
Institution: Beth Israel Deaconess Medical Center

Mentor: Brian O'Gara, M.D., M.P.H

Project(s) Available:

1. Lung protective properties of the inhaled anesthetics

We have recently completed a clinical trial investigating whether the volatile anesthetic sevoflurane can limit lung inflammation during cardiac surgery, as compared to propofol. We plan a follow up translational study diving deeper into the cell types involved in perioperative lung injury and their potential modulation by a subanesthetic dose of the volatile anesthetics. Student opportunities could include recruitment (screening), intraoperative data collection, medical record abstraction, specimen collection/processing, and data analysis.

2. Cognitive prehabilitation to prevent postoperative delirium and POCD

Our group recently completed a feasibility trial of a mobile application-based cognitive prehabilitation regimen to prevent delirium and POCD following cardiac surgery. We plan a follow up efficacy trial, in which a student could participate as a blinded or unblinded study investigator. Responsibilities include screening, consenting, participant follow up and mobile application instructions, data collection, administration of cognitive exams and analysis.

3. Intraoperative Virtual Reality

We are currently wrapping up an innovative clinical trial investigating whether the use of virtual reality immersion can reduce intraoperative anesthetic requirements during upper extremity surgery. Given the success of implementing this trial we anticipate applying this technology to other patient populations (ex. pain patients). Interested students can participate in study design, recruitment (screening, consenting), intraoperative VR administration, survey administration, data collection and analysis.

Institution: Beth Israel Deaconess Medical Center

Mentor: Balachundhar Subramaniam, MD

Project(s) Available: Perioperative multimodal general AnesThesia FocusIng on Specific CNS targets in patients undergoing carDiac surgERies -The PATHFINDER study: a feasibility trial

In this study investigators are looking to employ a rational strategy of EEG-guided multimodal general anesthesia (MMGA) using specific sedative and analgesic brainstem/ cortical targets. The target population of this research includes cardiac surgery patients with age >60 years undergoing cardiopulmonary bypass. By using the EEG intra-operatively and titrating different classes of medications to brainwave patterns, we hope to maximize therapeutic benefit and minimize side effects. In doing so, we hope to learn more about the feasibility of implementing multimodal general anesthesia techniques in the OR and EEG-guided sedation until extubation in the ICU. Primary outcomes include rates of postoperative delirium (POD) and postoperative cognitive dysfunction (POCD), and secondary outcomes include hospital length of stay, ICU stay, time to extubation, postoperative analgesic use, etc.

Students will have the opportunity to participate in patient recruitment, data collection (including intraoperative observation), analysis of EEG recordings, and data analysis.

PANDORA: Scheduled prophylactic 6-hourly intravenous acetaminophen to prevent postoperative delirium in older cardiac surgical patients

In this study investigators aim to evaluate a prophylactic intervention for postoperative delirium, one of the most common and detrimental complications of cardiac surgery in older adults. The central hypothesis is that scheduled prophylactic 6-hourly IV acetaminophen can prevent postoperative delirium in older cardiac surgical

patients when administered in the first 48 hours following surgery. Through this trial, we will determine the effect of IV acetaminophen on; 1) the incidence of postoperative delirium, 2) the use of opioids and other rescue analgesics in the first 48 postoperative hours, daily pain scores at rest and exertion, and length of stay in the Intensive Care Unit and overall hospital length of stay 3) longer-term cognitive, physical, and self-care functional recovery after surgery. Interested students will have the opportunity to participate in patient screening and recruitment, administration of neurocognitive and delirium assessments, adverse event monitoring and data collection/analysis.

Institution: Beth Israel Deaconess Medical Center

Mentor: Shahzad Shaefi, MD, MPH

Project(s) Available: Carbon Monoxide in Cardiac Arrest

We are interested in creating a preclinical murine model of cardiac arrest and assessing the effects of CO on the disease physiology and outcomes. The student in the proposed project will be exposed to the workings of small animal models as well as basic techniques of experimental design, execution and eventual publishing. We aim to carry the knowledge gained in these studies into larger animal models and eventually into human treatment.

Oxygen Titration in Septic Shock

We aim to develop a clinical trial investigating the effect of varying oxygen titrations on septic shock patient outcomes. The student in this proposed trial would be closely involved with the development and execution of a large clinical trial, including gaining an understanding of human subjects research, patient screening, enrollment and consenting as well as grant writing, manuscript preparation and fundamentals of biostatistics and epidemiological research within clinical trials.

Biomarkers Associated with the Surgical Experience in the Operating Room (BASE-OR)

The purpose of this study is to further investigate the mechanistic underpinnings of the stress and inflammation response to surgery and anesthesia. In order to fully elucidate this, we will establish a plasma, urine and tissue repository of samples collected from surgical patients at BIDMC. These samples will be assessed at a future date for inflammatory and immunologic biomarkers with the aim of uncovering presently unclear mechanisms of postoperative dysfunction. Students will have the opportunity to participate in patient screening, enrollment and consenting as well specimen acquisition/processing, data collection and analysis.

Biomarkers Associated with a Subject's Experience in the Intensive Care Unit (BASE-ICU)

The purpose of this study is to further investigate the mechanistic underpinnings of morbidities experienced in the critically ill population. In order to fully elucidate this, we will establish a plasma and urine repository of samples collected from patients admitted to the intensive care unit (ICU) at BIDMC. These samples will be assessed at a future date for inflammatory and immunologic biomarkers with the aim of uncovering presently unclear mechanisms of dysfunction sustained in the ICU. Students will have the opportunity to participate in patient screening, enrollment and consenting as well specimen acquisition/processing, data collection and analysis.

Institution: Beth Israel Deaconess Medical Center

Mentor: Simon Robson, M.B., Ch.B., FRCP, Ph.D.

Project(s) Available: Purinergic Signals in NASH and Liver Fibrosis

The research interests in Robson laboratory are in purinergic signaling and our focus has been on the vascular and immune ectonucleotidases of the CD39 family. These signaling pathways are crucial in modulating inflammation and immune responses in the liver and gastrointestinal tract, such as in inflammatory bowel disease (IBD), as well as in non-alcoholic steatohepatitis (NASH) and are linked to development of liver fibrosis.

We have identified ectonucleotidase activity in the vasculature and immunoregulatory cells and confirmed that CD39 has identity with the ATP or nucleoside triphosphate diphosphohydrolase (EC 3.6.1.5; ENTPD1). Recent work has detailed the functional consequences of plasma membrane expression of CD39 and related family members by dendritic cells, regulatory T cells, T helper type 17 (Th17) and natural killer T (NKT) cells. We have developed Cd39-deficient, floxed mice and CD39 transgenic mice. Modulation of CD39 impacts survival and in models of inflammation and hepatic/intestinal fibrogenesis.

The proposed FAER scholarly project will target and help define the mechanism of purinergic signaling in regulation of macrophage activation and generation of pro-fibrogenic stimuli in mouse liver toxic metabolic injury and fatty liver models.

Specifically:

1. Phenotype of CD39-deficient and wildtype macrophages will be studied in vitro and in co-culture with hepatic stellate cells in presence of exogenous ATP/adenosine.
2. Identification of ATP receptor which mediates hyper-inflammatory responses in absence of Cd39 will be studied (P2X7) using chemical inhibitors and siRNA screens.
3. Putative fibrogenic/fibrolytic soluble mediators released by macrophages in response to ATP/Adenosine will be identified in macrophage/HSC co-culture system using neutralizing antibodies.

Institution: Beth Israel Deaconess Medical Center

Mentor: Maria Serena Longhi, MD, PhD

Project(s) Available: Dr. Longhi's research aims at defining how immune responses are regulated in chronic inflammatory statuses and in autoimmune disorders, including inflammatory bowel disease and autoimmune hepatitis.

Her research program includes these areas of interest:

a) Interactions between purinergic, hydrocarbon and oxygen mediated pathways in inflammatory bowel disease: as part of these investigations, Dr. Longhi's laboratory has found that effector Th17 cells obtained from the peripheral blood and lamina propria of Crohn's disease patients express low levels of CD39, an ectonucleotidase that is key to immune homeostasis by hydrolyzing pro-inflammatory nucleotides into immunosuppressive adenosine. Defective CD39 expression derives from impaired response of Th17 cells to ligands of aryl hydrocarbon receptor (AhR), a receptor for toxins/xenobiotics that also modulates adaptive immunity. Recent studies from her laboratory have shown that in Crohn's disease poor response to AhR ligands results from low oxygen levels, derived from protracted tissue inflammation. Her current research in this area aims at defining how alterations in the CD39, AhR and oxygen pathways can be therapeutically corrected.

b) Regulation of AhR signaling in autoimmune hepatitis: Dr. Longhi's work in this research area aims at identifying key mechanisms leading to functional impairment of regulatory T cells (Treg), a lymphocyte subset central to immunotolerance maintenance. As part of these investigations Dr. Longhi's laboratory is currently defining the alterations in AhR signaling pathways leading to Treg dysfunction in this autoimmune condition.

c) Post-transcriptional regulation of CD39 in inflammatory bowel disease: as part of these studies, Dr. Longhi is defining the role of endogenous antisense RNAs, as modulators of CD39 expression and activity in both regulatory and effector cells in inflammatory bowel disease. Factors contributing to antisense RNA upregulation in Tregs and Th17 cells are also investigated.

For all three projects interested students will be involved in different aspects of the research project, including sample collection and processing, basic experimental techniques like cell isolation, culture and differentiation, data analysis and interpretation.

Institution: Brigham and Women's Hospital

Mentor: Richard Urman, M.D. , M.B.A.

Project(s) Available: Study Title: Novel Computational Methods for Continuous Objective Multimodal Pain Assessment Sensing System (COMPASS)

Pain is a complex human experience and a symptom of numerous medical conditions with anatomic, physiologic, psychosocial, and cultural determinants. Clinicians rely on patients' self-reported information as well as assessments of multiple clinical cues, and few methods are available for objective assessment of pain. The most common measures available for pain assessment are visual analog scales, numerical rating scales, and verbal rating scales. These self-reporting measures, which come from patients' individual assessments, are subject to high variability. Consequently, objective measurement of pain has long been clinicians' holy grail for effective pain management.

The main goal of this National Science Foundation (NSF) funded study is to develop a Continuous Objective Multimodal Pain Assessment Sensing System (COMPASS), to objectively and accurately measure pain for clinical use, with multimodal data coming from facial-expressions and non-invasive physiological sensors. The study focuses on chronic Low Back Pain, although the science and methods being developed are broadly applicable to other types of pain. The long-term goal is to enable objective chronic pain assessment and management without undesirable and unintended consequences, and potentially extend its use to other patient states such as stress, depression, and emotion.

COMPASS is built on the premise that pain can be assessed accurately and reliably through integrations of non-invasive, multimodal sensor data to assess pain objectively.

These non-invasive modalities will include Facial Expression, Electroencephalography (EEG), Eye movement, Galvanic Skin Response, Electrocardiogram (ECG), Electromyography (EMG), Skin Temperature, Respiratory Rate, and Blood Pressure. The study will also investigate optimal sensor selection to assess pain objectively and accurately with fewer sensors. The methodology includes developing feature extraction methods, machine learning models, and data fusion algorithms to objectively assess pain. We will design experiments to collect a large set of clinical data from chronic low-back pain patients and then train and validate the performance of COMPASS.

Institution: Cleveland Clinic Foundation

Mentor: Daniel Sessler, MD

Project(s) Available: POISE-3, a 10,00-patients multicenter factorial RCT.
Hypotension prediction index evaluation, a 300-patient single-center RCT.
Two RCTs of regional blocks for thoracic surgery.
Many others!
Students can and do participate in all aspects of trials.

Institution: Icahn School of Medicine at Mount Sinai

Mentor: Daniel Katz, M.D.

Project(s) Available: Patient Safety Innovation Grant, Icahn School of Medicine
Practice Pattern Changes Following the Implementation of Triton, an FDA-cleared Technology for Quantification of Blood Loss (QBL): A Performance Improvement Study.

The goal of this project is to evaluate how practice patterns change after the implementation of a QBL strategy. FAER Student(s) will be examining the data from our EMR and looking into how we can leverage this new technology to change clinical care. We will be examining the distributions of blood loss and looking at the literature to design and implement practice changes that we will then study.

In addition, the student will be observing in the clinical and operating rooms settings.

Industry Supported Research Grant, Icahn School of Medicine

Utility of Thromboelastometry in Parturients Experiencing Large Volume Loss in Cesarean Section

The goal of this project is to examine the utility of thromboelastometry in patients experiencing major obstetric hemorrhage.

FAER Student will be participating in the consenting process , as well as the the testing analysis phase after the blood draw.

FAER Student will also be observing the clinical processes in and out of the Operating Rooms and Labor and Delivery Rooms.

Institution: Massachusetts General Hospital

Mentor: Jianren Mao, M.D., Ph.D.

Project(s) Available: The MGH Center for Translational Pain Research is a combined preclinical and clinical research facility. We are testing a new pharmacological therapy that could improve opioid analgesic effect and reduce opioid side effects such as opioid-induced hyperalgesia.

The student will learn clinical study design, subject recruitment, and research data collection. The student will have the opportunity to be exposed to laboratory studies of pain and opioid-related disorders using the state-of-art neuroscience techniques.

Institution: Massachusetts General Hospital

Mentor: Joseph Cotten, M.D., Ph.D.

Project(s) Available:

1) We are interested in the molecular mechanism(s) by which inhaled, halogenated anesthetic gases activate TASK potassium channels. Using random and targeted mutagenesis and guided by several recent potassium channel crystal structures, we will identify regions of the TASK potassium channel critical for activation by halogenated anesthetics. We will identify amino acid residues in TASK-3 important for anesthetic regulation using either a yeast-based or a mammalian cell line-based functional assay combined with next generation DNA sequencing.

2) Opioid sensitivity in providing analgesia and in causing respiratory depression is modified by exposure to hypoxia as determined in patients with sleep apnea and in patient living at high altitude. In a rat model, we will study the effects of hypoxia, normoxia, and hyperoxia on opioid sensitivity and tolerance.

The student will focus on either molecular biology/ion channel or rodent studies. A unique and important role will be defined based on the student's interests. The student will work closely with the mentor and/or his research assistant to master multiple basic laboratory skills in molecular biology, ion channel electrophysiology, basic electronics, respiratory physiology, and rodent handling/experimentation.

Institution: Massachusetts General Hospital

Mentor: Stuart Forman, M.D., Ph.D.

Project(s) Available: Wild-type zebrafish embryos (up to 7 days post-fertilization) will be used to screen libraries of compounds for suppression of motor responses to environmental stimuli, using a high-throughput programmable video analysis tool. Active compounds will be further characterized for potency and reversibility. Zebrafish colonies with knockout or knockin of specific genes associated with general anesthesia sensitivity will be created, and used for further testing of general anesthetics.

Students will participate in lab meetings, present their findings, and work with labmates to summarize their work in the form of Powerpoint slides or a poster. Students will also:

- 1) Learn how to use zebrafish for drug assays of both hypnosis and sedation.
- 2) Perform high-throughput screening tests on libraries of novel compounds.
- 3) Perform basic statistical analyses and understand key experimental concepts such as repeatability, statistical significance, and power analysis.
- 4) Learn to maintain a research notebook, participate in weekly lab meetings, and present their summarized results in written and oral form.
- 5) Participate in weekly reading and discussions of literature related to anesthetic pharmacology and mechanisms. Attendance at weekly Grand Rounds conferences will be encouraged.
- 6) Observe and learn about clinical anesthesia in the MGH operating rooms and affiliated divisions (OB, Pain, ICU).

Institution: Massachusetts General Hospital

Mentor: J.A. Jeevendra Martyn, M.D., F.R.C.A., F.C.C.M.

Project(s) Available: The project will examine changes in motor neuron numbers with time using burn injury and sepsis as relevant models. The role of microglia in these changes and how the motor neuron changes affect muscle synapse and muscle mass will be studied. Therapeutic maneuvers to attenuate these motor neuron changes will also be tested.

The student will be taught simple basic experiments on PCR, western blots and in vivo rodents experiments on establishment of various pathologic states described above.

Institution: Massachusetts General Hospital

Mentor: Shiqian Shen, M.D.

Project(s) Available: Accumulating evidence suggest a critical role for neuro-immune interactions in pain perception, and in the transition from acute to chronic pain. Our lab focuses on dissecting key immunological events that are implicated in the development of neuropathic pain.

Taking advantage of preclinical animal models of pain, particularly chemotherapy-induced peripheral neuropathy and sciatic nerve chronic-constriction injury, we will examine the underlying contribution from different subset of immune cells during the onset and maintenance of neuropathic pain.

Student is expected to participate in the experiments using animal models of pain, and is expected to learn how to perform nociceptive behavior testing, including von Frey Filaments, Hargreaves apparatus, and facial grooming. Perspective student will participate in scientific literature review, experimental design, data interpretation, and troubleshooting.

Institution: Massachusetts General Hospital

Mentor: Zhongcong Xie, M.D., Ph.D.

Project(s) Available: Recent population studies have suggested that children who undergo anesthesia and surgery at an earlier age could have an increased risk for cognitive impairment. We have proposed to develop and validate biomarkers in mouse models that can later be used to inform and effectively translate to clinical trials in children to study anesthesia- and surgery-induced cognitive impairment. Our Preliminary studies show that anesthetic sevoflurane can increase levels of brain P-Tau, inhibit neurogenesis, cause cognitive impairment and increase blood Tau levels in young mice. Therefore, we hypothesize that Tau and P-Tau in blood and urine serve as the biomarkers for anesthesia- and surgery-induced cognitive impairment in young mice, and P-Tau inhibits migration of neural progenitor cells (NPCs) by de-stabilizing their microtubules. The results of this project would ultimately lead to safer anesthesia care and better postoperative outcomes for children.

The student performs the research under the supervision of the mentors. Specifically, the student assesses the effects of 24 hours treatment with DMED on cell death and inflammation in H4 human neuroglioma cells stably transfected to express human full-length APP (H4-APP cells). The student detects the cell viability, caspase-3 activation and levels of IL-6 by using MTT assay (Thermo Fisher Scientific, Waltham, MA), Western Blot with caspase-3 antibody (Cell signaling technology, Danvers, MA) and IL-6 ELISA kit (Thermo Fisher Scientific, Waltham, MA).

During this project, the student is in charge from the cell culture and drug delivery process and also performs the cells and protein analysis for MTT, Western blot and ELISA test with the help of lab colleague. Finally, the student preforms the data analysis for above experiments.

Institution: Massachusetts General Hospital

Mentor: Ken Solt, M.D.

Project(s) Available: Our laboratory aims to elucidate the neural circuits involved in anesthetic-induced unconsciousness and emergence from general anesthesia, with the long-term goal of developing novel methods to rapidly reverse the effects of general anesthesia to restore consciousness and cognition. This project will involve the use of various neural circuit manipulations in rodents to elicit changes in arousal state, including (but not limited to) chemogenetics and optogenetics. EEG and intracranial recordings will also be used to assess changes in neurophysiology. The student must be willing to work with rodents.

With appropriate supervision by senior lab members, the student will learn how to handle and anesthetize laboratory animals, and will participate in various activities including stereotaxic neurosurgery, behavioral experiments, neurophysiological recordings, histology, and data analysis. The student will attend weekly lab meetings to present brief progress reports and learn about other ongoing projects. At the end of the fellowship, the student will be expected to summarize and presents his/her work at the final lab meeting.

Institution: Massachusetts General Hospital

Mentor: Lorenzo Berra, M.D.

Project(s) Available: Lung rescue team: the goal of this interventional crossover study, in intubated and mechanically ventilated Acute Respiratory Distress Syndrome (ARDS) patients, is to compare two positive end-expiratory pressure (PEEP) titration techniques regarding: respiratory mechanics, gas exchange, changes in aeration and distribution of ventilation and its impact on cardiac function, specially the right heart (RH). The PEEP titration techniques are: incremental PEEP titration (PEEPinc) and Lung recruitment maneuver plus incremental (LRM plus PEEPdec).

iNO cardiac surgery: the goal of this phase 3 randomized, controlled clinical trial is to investigate the possible beneficial effects of nitric oxide on kidney protection in patients undergoing cardiac surgery with estimated CPB time > 90 minutes. Study gas is delivered through CPB and mechanical ventilator/HFNC for 24 hours from the beginning of CPB. Patient hospital course is monitored for detection of AKI, hemodynamics, respiratory and other clinical outcomes are assessed. Moreover, plasma and urine samples are processed and analysis are performed in order to investigate no metabolites and kidney damage biomarkers.

The student will join the research team led by Drs. Berra and Kacmarek, with 2 MD research fellows and 1 post-graduate student. We actively perform on several study protocols in the field of management of ventilator and airway care of patient admitted to the ICU. Student's duties include but not limited to:

- a) Participate in ongoing research project on lung/heart interaction and respiratory care or nitric oxide and cardiac surgery
- b) Record data of procedures and results
- c) Learn clinical trials and clinical research compliance
- d) Report analyzed data to PI and participate in interpretation of results of studies, compared hypothesis and research methodology
- e) Participate actively in enrollment of patients, study procedures and samples analysis
- f) Learn basics application of statistics for the analysis of clinically relevant data
- g) Present at weekly research team meeting
- h) Develop a poster presentation for the annual ASA meeting to summarize preliminary or definitive results of study s/he takes part in

Institution: Massachusetts General Hospital

Mentor: Yi Zhang, M.D.

