and time spent with biological mothers in early home environment play an important role in the development of discordance in dizygotic twin pairs. However, more variables could be tested in the future to increase the specificity of the model. The case study of these twins was important in identifying any major medical illnesses or risk factors that might alter data collection in later stages of the study. Further investigation of the twins' microbial and metabolic profile, could guide the development of nutritional and pharmacologic interventions to manage obesity.

090

**Gedallovich, Seren Michelle**

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  
Mentor: Chyi-Song Hsieh, MD, PhD

**Culture and characterization of fastidious human gut microbiota from patients with inflammatory bowel disease (IBD)**

Gedallovich SM; Hsieh C

**Introduction:** Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, is a debilitating and recurring condition that affects over 1.4 million people in the United States. IBD is thought to arise from an exaggerated immune response to commensal human gut microbiota, though specific species involved in disease pathogenesis have yet to be identified. The overall aim of the present study was to isolate pure cultures of bacterial species that are hypothetically linked to IBD pathogenesis, by first developing an optimal culturing protocol, with the eventual goal of inoculation of these species into gnotobiotic and germfree mice. Manipulation of these species in murine models may provide insight into the dynamics of the gut mucosal inflammatory response.

**Methods:** Stool samples from patients with active IBD were cultured in solid and liquid media for bacterial growth, under anaerobic and aerobic conditions. Different media preparations were tested for selective growth of bacterial species of interest, specifically Wilkins-Chalgren, Gut Microbiota Medium, and Brain Heart Infusion. Successfully cultured gut microbiota were identified through DNA extraction and subsequent sequencing of the 16S rRNA region.

**Results:** Overall, eight bacterial species were isolated in pure culture and stored in glycerol for future manipulation in murine models. Wilkins-Chalgren medium preferentially grew out Clostridium species (71.4%), with the remaining 28.6% made up of E. coli and Bifidobacterium breve colonies. Surprisingly little microbial diversity was captured with Gut Microbiota Medium, with 75% of colonies identified as Bifidobacterium breve, and the remaining 25% made up of Pediococcus acidilactici and Enterococcus raffinosus. Brain Heart Infusion medium gave a wide spread of species, with no one species accounting for the majority of results.

**Conclusions:** The results of this study suggest that modifications to the culturing technique, including broader colony sampling, will likely increase the diversity of culturable microbiota detected in the stool samples. Future goals of this study include inoculation of germfree and antibiotic-treated mice with the bacterial cultures. Murine stool will be analyzed for colonization by the inoculated bacterial species through DNA extraction and 16S sequencing. Additionally, immune responses of the murine gut mucosa will be analyzed to assess inflammatory responses to the fecal microbiota. If successful, these protocols will enhance our understanding of the inflammatory response in human gut mucosa during an IBD flare, by allowing researchers to model specific commensal bacterial community compositions in mouse models.

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**Liu, Sonya**

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  
Mentors: Rajendra Apte, MD, PhD; Abdoulaye Sene, PhD

**Nicotinamide phosphoribosyltransferase inhibition on LPS-induced cytokine production in mouse macrophages**

Liu SY; Sene A; Apte RS

**Introduction:** Nicotinamide phosphoribosyltransferase (Nampt) is an enzyme involved in re-synthesis of nicotinamide adenine dinucleotide (NAD). Previous research suggests links between intracellular NAD levels and inflammatory pathways, and upregulation of Nampt in inflammation. This study was carried out to examine the effects of Nampt depletion on macrophages' response to lipopolysaccharide (LPS) by measuring pro-inflammatory cytokine (TNF-alpha and IL-6) and anti-inflammatory cytokine production (IL-10).

**Methods:** Nampt activity was inhibited in macrophages in vivo by conditionally knocking out the Nampt gene in primary mouse macrophages and in vitro by using Nampt-specific inhibitor FK866 in the mouse macrophage cell line RAW264.7. Gene expression (mRNA levels) of the cytokines was measured with real-time PCR. Secreted IL-6 and IL-10 protein levels were measured with enzyme-linked immunosorbent assays (ELISAs).

**Results:** Nampt mRNA was significantly decreased in peritoneal macrophages (but not bone marrow derived macrophages) of conditionally knocked out (CKO) mice, which did not affect TNF-alpha mRNA levels. In vitro, Nampt mRNA levels in RAW264.7 cells increased with increasing FK866 concentration to compensate for the blocked Nampt protein. Compared to control, TNF-alpha mRNA levels increased in LPS-stimulated RAW264.7 cells only at low FK866 concentrations. Both IL-6 mRNA and protein levels in LPS-stimulated cells steadily decreased with increasing FK866. Compared to unstimulated RAW264.7 cells, mRNA levels of the anti-inflammatory cytokine IL-10 increased in LPS-stimulated cells at FK866 concentrations less than 1 uM, while IL-10 protein secretion was decreased in all LPS-stimulated cells, especially at higher FK866 concentrations.