Project(s) Available: Retrospective study on post operative pain management in Patients with Opioid Use disorder.

Students will assist in data collection, statistical analysis (with supervision and help from PI and statistician), literature review, and manuscript writing.

Institution: Massachusetts General Hospital

Mentor: Fumito Ichinose, M.D., Ph.D.

Project(s) Available: Sudden CA is a leading cause of death worldwide. Despite advances in cardiopulmonary resuscitation (CPR) methods only 10-20% of adult out-of-hospital CA (OHCA) victims survive to hospital discharge and up to 60% of survivors have moderate to severe cognitive deficits 3 months after resuscitation. Most of the recent pharmacological interventional studies in CA have shown no benefit in improvement on mortality and other outcomes. Endothelial-derived nitric oxide (NO) maintains vascular homeostasis and prevents organ injury induced by ischemia and reperfusion (I/R). In the presence of hemolysis, Hb is released into the circulation in the form of oxyhemoglobin (Oxy-Hb), which depletes vascular NO via the dioxygenation reaction to form methemoglobin (Met-Hb). Nitric oxide depletion by plasma free Hb produces vasoconstriction, impaired tissue perfusion and inflammation. We previously showed in preclinical studies that breathing NO after CPR improves outcomes in mice, rats, and pigs subjected to experimental CA. We also reported that hemolysis and plasma NO consumption are increased in post-arrest patients and mice subjected to experimental CA, and breathing NO decreases plasma NO consumption in post-CA mice. However, the extent of hemolysis after CA in humans and its correlation with plasma NO consumption over time has not been clearly elucidated. In this study we aim (I) to measure levels of hemolysis in patients resuscitated from OHCA, (II) to measure levels of plasma NO consumptions, and (III) analyze the correlation of these parameters with clinical outcomes in existing cohort of plasma samples obtain in the Neuroprotect trial.

Student will assist PI to measure plasma free Hb and NO consumption such as:

- 1) Assist measurements of plasma free Hb using an assay kit
- 2) Assist measurements of plasma NO consumption with chemiluminescence
- 3) Assist analysis of the data

Institution: Mayo Clinic

Mentor: Micheal Joyner, M.D.

Project(s) Available:

- IRB 19-10298 High Resolution Phenotyping of Twins Highly Divergent For Exercise and Lifestyle
- IRB 19-009290 Exercise and Hypoxic Responses to Isovolemic Hemodilution in Rare Hemoglobin Variant Humans
- IRB 19-002893 Physiological Validation of Current Machine Learning Models for Hemodynamic Instability in Humans
- IRB 19-000901 Effects of Left and Right Shifted Oxygen-Hemoglobin Dissociation Curves on Skeletal Muscle Blood Flow and Oxygenation during Handgrip and Cycling Exercise

Student Role for all listed projects:

The student will work closely with Dr. Joyner and his research fellows to understand the fundamental biological questions. They will also participate during the invasive studies on instrumenting subjects, obtaining/analyzing samples, and also analyzing data. The goal will be generation of an abstract for presentation at a major meeting and inclusion as a co-author on a subsequent manuscript.

Institution: Mayo Clinic

Mentor: Carlos Mantilla, M.D. Ph.D.

Project(s) Available: Available Projects:

- Opioid-induced respiratory depression
- Clinical assessment of diaphragm muscle function

Student Role:

The student will work closely with Dr. Mantilla and his research fellows using techniques such as whole-body plethysmography, lung mechanics and wireless telemetry of respiratory function. The studies will assess the impact of physiological changes in motor neurons, muscle fibers and neuromuscular junctions across diseases and conditions that limit the ability to sustain breathing and perform expulsive maneuvers such as coughing and sneezing that are necessary to maintain clear airways. Students will participate in data collection, analyses and interpretation with the goal of generating an abstract for presentation at a major meeting and inclusion as a co-author on a subsequent manuscript.

Institution: Mayo Clinic

Mentor: Christina Pabelick, M.D.

Project(s) Available: Basic science

Research topic: "Pediatric Airways smooth muscle cells as a model for pediatric airway disease"

Research topic: "Sex differences in neonatal/pediatric asthma"

Student's role: The student will be mentored by me and a fellow throughout their internship. The student will help with literature searches for the given topic, learn basic lab techniques and a variety of methods (e.g. western blot, calcium imaging, immunohistochemistry) to be able to address the above mentioned questions. The student will learn data analysis, interpretation of their results and will present his or her findings at lab meetings. Towards the end, the student will write an abstract to be submitted for the ASA meeting as well as the American Thoracic Society meeting. Throughout their time with me, the students will have an opportunity to shadow me and my colleagues in the operating room and attend resident lectures as well as medical student lectures provided by Mayo's IMSP program.

Institution: Medical College of Wisconsin

Mentor: David Stowe, MD, PhD

Project(s) Available: Type: Basic Science Research

Topic Title: Mitochondrial Function in Health and Disease

Overview: The Stowe laboratory is currently active in several areas: A) Mechanism and timing of activation of cardiac mitochondrial (m) small and large K⁺-sensitive Ca²⁺ (SKCa and BKCa) channels; assessment of their protective role against acute cardiac injury; identification of specific mSKCa splice variants in several species, including human; and exploration of the molecular and biophysical mechanisms underlying protection with opening of these mitochondrial channels. B) Mitigation of Ca²⁺ dys-regulation and excess reactive O₂ species emission after injury to the heart, brain and liver. C) Regulation of mCa²⁺ flux through Ca²⁺ channels and Ca²⁺ exchangers with H⁺, K⁺ and Na⁺; and exploration of dynamic mCa²⁺ buffering mechanisms. D) Ischemia-induced nitration of nucleotide transporters VDAC and ANT on promoting damage to mitochondria and cells with identification of specific residues that may be targeted to protect against damage. The Stowe lab collaborates in other funded projects with researchers who share similar goals but who have different skill sets and knowledge. The research is funded through VA Merit, NIH, or MCW grants.

Student Role: An individual FAER student under Dr. Stowe's mentorship would be responsible for researching the literature, learning research techniques, conducting experiments with the proper controls, application of unbiased treatment of the data, data analysis, data compilation, data interpretation, and preparation of abstracts and posters related to findings. Dr. Stowe has mentored 2 PhD students, and 7 MS students, and co-mentored many other graduate students. He has trained 25 post-doctoral fellows, 33 NIH or FAER medical students in research training and 23 undergraduate students interested in pursuing research careers. His role as a FAER mentor, at any level of training, is to expose the student to high quality research projects with plenty of collaborators and laboratory staff to share in the training. The goal for the mentee is to develop a well-planned approach to conduct, analyze, interpret, and report on experimental results. The research is intended to help FAER students to develop eventually into independent and successful researchers, particularly those who also have clinical ambitions.

Institution: Medical College of Wisconsin

Mentor: Julie Freed, MD, PhD

Project(s) Available: Project #1: The Role of Sphingolipids in Maintaining Vascular Homeostasis

Description:

Our laboratory studies how bioactive lipids, known as sphingolipids, ultimately regulate microvascular function. We assess microvascular function by examining vascular reactivity in response to flow. This is highly translational work as it is done in human microvessels.

How the student will Participate:

The student can assist members in the laboratory to conduct the vessel experiments. The student may also learn cell culture and perform studies examining how these lipids affect the overall cellular redox state of the cell.

Project #2: Prehabilitation of Frail Surgical Cancer Patients Using Remote Ischemic Preconditioning

Description:

This is a joint project between the Dept of Anesthesiology and Physical Medicine and Rehabilitation. We use ischemic preconditioning to decrease frailty and improve functional capacity prior to surgery as a means to improve surgical outcomes.

How the student will Participate:

The student can assist with frailty testing as well as perform cognitive testing in enrolled subjects.

Institution: Medical College of Wisconsin

Mentor: Wai-Meng Kwok, PhD

Project(s) Available:

Description: Mitochondria are key regulators and buffers of intracellular Ca^{2+} . Excess Ca^{2+} , seen in pathologies, can overload the buffering capacity and trigger opening of the mitochondrial permeability transition pore that leads to cell death. Several ion channels and transporters work in concert to regulate mitochondrial Ca^{2+} influx and efflux. The calcium-hydrogen exchanger (CHE) on the inner mitochondrial membrane (IMM) contributes to Ca^{2+} efflux, but its contribution in regulating cardiac mitochondrial function is not well understood. The goal of this project is to test the hypothesis that cardiac mitochondrial CHE activity is enhanced in response to stress, and consequently is a key contributor in regulating Ca^{2+} across the IMM. The experimental approach will utilize a high-resolution respirometer to monitor mitochondrial respiration, membrane potential, Ca^{2+} uptake and efflux rates under various conditions. The overall long term goal is to determine the molecular mechanism that underlie modulation of CHE.

How the student will Participate: During the research fellowship, the student will acquire proficiency in the relevant laboratory techniques, including isolating cardiac mitochondria, measuring mitochondrial respiration using various substrates and monitoring Ca^{2+} uptake and efflux using Ca^{2+} -sensitive dyes. The student is expected to conduct the experiments, learn to analyze the acquired data, contribute to the design of the experiments and participate in research group meetings. The research is expected to culminate in a presentation by the student as the presenting first author at a national meeting.

Institution: Medical University of South Carolina

Mentor: Sylvia Wilson, M.D.

Project(s) Available:

1. Quadratus Lumborum versus Transversus Abdominis Plane Nerve Block: A Comparison in Regional Anesthesia

Techniques with an Enhanced Recovery After Surgery Pathway - After completing necessary (CITI) training modules the student will be involved in all aspects of conducting research procedures. The student will be trained in screening subjects for eligibility, obtaining written consent, obtaining HIPAA authorization, collecting data, data analysis and data entry. With the assistance of the Principal Investigator and the research departmental staff students will explain the study to potential subjects prior to consent. He or she will be given the opportunity to interact with numerous faculty and be involved in writing abstracts and/or publications. The student will also be given exposure to a clinical anesthesia environment.

Institution: Memorial Sloan Kettering Cancer Center

Mentor: Rebecca Twersky, MD, MPH, FASA

Project(s) Available:

1. Cluster-Randomized, Prospective Assessment of Postoperative Pain Management in Patients Undergoing Bilateral Mastectomy with Immediate Reconstruction (BMw/IR) Using Preoperative Paravertebral (PVB), Serratus+PECS-1, or PVB+PECS-1 Nerve Blocks: A novel clinically integrated trial (CIRT) to prospectively obtain high-quality data using standard EMR data in a large ambulatory surgery cancer center in women undergoing mastectomy with immediate reconstruction. The study design involves 3 arms, using a cluster scheme with randomization at the treatment level on a monthly basis. With this design, eligible patients will be randomized to receive: either a paravertebral (PVB) block alone, a serratus and PECS-1 block combination, or a PVB and PECS-1 combination. The project will compare the opioid-consumption and postop pain related outcomes.
2. Evaluation of perioperative clinical outcomes and patient reported outcomes following ambulatory surgery at Josie Robertson Surgery Center (JRSC) using Enhanced Recovery After Surgery (ERAS) programs and electronic self-reporting symptom tracker MSK Engage system. Goals: a. test for an association between important periop outcomes & post-discharge symptoms/recovery, b. evaluate the impact of opioid minimization on postop & postdischarge pain, c. test for an association between periop outcomes & post-discharge recovery 10 days after surgery, d. test for an association between high-risk conditions & recovery after discharge, e. determine frequency of frailty & postoperative cognitive impairment in ambulatory oncology geriatric patients, f. determine if ERAS implementation is associated with improved post-discharge recovery patterns.
3. Double Blind, Randomized, Placebo Controlled Trial of Locally Instilled Bupivacaine in the Surgical Bed After Unilateral Mastectomy Without Reconstruction: a prospective randomized controlled clinical trial focused on improving pain control following mastectomy procedures in patients not undergoing immediate reconstruction and who do not receive intraoperative regional nerve blocks. The rationale for the study comes from literature showing a reduction in pain, opioid use, and nausea with continuous infusion of a long-acting anesthetic via an indwelling pump after breast procedures (bupivacaine, a long acting local anesthetic, into the mastectomy cavity after skin closure, and leaves it to dwell for 2 hours). Metrics: pain - BPI scale, Impact Score for PONV.

Institution: Memorial Sloan Kettering Cancer Center

Mentor: Hanae Tokita, MD

Project(s) Available:

1. Cluster-Randomized, Prospective Assessment of Postoperative Pain Management in Patients Undergoing Bilateral Mastectomy with Immediate Reconstruction (BMw/IR) Using Preoperative Paravertebral (PVB), Serratus+PECS-1, or PVB+PECS-1 Nerve Blocks: A novel clinically integrated trial (CIRT) to prospectively obtain high-quality data using standard EMR data in a large ambulatory surgery cancer center in women undergoing mastectomy with immediate reconstruction. The study design involves 3 arms, using a cluster scheme with randomization at the treatment level on a monthly basis. With this design, eligible patients will be randomized to receive: either a paravertebral (PVB) block alone, a serratus and PECS-1 block combination, or a PVB and PECS-1 combination. The project will compare the opioid-consumption and postop pain related outcomes.
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frequency of frailty & postoperative cognitive impairment in ambulatory oncology geriatric patients, f. determine if ERAS implementation is associated with improved post-discharge recovery patterns.

Institution: Montefiore Medical Center/Albert Einstein College of Medicine

Mentor: Jonathan Leff, M.D.

Project(s) Available:

1. Surgical prehabilitation is a new paradigm shift in perioperative medicine, and this entails taking care of modifiable factors that are associated with surgical outcomes. Prehabilitation in cardiac surgery has been associated with improved outcomes. We are planning to conduct a retrospective chart review of patients undergone CABG alone and CABG valve surgeries with a latency of 3 weeks or more between the preoperative anesthesia clinic visit and surgery. The purpose of the study is to evaluate whether modifiable pre-surgical factors were addressed in the pre-operative clinic. The student will be reviewing the medical charts, collecting information from pre-operative clinic notes, will use an existing database for other study-related outcomes.

2. Hypoalbuminemia is a well-recognized predictor of poor surgical outcomes after cardiac surgery. However, the change in albumin values in the postoperative period compared to the baseline values and the association with surgical outcomes are not thoroughly studied. The purpose of this retrospective study is to evaluate the role of delta albumin (pre-operative minus POD1 albumin) in predicting acute kidney injury, delirium, and surgical site infections. Patients underwent cardiac surgery with a record of pre and post albumin values will be included in the study. This is a database-driven study; the student will review the medical records to query the missing data points and also to validate the data points in the database. Student responsibility will include meeting with the statistician and helping in the preparation of the manuscript.

Institution: Montefiore Medical Center/Albert Einstein College of Medicine

Mentor: David Adams, M.D.

Project(s) Available:

1. The erector spinae plane (ESP) block is a relatively new regional technique introduced as a mode of analgesia for thoracic and abdominal surgeries. The use of ESP block in spine surgeries has not been studied extensively. The purpose of this randomized controlled study is to evaluate the efficacy of ESP block in patients undergoing elective laminectomies. The primary outcome of the study is 24-hour opioid consumption, and secondary outcomes are LOS and adverse events. The student will be responsible for screening the patients, helping with the consenting process and collecting the data in the intra and post-operative period.

2. The traditional method for preoperative evaluation of diabetic management is through the surveillance of HbA1C values. However, the association between HbA1C values and surgical outcomes is controversial. Fructosamine is an alternative reliable test; due to relatively short half-life compared with HbA1c, fructosamine is a better measure of glycemic control in the preceding 2- to 3-week period. In this observational cohort study, preoperative fructosamine values will be correlated to surgical outcomes. The study will be conducted in patients undergoing spinal fusion procedures. The student will be responsible for screening the patients, helping with the consenting process, and collecting the data in the intra and post-operative period and maintain the database.

Institution: Montefiore Medical Center/Albert Einstein College of Medicine

Mentor: Jerry Chao, M.D. M.S

Project(s) Available: Enhanced recovery after surgery (ERAS) protocol is well established in many surgical disciplines and leads to a decrease in the length of hospital stay and morbidity. This is a prospective, randomized controlled trial assessing the effect of an ERAS Protocol for patients undergoing bariatric surgery and rates of 30-day complications. The components of the protocol will include (i) preoperative interventions, (ii) intraoperative interventions, and (iii) postoperative interventions designed for patients scheduled for bariatric surgery. Subjects randomized to the intervention will receive all three perioperative components of the ERAS Protocol. Controls will be randomized to receive standard of care (no ERAS) at our institution. The endpoints of the study will be 30-

day complications, including ED visits for clinically significant events and 30-day re-admissions. The student will be responsible for screening the patients, helping with the consenting process, and collecting the data in the intra and post-operative period and maintaining the database.

Institution: Montefiore Medical Center/Albert Einstein College of Medicine

Mentor: Iyabo Muse, M.D.

Project(s) Available: The Food and Drug Administration (FDA) just approved 1% Chloroprocaine HCL for use in spinal anesthesia. In this double-blinded, randomized controlled study preservative-free, 1% chloroprocaine HCL will be compared to hyperbaric bupivacaine in ambulatory hemorrhoidectomies. The Primary outcomes will be recovery time (return of motor and sensory function) and fit to discharge time from the PACU. Secondary outcomes will be evidence of hypotension during the case, and evidence of TNS (transient neurologic symptoms) 24hr after the procedure. The student will be responsible for screening the patients, helping with the consenting process, and collecting the data in the intra and post-operative period and maintaining the database.

Institution: Montefiore Medical Center/Albert Einstein College of Medicine

Mentor: Naum Shaparin, M.D. M.B.A.

Project(s) Available: Approximately 8% of the US adult population has high impact chronic pain and has been linked to restrictions in mobility and daily activities, dependence on opioids, anxiety, and depression, and poor perceived health or reduced quality of life. In this retrospective study we are evaluating the association between different treatment modalities of chronic pain and utilization of healthcare resources and explicitly looking into patients and provider factors associated with high utilization of healthcare resources. We will query our internal database for identifying patients with moderate to severe chronic pain and plan to collect all the demographic and clinical factors. This is a database-driven study, and no medical records will be queried. Student responsibility will be gathering the data, meeting with the statistician and helping in the preparation of the manuscript.

Institution: NYPH (Columbia Campus) Program

Mentor: Charles Emala, MS, MD

Project(s) Available: Project #1:

Basic Science

Title: Airway GABAA receptors and reactive airway disease

Description: Dr. Emala's main area of research interest is in the understanding of interactions between signal transduction pathways in airway nerves and smooth muscle and how these interactions contribute to diseases such as asthma. A broader understanding of the non-neuronal expression and function of GABAA receptors in smooth muscle is a central focus.

Project #1 Student Role: Assist with measuring ex vivo airway smooth muscle contraction and relaxation of human and mouse airways in a perfused organ bath system. Assist with cell based assays measuring intracellular calcium, plasma membrane potential, and intracellular second messengers. ELISA and western blotting of phosphoproteins will be performed. The student will participate and present at weekly lab meetings and participate in laboratory journal clubs. The student will have the opportunity to attend research seminars in the department of anesthesiology and neighboring basic science departments. The student may have the opportunity to contribute to the writing of meeting abstracts and primary manuscripts associated with this research.

Project #2:

Basic Science

Title: Natural phytochemicals relax airway smooth muscle and reduce lung inflammation

Description: Dr. Emala's main area of research interest is in the understanding of interactions between signal transduction pathways in airway nerves and smooth muscle and how these interactions contribute to diseases such as asthma. The laboratory has demonstrated that phytochemicals of the flavonoid and ginger family have dual beneficial effects in asthma; smooth muscle relaxation and anti-inflammation.

Student Role: Assist with measuring ex vivo airway smooth muscle contraction and relaxation of human and mouse airways in a perfused organ bath system. Evaluate histologic changes in fixed lung samples from asthmatic mice chronically treated with phytochemicals. The student will participate and present at weekly lab meetings and participate in laboratory journal clubs. The student will have the opportunity to attend research seminars in the department of anesthesiology and neighboring basic science departments. The student may have the opportunity to contribute to the writing of meeting abstracts and primary manuscripts associated with this research.

Institution: NYPH (Columbia Campus) Program

Mentor: Jeanine D'Armiento, MD, PhD

Project(s) Available:

Project #1

Type of Research: Basic Science

Research Topic: Lung Smoke Exposure and Injury

Overview: Studies in the laboratory have identified that the use of an inhaled MMP inhibitor protects mice from the development of injury in a model of ARDs. This protection is consistent with blockade of neutrophil influx into the lung. Present studies are exploring the use of these compounds long term and the lasting improvement in lung function in this model system.

Project #1 Student Role: Summer students will perform Western Blot analysis and PCR analysis to explore the mechanism by inhaled MMP inhibitors block tissue destruction and protect lung function.

Project #2

Type of Research: Basic Science

Research Topic: Alternative Pathways in Lymphangiomyomatosis (LAM) pathogenesis

Overview: Studies in the laboratory have identified that unique tyrosine kinase inhibitors block the growth of LAM lung cells. The blockade of this growth is independent of the mTOR pathway, which is thought to be necessary for the growth of LAM cells. The summer project will further explore this pathway to identify the unique molecules involved in LAM cell growth. The identification of novel compounds to block growth of these cells has the potential to lead to unique therapies of the disease.

Student Role: Summer students will perform Western Blot analysis and PCR analysis on LAM cells and tissue samples from animal models and pathology specimens to explore these pathways.

Institution: NYPH (Columbia Campus) Program

Mentor: Paul Garcia, MD, PhD

Project(s) Available:

Clinical Research

Thalamocortical oscillations and their influence on emergence and recovery from anesthesia

It is becoming increasingly apparent that optimal emergence from anesthesia requires the initiation of networks specific for arousal and consciousness. Certain EEG features during the emergence process can predict normal vs abnormal recoveries from general anesthesia. We are enrolling patients in several studies focused on pharmacologic interventions designed to influence thalamocortical oscillations during surgical anesthesia. Frontal EEG electrodes will be used to continuously monitor patients from induction through maintenance and emergence. EEG signatures that define the transition from unconscious to conscious will be characterized while administering anesthesia via a standard protocol.

Student Role: The MSARF student will receive advanced training in clinical research techniques such as spectral analysis of EEG data, statistical techniques, and scientific communication skills.

Laboratory Research

Pre-clinical investigations of neurodegenerative disease and emergence and recovery from anesthesia

Many anesthetic drugs have been linked to worsening of memory in animal models. The clinical concern for long-term adverse cognitive consequences in vulnerable patients remains high. We have developed specific measurements of abnormal recovery in rodents that mimic cognitive problems in the immediate (hours to days) post-anesthesia time-period. By investigating activity levels and latency to appearance of normal waking behaviors, we can rigorously determine the influence certain disease states have on emergence and recovery. Our aim is to identify neuroprotective strategies through an examination of the pharmacologic and neurophysiologic determinants of post-anesthesia behavior.

Student Role: The MSARF student will learn in vivo anesthetic techniques with rodents, behavioral testing, statistical techniques, and scientific communication skills.

Institution: NYPH (Columbia Campus) Program

Mentor: May Hua, MD, MSc

Project(s) Available:

Type of Research: Health Services and Outcomes Research

Project Research Topic: Use of palliative care and end-of-life care in critically ill patients, high-risk surgical patients and other patients with serious illness.

Project Overview - 3 projects are available: 1) Examining the effect of implementing a hospital-based palliative care service on treatment intensity for patients with dementia 2) Examining the association between statewide

end-of-life care legislation and place of death 3) Examining variation in discharge to hospice among critically ill patients

Project Student Role: Under the supervision by the PI and a biostatistician, the student will be involved in analyzing and presenting data and writing a manuscript for publication.

Project Mentor Names: May Hua, MD, MS

Institution: NYPH (Columbia Campus) Program

Mentor: Caleb Ing, MD, MS

Project(s) Available:

Type of Research: Perioperative Outcomes (Health Services)

Research Topic: Epidemiology of perioperative complications and adverse outcomes in pediatric patients.

Overview: The project consists of evaluating short and long-term complications and adverse outcomes in children undergoing surgical procedures. This includes evaluation of causes, risk factors, and methods for prevention of a variety of adverse outcomes. The specific complications and datasets to be used will be determined after discussion with the candidate.

Student Role: The student's responsibilities will involve literature review which involves identifying and reading relevant articles and aiding in the writing of a manuscript. Interpreting data and generating tables and figures, as well as potentially some minor data analysis depending on the experience of the student.

Mentor Names: Caleb Ing, MD, MS

Institution: NYPH (Columbia Campus) Program

Mentor: H.T. Lee, MD, PhD

Project(s) Available:

Type of Research: Basic Science

Research Topic: Acute kidney injury and multiple organ dysfunction

Overview: Dr. Lee's research focuses on the pathomechanisms of perioperative acute kidney injury, AKI induced remote organ dysfunction and translational approaches to attenuate this injury. One focus of the laboratory is the role of Purinergic and Toll like receptors on acute kidney injury in vivo as well as in vitro.

Student Role: Assist with in vitro cell signaling experiments. The medical student will learn in vitro cell death assays, immunoblotting and RTPCR under the supervision of PI and postdoctoral fellows. The student will work with cultured cell lines and tissues obtained from animal models to investigate the expression of mRNA and proteins involved in cellular injury and protection following ischemia reperfusion injury. The student will be encouraged to analyze and present their data in written and oral form and participate in weekly laboratory meetings.

Institution: NYPH (Columbia Campus) Program

Mentor: Richard Levy, MD

Project(s) Available:

Project #1

Research Type: Basic

Research Topic: Age-specific Propofol Toxicity

Overview: Propofol infusion syndrome (PRIS) is a potentially life-threatening side-effect of treatment with the sedative/hypnotic, propofol. Young children appear to be at higher risk than older patients. However, the underlying cause of PRIS is unknown. Recently, we identified a novel mechanism of propofol toxicity in cardiac mitochondria of immature mice. In this project, we aim to determine the exact cause of propofol toxicity and will attempt to develop mitigating strategies.

Student Role: Assist in rodent exposures and data analysis. Assist in measuring various aspects of mitochondrial function in the mouse brain through a variety of basic science techniques.

Project #2

Research Type: Basic

Research Topic: Assessing the Permeability Transition Pore (PTP) in Developing Mitochondria

Overview: The PTP is a voltage-gated, non-specific, non-selective mega-channel present on the inner mitochondrial membrane. Although the presence of the pore and its functional importance have been well established, its exact proteinaceous molecular identity remains elusive. Mounting evidence suggests that opening of the pore within mitochondria plays a pathological role in a variety of cardiac disease processes while physiological regulation of the PTP may be important for normal cellular development and differentiation. In this project, we aim to identify novel proteins that may regulate the PTP or serve as pore components. Furthermore, we aim to determine the role of the PTP in cardiomyocyte mitochondrial maturation.

Student Role: Assist in isolation of cardiomyocyte mitochondria from newborn and juvenile rodents. Assist in measuring various aspects of mitochondrial function in the mouse heart through a variety of basic science techniques.

Institution: NYPH (Columbia Campus) Program

Mentor: Gebhard Wagener, MD

Project(s) Available:

Type of Research: Clinical (Patient-oriented) research

Research Topic: Specialized Pro-resolution Markers (SPMs) after major abdominal surgery

Overview: The aim of this project is to assess if Specialized Pro-resolution Markers (SPMs) are detectable after major abdominal surgery such as Whipple procedures or hepatectomies and if their levels correlate with outcome. SPMs have been described mostly in preclinical models and are thought to mediate the resolution of inflammation and prevention of progression to chronic inflammatory after an inflammatory insult. Little is known if and when SPMs are detectable in humans after acute inflammatory insults such as abdominal surgery

Student Role: The student's responsibilities will to collect urine and plasma samples on patients undergoing major abdominal surgery and collect the necessary clinical data. The student will be able to follow up with the patient in the operating room and then postoperatively in the ICU or floor. Additionally the student will help with analysis of the data (after the samples were analyzed for SPMs) and preparation of a manuscript. This project will further allow the student to observe the clinical work of the PI in the operating rooms and the ICU.

Institution: Ohio State University Wexner Medical Center

Mentor: Tristan E Weaver, M.D.

Project(s) Available:

Project#1

Project Title: "Opioid consumption after Hospital Discharge in Radical Cystectomy".

Project description: Surgical patients at The Ohio State University, and across the country, who are admitted for at least 2 days in the hospital, are overprescribed a significant amount of opioid medications when discharged to home. Our hypothesis is that the opioid medication (oral morphine equivalent) prescribed to treat pain after cystectomy exceeds by a large margin (30-50%) the actual patients' requirement and results as a leftover medication.

Study population: Adult patients ≥ 18 years old, scheduled to undergo a cystectomy, who give written informed consent to participate in the study and who meet all inclusion and no exclusion criteria.

Data collection: Data will be collected by weekly follow-up phone survey. Considering this an observational study aimed to explore and describe opioid consumption post-discharge, no formal inferential statistical analyses will be performed.. Continuous variables will be expressed using means, medians, standard deviations and other appropriate measures of spread and categorical variables using frequencies and percentages. Estimated means and confidence intervals will be provided for the outcome variables of interest. Continuous variables will be expressed using means, medians, standard deviations

- Medical Student activities:
- a) The medical student will be trained to screen possible candidates for the study.
 - b) The student will assist the postdocs or research fellows to perform the informed consent, patient enrollment, collect demographics, medical history and medications.
 - c) The student will have the opportunity to interact and assist the anesthesiologist on the case with any study procedures, which will provide him/her a more accurate knowledge of the clinical work of the anesthesiologist.
 - d) The student will be instructed on how to perform the necessary intraoperative assessments and how to record the data on the case report forms.
 - e) In this particular study, the MS will perform follow-up telephone interviews to discharged patients.
 - f) Finally, the student will transfer the data to a database for analysis, and will interact with one of the lab's statistician to learn how to register the data and to interpret the results of the data analysis.
 - g) The student will be expected prepare an abstract and/or poster to present at the local OSUMC Research Day and at an Anesthesiology National Meeting

Institution: Ohio State University Wexner Medical Center

Mentor: Michael Kushelev, Assistant Professor - Clinical

Project(s) Available:

Project #2

Project title: "Intravenous and Perineural Dexamethasone for Brachial Plexus Block in Hand Surgery"

Project description: This is a randomized prospective single-blinded controlled trial. Brachial plexus block with local anesthetics can alleviate the pain and reduce the need for postoperative analgesics. Local anesthetics have been correlated with enhancement of inflammatory response, altered nerve permeability, and neurotoxicity and may be responsible for "rebound" hyperalgesia when the block wears off. In clinical settings, no evidence of perineural dexamethasone toxicity or neurologic complications. Dexamethasone has also been used intravenously demonstrating similar prolongation of analgesia effects. We hypothesized that

the co-administration of perineural and intravenous dexamethasone will prolong the duration of ropivacaine-induced local analgesia when compared with ropivacaine local block alone or when administered in conjunction with IV dexamethasone.

Objectives: 1) Primary outcome: duration of anesthetic blockade measured by the time from performing the perineural block to the first reported pain at the surgical site between groups. 2) Secondary outcome: to compare duration of block between groups, to compare overall patient satisfaction, to compare 48-hours postoperative opioid consumption, PONV incidence, rebound pain.

Medical Student activities:

- a) The medical student will be trained to screen possible candidates for the study
- b) The student will assist the postdocs or research fellows to perform the informed consent, patient enrollment, collect demographics, medical history and medications.
- c) The student will have the opportunity to interact and assist the anesthesiologist on the case with any study procedures, which will provide him/her a more accurate knowledge of the clinical work of the anesthesiologist.
- d) The student will be instructed on how to perform the necessary intraoperative assessments and how to record the data on the case report forms.
- e) The MS will perform follow-up telephone interviews to discharged patients
- f) The student will transfer the data to a database for analysis, and will interact with one of the lab's statistician to learn how to register the data and to interpret the results of the data analysis.
- g) The student will be expected prepare an abstract and/or poster to present at OSUMC Research Day and at an Anesthesiology National Meeting

Institution: Ohio State University Wexner Medical Center

Mentor: Galina Dimitrova, Associate Professor-Clinical

Project(s) Available:

Project #3

Project Title: A Prospective, Randomized, Parallel-group Single Center Study to Evaluate the Use of Thromboelastometry (ROTEM) in Patients Undergoing Spine Surgeries"

Project description: This is a prospective, randomized parallel-group, single center study in patients undergoing elective major spine surgery. Patients will be randomized to guide blood transfusion administration with ROTEM or laboratory coagulation tests. Randomization list will be computer-generated at a ratio 1:1.

Primary outcome: Compare the overall amount of intra-operative RBC and FFP guided with ROTEM versus laboratory coagulation tests in patients undergoing major spinal surgeries. •

Secondary outcomes:

- Compare the amount of Cryoprecipitate and Platelets transfused intraoperative between both groups.
- Compare the amount of all blood products transfused at 6, 12, and 24 hours postoperative.
- Compare the incidence and requirements of fibrinogen concentrate, PCC, antithrombin concentrate, factor XIII concentrate, and activated recombinant factor VII, or any other hemostatic therapy. Compare variables that affect coagulopathy such as acidosis and hypothermia.
- Compare hemodynamic variables during surgery.
- Compare postoperative time of mechanical ventilation
- Compare length of ICU stay and overall hospital stay
- Compare total in hospital need for transfusion
- Compare postoperative coagulation status on days 1 and 3 if available
- Compare overall infection rate

- Compare 30 days mortality

Student Role:

- a) The medical student will be trained to screen possible candidates for the study
- b) The student will assist the postdocs or research fellows to perform the informed consent, patient enrollment, collect demographics, medical history and medications.
- c) The student will have the opportunity to interact and assist the anesthesiologist on the case with any study procedures, which will provide him/her a more accurate knowledge of the clinical work of the anesthesiologist.
- d) The student will be instructed on how to perform the necessary intraoperative assessments and how to record the data on the case report forms.
- e) The student will transfer the data to a database for analysis, and will interact with one of the lab's statistician to learn how to register the data and to interpret the results of the data analysis.
- f) The student will be expected prepare an abstract and/or poster to present at OSUMC Research Day and at an Anesthesiology National Meeting

Institution: Oregon Health & Science University

Mentor: Michael Hutchens, M.D.

Project(s) Available:

Translational Science

Research Topic: Role of heart-derived cardiac LIM protein in acute cardiorenal syndrome

Mentor(s): Michael Hutchens, MD, MA

Project Overview: Acute cardiorenal syndrome is a common and deadly perioperative complication which may lead to chronic kidney disease. The Hutchens lab focuses on heart-kidney signaling in acute cardiorenal syndrome with the goal of intervening to prevent this AKI-CKD transition. This long-term project includes extensive evaluation of a specific heart-kidney signal, the transcriptional modifier cardiac LIM protein, in cardiorenal syndrome induced by cardiac arrest and cardiopulmonary resuscitation in the mouse. Numerous projects for students are available, ranging from detailed investigation of mouse physiology around cardiac arrest and resuscitation to the molecular biology of a filtered protein signal in the tubular epithelium.

Student Role: The student will collect and analyze data, prepare figures, present data, and help with manuscript writing.

Clinical Research

Research Topic: Risk of Chronic Kidney Disease (CKD) after cardiac arrest.

Mentor: Michael Hutchens, MD, MA

Project Overview: Although clinical data suggest a relationship between cardiovascular crisis and early development of CKD, and animal models demonstrate a mechanistic association, no clinical study yet quantifies the risk of CKD associated with prior cardiac arrest and cardiopulmonary resuscitation. This study will use a large clinical dataset to determine how many of approximately 17,000 long-term cardiac arrest survivors go on to develop CKD, and to determine associated risk factors.

Student Role: The student will analyze data, prepare figures, present data, and help with manuscript writing.

Institution: Oregon Health & Science University

Mentor: Glenn Woodworth, M.D.

Project(s) Available:

Health Services

Research Topic: Using simulation to teach resident anesthesiologists pharmacokinetics of infusions

Mentor(s): Glenn Woodworth, MD

Project Overview: Effectiveness of teaching will be evaluated with pre- and post- knowledge testing in comparison to a control group that is taught without simulation. Areas to be studied are simulation to teach to teach the pharmacokinetics of medication infusions.

Student Role: Student would be involved in data acquisition and analysis of one of the areas of research. They would also assist with manuscript preparation.

Health Services

Research Topic: Validity of faculty assessments for EPAs and Procedures

Mentor(s): Glenn Woodworth, MD

Project Overview: Faculty assessments are being collected for EPAs and Procedural skills. Goal is to create descriptive statistics of the assessment data to better understand the level of competency reached by graduating residents

Student Role: Student would be involved in data analysis, as well as manuscript preparation.

Institution: Oregon Health & Science University

Mentor: Eric Schnell, M.D., Ph.D.

Project(s) Available:

Basic Science

Research Topic: Neuronal Circuit Rearrangements following Brain Injury

Mentor(s): Eric Schnell, MD, PhD

Project Overview: Our research focuses on neuronal circuit rearrangements that result from brain injury. We combine translational models of injury with immunohistochemical and electrophysiologic assays of brain structure and function, and have been analyzing how anesthetic drugs alter hippocampal gene expression and neuronal circuit function.

Student Role: The student would assist in studies of the anesthetic modulation of adult neurogenesis and in the analysis of signaling pathways involved in neuronal circuit integration of new neurons.

Institution: Oregon Health & Science University

Mentor: Ines Koerner, M.D., Ph.D.

Project(s) Available:

Basic Science

Research Topic: Role of microglia in neurogenesis and regeneration after cardiac arrest

Mentor(s): Ines P. Koerner, MD, PhD

Project Overview: The project explores how microglia, the brain resident immune cells, support formation of new neurons in the hippocampus, and how these adult-born neurons improve memory function of mice after cardiac arrest.

Student Role: The student will assist with image acquisition and analysis to quantify adult-born neurons.

Institution: Oregon Health & Science University

Mentor: Nabil Alkayed, M.D., Ph.D.

Project(s) Available:

Topic: GPR39 as a therapeutic target in hypertension.

Mentor(s): Nabil J. Alkayed, MD, PhD

Project Overview: The project investigates the role of the GPR39 as a mediator and potential target in the treatment of hypertension.

Student Role: The student will assist in administering treatment and collecting and analyzing data.

Topic: Role of GPR39 in Vascular Cognitive Impairment.

Mentor(s): Nabil J. Alkayed, MD, PhD

Project Overview: The project investigates the role of GPR-39 in aging-related vascular cognitive impairment.

Student Role: The student will assist in administering treatment and collecting and analyzing data.

Institution: Oregon Health & Science University

Mentor: Austin Peters, M.D.

Project(s) Available:

Title: Effects of Ketamine on Circulating Protein Biomarkers and Patient Outcomes after Traumatic Brain Injury

Project 1 Description: Using mice, I model a traumatic brain injury and subsequently implant a pump that infuses ketamine. At a later time, blood is collected and analyzed via ELISA to quantify proteins released from the brain into the blood stream, with the intention to determine whether ketamine normalizes these biomarkers as compared to controls. This will validate whether certain protein biomarkers can be used to measure therapeutic efficacy and/or predict recovery after traumatic brain injury.

Project 2 Description: Retrospective study of data obtained from the Tranexamic Acid for Traumatic Brian Injury trial, in which a portion of TBI patients received ketamine, and clinical data was collected that will allow me to see if ketamine was associated with differential trajectory of blood based protein biomarkers in the first week after injury, and whether ketamine-exposed patients had different outcomes from those who were not exposed to ketamine.

Institution: Rutgers/ New Jersey Medical School

Mentor: Yuan-Xiang Tao, PhD, MD.

Project(s) Available:

Title: Role of dorsal root ganglion FTO, a RNA demethylase, in neuropathic pain.

Project Overview: RNA modifications were recently rediscovered as essential regulators of gene expression. N6-methyladenosine (m6A) is identified as the most prevalent internal modification of eukaryotic RNA. The m6A modification controls RNA metabolism including RNA degradation and has been linked to human diseases such as obesity and cancer. However, its role in chronic neuropathic pain is unknown. FTO (fat mass and obesity-associated protein) is a well-characterized RNA demethylase. We propose that peripheral nerve injury increases the expression of FTO in the injured dorsal root ganglion (DRG) and that this increase contributes to neuropathic pain. We will first examine whether peripheral nerve injury upregulates the expression of FTO and increases the level of m6A on specific RNAs in the DRG. We will then determine whether pharmacological inhibition or genetic knockdown of DRG FTO attenuates nerve injury-induced pain hypersensitivity during the development and maintenance periods. Finally, we will define whether FTO contributes neuropathic pain through regulating expression of mu opioid receptor mRNA in the DRG. These studies will not only advance our understanding of posttranscriptional mechanisms of neuropathic pain, but will also open a door to develop a new strategy for the prevention and treatment of this disorder.

Student Role: The student will be involved in partial phases of the project, including preclinical SNL model preparation, behavioral tests, tissue harvest, RT-PCR, data collection and analysis, and abstract/manuscript preparation.

Institution: Rutgers/ New Jersey Medical School

Mentor: Jiang-Hong Ye, Professor

Project(s) Available:

1. Lateral habenula (LHb) Deep Brain Stimulation (DBS) for Opioid-induced hyperalgesia:

Long-term use of opioids in the treatment of chronic pain is limited by the development of tolerance and opioid-induced hyperalgesia (OIH)– paradoxical sensitization to noxious (hyperalgesia) and non-noxious (allodynia) stimuli.

Novel adjunctive therapies are needed to increase the efficacy and prolong the duration of action of opioids in chronic pain treatment.