**Conclusions:** This is the first study of Nampt that involves in vivo Nampt inhibition using a conditional knockout mouse model. Our results indicate that Nampt can be successfully depleted in mature macrophages and suggest that Nampt modulates inflammatory signaling pathways. Further experimentation using this CKO model is required to dissect the effects. Nampt inhibition could also be investigated as a potential treatment of inflammatory disorders.

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**Markov, Alexander**

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: David M Alvarado PhD; Srikanth Santhanam PhD; Matthew A Ciorba MD

**Using public data to identify potential modulators of CRC survival in the kynurenine pathway**

Markov AM; Alvarado DM; Santhanam S; Ciorba MA

**Introduction:** Tryptophan metabolism along the kynurenine pathway (KP) has widely been implicated in aiding cancers evade immunesurveillance. In recent years, kynurenic acid (KYNA) and the enzymes which produce it, kynurenine transesterases I – IV (KATs), have come into the spotlight as potential therapeutic targets for colorectal cancer. In this study, we investigate the relationship between KAT enzyme expression levels and CRC survival using publicly available data.

**Methods:** Colon and rectal adenocarcinoma (COADREAD) patient data compiled by the Cancer Genome Atlas (TCGA) was accessed using the UCSC Cancer Genomics Browser (N=433) and the cBioportal for Cancer Genomics Database (N=365). The gene expression of KP enzymes was compared on both a global level and based on cancer stage. Association between gene expression and overall survival (OS) were probed using Kaplan Meyer (KM) curves. High and low gene expression were defined as being the top and bottom quartiles respectively. Statistical significance was determined with a Log-Rank (Mantel-Cox) test.

**Results:** KAT I, II, III and IV were present in all primary tumor samples, with KAT IV being the most highly expressed enzyme in entirety of the pathway. We found that high levels of KAT expression were significantly ( $p < 0.05$ ) associated with improved 3-year survival for KAT II and KAT IV and near significantly ( $p < 0.10$ ) for KAT III. Paradoxically, high KAT I expression is associated with worse survival. This relationship is statistically significant for 2-year survival ( $p < 0.05$ ) and near significant for 3-year survival ( $p < 0.10$ ).

**Conclusions:** In this study we demonstrated that KAT enzyme expression is significantly associated with patient clinical outcome, particularly 3-year survival. These findings are in line with the notion that KYNA production is detrimental to tumor growth and proliferation. Interestingly, however, patients with high KAT I expressing tumors had a less favorable survival than those with low expression. At this time, we cannot make sense of this finding although it reaffirms the need for further investigation into the relationship between KYNA, cancer proliferation and the KAT enzymes.

061

**Mathur, Shagun**

T35 NIH NIDDK Short-Term Training Program

Summer Research Program

Current Doctoral Program of Study: Medicine

Washington University in St. Louis

Department: Anesthesiology

Mentor: Michael Avidan, MBCh

**Intraoperative awareness with explicit recall: a sub-study of SATISFY-SOS**

Mathur S; Soares A; Wildes T; Sharma A; Avidan M

**Introduction:** Unintended intraoperative awareness with explicit recall (AWR) is a dreaded complication. Patients who experience AWR often report recollections of hearing things, of being unable to breathe, or of pain, paralysis, and panic. Because of recently implemented interventions at our institution, we hypothesize that i) the incidence of AWR would be significantly lower than 0.2%, and ii) AWR experiences would be associated with known risk factors.

**Methods:** We conducted a prospective cohort study including a modified Brice questionnaire and an additional structured interview to determine the incidence of AWR following our interventions. There were a total of 16,807 unique respondents for the study.

**Results:** 721 patients surveyed using the modified Brice interview reported having recollections of hearing, pain, paralysis, and/or distress. 282 patients with either pain, paralysis, and/or distress were contacted via telephone and given a structured interview. Of the 149 who participated, 117 had memories of their surgical experience, and 91 of these had memories during their surgery. Of these 91, 31 patients expected to be conscious and 80 had unexpected consciousness. 23 of these patients had received general anesthesia, and 11 of these cases were incidences of definite awareness, an incidence of 0.06%. When examining the anesthetic records of these patients, we found that in most instances, low anesthetic concentration was responsible for their consciousness.

**Conclusions:** The results of this study indicate that the intervention methods used to prevent AWR are not currently sufficient to lower the incidence of awareness. While the incidence of awareness was lower than the reported incidence, it was not lower by a significant order of magnitude. AWR was associated with the most common risk factor, low anesthetic concentration, something which could be prevented by using BIS and ETAC alerts to monitor patients' level of anesthetic and consciousness.