One of the prominent treatments is DBS, in which implanted electrodes deliver electrical stimulation to stereotactically targeted brain regions. DBS in selected brain regions has shown significant therapeutic benefits for otherwise treatment-resistant movement disorders, including Parkinson's disease. DBS research has been extended to various brain regions for the treatment of neuropsychiatric conditions such as obsessive-compulsive disorder and depression (Krack, 2010; Mathews, 2011). Recent research has indicated that DBS may also be an effective treatment for addiction. DBS was tested for its effect on response to alcohol, cocaine, heroin, morphine, and nicotine, showing promising results in several regions of the reward system. We postulate that better results may be obtained by targeting more remote limbic regions that regulate the mesolimbic dopaminergic system, such as the LHb.

2. Cannabis anti-nociception reduces relapse to use of opioids

Opioid misuse and overdose in the United States have reached the highest rates in recorded history. Recent clinical evidence indicates that medical cannabis is linked to significantly decreases opioid overdose mortality rates, suggesting that cannabis may play a beneficial role in the opioid crisis, yet the mechanisms of this association have not been well explored.

Repeated use of opioids can lead to tolerance and dependence, and the emergence of heightened pain sensitivity to noxious stimuli termed hyperalgesia, which may drive continued or escalated use of opioids to manage worsening pain symptoms. Cannabis can also treat pain. The central hypothesis of this project is that cannabis may relieve hyperalgesia in opioid-dependent individuals, and thus reduce the relapse and escalation of the use of opioids. We propose to test the hypothesis by examining the effect of cannabis on hyperalgesia and relapse to opioids use in opioid-dependent animals

Students will participate in animal experiments including testing pain before and after the use of DBS or cannabis.

Institution: Rutgers/ New Jersey Medical School

Mentor: Huijuan Hu, Associate Professor

Project(s) Available:

Project title: Role of calcium release-activated calcium channels (CRACs) in pain

Mentor: Huijuan Hu, Ph.D.

Project overview: Research in my lab aims to identify key molecule targets that are involved in pain plasticity. Currently, we are interested in calcium release-activated calcium channels (CRACs), which are composed of three pore-forming subunits Orai1/2/3 and activated by STIM1 and STIM2 (Ca²⁺ sensors, mainly located on the surface of the ER membrane). We found that both Orai1 and Orai3 mediate SOCE and contribute to neuronal excitability in DRG neurons. Our pilot data demonstrated that Orai3, not Orai1, was markedly increased in the DRG and that SOCE in DRG neurons was significantly enhanced under inflammatory pain conditions. Moreover, we found that peripheral inhibition of STIMs or OraIs markedly decreased chemical-induced nociceptive behavior, suggesting that CRACs in DRG neurons are involved in peripheral mechanisms of pain. Despite we have shown the importance of Orai1 in central sensitization, whether it contributes to peripheral sensitization remains unknown. More importantly, whether Orai3 contributes to pain hypersensitivity has never been explored. Based on our recently published data and pilot results, we hypothesize that Orai3 and Orai1 as an integrating calcium signal contribute to peripheral sensitization. We will investigate whether expression and function of Orai3 and Orai1 are altered under chronic pain conditions. We will investigate whether CRACs contribute peripheral sensitization using the knockdown approach and sensory neuron-specific conditional Orai1 and Orai3 knockout (KO) mice. Finally, we will determine whether CRACs are responsible for TRPV1^{ER}-mediated Ca²⁺ entry. We will examine capsaicin- and endogenous TRPV1 agonist 20-HETE-induced Ca²⁺ entry in DRG neurons, synaptic transmission and pain hypersensitivity using conditional Orai1 and Orai3 KO mice and their littermate wild type mice. We will use a combination of molecular, electrophysiology, live-cell imaging and behavioral techniques to elucidate role of Orai1 and Orai3 in peripheral sensitization.

Student role: The student will be involved in one of these studies. He/she will be trained to perform experiments related to this project including cell culture, calcium imaging, Western blot analysis, RT-PCR. He/she will be responsible for data analysis and abstract/manuscript preparation.

Institution: Stanford University School of Medicine

Mentor: Samuel Rodriguez, M.D.

Project(s) Available: Immersive technologies in a laboratory induced pain model – several studies focusing on various parameters (hardware/software) in healthy volunteers undergoing a cold pressor challenge. Students will be responsible for consenting patients and running various protocols on healthy volunteers. They will have the opportunity to design their own pilot study if interested as well as participating in upcoming IRB approved trials. Virtual Reality and Augmented Reality for Rehabilitation in Pediatric Pain – Investigating clinical protocols and efficacy of using immersive technologies for pediatric patients with acute/chronic pain in the inpatient and outpatient settings. Students will be expected to consent patients and guide them through VR/AR protocols in the inpatient and outpatient setting. Students will be able to participate in designing games and protocols for this and future projects if interested.

Institution: Stanford University School of Medicine

Mentor: Pervez Sultan, M.D.

Project(s) Available:

Project 1 – Development of new 6-week postpartum quality of recovery scoring tool

Background: Childbirth is one of the most common reasons why adults seek in-patient medical management. Despite the large numbers of women delivering globally, recovery following childbirth is a largely unexplored entity. In this study, we aim to develop a new quality of recovery scoring measure using methodology endorsed by the PROMIS (patient reported outcome measurement instrument) group.

Aim: To pilot test a new quality of recovery patient-reported outcome measure (PROM), which will subsequently be field tested in a larger sample size.

Methods: The student, under direct supervision, will ask women to complete the PROM as women recover from childbirth at 6 weeks postpartum during clinic visits. Women will be recruited prior to the student starts their attachment.

Project 2 – Prediction of recovery following childbirth – Part 1

Background: There are currently no biomarkers that can predict worse postpartum recovery following childbirth. A significant number of women still have not recovered to their baseline by 6 weeks postpartum.

Aim: To determine whether pre-operative biomarkers can be used to predict worse in-patient recovery in women undergoing elective cesarean delivery. Mass cytometry and plasma biomarkers (olink.com) will be assayed and correlated with in-patient recovery scores in a subset of women undergoing elective cesarean delivery.

Methods: The student, under close supervision, will recruit 10 women into this small single-center study and women will also be asked to complete a survey (Obstetric Quality of Recovery-11) 24 hours following delivery.

Project 3 – Prediction of recovery following childbirth – Part 2

Background: The ObsQoR-11 patient-reported outcome measure (PROM) is a validated measure of the quality of recovery following childbirth. No Spanish version currently exists.

Aim: to translate the ObsQoR-11 PROM and validate its use in this population.

Methods: The student will, under direct supervision, help with translation (with an interpreter / medical physician fluent in Spanish). They will then validate this in a subset of 50 women undergoing all delivery types at Stanford University School of Medicine by asking Spanish speaking women to complete the survey 24 hours after delivery.

Institution: Stanford University School of Medicine

Mentor: Eric Gross, M.D., Ph.D.

Project(s) Available: Approximately 560 million people in the world have a genetic variant limiting the ability to break down reactive aldehydes and having a flushing response after alcohol consumption. However, these

aldehydes are also produced during cellular injury, particularly for surgeries which result in organ ischemia-reperfusion (such as cardiac bypass and solid organ transplants) and are known to cause both pain and cellular injury.

We are studying how this genetic variant that limits reactive aldehyde metabolism may affect outcomes to surgery and influence responses to pain and injury (see Gross ER, Science Translational Medicine, Annals of Internal Medicine, and Annual Reviews of Pharmacology and Toxicology). We have ongoing basic science and clinical projects where our overall aim is to develop a precision anesthesia platform for those with this genetic variant in order to allow for optimal recovery from surgery. This will help us to also understand how to improve surgical recovery for all patients.

Student Role:

Several portions of the project are reasonable to accomplish within an 8-week time period and is suitable in challenge and scope for a medical student. Each mini-project listed here will consist of a variety of tasks and the student will meet with the mentor at least weekly to discuss progress. Further, the student will have six hours per week of clinical exposure and be the only student assigned to the project.

Basic Science Mini-Project: The student will measure reactive aldehyde metabolism to test whether volatile anesthetics can increase reactive aldehyde metabolism in liver homogenates of rodents with the genetic variant versus rodents which do not have the genetic variant. The student will be able to determine how volatile anesthetics modify reactive aldehyde metabolism for these rodents and provide pre-clinical data so this drug can be further moved towards testing in the clinic.

Clinical science Mini-Project: Using next generation mass spectrometry technology, we are establishing techniques to measure levels of reactive aldehydes in patients undergoing surgery. We will collect samples during surgery and quantify the level of reactive aldehydes that are produced during surgical surgery. The student will work on enrolling patients, collecting and processing samples, analyzing the data and interpreting the data to determine how the levels of aldehydes change during surgery in people and to gain a better understanding of mass spectrometry.

Institution: Stanford University School of Medicine

Mentor: Titilola Falasinnu, Ph.D.

Project(s) Available:

- Emergency Department Management of Acute Pain Episodes in rheumatic diseases.
- The goal of this project examine whether patients with rheumatic diseases receive disparate care for pain in the emergency department using a structured medical record review of visits between January 1, 2018 and December 31, 2018. We will compare emergency department pain management practice for patients with rheumatic disease by disease group, gender and race/ethnicity. The primary outcomes of interest are time from pain score to receipt of pain medication, total time in the emergency department waiting room, and type, dose, and route of administration of medication received. Differences in the time variables by disease group, gender, and race/ethnicity will be assessed using survival analysis techniques, in particular the log-rank test. Finding from this research will inform the development of guidelines for managing acute pain manifestations of rheumatic diseases.
- I will provide training on designing a chart abstraction tool in Qualtrics and Redcap. I will also provide guidance on validation of questionnaire and data cleaning. Other learning opportunities include teaching basics of data analyses, descriptive statistics and epidemiological principles. I will also engage the student (as a coauthor) in the manuscript writing process – teaching basics of scientific writing.

Institution: Stanford University School of Medicine

Mentor: Ian Carroll, M.D.

Project(s) Available:

Project #1: Under fluoroscopy epidural injections with contrast are often shown to spread only on one side of the midline. While the existence of a plica mediana dorsalis restricting epidural flow has been previously described, its importance in contributing to unilateral epidural blockade or limiting the efficacy of epidural blood patches have been poorly explored. This study will consist of a retrospective cohorts study of over 300 patient's who underwent epidural injection under fluoroscopy with contrast injection as part of Stanford's CSF leak headache program. Patient factors including the site of epidural injection (cervical, thoracic, or lumbar), patient age, gender, and duration of symptoms will be looked at as potential predictors of restricted epidural flow due to a plica mediana dorsalis. Findings have direct implications for alternative ways of approaching unilateral epidural blockade and unsuccessful bedside epidural blood patch-i.e. accessing the contralateral side. This project should take approximately 4-5 weeks for data collection, and approximately 2-3 weeks for manuscript preparation.

Project #2: Elevated total CSF protein and elevated serum prolactin have both been reported among patients with spontaneous CSF leaks. However no systematic research has been conducted to determine whether the presence of elevated CSF protein or elevated serum prolactin predict positive response to epidural blood patch among patients with orthostatic headaches suspected to have CSF leaks. We will conduct a case control study among 130 patient's with orthostatic headaches who underwent epidural blood patching at Stanford's CSF leak headache program. Logistic progression will be used to examine if these lab findings predict the odds of a positive response to epidural blood patching among patients with orthostatic headaches, and whether these lab findings better predict a positive response to treatment when compared to traditional neuroimaging findings. This project should take approximately 4-5 weeks for data collection, and approximately 2-3 weeks for manuscript preparation.

Institution: Stanford University School of Medicine

Mentor: Ban Tsui, M.D.

Project(s) Available:

1. Enhanced Recovery after Cardiac Surgery with Erector Spinae Plane (ESP) Catheters

ESP may reduce perioperative anesthetic exposure and perioperative opioid use that can lead to a less detrimental effect on brain development. The project's aims are to determine whether regional anesthesia can improve neurologic outcomes utilizing electroencephalogram (EEG) and to examine whether blood metabolic changes can predict the neurologic outcome using nuclear magnetic resonance spectroscopy (NMRs). The student will learn and work with pediatric cardiac surgeons, anesthesiologists, cardiologists, intensivists, and neurologists.

2. Electrical Epidural Stimulation Test for Confirmation of Epidural Catheter Placement in Laboring Women

Combined spinal-epidural is an established technique for providing labor analgesia to obstetric patients. Historically though, after rapid onset analgesia, the epidural catheter remains untestable in placement and effectiveness. It was previously determined that the motor threshold current of an epidural stimulation test was unaffected by local anesthetic and placement confirmation. The student will gain experience with laboring patients, and to coordinate closely with regional anesthesiologists and OB-GYN physicians to investigate the ability of the EST to confirm the placement of the epidural catheter.

3. Umbilical Vessel Catheterization under ECG Monitoring and Guidance

Umbilical Venous Catheters (UVC) are typically placed with poor guidance and some radiological confirmation, however, misplacement of the catheter in other unintended anatomical areas or migration of the catheter placement could prove detrimental in critically ill infants. A previous study suggests the use of electrocardiograms to guide the placement of the UVC and provide a tool for around-the-clock monitoring. The student will engage

with neonates and families in the NICU, work closely with neonatologists in the development of biotechnological solutions in neonatal UVC placement.

4. Pediatric Scoliosis Surgery: Enhanced Recovery with ESPB

We propose the use of the ESPB to reduce perioperative opioid use and morbidity after surgery, and radically improve pain management. Students will work closely with orthopedic surgeons and pediatric anesthesiologists while assisting in the implementation of ESPB within pediatric scoliosis surgeries.

Institution: Stanford University School of Medicine

Mentor: Boris Heifets, M.D., Ph.D.

Project(s) Available:

1. Separating MDMA ('ecstasy')'s therapeutic pro-social effects from its abuse potential.

MDMA is an abused drug that also has therapeutic potential for several conditions including Post-Traumatic Stress Disorder. We model behaviors in mice related to sociability and drug reward, both of which are strongly influenced by the drug MDMA, which has effects on both behaviors in humans. Using a combination of genetic, pharmacological, optogenetic and chemogenetic manipulations, we dissect the circuitry related to these various drug effects in search of a therapy capable of enhancing sociability yet with low abuse potential.

2. Investigating the neural circuitry of ketamine's antidepressant effect in humans and mice

Ketamine is an anesthetic drug with a long history of safe use in the operating room environment, and recently it has also been found to have profound antidepressant effects when given outside of the operating room. Although animal studies suggest that ketamine's antidepressant mechanism relies on NMDA receptor antagonism and activation of specific intracellular signaling pathways, mechanistic trials in humans do not support this idea. We are using findings obtained from human studies of ketamine's antidepressant mechanism to inform refined animal models of ketamine's antidepressant effect. We are using whole-brain unbiased neuronal ensemble detection methods to identify neural circuits that are necessary and sufficient to account for ketamine's antidepressant mechanism.

3. How does ketamine engage the endogenous opioid system?

We have recently found that an opioid receptor antagonist, naltrexone, can completely block the antidepressant effect of ketamine in patients with treatment resistant depression. This data suggests that ketamine can modulate the endogenous opioid system for therapeutic benefit. Using transgenic mouse lines that allow for selective controls of various populations of endogenous opioid-releasing neurons, we are probing the role that ketamine has in modulating behaviors related to these neural circuits.

4. Hallucinogens and creativity: establishing animal models with relevance to humans.

Classical hallucinogenic drugs like psilocybin have garnered significant recent media attention for their possible role in treating a host of psychiatric disorders, and for their potential to enhance creativity. We are studying behavioral processes relating to perception, learning, and creativity in both human studies and in mouse models.

Institution: Stanford University School of Medicine

Mentor: Pamela Flood, M.D., M.A.

Project(s) Available:

Project 1: Effect of gabapentin on persistent pain and opioid use after cesarean section: This is a double-blind randomized trial of titrated outpatient use of gabapentin on time to opioid cessation in high risk women. Secondary outcomes include pain, psychological outcome (anxiety, postpartum depression) and functional outcomes (fatigue and physical function), assessed with weekly questionnaires and corroborated with Fitbit activity trackers.

The student would have the ability to directly interact with participants through enrollment and have the opportunity to participate in preliminary data analysis that could result in an abstract for presentation, or a potential publication. The student would also have the opportunity to work within the clinical obstetrical, pain management, and general operating room environments.

Project 2: Association between anesthesia, childbirth, chronic headache and back pain. This is a retrospective study using recently collected data on patients with chronic headache and/or back pain related to their history of childbirth and child-raising. This is a study that requires data analysis and would be appropriate for a student with some preexisting data analysis skills. The student would also have the opportunity to work within the clinical obstetrical, pain management, and general operating room environments.

Institution: Stanford University School of Medicine

Mentor: Alex Butwick, M.D., F.R.C.A.

Project(s) Available: The aim of the proposed work will be to examine trends and practices related to screening, identification, and treatment for antepartum anemia. First, we will survey attending obstetricians who practice at our tertiary care obstetric center to assess the

Institution: Stanford University School of Medicine

Mentor: Jessica Brodt, M.B.B.S. (M.D. equivalent)

Project(s) Available: Enhanced Recovery after Cardiac Surgery with Erector Spinae Plane (ESP) Catheters
Traditional management of perioperative pain in adult cardiac patients relies heavily on systemic opioids. To mitigate this, we propose the use of regional anesthesia via ESP catheters as a means of improving pain management and postoperative recovery after cardiac surgery. Specifically, this research is examining whether local anesthetic via ESP catheters, when used for patients undergoing sternotomy for cardiac surgery, reduces postoperative pain score, opioid requirements, levels of inflammatory biomarkers and ICU length of stay. Students will gain exposure to inflammatory biomarker analysis, will have interactions with patients in the cardiac OR and cardiovascular ICU, and will work closely with cardiothoracic and regional anesthesiologists as well as cardiac surgeons.

Institution: SUNY Downstate Medical Center

Mentor: Ketan Shevde, M.D.

Project(s) Available:

#1

A Comparison of Insulin Sensitivity and Management in Hyperglycemic Patients in the Perioperative Period: ESRD vs. non-ESRD

In this project, we monitor the perioperative plasma glucose in hyperglycemic patients undergoing all surgical procedures, independent of anesthesia. We evaluate the change in blood glucose following exogenous insulin administration to determine whether there is a significantly different response between ESRD and non-ESRD patients. We hypothesize that patients with ESRD and preoperative hyperglycemia will have heightened insulin sensitivity due to delayed renal clearance of insulin, and will demonstrate a more significant decrease in blood glucose following insulin administration compared to non-ESRD patients. For the purpose of this study hyperglycemia will be considered as blood sugar levels of 150 mg/dL or higher and major surgical procedures will be considered to be arterio-venous access procedures, major abdominal, orthopedic, and thoracic procedures. The student will assist with protocol implementation, patient recruitment, data collection and analysis.

#2

Blood Pressure Cuff Study-

Currently at Downstate Medical Center and other University Hospitals reusable blood pressure cuff sleeve usage is the standard. Initially, we are planning to determine the number/percentage of times that the protective sleeves are used. To do so, we will perform an observational study of the clinical practice as it currently exists regarding the use of the sleeves. This will entail observing subjects in the ORs at Downstate and counting the number of blood pressure cuffs applied over the protective barriers and those applied directly on the patient's arm without the protective barrier. In addition, blood pressure cuffs are being tested for transmission of pathogens from the blood pressure cuffs to patients through collaboration with the Pathology Department lab at SUNY Downstate Medical Center.

The student will assist with data collection, data management, entry and analysis.

Institution: SUNY Downstate Medical Center

Mentor: Ming Zhang, M.D., Ph.D.

Project(s) Available: Complement activity in synovial fluid and its impact on cultured chondrocytes-

The pathogenesis of arthritis can be attributed in part to the increased presence of complement factors. The study involves collecting synovial fluid from patients undergoing total knee arthroplasty. Chondrocytes are then isolated from the resected femoral and tibial tissues. These cells are cultured in synovial fluid with varying levels of complement. The control consists of chondrocyte growth in supplemented DMEM media alone. We will analyze the level of endogenous complement via ELISA assays while the induced expression of complement related inflammatory factors will be measured by RT-qPCR and western blot. In addition, we collect 5-10 ml of blood samples from the patients to compare the levels of complement related factors in the blood versus those levels in the synovial fluid. This study will provide important insights into the cytotoxic effects of complement on chondrocytes in the human arthritic knee joint.

The student will assist in protocol implementation, patient recruitment, sample collection data collection and analysis.

Institution: SUNY Downstate Medical Center

Mentor: Gina Subtirelu, M.D.

Project(s) Available: We will prospectively compare changes in optic nerve sheath diameter (ONSD) during anesthesia maintenance with sevoflurane-only anesthesia versus anesthesia maintenance with propofol in patients undergoing urologic and gynecologic surgery in the steep Trendelenburg position. We hypothesize that ONSD will be significantly smaller (% change) during anesthesia maintenance with propofol versus anesthesia maintenance with sevoflurane. We will measure the percentage of change in ONSD during anesthesia maintenance with sevoflurane versus propofol. Group A will begin anesthesia maintenance with sevoflurane. Then will be switched after 30 minutes to anesthesia maintenance with propofol then will be switched to sevoflurane.

The student will assist with protocol implementation, patient recruitment optic nerve measurement, data collection and analysis.

Institution: SUNY Downstate Medical Center

Mentor: Daisy Lin, Ph.D.

Project(s) Available: The developing brain is extremely sensitive to drug exposure and can undergo long-lasting changes that impact its function during adulthood. By using molecular/cellular/epigenetics, electrophysical and behavioral tools, our lab investigates the impact of drugs, such as anesthetics, on the developing brain. We aim to understand the long-term effects of different anesthetics on their target receptors in the neonatal brain and the resulting changes in neuronal functional output in adulthood. With this approach, we are working toward developing neurodevelopmental abnormalities and disease vulnerabilities associated with specific anesthetic exposure during early brain development. we hope to gain a comprehensive understanding on the mechanisms of different anesthetics on the developing brain to assist optimum treatment approaches in pediatric anesthesiology.

The student will assist in anesthetizing neonatal mice, surgical dissection of mice and carryout molecular/cellular/epigenetics, electrophysical and/or behavioral experiments.

Institution: SUNY Downstate Medical Center

Mentor: Ira Kass, Ph.D.

Project(s) Available:

Project #1

The developing brain is extremely sensitive to drug exposure and can undergo long-lasting changes that impact its function during adulthood. By using molecular/cellular/epigenetics, electrophysical and behavioral tools, our lab investigates the impact of drugs, such as anesthetics, on the developing brain. We aim to understand the long-term effects of different anesthetics on their target receptors in the neonatal brain and the resulting changes in neuronal functional output in adulthood. With this approach, we are working toward developing neurodevelopmental abnormalities and disease vulnerabilities associated with specific anesthetic exposure during early brain development. We hope to gain a comprehensive understanding on the mechanisms of different anesthetics on the developing brain to assist optimum treatment approaches in pediatric anesthesiology.

The student will assist in anesthetizing neonatal mice, surgical dissection of mice and carryout molecular/cellular/epigenetics, electrophysical and/or behavioral experiments.

Project #2

Early life exposure to anesthetics and seizure development later in life.

Our long-term goal is to gain a comprehensive understanding of neurological change/disease vulnerability associated with each type of anesthetic in order to develop a safe treatment approach. The overall objective for this study, which is one of the series of steps toward attainment of our long-term goal, is to identify an association between exposure to GABAA receptor targeted anesthetics in young children and an increased risk of seizure disorder later on in life.

The student will assist in carrying out molecular/cellular/epigenetics, electrophysical and/or behavioral experiments.

Project #3

Analyzing patient EKG and correlating it with EEG from BIS monitor to assess anesthetic state and other pathophysiologic brain conditions from EKG analysis alone.

The student will assist with EKGs, protocol implementation, data collection and analysis.

Institution: SUNY Downstate Medical Center

Mentor: Panayiotis Tsokas, Ph.D.

Project(s) Available: Development of novel amnesic agents using a strategy of blocking Protein Kinase M-zeta (PKM-zeta is a brain-specific, constitutively active isoform which plays a key role in the maintenance of long-term memory. We have devised an antisense oligodeoxynucleotide (ODN) sequence which specifically blocks new PKM-zeta synthesis from the PKM- zeta mRNA. In vivo intrahippocampal injection of the antisense ODN blocks long- term synaptic potentiation (LTP) and long-term memory formation. We are planning on modifying the ODN so that it can cross the blood brain barrier and block the formation of new memories during anesthesia.

The student will perform the intrahippocampal injections of different drugs. This will involve cranial surgery and the implantation of cannulae into the brain. Students with prior laboratory experience may become involved with other aspects of the project. Knowledge of basic techniques in protein biochemistry (western blotting) and tissue staining (immunohistochemistry) would therefore be useful, but not necessary.

Institution: SUNY Downstate Medical Center

Mentor: Ivan Velickovic, M.D.

Project(s) Available:

#1

Studies show certain components of the complement system are present in fetal serum at approximately eighteen weeks gestation. As the fetus matures, such complement levels increase proportionally to fetal maturity. Deficiency of complement factors in neonates correlated with gestational age and may predispose the infants to severe invasive bacterial infection. However, new factors of complement system, particularly those of MBL pathway, are not well studied in the fetal circulation. The aim of this study is to quantify the profile of the initial molecules in three complement pathways in cord blood.

The student will assist with chart review, data entry and data analysis.

#2

Is Obesity a relative contraindication for Quadratus Lumborum Block in post-caesarian obstetrical patients? A retrospective chart review.

We will retrospectively compare the rate of QL block failure as defined by post operative pain requiring supplemental analgesia in cesarean delivery patients with BMI greater than or equal to 30 and less than 30. we hypothesize that the rate of QL block failure will be higher in patients with a day-of-surgery BMI greater than or equal to 30.

Students will assist with chart review, data management and data analysis.

Institution: SUNY Downstate Medical Center

Mentor: James Cottrell, M.D.

Project(s) Available: The project examines the relationship between Alzheimer's Disease and the susceptibility to or exacerbation of postoperative cognitive dysfunction (POCD). Using biochemistry, immunocytochemistry, brain slice electrophysiology and behavioral methods, we st

Institution: University of Alabama at Birmingham

Mentor: Brant Wagener, M.D., Ph.D.

Project(s) Available: Essential role of RAGE in amyloid beta (A β)-mediated alveolar epithelial injury
Pseudomonas aeruginosa type III secretion toxins are virulence determinants that initiate the generation of alveolar epithelial and endothelial cell amyloid proteins. Emerging published evidence and our preliminary work suggest that these A β species affect epithelial paracellular permeability and transepithelial ion transport. Furthermore, vitamin E modulates the release of A β by lung epithelial and endothelial cells, possibly via the inhibition of RAGE signaling. In this project, we are testing the hypothesis that P. aeruginosa-induced release of epithelial amyloid proteins causes an increase in alveolar epithelial paracellular permeability via a RAGE-dependent mechanism that is inhibited by pretreatment with Vitamin E. Students will be able to experiment with alveolar epithelial and endothelial cells to determine their permeability response to cytotoxic A β species. They will determine roles for RAGE and Vitamin E in pulmonary barrier dysfunction. Students will be able to observe animal experiments and work with tissue derived from these experiments. Endpoints of these experiments will be measures of cell permeability by ECIS and Western blotting among other laboratory techniques.

The Role of Sex Dimorphism in Post-TBI Bacterial Pneumonia

Traumatic brain injury (TBI) is the leading cause of injury-related death under the age of 45 caused in part by the high incidence of post-traumatic bacterial pneumonia. TBI induces a systemic immunosuppressed state via a vagal response that acts via the $\alpha 7$ nicotinic acetylcholine receptor ($\alpha 7$ nAChR) expressed on macrophages. Furthermore, our data suggests that gender differences may account for increased survival after post-traumatic bacterial pneumonia. If true, this could lead to novel therapies shortly after TBI that may lead to decreased morbidity and mortality for patients.

Students will be able to experiment with male and female alveolar macrophages to determine their immune response to Pseudomonas aeruginosa. They will be able to test the effect of $\alpha 7$ nAChR and estrogen receptor activators and inhibitors on this immune response. Students will be able to observe animal experiments and work with tissue derived from these experiments. Endpoints of these experiments will be measures of immune response by ELISA and Western blotting among other laboratory techniques.

Institution: University of Alabama at Birmingham

Mentor: Sadis Matalon, Ph.D.

Project(s) Available:

Title: Novel insight into preeclampsia and fetal growth restriction: role of extracellular heme

Brief description of the project: Our published studies show that brief exposure of pregnant mice to halogens (chlorine and bromine) results in a preeclampsia-type disease and fetal growth restriction. The mechanisms responsible for damaging the placenta have not been elucidated. We propose that reactive intermediates generated by the interaction of halogens and lung epithelial cells result in the generation of long lived reactive intermediates which damage red blood cells causing release of hemoglobin in the plasma. Hemoglobin is readily oxidized to heme, a pro-oxidant known to cause severe damage to proteins, lipids and DNA. To test our hypothesis, we will exposed pregnant mice at E13 (gestation day 13) to chlorine for 400 ppm for 30 min and return them to room air. We will use ultrasound to perform serial measurements of fetal length and damage to the maternal hearts at E15, E17 and E19, as we have done in the past (PMID: 28607126). In addition pregnant mice will be sacrificed at E15, E17 and E19 and blood, placentas and lungs will be collected and a variety of biochemical, immunological and physiological measurements will be performed. In the second set of experiments, we will administer hemopexin (a human protein with high affinity to heme) and these studies will be repeated.

Role of the student to the project: The student will be involved in all aspects of this project. He/she will learn how to expose mice to halogens, perform ultrasound measurements as well as a variety of biochemical, physiological and immunological measurements. In addition, the students will be introduced to the clinical aspect of this project, which involves collecting plasma samples and placenta samples from pre-eclamptic women.

Institution: University of Alabama at Birmingham

Mentor: Aftab Ahmad, Ph.D.

Project(s) Available:

Title: Effect of anesthetics on survival and inflammatory pathways.

Background: Anesthetics are routinely used for surgery. Increasing evidence suggest that anesthetics can influence the outcome of such surgeries. Studies have shown that anesthetics can also alter cancer metastasis. Anesthetics are also known to alter the extracellular milieu, which include extracellular vesicles and extracellular nucleic acids. These extracellular molecules are increasingly being recognized in disease and development. They can alter cell growth and inflammation through activation of signaling pathways. The purpose of these studies is (a) to characterize nucleic acid types released in response to specific anesthetics, and (b) to determine whether anesthetics can influence cell growth and inflammatory pathways. These studies could lead to better understand the role of anesthetics in outcomes following surgery.

Approach: These studies will be carried out using in vivo followed by in vitro cell culture-based assays. Animals will be exposed to at least two anesthetics and blood will be collected. Initially extracellular vesicles will be isolated from the plasma of these animals. Total nucleic acids will also be isolated and quantified for the amount of RNA, DNA and microRNA species using standards. A NFkB-reporter cell line will be used to screen for anesthetic effects on inflammation by exposing these cell lines to anesthetics. Additionally, extracellular vesicles isolated from anesthetized animals will be added to cells following which cell growth and inflammatory markers will be assessed.

Student's role: The student will be involved in all aspects of the project and will be trained to carry out the work. The student will have hands-on experience in culturing cells and performing cellular assays. The student will isolate, characterize and quantify extracellular vesicles and extracellular nucleic acids using a fluorimeter and nanosight particle analyzer. The student will conduct reporter assays using a luminometer. The student will be included in authorship arising from the work and present at meetings.

Institution: University of Alabama at Birmingham

Mentor: Kevin Harrod, Ph.D.

Project(s) Available: Dr. Harrod's Project

RESEARCH TOPIC

1. Influenza and secondary pneumococcal infections
2. Modulating Endoplasmic reticulum stress as a novel antiviral intervention
3. Influenza mediated regulation of airway ion channel biology

OVERVIEW

Dr. Kevin Harrod's current research portfolio is not limited to, but includes the above topics. His research goals are grounded in the use of emerging or high throughput technologies to elucidate system-wide knowledge of host-pathogen interactions in respiratory infection. He has a primary focus in the molecular mechanisms underlying pathogenesis, immunity and host defense to respiratory viruses such as influenza, and a long-standing interest in community-acquired bacterial infections of the lung including sepsis. He has a broad background in lung, cell, and molecular biology, infectious disease of the respiratory tract using both bacterial and viral pathogens. A particular focus on translational approaches is a priority for this laboratory.

STUDENT ROLE

The student role will focus on in vivo and/or in vitro projects related to the topics listed above. Projects will employ a variety of molecular biology and virology techniques. Computational biology and bioinformatics projects are available as well.

Institution: University of Alabama at Birmingham

Mentor: Jennifer DeBerry, Ph.D.

Project(s) Available: Opsin-based neuromodulation to recover lower urinary tract function after paralysis
Loss of volitional control over urine storage and voiding after spinal cord injury (SCI) has a profound negative impact on an individual's independence, general health, and quality of life. Normal lower urinary tract function requires opposing, but coordinated, activity between the detrusor (i.e., smooth muscle of the urinary bladder) and the striated muscle of the external urethral sphincter (EUS). Following SCI rostral to bladder innervation, there is an acute period of spinal shock when the bladder is flaccid. This is followed by a gradual re-emergence of detrusor contractility that is mediated by a spinal reflex loop, which is typically only functional during postnatal development before volitional control develops. In contrast, the EUS quickly recovers tonic contractile activity. Thus, when detrusor contractility re-emerges, its coordination with EUS relaxation is lost. The result is detrusor-sphincter dyssynergia and urinary retention, which can trigger autonomic dysreflexia. The current standard of practice for bladder emptying after SCI introduces susceptibility to urogenital infection and long-term damage. Optogenetics is an innovative technology that allows for optical control of excitable cells via light-gated ion channels and pumps.

The aim of this project is to use a combination of excitatory and inhibitory light-gated proteins expressed in sensorimotor pathways (bladder and EUS) to recover lower urinary tract function after paralysis. The model we use is a mouse model of mid-thoracic spinal contusion injury. Participants will have the opportunity to perform hands-on work including advanced neurosurgical procedures, in vivo urodynamic testing, and in vitro analysis of post-mortem tissues.

Institution: University of Alabama at Birmingham

Mentor: Songwei Wu, M.D.

Project(s) Available: Endothelial derangement in pulmonary arterial hypertension
Lung vascular endothelial cells (ECs) are main participants in initiation and progression of pulmonary arterial hypertension (PAH). Dysregulated EC proliferation leads to disordered angiogenesis with intraluminal growth causing arteriolar occlusion and obliteration. Endothelial-to-mesenchymal transition (EndMT) can result in pulmonary artery muscularization, which contributes to the distinct pathologic characteristics of PAH. We recently observed that pulmonary microvascular ECs produce and release vascular endothelial growth factor (VEGF) under conditions known to produce PAH. This microvascular EC-derived VEGF exerts a strong chemotactic effect on macrovascular ECs and smooth muscle cells (SMCs) in a neuropilin-2 (NRP2)-dependent manner. We revealed that PAH also caused activation of the Hippo pathway transducers YAP and TAZ, and a VEGF-dependent rise in HMGA1 protein, which has recently been identified to promote EndMT in PAH. Our evidence also indicates the distal migration of the larger vessel ECs into alveolar capillaries in lungs from rats with experimental PAH as well as in arteriolar plexiform lesions from patients with severe PAH. Hence, this project will test the CENTRAL HYPOTHESIS that microvascular EC-derived VEGF signaling promotes migration and deranged proliferation of macrovascular ECs and SMCs into distal microvascular beds to initiate vascular remodeling leading to a rise in pulmonary vascular resistance and progression of PAH. Specific Aims will test: [1] VEGF derived from microvascular ECs acts through NRP2 to trigger distally-directed macrovascular EC/SMC migration; [2] VEGF-NRP2 signaling effects the migrated macrovascular ECs/SMCs to stimulate proliferation and EndMT; [3] VEGF-NRP2 signaling promotes hemodynamic decline in PAH.

The students will learn a number of cell and molecular biology techniques including: cell culture, RNA extraction, qPCR, immunoblotting, and immunofluorescence to assess YAP/TAZ activation and EndMT in pulmonary macrovascular ECs, have the opportunity to present their work at research conferences and potentially be listed as coauthors of related publications.

Institution: University of Alabama at Birmingham

Mentor: Jianguo Gu, M.B., Ph.D.

Project(s) Available:

Project 1: This project is to study the roles of ion channels including voltage-gated potassium channels in mediating pathological pain induced by cold temperatures. The long-term goal of this research project is to develop therapeutic compounds targeting these channels for clinical treatment of cold pain in patients.

Project 2: This project focuses on cellular and molecular mechanisms underlying the transduction and encoding of mechanical stimulation such as gentle touch. The long term goal of this project is to identify therapeutic targets for treating sensory disorders such as mechanical allodynia (i.e., pain induced by gentle touch) seen in patients with neuropathic and inflammatory diseases.

Project 3: Nodes of Ranvier are highly specialized axonal regions on myelinated nerve fibers of sensory, motor and central nervous systems where action potentials are propagated by saltatory conduction. Saltatory conduction through nodes of Ranvier ensures timely sensory and motor responses and precise signal processing in the CNS. A number of neurological diseases affect nodes of Ranvier to impair saltatory conduction leading to motor disorders, such as paralysis and sensory dysfunctions, such as pain, numbness, and other abnormal sensations. Knowledge of ion channels and their functions at mammalian nodes of Ranvier is a key to fully understanding saltatory conduction under both physiological and pathological conditions, and for potential treatments of those sensory and motor disorders. The overall goal of this project is to study ion channel mechanisms for securing saltatory conduction of action potentials at mammalian nodes of Ranvier.

STUDENT ROLE

As a trainee working in Dr. Gu's lab, you will learn to assess pain in animals after tissue inflammation and nerve injury to help in understanding the mechanisms underlying these pain conditions and to identify effective treatments for alleviating these pain conditions. Specifically, you will perform behavioral tests to assess neuropathic and inflammatory pain using methods such as von Frey Test for mechanical sensitivity, and the orofacial operant test for thermal sensitivity and mechanical sensitivity in orofacial regions. You will also give animals testing compounds to see if pain in the animals is relieved by the testing drugs.

Institution: University of Alabama at Birmingham

Mentor: Saurabh Aggarwal, M.D., Ph.D.

Project(s) Available: Role of Cigarette Smoking in HIV-associated Pulmonary Arterial Hypertension
HIV-associated vascular dysfunction such as pulmonary arterial hypertension (HIV-PAH) is a well-recognized cardiovascular complication of HIV infection with an adverse prognosis. However, the exact pathogenic mechanism that links HIV to PAH is not known. The overall objective of the project is to determine whether cigarette smoking (CS) disproportionately increases the risk of developing vascular endothelial and smooth muscle cell dysfunction in individuals living with HIV.

The FAER students will participate in the project and test the following aim:

Establish a direct link between CS and endothelial dysfunction in HIV positive patients. Smokers and non-smokers with and without HIV-1 infection will be recruited at the UAB HIV 1917 clinic. To evaluate vascular function, the following non-invasive measurements will be performed:

- a) Assessment of Biochemical Plasma Markers of Endothelial Function. To determine the role of CS in endothelial dysfunction in HIV, endothelium-derived mediators of vascular tone, such as nitrite/nitrate levels, cyclic GMP (a readout of nitric oxide function), endothelin-1, thromboxane, and prostacyclin will be measured by ELISA in patient plasma. Decrease in nitrite/nitrate, cGMP, and prostacyclin levels, while an increase in endothelin 1 will be considered as impairment of endothelial dependent vasodilation.
- b) Assessment of Endothelial dependent vasodilation. Blood pressure will be recorded by Pulse Wave analysis (indicator of vascular stiffness). Endothelial function in patients will be assessed by flow mediated dilatation, as it is non-invasive and measures by ultrasound the response of the brachial artery to increased shear stress. Shear stress increases vasodilation, which is dependent upon the release of nitric oxide by endothelial cells.
- c) Vascular smooth muscle function will be assessed by measuring with ultrasound, the dilation of brachial artery, before and after administration of a sublingual nitroglycerin (0.4 mg). Administration of nitroglycerin causes vasodilation which is dependent upon vascular smooth muscle cells and independent of endothelial cells.

Institution: University of Alabama at Birmingham

Mentor: Nagababu Enika, Ph.D.

Project(s) Available: S-nitrosothiols based therapeutic approaches for the management and treatment of cardiovascular diseases

Nitric oxide has been established as an important signaling molecule in the regulation of myocardial and vascular functions. Dysregulation of any of

Institution: University of Alabama at Birmingham

Mentor: Shama Ahmad, Ph.D.

Project(s) Available:

Title: Circulating catecholamines in bromine-induced cardiac dysfunction

Background: Halogens are widely used highly toxic chemicals that pose potential threat to humans due to their abundance. Halogens such bromine (Br₂) cause severe pulmonary and systemic injuries however, the mechanisms of their toxicity are largely unknown. Our studies have demonstrated that Br₂ inhalation and subsequent formation of reactive brominated species caused acute cardiac injury and myocardial damage that can lead to heart failure. In an attempt to attribute hyper-adrenergic drive to acute cardiac damage we measured circulating and LV tissue catecholamines. We found that increase in LV shortening correlated with decrease in circulating and cardiac tissue catecholamines. We therefore, hypothesized that brominated lipids formed on the moist pulmonary bed may react and either destroy or modify the antigenic sites of these catecholamines. The purpose of these studies is (a) to determine if plasma catecholamines are modified by brominated lipids and (b) to determine if brominated lipids modify intracellular production of catecholamines. These studies could lead us to better understand of the role circulating catecholamines in halogen-induced cardiac injury.

Approach: The studies will initially be carried out using plasma and cardiac tissues already collected from control or Br₂-exposed rats. In vitro cell culture based assays will also be utilized. Plasma and cardiac samples will be assayed for catecholamines using a rapid sandwich ELISA kit for the quantitative measurement of catecholamines in rat plasma, and tissue samples. Some samples will then be treated with brominated lipids and reassessed for catecholamine content. Immunoprecipitation and subsequent western blots will be performed to measure the catecholamine-antibody interaction after treatment. cardiac cells will be grown and assessed for catecholamine production before and after treatment with brominated lipids.

Institution: University of California (Davis) Health System Program

Mentor: Neal Fleming, MD, PhD

Project(s) Available: Sugammadex: Renal Failure - An evaluation of the utility of sugammadex for reversal of neuromuscular blockade in patients undergoing renal transplantation.