**No Poster** **Mendez, James**  
T35 NIH NIDDK Short-Term Training Program; Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Internal Medicine  
Division: Cardiology  
Mentor: Ari Cedars, MD

**The effects of disease specific health knowledge on hospitalization rates in adult congenital heart disease**

Mendez J; Cedars A

**Introduction:** A patient's education and knowledge relating to his or her specific adult congenital heart disease (ACHD) may have an effect on compliance with medical follow-up and self care. It has been shown that follow-up care received at specialized ACHD centers in Canada improves patient outcomes (Mylotte et al). It was our intent to examine whether ACHD patient knowledge regarding their specific disease will affect overall compliance with follow-up and ultimately, rates of inpatient hospitalization.

**Methods:** This is a retrospective, observational cohort study. We began by gleaning the electronic medical records of 100 patients. All patients were adults (over the age of 18) and had been regular patients of the Washington University Center for Adults with Congenital Heart Disease ("The Center"). The main data points that were extracted were: Date when the patient was first seen at The Center, the date when the patient was most recently seen at The Center and the number of inpatient admissions with each associated discharge diagnosis. Additional information was also collected.

**Results:** Analysis has not yet taken place. We will investigate the correlation between disease specific health knowledge, income, denial of impact, and intelligence, (data that have been previously obtained as a part of this ongoing study) and rate of hospitalization calculated as number of hospitalizations per patient year. We will separate hospitalizations based on whether they are anticipated, and therefore likely unavoidable, or unanticipated. Any correlation identified will then be analyzed for clinical variables which may be confounding results.

**Conclusions:** If the data shows, as we expect it to, that the odds of being hospitalized due to ACHD lesions is significantly reduced in association with a patient's disease specific health knowledge, this finding will provide further support to the importance of patient education. Other factors would have to be addressed as well however, as this study was only conducted at a single ACHD center under the care of a limited number of the same physicians. If the results do not show significant correlation between knowledge and reduced admissions, then this calls into question our current assumptions regarding the importance of disease specific health knowledge on outcomes.

**121** **Rosano, Kristen**  
T35 NIH NIDDK Short-Term Training Program  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Pediatrics  
Division: Newborn Medicine  
Mentors: Daniel Wegner; Jennifer Wambach, MD, MS; F Sessions Cole, MD

**Multiplexed direct genomic selection to detect rare, deleterious variants associated with Respiratory Distress Syndrome in late preterm and term infants**

Rosano KK; Wegner DJ; Kuzniewicz M; Wambach JA; Cole FS

**Introduction:** Respiratory Distress Syndrome (RDS) in early preterm infants is due to surfactant deficiency as a result of prematurity, but the causes of RDS in late preterm and term infants are not as well understood. The aim of this research is to screen 11 candidate genes for potential disease-causing variants and compare the frequency of these variants between affected and unaffected individuals. Understanding the genetic causes of RDS will allow for the development of more targeted therapies.

**Methods:** Multiplexed direct genomic selection (MDiGS) was used to facilitate the sequencing of 11 candidate genes in 255 late preterm and term infants, both affected and unaffected by RDS. This method utilizes biochemical "barcodes" ligated to each individual genomic library so that multiple individuals can be pooled into one lane of an Illumina sequencing instrument, greatly decreasing cost and increasing the statistical power of the study. Bacterial artificial chromosomes (BACs) were used to capture the genes of interest identified as candidates for RDS (ABCA3, CCDC39, CCDC40, AQP3, AQP4, AQP5, SCNN1A, SCNN1B, SCNN1D, SCNN1G, and ACADL).

**Results:** Results are pending, but the expectation is to find a number of variants – including single nucleotide polymorphisms, insertions and deletions, and copy number variants – all of which can be detected by MDiGS, in both affected and unaffected individuals. A positive result would be a variant, or set of variants, that is more common in affected individuals than unaffected individuals, which could indicate a causative damaging variant that plays a role in RDS.

**Conclusions:** Identifying the genetic variant or variants underlying Respiratory Distress Syndrome in late preterm and term infants could have a number of implications for treatment of this disease by helping to explain its molecular basis. This would lead to more effective treatments that target the specific process or processes involved. Differentiating between varying genotypes among affected individuals would also lead to more personalized therapies to optimize treatment for each specific case.

033

**Sartor, Lauren**

T35 NIH NIDDK Short-Term Training Program; Dean's Fellowship  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Surgery  
Division: Urologic Surgery  
Mentor: Steven Brandes, MD

**Long-term urinary function and sexual health follow-up on patients who underwent hypospadias repair in childhood**

Sartor L; Leopold Z; Vetter J; Paradis A; Brandes S

**Introduction:** Hypospadias is a common congenital disorder affecting 1 in 300 male newborns. Surgical repair for hypospadias typically occurs in early childhood. Current literature focuses on the short-term postoperative outcomes. However, a number of complications related to the surgery emerge after puberty. Complications resulting from hypospadias repair can greatly affect the urinary function and sexual health. There is a paucity of literature on patients who had hypospadias repair in childhood. Our study aims to assess the urinary and sexual health outcomes of patients who had hypospadias repair in childhood using an online questionnaire sent via email.

**Methods:** The surgical data of 672 men over the age of 16 who underwent hypospadias repair at St. Louis Children Hospital (SLCH) between 1988 and 2001 were examined. The phone number and mailing address in the medical records were used to contact the patient and obtain their email address. This provided access to a 27 question REDCap questionnaire that was a compilation of both validated and previously used questions that assess urinary and sexual health (AUA symptom score, ICIQ-SF, PDQ, SHIM, Mulhall Hardness Question, SEAR questionnaire, and PPPS). We obtained 68 email addresses and 30 completed surveys. Of the 30, 25 patients had their initial hypospadias repair at SLCH.

**Results:** Using univariate analysis and  $p < 0.05$ , patient responses were stratified based on 3 factors: surgery type, presence of curvature, and distal vs. proximal meatus (meatal location at the time of surgery). 28% had the island onlay procedure, 32% had the MAGPI procedure, and 40% of men were grouped as other, which consisted of patients who had circumcision, TIP, Mathieu, Thiersch, and GAP surgery type. The MAGPI procedure as compared to the other surgery types led to poorer urinary outcomes,  $p < 0.016$ . 36% of patients had curvature at the time of surgery. 32% of our patients had proximal hypospadias (midshaft or penoscrotal). As expected, both the presence of curvature and proximal hypospadias were significant for having lower confidence and self-esteem.

**Conclusions:** Hypospadias surgery in childhood has an impact on a patient's wellbeing in adulthood. A long-term follow-up on patients is important for improving outcomes in adulthood. Our study will continue to recruit patients to determine the optimal surgical approach based on the degree of the deformity.

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**Sindhar, Sampat**

T35 NIH NIDDK Short-Term Training Program  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Pediatrics  
Division: Genetics and Genomic Medicine  
Mentor: Beth A Kozel MD, PhD

**Investigating the true incidence of hypercalcemia in Williams Syndrome**

Sindhar S; Lugo M; Danback J; Yu E; Brink B; Deitzen D; Elder R; Pober B; Kozel BA

**Introduction:** Williams Syndrome (WS), a rare genetic disorder caused by a deletion of 26-28 genes on chromosome 7q11.23, is characterized by elfin facies, cardiovascular abnormalities, and endocrinological changes, particularly hypercalcemia. However, the etiology of hypercalcemia in WS is unknown and literature on the incidence and effect of hypercalcemia in these patients is scarce. Here we determined the true incidence of hypercalcemia in patients with WS across the lifespan and assessed whether an association exists between deletion size and hypercalcemia.

**Methods:** A retrospective chart review was conducted on 215 patients in the WS databases at Washington University, Yale University and Harvard University's School of Medicine. Calcium values were compared to age appropriate norms using the student t-test.

**Results:** We collected 865 calcium levels from 215 different patients. Individuals with WS tended to have higher calcium levels than those without WS ( $p < 0.001$ ). Overall, 27% of patients had at least one elevated calcium level as determined by house laboratory norms. Incorporating pediatric norms from St. Louis Children's Hospital (SLCH) dropped the prevalence of hypercalcemia to 24%. The disparity between hypercalcemia based on house lab standards and SLCH standards was exaggerated in patients age 0-1 yo (34% as compared to 13% according to SLCH norms) and age 1-2 yo (36% as compared to 29%). Hypercalcemia requiring intervention was seen in only 7% of patients, most of which occurred in the 12-24 month range. Chi-squared analysis showed having a larger deletion sizes ( $>2$  Mb) was not correlated with a history of clinically significant hypercalcemia.

**Conclusions:** This study shows that patients with Williams Syndrome, on average, have higher serum calcium values than their age-matched peers. Increases in calcium are mild, with only 7% requiring intervention for significantly elevated levels. Most childhood cases of treated hypercalcemia occurred between 12-24 months but other associated features that might suggest causality could not be identified with our data set. Many adult cases of hypercalcemia in WS appear to be secondary to other medical events and clinicians would be wise to investigate further in this population.