Dexmedetomidine for sedation of pediatric patients - A Phase 4 trial of the utility of dexmedetomidine for sedation of children undergoing MRI scans

Calibration and Validation of Patient Monitoring Device for Pressure Injury Prevention and Fall Detection - The initial clinical evaluation of a wireless device that has been developed as an aid in preventing bedsores and detecting patient falls.

Prospective Observational Study Characterizing Noninvasive Hemoglobin (SpHb) Measured with Pulse CO-Oximetry Technology in a Variety of Surgical Cases - A prospective, non-blinded, non-randomized, non-interventional study designed to collect additional data to evaluate, calibrate and improve the performance and understanding of the non-invasive SpHb technology.

Validation of PVI as a Parameter to Predict Fluid Responsiveness - This is an observational, retrospective, data analysis study to compare the new rPVI parameter to the older PVI and PPV standards.

Evaluation of dynamic monitors for the prediction of volume responsiveness in patients with and without diastolic dysfunction - A study to compare the predictive threshold for CO response to a fluid bolus in patients with normal or abnormal left ventricular diastolic function.

Institution: University of California (Davis) Health System Program

Mentor: Richard Applegate, MD

Project(s) Available: EEG Data Collection in Critically Ill Patients - A prospective, non-randomized, sequential data collection study of adult patients in the ICU designed to evaluate the utility of the SedLine monitor as a guide for sedation.

Comparison of Depth of Sedation Performance between SedLine and Comparitor Device during General Anesthesia - Directly compare the performance of the SedLine and BIS processed EEG monitors.

SedLine in pediatrics - An evaluation of the utility of the SedLine monitor as a guide to anesthetic depth in pediatric patients.

Patient Centered Outcome Research Institute: A Randomized Controlled Trial of Regional Versus General Anesthesia for Promoting Independence After Hip Fracture Surgery - A multi-center trial of the effects of operative anesthetic on post-operative outcomes.

Patient self-reported duration of analgesia after shoulder surgery and interscalene block with and without perineural adjuncts. - A prospective study of the impact of local anesthetic adjuncts on post-operative pain.

Transversus Abdominis plane (TAP) blocks with Ropivacaine Continuous Infusion Catheters vs Single Dose Liposomal Bupivacaine. - A prospective randomized controlled trial for pain control after renal transplant surgery

Institution: University of California, Los Angeles

Mentor: Maxime Cannesson, M.D., Ph.D.

Project(s) Available:

1. Machine learning of electronic health record data, physiological waveforms, and genomic data to predict post-operative complications and prevent failure to rescue after major surgery:

The goal of this proposal is to apply machine learning approaches to multiple data sources including EHR data, high-fidelity physiological waveform data, and genomic data that have never been used together in the acute care setting to predict postoperative major complications and decrease failure-to-rescue after surgery.

2. Biomedical Informatics Tools for Applied Perioperative Physiology:

The objective of this proposal is to focus the resources of an interdisciplinary team from academia, industry, and clinical medicine to create, develop, and organize large surgical datasets combining EHR and high fidelity physiological waveform data, to make these datasets freely accessible, and to develop new predictive/forecasting monitoring systems for the surgical patients. The study will begin with the development of a machine learning algorithm to predict cardiovascular collapse during surgery. This algorithm development will be based on physiological signatures predictive of cardiovascular collapse identified in the animal models of shock. The study hypothesis is that the combination of two separate OR databases containing EHR and physiological waveforms will allow for training and development of monitoring solutions, predictive and/or prescriptive analytics tools, clinical decision support, and validate them on an independent, external validation database.

3. Machine Learning of Physiological Waveforms and Electronic Health Record to Data to Predict, Diagnose, and Treat Hemodynamic Instability in Surgical Patients:

The goal of this proposal is to develop, validate, and test real-time intraoperative risk prediction tools based on EHR data and high-fidelity physiological waveforms to predict cardiorespiratory instability (CRI) and make the databases of intraoperative data and waveforms used for these developments freely accessible. The goal of this proposal is to apply machine learning approaches to the complex and time compressed environment of high-risk surgery where greater patient and disease variability exist and shorter period of time is available to deliver truly personalized medicine approaches.

Institution: University of California, Los Angeles

Mentor: Soban Umar, M.D., Ph.D.

Project(s) Available:

1. Multi-Organ Transcriptomic Analysis in Experimental Pulmonary Hypertension: The applicant will have the opportunity to work with research fellows and the PI on projects investigating transcriptomic signature of various organs in experimental pulmonary hypertension. The applicants will have the opportunity to learn basic in vivo and in vitro animal physiology, molecular biology, immunohistochemistry and biochemical lab techniques.

2. Investigating the Inotropic Effects and Rescue Potential of Intralipid in Septic Cardiomyopathy: The applicants will have the opportunity to learn basic in vivo and in vitro animal physiology, echocardiography, molecular biology, immunohistochemistry and biochemical lab techniques.

Institution: University of California, Los Angeles

Mentor: Andrew Hudson, M.D., Ph.D.

Project(s) Available: Anesthetic perturbation of synaptic transmission in vivo assessed via calcium imaging:

How do anesthetics interrupt the propagation of information through the cortical network? This project will utilize the genetically-encoded calcium indicator GCaMP6 to report neuronal activity in vivo in superficial frontal cortex of the mouse. Activity in the imaged area will be driven through electrical and optogenetic stimulation of the cortical and thalamic afferents to that area, to allow a thorough characterization of the change in the input-output relationship between neurons as a function of volatile anesthetic dose. This project will have the opportunity for the student to participate in experimental data collection utilizing in vivo 2 photon resonance scanning

microscopy, signal processing, and statistical analysis. Students will have the opportunity to observe animal surgery and injection of viral vectors.

Characterization of anesthetic dose responses in globus pallidus of mouse:

The basal ganglia play a huge role in action selection and motivation that directly impact the arousal signals propagated throughout the brain by the central thalamus, yet their contributions to anesthetic-induced unconsciousness remain relatively unexplored. This project utilizes high density depth-electrode recordings of action potentials and field potentials to characterize shifts in the relationship between the cortex, globus pallidus, and central thalamus as a function of anesthetic dose. This project will have the opportunity for the student to participate in experimental data recording utilizing a high density electrode-array system, signal processing, and statistical analysis of electrophysiology data. Students will have the opportunity to observe animal surgeries.

Institution: University of California, San Francisco

Mentor: Judith Hellman, MD

Project(s) Available:

Project Title: Innate immune modulation by the endocannabinoid system

Student Role: My laboratory is focused understanding the mechanisms of injury and organ failure in sepsis and other acute inflammatory disorders. We have active project defining the role of innate immunity, and endothelial and leukocyte signaling pathways in sepsis and injury, and the immunomodulatory effects of the endocannabinoid and endovanilloid systems in sepsis and acute inflammation. The student will have the opportunity to participate in studies focused on understanding the effects of cannabinoids on inflammatory activation of endothelial cells and leukocytes, and the roles of cannabinoid receptor 1 (CB1R) and the transient receptor potential vanilloid 1 (TRPV1) in mediating the immune effects of cannabinoids. They will gain experience in measuring parameters of inflammation and injury in vitro and in vivo in models of sepsis and inflammation. They will also have on average 6 hours per week clinical exposure in the ICU and/or OR. The student will, with my guidance, develop and create an abstract and poster based on their summer project, which they will present at the ASA Annual meeting.

Institution: University of California, San Francisco

Mentor: Hua Su, MD, MS

Project(s) Available:

Research Topic: Developing innovative therapies for the treatment of brain arteriovenous malformation.

Overview: Brain arteriovenous malformation (bAVM) is an important cause of intracranial hemorrhage. Available therapies are all invasive and have potentially high morbidity. Excessive VEGF expression is a fundamental part of the bAVM pathology. Compelling evidence show interruption of VEGF signaling could be a therapeutic strategy. Soluble FLT (sFLT1) binds to VEGF in the tissue, thus reducing its downstream signaling through membrane-bound VEGFRs. Soluble FLT1 in an AAV construct packaged in AAV serotype 2 capsid (AAV2) inhibited choroidal neovascularization in a non-human primate model. However, AAV2 does not cross the blood- brain barrier (BBB). We have test a non-invasive route, intravenous, using AAV serotype 9 (AAV9), because AAV9 enters the brain parenchyma much more effectively. We showed that systemic delivery of AAV9-sFLT1 reduced brain AVM severity in 2 mouse models. However, liver inflammation and growth arrest have been noticed. To reduce systemic side effect, we are testing a strategy to deliver sFLT1 to brain endothelial cell specifically. The goal of the project is to test if intravenous delivery of AAV-sFLT will prevent progression of or reverse the AVM phenotype with minimum side effect.

Student Role: Students will participate in ongoing projects. They will perform tissue section, histological and immunohistological staining, quantify vessel density and the number of abnormal vessels on tissue sections, and analyze gene expression through qPCR and western blot. The goal for the students is to learn basic lab techniques, principles for design research projects, data analyses and interpretations. They are expecting to be co- authors on publications resulting from their activities during the fellowship period.

Institution: University of California, San Francisco

Mentor: Arthur Wallace, MD, PhD

Project(s) Available:

Project Title: AVD-M: Audiovisual Detection Monitor Development: Respiration, Heart Rate, Pulse Oximetry, Perfusion, Etc.

Project Overview

Complications from opiate use have prompted attention towards reevaluating current systems in place used to monitor patient vital signs. Respiratory depression by opioids may quickly lead to apnea, respiratory and cardiac arrest, and death. At the present time, there is no monitor for continuous, non-contact, remote monitoring of respiration, heart rate, oxygen saturation, and perfusion in hospitals. Utilizing a multi-camera optical system as a

development platform, the AVD-M system utilizes two stereoscopic RGB cameras, an IR camera, a 3D vision depth camera, acoustic location, skeletal tracking, facial tracking, and machine vision to create a new class of medical monitors. The AVD-M system is capable of automatically monitoring and measuring respiration, heart rate, and oxygen saturation remotely. Algorithms to measure cardiac output will be developed. Conventional finger and nose-based pulse oximetry devices face inherent flaws such as when patients remove or displace the sensor during critical times. The AVD-M patient monitor employs human-centered design to prevent respiratory and cardiac arrest in hospitalized patients.

Student's Role: Student will learn computer programming utilizing National Instruments LabView. They will work with the AVD-M system to develop and test the new algorithms. They will do clinical testing of the pulse oximetry, heart rate, respiratory rate, and perfusion algorithms in volunteers and patients.

Institution: University of California, San Francisco

Mentor: Helen Kim, MPH, PhD

Project(s) Available: Predictors of hemorrhage and outcome in patients with cerebrovascular malformations
Project Overview

We have several NIH-funded research projects focused on predictors and modifiers of clinical course in patients with cerebrovascular malformations, which are a major cause of hemorrhagic strokes in younger people. First, the UCSF Brain Arteriovenous Malformation Study Project tracks treatment results and patient outcomes for all sporadic bAVM patients seen at UCSF. Second, we are the coordinating center for the Brain Vascular Malformation Consortium, a multicenter effort studying the clinical behavior and genetics of familial cerebral cavernous malformations (CCM), Sturge-Weber Syndrome (SWS), and Hereditary Hemorrhagic Telangiectasia (HHT). Although the mechanisms underlying these vascular diseases differ, patients often present with similar clinical symptoms, and there is no primary medical treatment available. We collect detailed clinical and imaging data at baseline and outcomes at follow-up, as well as blood/saliva and tissue specimens for functional studies.

Project Student Role

The student will have the opportunity to participate in current projects, and will gain hands on experience in designing clinical research studies, patient recruitment, data collection, and/or data analysis. Examples of possible projects include but are not limited to: (1) clinical outcomes and quality of life in cerebrovascular malformation patients; (2) treatment complications or outcomes in cerebrovascular malformation patients; (3) bioinformatics analysis of exome sequencing data; (4) candidate gene studies using genome-wide association data; (5) functional and/or biomarker studies in tissue or stored plasma or serum samples; and (6) racial/ethnic differences in outcomes.

Institution: University of Colorado Denver

Mentor: Slobodan Todorovic, M.D., Ph.D.

Project(s) Available: Overview of Project- Neuronal T-type voltage-gated calcium channels (T-channels) exist in three isoforms: Cav3.1, Cav3.2 and Cav3.3. Our recent studies documented supportive role of Cav3.2 isoform in painful diabetic neuropathy. However, the roles of Cav3.1 and Cav3.3 isoforms in painful diabetic neuropathy are not well studied. Hence, we plan to use our streptazocin-induced model of type 1 diabetes in mice to investigate the roles of Cav3.1 and Cav3.3 isoforms in painful diabetic neuropathy. We will inject streptazocin into a cohort of wild-type mice and age-matched cohorts of Cav3.1 and Cav3.3 null mice. We will then determine daily blood glucose levels, daily body weights as well as sensitivity of mice to mechanical and thermal painful stimuli for up to 6 weeks after injections of streptazocin. We expect that results of our study will further our knowledge of painful diabetic neuropathy which is a medical condition very resistant to current pain therapies. We use rats and mice to probe the role of T-type calcium channel inhibitors in alleviating pain post-surgery. We make a small incision on the paw of the animals under anesthesia and test for mechanical and thermal hyperalgesia for the 7 days post-operatively. Drugs are injected directly into the paw, in the spinal cord intrathecally or intraperitoneally. Mouse genetic is used as in the other project in order to identify the isoform of T-type calcium channels that is involved in hyperalgesia post-surgery. We hope that we can establish new pain therapies in the perioperative period that do not cause dangerous side effects and addiction.

Institution: University of Colorado Denver

Mentor: Tobias Eckle, M.D., Ph.D.

Project(s) Available: Epidemiologic studies in humans indicate that susceptibility to hypoxic events such as ischemic myocardial tissue injury is time-of-the-day dependent, with more severe injury occurring after a longer period without daylight. Current findings from my lab indicate that light-exposure could function to attenuate ischemic myocardial injury. In fact, we observed a time-dependent reduction in myocardial infarct size and troponin I release following light treatment. A search for light inducible circadian rhythm proteins revealed a robust induction of cardiac Period 2 (Per2) protein levels upon intense light exposure. Based on these findings, we hypothesize that intense light therapy provides robust cardio-protection by stabilizing cardiac Per2. The student will assist with studies using intense light exposure in mouse models for myocardial ischemia or assist with a clinical trial on intense light therapy in patients undergoing cardiac surgery.

Institution: University of Colorado Denver

Mentor: Fabrice Dabertrand, Ph.D.

Project(s) Available:

1. Sex differences in hippocampal vascular dysfunction after cardiopulmonary resuscitation from cardiac arrest
Stroke and cardiac arrest are remarkably sexually dimorphic diseases, and both induce cerebral ischemia. However, progress in understanding vascular cognitive impairment after ischemia, and then developing sex-specific treatments, has been in part limited by challenges in studying brain microcirculation from mouse models. We are studying endothelial dysfunction in isolated hippocampal arterioles from male and female mice subjected to cardiac arrest with cardiopulmonary resuscitation. We engage novel, state-of-the-art experimental approaches using intact native tissue in collaboration with a well-established model from Dr. Herson laboratory.

2. Pericyte contractility in CADASIL

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a genetic syndrome caused by mutations in the myocyte- and pericyte-expressed NOTCH3 receptor, resulting in brain microcirculation dysfunction that manifests clinically as stroke and dementia. Using a well-established genetic CADASIL mouse model, we propose to investigate and characterize pericyte contractility ex vivo using a

self-developed novel preparation of intact, pressurized, intracerebral arterioles and capillaries, and in vivo with state-of-the-art two-photon microscopy.

Institution: University of Colorado Denver

Mentor: Jamie Peters, Ph.D.

Project(s) Available:

1. Preclinical testing of novel psychedelics to treat heroin addiction

This project applies basic behavioral pharmacology to a preclinical model of heroin addiction to screen potential new therapeutics for opioid withdrawal and relapse. We are interested in screening a number of compounds related to and/or derived from the West African shrub iboga. These include noribogaine, as well as chemically modified derivatives designed to further reduce side effects. The major limitation of using the parent compound, ibogaine, to treat addiction is its hERG inhibiting properties. This leads to cardiac toxicity and in some cases cardiac arrest. Noribogaine, the major metabolite of ibogaine, also functions as a hERG inhibitor, but elicits fewer tremors and has reduced psychedelic properties. We are actively pursuing related compounds engineered to produce no hallucinations and no hERG inhibition, while maintaining their therapeutic efficacy. Using our well-established preclinical model of heroin addiction in rats, we can examine the therapeutic potential of these compounds on a number of important variables, such as opioid withdrawal-induced mechanical pain, cognitive function, and relapse.

2. Identifying the neural basis of heroin preference

This project entails both basic behavioral pharmacology as well as neural circuit analysis in a preclinical model of heroin versus food choice. In this model, rats are allowed to freely choose between food pellets versus an intravenous heroin infusion. We are screening a number of compounds in an effort to shift choice toward food, thereby reducing voluntary heroin intake. Initial compounds of interest include a dual-orexin receptor antagonist (DORA-12) and oxytocin. Orexin and oxytocin are both produced in the hypothalamus, but in distinct neuronal populations. If the systemic administration of either compound is effective in reducing heroin preference, we will begin to probe the neural circuitry responsible for these effects. This would involve invasive brain surgeries in rats to target the hypothalamic peptide systems with viral strategies that allow us to remote control neurons and examine the impact on heroin versus food choice. Brain tissue will be subsequently examined to verify the success of the viral strategy, and to count the number of orexin versus oxytocin cells, as well as to correlate these numbers with behavioral measures.

Institution: University of Colorado Denver

Mentor: Nidia Quillinan, Ph.D.

Project(s) Available:

Title: TrkB receptor agonism to reverse cognitive deficit after cerebellar stroke

Description: The overall goal of this study is to assess the functional benefit of delayed interventions using behavioral analysis of cognition and biochemical/molecular analyses of signaling pathways. This project builds upon ongoing projects in the laboratory that show memory and hippocampal plasticity deficits after cerebellar stroke. Preliminary data suggests that plasticity deficits can be reversed ex vivo by stimulating the neurotrophic receptor TrkB. This project will determine whether in vivo administration of a TrkB agonist can restore plasticity genes and memory function at delayed time points after cerebellar stroke.

Student Role: The students will generate cerebellar strokes by photothrombosis and perform neurobehavioral testing of memory function in rodents. The student will also isolate brain tissue after completion of neurobehavioral experiments and use quantitative RT-PCR to measure expression of hippocampal plasticity genes. The student will be trained in scientific rigor (blinding, randomization, statistical analysis) and will present their research to laboratory.

Institution: University of Colorado Denver

Mentor: Paco Herson, Ph.D.

Project(s) Available:

Title: Therapeutic interventions to improve outcome following cerebral ischemia

Description: The overall goal of this study is to assess the functional benefit of delayed interventions using behavioral analysis of cognition, histological analysis of injury and biochemical/molecular analyses of signaling pathways. This project builds upon ongoing projects in the laboratory that show that alterations in excitation/inhibition signaling contributes to cognitive deficits after experimental ischemic stroke. We will use a combination of genetic and pharmacological manipulations to further validate the therapeutic targets being studied in the laboratory. The laboratory is comprised of clinician-scientists and PhD scientists working together to address translational basic science projects.

Student Role: The student will participate in data collection and analysis. In particular, the student will learn to perform neurobehavioral testing to assess the functional benefit of post-ischemic therapeutic interventions. The student will perform the behavioral testing in a randomized and blinded manner, perform statistical analysis upon completion (and unblinding) and present data at one National or Regional research conference. The student will be included as an author when the data is published in a peer-reviewed Journal.

Institution: University of Kentucky College of Medicine

Mentor: Sara Hall, M.D.

Project(s) Available: Communication and Comfort Measures for Pediatric Surgical Patients. This observational research project seeks to evaluate whether there is an improvement in patient comfort and parent satisfaction with the addition of patient communication ability and communication method to a standardized post-anesthesiology handoff for pediatric outpatients undergoing elective surgery. The study aims are to compare recovery room duration, staff satisfaction, and family satisfaction with the use of the communication card. The student will be expected to work with the primary mentor in facilitating the use of the standardized patient handoff, including the collection of information from legally-authorized representatives, focusing on patient communication ability and the use of non-traditional patient communication strategies. Students will also be expected to complete data collection and transfer data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Ultrasound Assessments of Gastric volumes in Pediatric Patients Before and After Premedication. The objective of this study is to determine if preoperative medication administration before corrective idiopathic scoliosis corrective surgery affects patient's intra-operative gastric volume. Pre and post-medication administration ultrasound measurements of gastric volume will be compared for patients aged 10 or older, to determine if there is a significant change in the volume of contents in the gastric antral area. The student will be expected to work with the primary mentor in recruiting and consenting patients, collecting baseline demographic information from recruited patients, facilitating research-focused bedside ultrasonography and data collection for study aims. Students will also be expected to transfer study data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Institution: University of Kentucky College of Medicine

Mentor: Sanjay Dwarakanath, M.D.