079

**Wang, Cynthia**

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: Dermatology  
Mentor: Cristina de Guzman Strong, PhD

**Elucidating the antimicrobial activity of S100 family proteins towards increased prophylactic capabilities**

Wang CX; Goodwin ZA; Strong C

**Introduction:** As one of the earliest-acting mechanisms in innate immunity, antimicrobial peptides (AMPs) expressed on the skin are critical for broad-spectrum antimicrobial defense. Recent evidence identified rapid evolution in a locus that harbors an AMP gene family (S100). We hypothesized increased antimicrobial activity in the S100 gene family members as a beneficial trait for modern human innate immunity. The purpose of this project is to examine the antimicrobial activity of S100 family proteins in order to understand the evolution of the epidermal barrier and the mechanisms behind these adaptations.

**Methods:** Bioinformatics: Multiple sequence alignment was performed with Geneious. HapMap data was gathered from the NCBI SNP database. Protein expression: Genes were cloned into pET-28b plasmids and transfected into *E. coli*. Protein expression was induced with IPTG and detected through Western Blot.

**Results:** Sequence alignment of the conserved domains of S100 proteins revealed great consensus sequence variability. Despite wide non-coding variation in the S100 genes, geographically distant populations (CEU, JPT, CHB) exhibited similar allele frequencies in the coding regions of a core set of S100 proteins compared to YRI, suggesting evolution of the S100 genes in the post-migration era. Population-specific variants such as missense mutations were found as well. Induction of protein expression for positive controls sNix and wtNix was confirmed through Western Blot. Although the protein of interest, hS100A7, was not detectable by Western, transcriptional induction of hS100A7 was PCR confirmed.

**Conclusions:** The successful induction of positive control protein expression shows that the parameters used for IPTG induction are valid and can be repeated. Further work is needed to confirm hS100A7 protein expression and perform protein purification for antimicrobial functional assays. This model can be used as a platform to evaluate other S100 protein variants, including those that are population-specific. By elucidating adaptive variants in the S100 family and other AMPs, we can gain novel insights into the evolutionary mechanisms behind antimicrobial activity towards developing enhanced prophylactic treatment.

034

**Wright, Alec**

T35 NIH NIDDK Short-Term Training Program  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Washington University in St. Louis  
Department: Surgery  
Division: Urologic Surgery  
Mentor: R Sherburne Figenshau, MD

**The role of positive surgical margins in outcomes following robot-assisted partial nephrectomy**

Wright AJ; Bauman TM; Potretzke TM; Vetter JM; Figenshau RS

**Introduction:** Robot-assisted partial nephrectomy (RAPN) is a safe and effective minimally invasive method for the treatment of resectable small renal tumors. Incomplete excision of these tumors can lead to the formation of positive surgical margins (PSMs) and consensus has yet to be reached on the role these PSMs play in the outcomes of patients following partial nephrectomy. Therefore, the purpose of this study was to investigate the relationship of PSMs with oncologic outcomes in the largest single-center series of RAPNs to date.

**Methods:** After receiving institutional review board approval a prospectively maintained database was reviewed for patients of two surgeons who received RAPN from 2007-2013. Patient clinico-pathologic information was analyzed for association with PSMs and multivariate analysis was performed using logistic regression. Kaplan-Meier analysis was used to compare local-recurrence free and overall survival between patients with PSM and negative surgical margins (NSMs). Cox proportional hazards analysis was used to assess the influence of multiple clinico-pathologic factors on overall survival.

**Results:** A total of 579 patients received RAPN in this series and 31 (5.4%) had PSMs following surgery. A multivariate analysis of single surgeon data showed PSMs were associated with higher estimated blood loss ( $p=0.008$ ). Kaplan-Meier analysis showed that PSMs were significantly associated with decreased local-recurrence free survival ( $p < 0.001$ ) and decreased overall survival ( $p = 0.007$ ). Cox proportional hazards analysis revealed positive margins [HR 4.17, (95% CI 1.27-13.70),  $p=0.019$ ], age [1.06, (1.01-1.11),  $p=0.011$ ], and Charlson-comorbidity index [1.55, (1.23-1.95),  $p < 0.001$ ] were all independently associated with decreased overall survival.

**Conclusions:** Our data support the conclusion that PSMs are associated with increased risk of local-recurrence. These results also suggest there are shared factors that associate PSMs with a decrease in overall survival, which may be a consideration for patient management. Collaborative, multi-institutional, long-term studies are needed to make more definitive conclusions about the impact of PSMs on outcomes.

032

**Xu, Zhuchen**

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: Su-Hsin Chang, PhD; Cynthia Herrick, MD, FACP

**Long-term outcomes of Roux-en-Y gastric bypass in adult bariatric patients at Washington University/Barnes Jewish Hospital**

Xu Z; Herrick C; Colditz GA; Eagon JC; Chang SH

**Introduction:** Morbid obesity (BMI>40 or BMI>35 with weight-related health conditions) is a growing problem in the US population. Surgical treatment is one of the recommended treatments for morbid obesity, especially if medical management was unsuccessful. Roux-en-Y gastric bypass (RYGB) is the most commonly performed bariatric surgery procedure. The purpose of this study is to examine the long-term effects of RYGB on weight management and post-surgery adverse events in morbidly obese adults.

**Methods:** We reviewed electronic medical records of 1,413 adults who received RYGB surgery by Dr. Christopher Eagon at Washington University/Barnes Jewish Hospital and abstracted weight data. We performed both unadjusted and adjusted analyses to determine patient's post-surgery changes in body mass index (BMI).

**Results:** Analyses will demonstrate the trajectories for BMI change over the course of patients' follow-up at Washington University/Barnes Jewish Hospital, up to a maximum of 18 years. We will also assess the prevalence of surgical complications.

**Conclusions:** The results of this study will contribute to our understanding of the benefit and the risk of RYGB surgery. Importantly, our study utilizes patients operated on by the same surgeon, which minimizes the confounding variable of the surgeon's level of training and skill in the institutional setting.

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**Zuckerman, Aaron**

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  
Mentor: Matthew Ciorba, MD

**Probiotic LGG as a safe and effective intestinal-specific radioprotectant**

Zuckerman AJ; Riehl TE; Thotala DK; Ciorba MA; Stenson WF

**Introduction:** In patients receiving radiation therapy (RT) for cancers of the gastrointestinal (GI) tract, diarrhea from small intestinal (SI) mucositis is the major side effect limiting completion of therapy. In a standard model of single-dose total-body irradiation (TBI), our group previously showed that the probiotic bacteria *Lactobacillus rhamnosus* GG (LGG) and its conditioned culture media (CM) prevents the epithelial cell damage (apoptosis and crypt dropout) that underlies SI mucositis in a TLR2-dependent manner. To examine the practicality of human translation, we aimed to define the intestinal specificity, clinical applicability and safety of LGG in preclinical models that closely resemble human RT.

**Methods:** Crypt survival was determined histologically in mice pretreated with one of several products derived from LGG and the TLR2 agonist lipoteichoic acid (LTA), LGG modified to produce mutant LTA, or PBS and followed by one dose of TBI. Extra-intestinal radioprotection was assessed with flow cytometry of peripheral venous blood before pretreatment and after IR and examined for T and B cell markers. A novel fractionated total abdominal-only IR (TAI) model was developed to simulate human RT protocols. Mice pretreated with LGG, LTA, or PBS were given 7 or 8 days of TAI and followed for survival. Tumor protection assays were performed with syngeneic colon cancer tumor grafts. Mean tumor volume was assessed daily.

**Results:** LGG, LGG-CM, LTA, and PAM3-CSK4 have crypt-protective effects in IR mice, while treatment with LGG or LGG-CM mutated for LTA has no benefit. All T and B cell markers decreased after IR and no protection was observed with LGG or LTA compared to control. In our model of fractionated TAI, LGG- and LTA-treated mice survive longer than controls and recover weight faster. LGG did not protect CT26 cancer cells from IR *in vitro* or *in vivo* compared to control.

**Conclusions:** Probiotic LGG exerts its radioprotective effect via a LTA/TLR2-dependent mechanism that is confined to the GI lumen, persists in a clinically-relevant fractionated TAI model, and does not reduce tumor radiosensitivity. These findings provide the basis for a clinical trial of probiotic LGG in humans undergoing radiation therapy for lower GI tumors.



## WUSTL, Office of the Provost

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### Ankomah, Felix

WUSTL, Office of the Provost  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Surgery  
Division: Cardiothoracic Surgery  
Mentor: Varun Puri, MD, MSCI

#### **Predictors and consequences of readmission after major thoracic surgery**

Ankomah FB; Puri V

**Introduction:** The frequency and consequences of early hospital readmissions highlight their negative impact on individual patient outcomes and healthcare costs as a whole. Various studies have attempted to identify strategies to reduce the incidence of hospital readmission, particularly after surgery. In thoracic surgery, especially post lung cancer resection, the literature is quite scant despite large readmission numbers. Our objective is to identify predictors of readmission after lung cancer resection. Specifically, to establish perioperative variables associated with increased incidence of 30 and 90-day readmission after lung resection.

**Methods:** A retrospective study of patients who have undergone lung resection at the Barnes-Jewish Hospital from 2008 to 2014 was conducted to establish the 30 and 90-day postoperative readmission rate and diagnoses. Univariate analyses of perioperative factors were conducted to identify variables that affect readmission. Logistic regression models predicting variables related to postoperative readmission and 30-day mortality will be fitted. Lastly, Cox model of long term survival will be fitted.