Project(s) Available: Intraoperative Right Ventricle Longitudinal Strain by Speckle Tracking Echocardiography: Comparison to Tricuspid Annular Plane Systolic Excursion and Fractional Area Change. The unique shape of the right ventricle(RV) makes it difficult to quantify its function during surgery. This study investigates if RV-FWS assessment by STE can be used as a marker for RV function and correlates with intraoperative assessments of TAPSE and FAC. The student will be expected to work with the primary mentor in recruiting and consenting patients, collecting baseline demographic information from recruited patients, facilitating research-focused Echo and data collection for study aims. Students will also be expected to transfer study data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Institution: University of Kentucky College of Medicine

Mentor: Syed Ali, M.D.

Project(s) Available: Duration of Various Factors Contributing to the Operating Room Turnover Time- This study investigates the duration of turnover by anesthesia technician, anesthesia resident, certified registered nurse anesthetist, surgical technician, operating room registered nurse, and the hospital environmental service. Students may help time events or record data, facilitating research-focused data collection for study aims. Students will also be expected to transfer study data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Noise Levels in Operating Rooms and Procedural Units During the Anesthesia Peri-Induction Period. This study investigates the noise levels in the OR during the induction period. Students may record noise levels and collect other data, for completion of study aims. Students will also be expected to transfer study data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Institution: University of Kentucky College of Medicine

Mentor: Kevin Hatton, M.D.

Project(s) Available: Haptoglobin is essential for free hemoglobin metabolism and elimination. In humans, there are three different haptoglobin phenotypes, each with a different effect on vasospasm risk after subarachnoid hemorrhage. The student will work with the primary mentor in his lab to determine the haptoglobin phenotype of subjects with aneurysmal subarachnoid hemorrhage (aSAH). The student will be taught basic laboratory safety and laboratory techniques for ELISA testing of blood plasma. In addition, the student will be expected to collect baseline demographic information from the electronic medical record. Students will transfer study data to an online database. Finally, the student will be expected to work on statistical analysis and present significant findings at a departmental research conference and a regional or national meeting.

In a different but related study, our lab is also evaluating changes in adaptive immunity in aneurysmal subarachnoid hemorrhage and its effect on vasospasm to further elucidate the neuroinflammatory cascade and investigate potential acquired immunity effects in vasospasm. The student will be taught basic laboratory safety and laboratory techniques for Flow cytometry and ELISA testing of blood and CSF. Students will transfer study data to an online electronic database. The student will work on statistical analysis and present significant findings at a departmental research conference and a regional or national meeting.

Finally, our lab is co-investigating the predictive potential of a miRNA panel on vasospasm and neurologic outcome after aSAH. Students will transfer study data to an online electronic database and collect baseline demographic information. Students will also learn about miRNA and the process to isolate and measure miRNA from plasma and CSF samples. The student will work on statistical analysis and present significant findings at a departmental research conference and a regional or national meeting.

Institution: University of Kentucky College of Medicine

Mentor: Daniel Wambold, M.D.

Project(s) Available: Thermal Effects on Ropivacaine. This is a double-blinded, randomized, investigational study of Ropivacaine, administered via single injection block pre-operatively, either at room temperature (20° to 25°C) in Arm A versus 4°C in Arm B, evaluated for time to onset of analgesia, cold sensitivity, and morphine equivalency units of adjunct pain medication in the 24 hours following administration. The student will be expected to work with the primary mentor in recruiting and consenting patients, collecting baseline demographic information from recruited patients, and facilitating research-focused data collection for study aims, including skin pinch and ice glove patient data. Students will also be expected to transfer study data to an online electronic database. Finally, the student will be expected to work with the primary mentor in the statistical analysis plan and will be expected to present significant findings at a departmental research conference and a regional or national meeting.

Institution: University of Maryland School of Medicine

Mentor: Tibor Kristian, Ph.D.,

Project(s) Available: Will focus on research on the Neuroprotective mechanisms of NAD precursor nicotinamide mononucleotide. One of the effect of NMN administration to animals is the inhibition of free radicals production following ischemic insult. The student will be engaged in project where the effect of NMN on different sources of free radicals will be examined.

Institution: University of Maryland School of Medicine

Mentor: Gary Fiskum, Ph.D.,

Project(s) Available:

1. Deleterious effects of hyperoxic resuscitation on brain region selective energy metabolism proteins following global cerebral ischemia Student will conduct high level stereologic quantification of specific proteins using light microscopy and immunoblots.

2. Quantitative assessment of neuroinflammatory proteins after polytrauma consisting of traumatic brain injury plus mild hemorrhagic shock. Student will conduct high level stereologic quantification of specific proteins using light microscopy and immunoblots.

Institution: University of Maryland School of Medicine

Mentor: Rebecca Henry, Ph.D.,

Project(s) Available:

1. Show that delayed intervention targeting specific microglial NOX2 mechanisms promotes the neurorestorative microglial phenotype and improves chronic cognitive function recovery after TBI.

Recently, we have demonstrated that NOX2 plays a critical role in secondary neuroinflammation after moderate-level TBI. Therefore, the goal of these experiments is to investigate the relative contribution of microglial NOX2 during chronic TBI on neurodegenerative and functional outcomes. To this end we have developed a novel NOX2fl/fl mouse model (Mouse Biology Program (KOMP), University of California, Davis; model 3) and will cross NOX2fl/fl with tamoxifen-inducible CreER models that will target microglia (Cx3cr1tm2.1(cre/ERT2)Jung/J; called Cx3Cr1CreERNOX2flox).

2. Investigate the effect of preexisting obesity on chronic neuroinflammatory and neurodegenerative responses following a TBI; investigation of potential interventions

There is now an increasing body of evidence suggesting that pre-existing high-fat diet induced obesity is associated with an exacerbation in neuroinflammatory responses and worsening outcomes following TBI.

Therefore, the goals of this experiment is to investigate the relative contribution of preexisting obesity on chronic neuroinflammatory responses following TBI and how dietary manipulation may affect this.

3. Investigate the effect of preexisting chronic stress on chronic neuroinflammatory and neurodegenerative responses following a TBI

The hypothalamic pituitary axis (HPA) plays a vital role in the regulation of the physiological stress response through coordinated release of stress hormones; the main one in humans being cortisol and corticosterone in rodents. Interestingly, TBI-induced dysregulation of the HPA has been reported in the clinical (25% patients with pituitary gland dysfunction up to 6 months following injury) and dysregulation of the HPA axis is one of the primary symptoms of neuropsychiatric disorders including depression, anxiety and post-traumatic stress disorder (PTSD). Post-TBI HPA axis dysfunction leads to inappropriate responses to stress, which in turn can dysregulate inflammation. Therefore, the goals of this set of experiments is to investigate the role c

Institution: University of Maryland School of Medicine

Mentor: Wei Chao, MD, Ph.D., FAHA

Project(s) Available:

Targeting inflammation in trauma

OVERVIEW:

Traumatic injury is a major cause of combat casualty and mortality. It has been well documented that traumatic injury rapidly activates the innate immune system and induces profound systemic hyper-inflammatory responses. These systemic inflammatory responses can cause severe collateral damage to the body by causing profound hemodynamic instability, tissue hypoxia, metabolic dysfunction, and organ failure. However, the mechanism leading to innate immune activation and organ failure after traumatic injury is unclear. microRNAs are a group of small and single-stranded non-coding RNAs. We have recently reported that cellular miRNAs are released from injured tissues during septic shock and cardiac hypoxic injury. In this project, we propose to test the specific role of circulating extracellular (ex) miRNAs in innate immune activation in a mouse model of poly-trauma.

STUDENT ROLE:

The student will learn to perform the trauma model in mice, which include superior mesenteric artery (SMA) occlusion, tibia fracture, and muscle crush injury. Under supervision, the FAER student will measure multiple inflammatory markers such as IL-1 β , IL-6, TNF α , and tissue injury markers such as KIM-1 and Ngal. Finally, the student will examine the plasma level of a panel of miRNAs in sham and trauma animals.

Institution: University of Maryland School of Medicine

Mentor: Junfang Wu, BM, MS, Ph.D.,

Project(s) Available:

1. The Function and Mechanisms of Voltage-Gated Proton Channel Hv1 in Spinal Cord Injury (SCI) and traumatic brain injury (TBI)
2. Dementia Following Spinal Cord Injury: Mechanism and Therapeutic Targeting
3. Spinal Mechanisms Underlying SCI-Induced Pain: Implications for Targeted Therapy

Institution: University of Maryland School of Medicine

Mentor: Peter Hu, Ph.D.,

Project(s) Available:

Description and Opportunities

Our research is focused on developing machine learning based predictive algorithms for near and long-term patient outcomes based on the continuous analysis of vital signs from the field to in-hospital resuscitation to the intensive care unit bedside. Currently, we have over 10 extramural funded projects. We have developed and tested a Bleeding Risk Index (BRI) Monitor for a minute-by-minute analysis of continuous photoplethysmograph (PPG) waveform. This monitor could be used for predicting future transfusion need in the field.

The following three potential projects may be of interest for the FAER students. 1. Oximetry and Non-invasive predictors of Intervention Need after Trauma. 2. Critical Care Air Transport Team Viewer for Advisory Alarms, Situational awareness, Mentoring, and Remote Decision-making. 3. Developing Reliable Telemedicine Platforms with Unreliable and Limited Communication Bandwidth.

Institution: University of Maryland School of Medicine

Mentor: Konstantin Birukov, M.D., Ph.D.,

Project(s) Available: Dr. Birukov's research expertise is cell and animal models of acute lung injury and signaling pathways which control organ function in healthy and injured lung. He developed a new research direction addressing novel, barrier-protective and anti-inflammatory properties of bioactive phospholipids present in our

body and developed synthetic phospholipase resistant analogs of natural phospholipids for testing in the models of lung injury and barrier dysfunction. The focus of the current studies by Dr. Birukov group is discovery of circulating factors and characterization of molecular mechanisms underlying deleterious effects of danger associated molecular patterns (DAMPs) in clinically relevant conditions: acute respiratory distress syndrome (ARDS), sepsis and traumatic brain injury.

Available projects will include:

1. Collection and analysis of blood samples from control and TBI and crush syndrome patients. Identification of circulating factors associated with morbidity and mortality in these syndromes
2. Testing effects of factors present in these blood samples in the cultures of human lung endothelial cells: their effects on vascular endothelial barrier, inflammatory response and cell survival

Institution: University of Maryland School of Medicine

Mentor: Megan Anders, M.D.,

Project(s) Available: High-quality cardio-pulmonary resuscitation in the operating room

Overview: There are well-established guidelines for treatment of patients who suffer cardiac arrest outside of the operating room. The causes of cardiac arrest during surgery are often very different, and these patients therefore require different treatments for successful recovery. In recent years, more attention has been focused on optimally adapting Advanced Cardiac Life Support (ACLS) to the perioperative period. The assessment of quality of care provided during an intraoperative cardiac arrest can be difficult due to the unique clinical situations and tailored responses by anesthesiologists.

Student Role: The student will evaluate evidence-based practices for intraoperative cardiopulmonary resuscitation and will analyze clinical records from a registry database to assess real-world compliance with best practices. A case review tool will be developed to help identify high-quality care for intraoperative arrest.

Institution: University of Maryland School of Medicine

Mentor: Marta Lipinski, Ph.D.,

Project(s) Available:

- Evaluation of age-related changes in autophagy and lysosomal function in the mouse brain.
- Evaluation of the effects of TBI on lipid homeostasis and autophagy-lysosomal function in the brain.
- Identification of plasma lipid biomarkers for TBI.

Institution: University of Maryland School of Medicine

Mentor: Bogdan Stoica, M.D.,

Project(s) Available: The project designed for FAER students will examine the role of changes in microRNAs expression in neuronal cell death and neuroinflammation and use primary neurons and microglia in vitro and experimental TBI in vivo.

Institution: University of Pennsylvania

Mentor: Roderic Eckenhoff, MD

Project(s) Available:

Project Title: Study of propofol binding to possible molecular target of propofol infusion syndrome

Project Category: Basic Science

Project Description: The pharmacology of anesthetic molecules is both very complex with many known (and many unknown) binding partners. This complex network of interactions provides a plethora of interesting questions related to anesthetic mechanisms as well as the many “off-target” effects of anesthesia. Traditional techniques often employed to study these interactions are generally not applicable to anesthetic molecules due to their small size and low binding affinities. Our lab has overcome some of these obstacles through the development of diazirine-based photoaffinity analogues of several anesthetics. This project seeks to study the molecular interaction of propofol with a mitochondrial protein that was identified during a proteomics experiment previously conducted by our lab. It is thought that this protein may play an important role in the development of propofol infusion syndrome (PRIS) which is a complication seen in some ICU patients on propofol sedation. The student would use a photo-analogue of propofol to conduct a photo-chemistry reaction with the target protein, and would then prepare the sample via protease digestion and purification. The binding sites would subsequently be identified via MS/MS sequencing analysis of the prepared sample. The result of this experiment would also involve learn basic molecular docking calculations of ligand/protein binding based on the binding sites identified via photolabeling.

Institution: University of Pennsylvania

Mentor: Maurizio Cereda, MD

Project(s) Available:

Project: An imaging approach to predict and contain lung injury (translational)

Acute lung injury results from the propagation of an inflammatory insult in the lung; it causes respiratory failure in almost 200,000 patients annually, and 60% of these will be dead within two years. Our goal is to design strategies to contain lung injury and to reduce its impact in patients. Our research focuses on the early mechanisms leading to acute lung injury. Dr. Cereda’s group studies how the distribution of local mechanical properties in the lungs governs the regional progression of pulmonary inflammation. They use a multifaceted quantitative approach that incorporates various techniques of morphologic, functional, and metabolic imaging (CT and MRI) in conjunction with standard measurements of tissue and systemic inflammation. With the support of a recent NIH grant, Dr. Cereda investigates new strategies of personalized care in a large animal model undergoing prolonged mechanical ventilation. Students will learn animal preparation and surgery techniques, help run the biological experiments associated with the project, and perform tissue analysis to measure regional inflammation in the lung. For those interested, students can learn 3D image reconstruction and analysis techniques, including deep learning based methodologies. There are no particular prerequisites for students. The involvement will depend on the student’s experience, availability, and most importantly interests. Importantly, the students will be exposed to a research environment where the focus is to rapidly narrow the gap between basic research and clinical investigation in critical care. Dr. Cereda has extensive experience in mentoring undergraduate students.

Institution: University of Pennsylvania

Mentor: Justin Clapp, PhD MPH

Project(s) Available:

1) How older patients and their caregivers consider the risk of cognitive impairment when deciding about elective surgery

Considerable translational and clinical research is beginning to illuminate the risks that surgery presents for postoperative cognitive function in older patients. Currently, however, cognitive risks are not routinely disclosed

in surgical informed consent discussions. This project seeks to understand how the inclusion of cognitive risks would factor into the decision-making processes of older patients and their caregivers regarding whether to pursue an elective surgery, what type of anesthesia to undergo, and whether to be assessed in a geriatric consultation as part of decision making. Interviews will first be undertaken with older residents and their caregivers at assisted living facilities. A second round of interviews will be undertaken with surgeons to understand their willingness to present cognitive risks, how they might do so, and what the barriers might be to doing so. This project would likely present the mentee with opportunities for participating in data collection and data analysis.

2) Role of referral in predisposing patients for/against consent to elective surgery

Our lab has spent several years examining how patients make decisions about elective surgery by studying surgical consultations. One of our core findings in these studies has been that patients enter surgical consultations with strong predispositions about whether to consent to surgery formed through upstream interactions. These predispositions in many cases trump the influence of the informed consent conversation, rendering normative models based on informed consent (e.g., “shared decision making”) of minimal relevance. A particularly important upstream interaction is with the provider who refers the patient to surgery: the manner in which this provider frames the purpose of the referral and the encounter with the surgeon appears to play a significant role in whether the patient ultimately decides to undergo or forego surgery. This study interviews referring providers about their framing of the surgical referral, then tracks those specific patients to the surgical consultation, which is observed and the patient interviewed. This project would likely present the mentee with opportunities for participating in data analysis and theory development, and possibly data collection.

3) Decisions about appropriateness of care in ICUs

Institution: University of Pennsylvania

Mentor: Meghan Lane-Fall, MD

Project(s) Available:

Project #1: In the Handoffs and Transitions in Critical Care (HATRICC) project, we have standardized communication at certain hospital transition points to decrease preventable patient harm. We are now evaluating the sustainability and ongoing effectiveness of this standardized communication. HATRICC involves the use of qualitative and quantitative methods to assess the effectiveness of provider communication when patients are transferred from the operating room to the intensive care unit. In this project, you would observe handoffs in the intensive care unit and help us develop strategies to provide feedback to doctors, nurses and advanced practice providers. You would also analyze already-collected data to discern trends in provider behavior over time. As a member of the Lane-Fall Lab, you would attend weekly team meetings and journal club sessions devoted to understanding the methodology used to assess and improve provider behavior. Scholars will be exposed to the dynamic environment of the surgical intensive care unit, and will have opportunities to shadow ICU clinicians, anesthesiologists, and surgeons, if desired.

Project #2: Understanding the patient and family experience of recovery after critical illness

Recently, we completed data collection on a longitudinal study of patients and families recovering from critical illness after life-threatening trauma. We are analyzing these data to characterize the patient and family experience of recovery to identify strategies to improve patient- and family-centered outcomes. As part of this project, you would learn how to analyze, synthesize, and present both qualitative and quantitative data related to critical illness recovery.

Project #3 Title: Penn TeleICU Value and Opportunity

Penn Medicine is a pioneer in telemedicine, having established one of the nation’s first teleICU programs in 2004. Although observed-to-expected mortality ratios have demonstrated improvement in Penn ICUs with teleICU coverage, the optimal use and scope of teleICU services at Penn remains unclear. This project is qualitative

evaluation of Penn teleICU services to characterize challenges and opportunities presented by this technology and to identify potential areas for refinement, optimization, and growth. As part of this project, you would observe the provision of tele-critical care and would interview both teleICU providers and bedside staff who interface with teleICU providers.

Institution: University of Pennsylvania

Mentor: Mark Neuman, MD MSCE

Project(s) Available: Evaluation of a system-wide EMR alert to encourage naloxone prescribing in high-risk patients.

Description of projects available to a summer student

Evaluation of a system-wide EMR alert to encourage naloxone prescribing in high-risk patients. According to the CDC, over 70,000 US adults died from drug overdoses in 2017, of which two thirds were opioid related. Over 11 million people in the US reported misuse of prescription opioids in 2017 and over 2 million people suffered from opioid use disorder. In 2018, the US Department of Health and Human Services put forward broad recommendations for co-prescribing of naloxone with opioids for individuals at high risk of opioid-related harm, such as those receiving high doses of opioid medications. In 2019, Penn Medicine, a major 6-hospital regional health system with six hospitals in PA and NJ, initiated pilot testing of an EMR-based “nudge” to encourage co-prescribing of naloxone for patients receiving outpatient opioid prescriptions with doses exceeding 50 morphine milligram equivalents per day. A cluster-randomized system-wide rollout of this alert across all Penn Medicine outpatient practices across Pennsylvania and New Jersey is anticipated in early 2020. The present project will evaluate the impact of this alert on the frequency of naloxone co-prescribing and opioid dispensing compared to control (standard care) using electronic health record data. Involved students will gain experience with study design, data management, and data analysis.

Institution: University of Pittsburgh

Mentor: Gregg Homanics, PhD

Project(s) Available:

Project Title: Epigenetic Effects of Ethanol

Project Description: Recent research in the lab suggests that an individual's ethanol phenotype is dictated in part by his

father's history of ethanol exposure prior to conceiving that individual. Remarkably, these transgenerational effects of ethanol appear to only affect male offspring. These exciting observations suggest that ethanol is an epimutagen (ie, alters the epigenetic program) that impacts germ cells in an enduring fashion. To further investigate the hypothesis that an individual's drinking and neurobiological sensitivity to ethanol are due in part to preconception ethanol exposure, we will 1) characterize the model in greater detail, 2) undertake studies to reveal the mechanism(s) that mediate these effects, and 3) examine if these effects represent true transgenerational epigenetic inheritance.

Student Role: Students will actively participate in experiments involving exposure of mice to alcohol, breeding mice,

testing the behavioral phenotype of mice (e.g., alcohol drinking, alcohol sensitivity, etc), and/or molecular characterization of the effects of alcohol on the brain (e.g., RT-PCR, ChIP assay, RNAseq, etc). Students will be expected to participate in data collection and data analysis, and ultimately contribute to manuscript preparation. This type of student project should ultimately result in co-authorship on a peer reviewed publication.

Institution: University of Pittsburgh

Mentor: A. Murat Kaynar, MD, MPH

Project(s) Available:

Project Title: The interaction of sustained inflammation and insulin signaling pathways in a Drosophila model of sepsis

Project Description: Sustained inflammation following recovery from sepsis is a major factor for increased morbidity (dementia, neuro-muscular dysfunction, accelerated atherosclerosis) and mortality in critically ill patients. Our laboratory developed a Drosophila model of surviving sepsis, where we infect flies with *S. aureus* and treat in a delayed fashion with linezolid. Despite survival advantage, the antibiotic treated survivors had sustained inflammation as shown by NF- κ B expression compared to sham controls. The survivors also had decreased glucose/glycogen storage. We are exploring the Insulin Receptor pathways to modify the sustained inflammation.