**Results:** Of 2248 patient procedures analyzed, forced expiratory volume in 1 second (FEV1;  $p < 0.0001$ ), diffusing capacity of the lungs for carbon monoxide (DLCO;  $p < 0.0001$ ), smoking history ( $p = 0.004$ ), length of stay after surgery ( $p = 0.002$ ), and postoperative intensive care unit (ICU) stay ( $p = 0.002$ ) were significant predictors of 30-day readmission. We anticipate identifying other risk factors of readmission, long term survival, and 30-day mortality. This will be a combination of modifiable and non-modifiable variables.

**Conclusions:** Establishing modifiable risk factors for postoperative readmission will aid in reducing readmissions after thoracic surgery, improve patient outcomes, decrease healthcare expenditure, and contribute to the knowledge base. This project was limited by incomplete follow-up information, addressed by excluding patients lost to postoperative follow up. Additionally, examination of patient-level factors such as medication nonadherence, which may impact readmission, seems unfeasible but presents an opportunity for future prospective research.

011

### De Freitas, Danielle

WUSTL, Office of the Provost  
Summer Research Program  
Current Doctoral Program of Study: Medicine  
Meharry Medical College  
Department: Orthopaedic Surgery  
Mentor: Scott J Luhmann, MD

#### **Proximal junctional kyphosis in adolescent idiopathic scoliosis**

De Freitas DG; Kassim S; Luhmann SJ

**Introduction:** Presently, there are several risk factors hypothesized for the development of proximal junctional kyphosis (PJK) after surgical correction of adolescent idiopathic scoliosis (AIS). This study investigated whether the degree of sagittal change of the upper instrumented vertebrae (UIV) influences the development of PJK. Our hypothesis was an iatrogenic decrease in kyphosis over the upper 1 to 2 instrumented vertebrae would be associated with PJK.

**Methods:** This study was a retrospective analysis of charts and radiographs of AIS patients who underwent posterior spinal fusion with a minimum 2 year follow-up. The study population consisted of 87 AIS patients (69 female; 18 male) with an average age of 14 years and an UIV between T2 and T4. PJK was quantified using the method of Glattes et al (UIV+2) and Lonner et al (UIV+1).

**Results:** The UIV was T2 in 14 patients, T3 in 35 patients, and T4 in 38 patients. Overall, T1-T5 kyphosis preoperatively was 13.1 degrees and postoperatively was 14.90. The major coronal Cobb preoperatively was 59.60 and postoperatively was 19.70, 67% improvement. Using the PJK UIV+1 criteria, 31 patients had PJK postoperatively (56 did not), and the PJK UIV+2 method 4 patients had PJK (83 did not). Using PJK UIV+1 method, for patients who did not develop PJK (PJK-) the mean preoperative UIV-1 was 6.70; those with PJK (PJK+) the UIV-1 was 8.60. The immediate postoperative mean UIV-1 was 5.80 (-13% change) for PJK- patients and 8.60 (0%) for PJK+ patients. The final UIV-1 for PJK- patients was 5.50 (-17%), and 12.90 (+50%) for PJK+ patients. The pre-operative UIV-2 for PJK- subjects was 10.0 and 11.20 for PJK+ patients. The immediate postoperative UIV-2 in PJK- patients was 8.40 (-16%) and in PJK+ patients was 11.70 (+6%). The final postoperative measures of UIV-2 in PJK- patients was 9.40 (-6%) and those with PJK was 15.30 (+37%).

**Conclusions:** Our data did not support our hypothesis that an iatrogenic decrease in kyphosis over the upper 1 and 2 instrumented vertebrae was associated with the development of PJK; interestingly the converse proved to be true. Therefore, the development of PJK may be due to more global factors.

**Iseyemi, Abigail**

WUSTL, Office of the Provost

Summer Research Program

Current Doctoral Program of Study: Medicine

Meharry Medical College

Department: Obstetrics &amp; Gynecology

Division: Clinical Research

Mentor: Jeffrey F Peipert, MD, PhD

**Risk factors for unintended pregnancy in the Contraceptive CHOICE Project**

Iseyemi AY; Peipert, JF; Zhao Q; McNicholas C; Eisenberg D; Madden T

**Introduction:** Unintended pregnancies comprise more than 50% of all pregnancies in the United States each year. These pregnancies cost over \$21 billion and are associated with a higher risk of poor maternal and child health outcomes. The purpose of this study is to examine socioeconomic status (SES) as an independent risk factor for unintended pregnancy when no-cost contraception is provided to all participants.

**Methods:** Data was taken from 9,136 CHOICE Project participants who were recruited between 2007 and 2011 and followed for up to three years. Women who experienced an unintended pregnancy while using an intrauterine device (IUD), an implant, depot medroxyprogesterone acetate (DMPA) injections, birth control pills, a hormonal patch, or a vaginal ring were included in the analysis. Factors evaluated included demographic characteristics (i.e. age, race/ethnicity, educational level and insurance), history of unintended pregnancy, history of sexually transmitted infection (STI), and current contraceptive method. Adjusted hazard ratios and their respective 95% confidence intervals (CI) estimated for time to unintended pregnancy, controlling for potential confounding variables.

**Results:** Baseline characteristics of participants were: mean age 25, 50% black, 35% with less than a high school education, 58% low SES (defined for those who reported either receiving public assistance or having difficulty paying for basic necessities) and 63% having experienced a previous unintended pregnancy. There were 369 unintended pregnancies during the study period. Among this group there was a significant number who were of low SES HR<sub>adj</sub>=1.40, 95% CI(1.05,1.87), in addition to a significant number of participants of young age, having public insurance, having a high school degree or less, a history of unintended pregnancy and a history of STI.

**Conclusions:** The results indicate that lower SES is an important risk factor for unintended pregnancy. Future research should focus on ways to remove obstacles for all women to access the most effective contraceptive methods. This, in turn, may decrease disparities and reduce the rate of unintended pregnancy.

## Junior Faculty Research

- No Poster**     **Harris, Lydia-Ann, PhD**  
Washington University in St. Louis  
Department: Center for Human Nutrition  
Division: Geriatrics and Nutritional Science  
**Whey protein causes insulin resistance via an FGF21 mediated mechanism**  
Harris LLS; Smith GI; Klein S; Mittendorfer B  
**Introduction:** Fibroblast growth factor 21 (FGF21) is produced by the liver and may have important metabolic functions (e.g., it increases energy expenditure, and decreases body fat and plasma triglyceride concentrations). Dietary protein and leucine restriction increase plasma FGF21 concentration and improve metabolic function in mice, which suggests that amino acids are important regulators of FGF21 production. However, the acute effect of amino acids and protein ingestion on plasma FGF21 concentration in people is not known. Accordingly, the goal of our study was to test the hypothesis that both protein and leucine ingestion attenuate the insulin-induced increase in plasma FGF21 concentration.  
**Methods:** Plasma FGF21 concentration was measured in 22 women during a hyperinsulinemic-euglycemic clamp procedure with and without concomitant ingestion of whey protein (0.6 g/kg fat-free mass) or an amount of leucine that matched the amount given with whey protein (n = 11).  
**Results:** We found that the plasma FGF21 increased from  $177 \pm 28$  pg/ml during basal, postabsorptive conditions to  $598 \pm 90$  pg/ml during the clamp procedure (insulin and glucose infusion) and protein ingestion prevented the clamp-induced increase in FGF21 concentration ( $142 \pm 37$  and  $201 \pm 45$  pg/ml during basal and clamp, respectively) whereas leucine ingestion had no effect on plasma FGF21 concentration, which increased ( $185$  pg/ml vs  $367$  pg/ml, respectively).  
**Conclusions:** Protein ingestion inhibits FGF21 production but this effect is not mediated by leucine.
- 058**     **Siddiqi, Shan, MD**  
Psychiatry Resident  
Washington University in St. Louis  
Department: Psychiatry  
Mentors: Kevin J Black, MD; Fay Y Womer, MD  
**Impact of a structured review session on medical student psychiatry subject examination performance**  
Siddiqi SH; Womer FY; Black KJ  
**Introduction:** The National Board of Medical Examiners (NBME) subject examinations are used as a standardized metric for performance in required clerkships for third-year medical students. While several medical schools have implemented a review session to help consolidate knowledge acquired during the clerkship, the effects of such an intervention are not yet well-established. One prior study reported an improvement in NBME psychiatry examination scores with a 1.5-hour review session, but this study was limited by a small sample size and selection bias introduced by the fact that attendance at the review session was optional.  
**Methods:** A 1.5-hour structured review session was conducted for medical students in the last week of each 4-week psychiatry clerkship between September 2014 and July 2015. Students were required to attend unless excused due to scheduling conflicts. Mean scores were compared with students who took the test in the corresponding time period during the previous two academic years. Endpoints included mean scaled scores, mean scores for the two lowest-performing students in each 4-week clerkship, percentage of students scoring 70 or less, and percentage of students scoring 99.  
**Results:** 83 students took the exam during the experimental period, while 176 took the exam during the control period. Mean scaled score improved from 85.3 to 87.8 ( $p < 0.05$ ) for all students and from 74.1 to 78.7 ( $p < 0.001$ ) for the two lowest scores in each 4-week clerkship. Percentage of students scoring 70 or less improved from 4.0% to 0% ( $p < 0.05$ ). Percentage of students achieving the maximum possible score appeared to increase from 7.4% to 13.2%, but did not reach significance.  
**Conclusions:** An end-of-clerkship review session led to increased mean scores on the NBME psychiatry subject examination, particularly for students at the lower end of the score range. Future research should investigate the impact of such an intervention in other specialties and other institutions.

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