Student Role: Student responsibilities may include maintenance of Drosophila colonies, data collection including survival analysis, activity level of sepsis surviving flies, and help with total protein measurement, Western blotting, and NF- κ B activity assays. The student will produce a research abstract with data from the summer project that would fit into a larger manuscript. This type of student project should ultimately result in co-authorship on a peer reviewed publication.

Institution: University of Pittsburgh

Mentor: Grace Lim, MD, MS

Project(s) Available:

Project Title: Quantitative and Qualitative Pain Phenotypes in Pregnant Women with Substance Use Disorder

Project Description: Best practices for the treatment of pain in pregnant women with substance use disorder (SUD) are not well-established. Existing clinical guidelines for treatment of this population are limited by the lack of high-quality evidence on basic differences between women with and without SUD. The primary aims of this prospective, longitudinal, clinical observational trial is to: 1) enroll a cohort of prenatal and postpartum women with and without SUD; 2) quantify objective clinical assessments of pain by mechanical and thermal temporal

summation as well as analgesia endpoints including pain ratings and opioid requirements; 3) collect patient-reported variables related to pain experience such as catastrophizing, resilience, expectations, and physical and affective dimensions of pain; 4) thoroughly assess qualitative characteristics around the pain experience in prenatal and postpartum periods using semi-structured interview across the peripartum spectrum. The results of these investigations will shed light on key differences in obstetric pain and analgesia between women with and without SUD, thereby supporting future discovery of effective treatments tailored to the needs of this under-represented population.

Student Role: The student may learn skills in: pain score modeling; data abstraction; qualitative research; quantitative research; clinical research using health record information; abstract and manuscript development and submission.

Institution: University of Pittsburgh

Mentor: Marsha Ritter Jones, MD, PhD

Project(s) Available:

Project Title: Local anesthetic effects on release of immune-related proteins from nonpeptidergic neurons

Project Description: Neural-immune communication has been shown to be important in many autoimmune diseases and chronic pain. While peptidergic sensory neurons, ones that release cgrp and substance P, have been demonstrated to play a role in this interaction, nonpeptidergic neurons have not been evaluated as extensively. Moreover, these nonpeptidergic afferents penetrate to the most superficial layers of the epidermis, suggesting they play an important role in the innate response to a pathogen. We have found that these neurons express mRNAs of some innate immune-related genes, i.e. S1008a. Our studies seek to understand how neurons use these innate immune-related proteins to communicate with the immune system and/or amongst cells in the dorsal root ganglia (DRG). We also seek to define what triggers the production and release of these proteins. Regional anesthesia decreases nerve conduction to minimize pain sensations, but little is known about how local anesthetics and adjuvants may impact the function of these neurons. These studies will lead to a better understanding of the neural-immune relationship, potentially intervenable targets for pain management, and the impact regional anesthesia on neural immune communication.

Student Role: The student will learn isolation and cell culture techniques of primary murine DRG neurons. The student will perform in vitro assays to evaluate for secreted proteins from cultured neurons treated with a variety of concentrations and local anesthetics. This effect will also be examined in combination with select regional anesthesia adjuvants. The student will participate in data collection and data analysis, and ultimately develop an abstract and contribute to manuscript preparation.

Institution: University of Pittsburgh

Mentor: Bradley Taylor, PhD

Project(s) Available:

Project Title: Surgery Establishes an opponent process of opioid receptor analgesia and neuronal pain sensitization – (1) Basic Science

Project Description: This project tests a new conceptual model of the transition from acute to chronic pain, based on the delicate balance between latent pain sensitization (LS) and endogenous analgesia that develops after painful tissue injury. First, injury activates pain pathways. Second, the spinal cord establishes MOR constitutive activity (MORCA) as it attempts to control pain. Third, over time, the body becomes dependent on MORCA, which paradoxically sensitizes pain pathways. The manuscript underlying this working hypothesis was featured on the cover of the September 20, 2013 issue of Science. The summer project will study how stress or drugs modulate opposing inhibitory and excitatory influences on nociceptive processing in a mouse model of postoperative pain.

Student Role: Hands-on participation in animal surgery and behavioral testing, immunohistochemistry, in situ hybridization, and data analysis. The student will produce a research abstract with data from the summer project

that would fit into a larger manuscript. This type of student project should ultimately result in co-authorship on a peer reviewed publication.

Project Title: Surgery establishes an opponent process of opioid receptor analgesia and neuronal pain sensitization – (2) Clinical

Project Description: This project tests a new conceptual model of the transition from acute to chronic pain, based on the delicate balance between latent pain sensitization (LS) and endogenous analgesia that develops after painful tissue injury. First, injury activates pain pathways. Second, the spinal cord establishes MOR constitutive activity (MORCA) as it attempts to control pain. Third, the subject rests within a pain-free period, although LS continues to render vulnerability to the transition to chronic post-operative pain. The summer project will study whether LS develops in humans after surgery.

Student Role: The student will conduct Quantitative Sensory Testing, observe administration of drug infusions, and perform data analysis. The student will produce a research abstract with data from the summer project that would fit into a larger manuscript. This type of student project should ultimately result in co-authorship on a peer reviewed publication.

Institution: University of Pittsburgh

Mentor: Brian Williams, MD, MBA

Project(s) Available:

Project Title: MultiModal PeriNeural Analgesia (MMPNA)

Project Description: Our group reported in vitro and in vivo safety of a 4-drug MMPNA drug combination comprised of preservative-free bupivacaine, buprenorphine, clonidine, and dexamethasone (BPV-BCD). To better characterize its analgesic potential, we are completing a prospective clinical trial of patients undergoing knee or hip replacement, comparing BPV-BCD against plain BPV. Data to be collected and analyzed include descriptive statistics addressing analgesic duration, rebound pain, and various physical therapy parameters. The mentor possesses investigational new drug approval from the FDA for this 4-drug nerve block mixture.

Student Role: The student will accompany the mentor on clinical activities in observing the MMPNA blocks that are being used for select prospective cases and study patients, and will observe some of the physical therapy processes for these patients after surgery. The student will be responsible for some prospective data review and verification, and mentored analysis of data (specifically, the SF-8 health status survey and the Quality of Recovery 15-item scale). The student will accompany the research coordinator for the administration of these and other patient surveys. The student will be introduced to new software (SPSS statistical software) and will produce a research abstract with data from the summer project that would fit into a larger manuscript. This type of student project should ultimately result in co-authorship on a peer reviewed publication.

Institution: University of Rochester

Mentor: Andrew Wojtovich, PhD

Project(s) Available:

Topic: Optogenetic control of mitochondrial reactive oxygen species - Reactive oxygen species (ROS) contribute to cellular damage in many pathologic processes, such as stroke. Mitochondria are a main site of ROS production and are central mediators of cell death. However, global antioxidant supplementation had little effect in clinical trials for diseases associated with increased oxidative damage. These clinical trials may have failed since mild levels of ROS are required to maintain cellular homeostasis. Moreover, ROS are emerging as signaling molecules that are required for the efficacy of several types of protective interventions. Thus, like many other physiological challenges, specific details such as dose, timing, and local environment contribute to ROS outcomes.

Overview: Oxidative damage is a major contributor to many diseases. However, in some situations reactive oxygen species (ROS) can help to protect the cell. We will take an optogenetic approach and utilize novel proteins that can generate ROS in response to light to determine what factors make some ROS beneficial and other ROS toxic. These new tools will be expressed as protein fusions using CRISPR/Cas9 technology with genes that encode known sites of ROS production. Using the genetic model organism *C. elegans* will further allow us to integrate our results with conserved stress response pathways and determine the role of ROS signaling in the context of neuronal ischemic sensitivity. This approach could potentially yield new therapeutic strategies for diseases in which ROS homeostasis has been disrupted.

Student Role: The student would be involved in *C. elegans* and cell culture, designing of experiments and collection of data. In addition, the student will learn how to isolate mitochondria and measure mitochondrial function. The student will be expected to keep accurate lab records and present at lab meetings.

Institution: University of Utah

Mentor: Natalie Silverton, MD

Project(s) Available: Measurement of Renal Blood Flow

There is a 30% incidence of Acute kidney injury (AKI) after cardiac surgery. AKI may be reduced by tailoring intra-operative hemodynamics to maintain renal perfusion and prevent renal ischemia. Currently there is no monitor of renal perfusion or renal ischemia available to guide kidney-protective hemodynamic management. Medullary ischemia is one of the important mechanisms of AKI. Urine oxygen tension (pUO₂) correlates well with medullary oxygen tension and renal blood flow, but is more easily accessible. We intend to develop and test a continuous monitor of urinary bladder pUO₂ and create a pUO₂ based goal-oriented hemodynamic management protocol. In this proposal, a fiber optic or hydrogel based pUO₂ probe will be integrated into the tip of a urinary catheter. Continuous pUO₂ measurements can then be used to guide therapy and hemodynamic management in the operating room and the intensive care unit. Opportunities for study design, data collection, and dissemination.

Institution: University of Utah

Mentor: Kai Kuck, PhD

Project(s) Available: Measurement of Renal Blood Flow

There is a 30% incidence of Acute kidney injury (AKI) after cardiac surgery. AKI may be reduced by tailoring intra-operative hemodynamics to maintain renal perfusion and prevent renal ischemia. Currently there is no monitor of renal perfusion or renal ischemia available to guide kidney-protective hemodynamic management. Medullary ischemia is one of the important mechanisms of AKI. Urine oxygen tension (pUO₂) correlates well with medullary oxygen tension and renal blood flow, but is more easily accessible. We intend to develop and test a continuous monitor of urinary bladder pUO₂ and create a pUO₂ based goal-oriented hemodynamic management protocol. In this proposal, a fiber optic or hydrogel based pUO₂ probe will be integrated into the tip of a urinary catheter. Continuous pUO₂ measurements can then be used to guide therapy and hemodynamic management in the operating room and the intensive care unit. Opportunities for study design, data collection, and dissemination.

Google Cardboard

We have developed a virtual reality game platform for pediatric anesthesia that provides a deeply immersive distraction. It is based on inexpensive, disposable hardware. The patient controls the game through breathing. The game incentivizes the patient to breathe in a way that promotes pre-oxygenation and deep inhalation of volatile anesthetic agent for induction. We propose to create a functional prototype and compare it in a clinical study to midazolam pre-medication. Opportunities for study design, data collection, and dissemination.

Advanced Video Laryngoscope

Laryngoscopes have hardly changed in the past 75 years. Video laryngoscopes have much more potential than what they deliver today, including the ability to detect anatomical features and the ability detect number of intubation attempts. The investigators are building a video database of intubation recordings and developing machine learning algorithm for video laryngoscopes. They need help classifying intubation videos, developing a survey, and provision of input for algorithm development. Opportunities for study design, data collection, and dissemination.

Institution: University of Utah

Mentor: Lara Brewer, PhD

Project(s) Available: Prompting Post-Op Patient to Breathe

The investigators are evaluating a “robonurse” device to keep patients safe. Opportunities for involvement include gaining clinical study experience, performing data analysis, and writing abstracts, manuscripts, and grants.

Institution: University of Utah

Mentor: Ken Johnson, MD

Project(s) Available: Prompting Post-Op Patient to Breathe

The investigators are evaluating a “robonurse” device to keep patients safe. Opportunities for involvement include gaining clinical study experience, performing data analysis, and writing abstracts, manuscripts, and grants. Anesthesia Perioperative Analytics at the U of U Covered Entity

Our department has an IRB umbrella to allow internal approval and electronic medical record data pull for retrospective research. This allows members of the department of anesthesiology who have completed IRB training requirements to quickly perform these types of studies without submitting full applications to the IRB. Data collected as standard of care may be reviewed.

Pain and inflammation biomarker signatures before and after total joint replacement: A look at opioid consumption.

The specific aims of this project are to determine the profile of differential mRNA expression, and plasma concentrations of selected proteins in pain, metabolism, and neuroinflammatory pathways, determine the profile of gene variants of selected proteins in pain, metabolism, and neuroinflammatory pathways., and explore the relationship between phenotype markers associated with physical function, pain interference, anxiety, depression, and pain catastrophizing with measures of gene variants, differential mRNA expression, and circulating concentrations of proteins involved in pain, metabolism, and neuroinflammatory pathways. Opportunities for involvement include data collection and analysis, abstract, grant and manuscript writing/authorship.

Institution: University of Utah

Mentor: Emily Hagn, MD

Project(s) Available: Echocardiographic Assessment of Cardiac Function during Outpatient Intravenous Lidocaine Infusions for Chronic Pain

The known effects of lidocaine and previous studies make it plausible that there may be previously unrecognized effects of lidocaine infusions on cardiac function, especially at higher-doses. In this study, we aim to use transthoracic echocardiography to assess whether or not changes in cardiac function are present during intravenous lidocaine infusions.

Comparison of changes in mRNA gene receptor expression on white blood cells between responders and non-responders of outpatient intravenous lidocaine infusions in chronic non-malignant pain

In hopes to improve patient selection for outpatient lidocaine infusion for chronic pain, the aim of this study is to explore the differences in mRNA gene receptor expression on white blood cells (WBCs) between responders and non-responders to current lidocaine infusions being performed at the University of Utah Pain Management Center. mRNA of interest include those that play a role in pain transmission and inflammation such as mu, adrenergic, immunomodulating, and metabolic-detecting receptors. These receptors are expressed both on neural tissue and on WBCs, thus allowing serum WBCs to act as a surrogate for pain transmission expression at neural junctions. This type of mRNA has been researched in chronic fatigue syndrome populations, demonstrating exaggerated post-exercise expression of WBC mRNA for several metabolic receptors associated with pain in patients who also described post-exercise malaise. Opportunities for study design, data collection, and dissemination.

Institution: University of Utah

Mentor: Markus Amann, PhD

Project(s) Available: Studies at the Utah Vascular Research Lab

Non-invasive and invasive studies in health and unhealthy human populations. Opportunities for study design, data collection, and dissemination.

Institution: University of Utah

Mentor: Derek Sakata, MD

Project(s) Available: Inhaled Remifentanyl

Elucidation of pharmacology and histology in swine. Participation in this study provides the opportunity to gain animal study experience, perform histologic tissue fixation

Evaluation of patient stress input device

Hand-held device measures hand clench, skin conductance, and has button for patient to press when in pain.

Opportunities include data analysis, device design refinement, manuscript writing/authorship.

Clinical evaluation of Intelliport Medication Management System for IV Bolus Injections.

Opportunities include study design, device design and refinement, clinical integration, and manuscript writing/authorship.

Prospective Real-time Operations OR Tool

Design of a prospective tool for analyzing OR scheduling. Opportunities include design of real-time HER data transfer protocols, user interface, financial/clinical algorithm development, abstract and manuscript writing/authorship.

Institution: University of Utah

Mentor: Talmage Egan, MD

Project(s) Available: PK/PD study of remifentanyl administration for chronic buprenorphine users: volunteer study in healthy subjects followed by prospective clinical study in long term opioid antagonist users. Opportunities for study design, data collection, and dissemination.

Institution: University of Utah

Mentor: Norman Taylor, MD, PhD

Project(s) Available: Resident

2017 - 2018 Advisor & Clinical Mentor, Lathan McCall, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Lathan McCall exclusively during the first two weeks of his anesthesiology residency, and served as his advisor and clinical mentor

2016 - 2018 Advisor & Clinical Mentor, Eric Abhold, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Eric Abhold exclusively during the first two weeks of his anesthesiology residency, and served as his advisor and clinical mentor

2015 - 2018 Advisor & Clinical Mentor, Mara Kenger, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Mara Kenger exclusively during the first two weeks of her anesthesiology residency

2014 - 2017 Supervisor, Grettel Zamora, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Grettel Zamora exclusively during the first two weeks of her anesthesiology residency

2013 - 2016 Advisor & Clinical Mentor, Jason Lee, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Jason Lee exclusively during the first two weeks of his anesthesiology residency, and I currently serve as his advisor and clinical mentor

2013 - 2014 Supervisor, Somi Kim, Massachusetts General Hospital, Oral Surgery Resident, I taught Dr. Somi Kim exclusively during the first two weeks of her anesthesia rotation during her residency

2012 - 2018 Supervisor, , Massachusetts General Hospital, Supervision and teaching of residents, 10 hrs/week, 45 weeks/year

2012 - 2018 Supervisor, , Massachusetts General Hospital, Intensive one on one tutorial of anesthesia resident in first month of training, 50 hrs/week, 2 weeks/year



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2012 - 2015 Advisor & Clinical Mentor, Caroline Hunter, Massachusetts General Hospital, Anesthesia Resident, I taught Dr. Caroline Hunter exclusively during the first two weeks of her anesthesiology residency, and served as her advisor and clinical mentor

Masters

2013 - 2014 Supervisor, , Massachusetts General Hospital, Supervision/research training of Masters student, 30 hours/week, 6 months/year

Medical Student

2018 Advisor/Mentor, John Hancock, University of Utah

2018 Advisor/Mentor, Sarah Nguyen, University of Utah

2012 - 2018 Supervisor, , Massachusetts General Hospital, Supervision and teaching of medical students, 10 hrs/week, 45 weeks/year

Institution: University of Vermont Medical Center

Mentor: Gabe Tharp, M.D., Ph.D.

Project(s) Available: Mechanisms of postoperative pulmonary complication (PPC) are not well defined. The current incidence of PPC is approximately 5% of all surgical cases. These complications range from mild respiratory failure to death. Patients at particularly high risk for PPC include those having laparoscopic abdominal surgery and the obese. This study is designed to measure markers of lung inflammation before and after robotic-assisted laparoscopic surgery in conjunction with state-of-the-art lung mechanics measurements. We hypothesize that subjects with impaired intraoperative lung mechanics will show elevated markers of lung injury following robotic-assisted laparoscopic abdominal surgery. We also hypothesize that obese patients will demonstrate more evidence of lung injury under these conditions. The results of this study will help us both understand novel mechanisms of PPC and also begin to design therapies to prevent PPC. The student will assist the principal investigator and co-investigators in the conduct of this prospective, observational study. The student will act as a member of the research team, including identifying and recruiting patients, assisting with data recording and sample gathering in the OR, and also with sample processing and storage. The student will have the opportunity to participate in data analysis.

Institution: University of Vermont Medical Center

Mentor: Mitchell Tsai, M.D., M.M.M.

Project(s) Available: Given the extent of research on OR management in the literature, it is surprising that there is little agreement across institutions on how to apply basic OR management metrics. For example, with trauma surgery services, managers may find it difficult to rationalize capacity-based services with traditional OR metrics: Higher utilization rates may decrease the capacity of the service, while allocating large blocks of OR time may need lead to poor utilization rates. The objective measurements, in essence, are conflicting. A Pareto optimal posits that none of the objective measurements can be improved without degrading another. By applying Pareto charts to OR management, this project will aim to demonstrate that the “optimum” for a surgical service occurs along a Pareto front. This goal is very different from traditional OR management, which attempts to find a single solution that satisfies the subjective preferences of a human decision maker under the pretense of objective data. The student will examine change in peri-operative processes using a systems-based multidisciplinary approach. The student will have the opportunity to explore operational and tactical issues directly affecting patient care and learn to understand the barriers and mechanisms to create change. The student will use a variety of resources to gather information, incorporate changes, and track outcomes, including database extraction tools and direct observation in anesthesia settings.

Institution: University of Vermont Medical Center

Mentor: Emmett Whitaker, M.D.

Project(s) Available: Preeclampsia is a hypertensive disease of pregnancy that affects up to 10% of pregnant women worldwide. While it is clear that offspring of pregnant women have neurocognitive deficits later in life, but the mechanisms that lead to these deficits remain unclear. The overall goal of our project is to examine the effects of preeclampsia on neonatal cerebrovascular function. Findings from this study will provide new insights into how offspring of preeclamptic mothers should be managed in the operating room with a particular focus on vascular dysfunction and cerebral perfusion. A FAER student would be involved in all aspects of the study, including small animal anesthesia and surgery, tissue harvest, data collection and analysis, and manuscript/abstract preparation.

Institution: University of Vermont Medical Center

Mentor: Melissa Davidson, MD

Project(s) Available: Self Determination Theory is a theory of human motivation addressing 3 universal, innate psychological needs (competence, autonomy, relatedness), which must be met in order for individuals to become more self-determined and intrinsically motivated. A multitude of SDT studies have been conducted in a variety of educational and health settings, including undergraduate and graduate medical education. Anesthesiology residents often complain they are not afforded enough autonomy during training, which according to SDT potentially thwarts their intrinsic motivation to learn. This study will compare resident and faculty perceptions of resident autonomy in one specific training activity (preoperative planning) using UVM Medical Center Department of Anesthesiology as a pilot prior to national survey. A validated SDT tool will be adapted for use and distributed to UVMMC faculty and residents. Data analysis and focus group meetings will be used to revise the survey for implementation nationally.

The student will work with principal investigator to adapt a validated tool for use in this study, which will include conducting focus groups with UVM Anesthesiology residents and faculty to elicit their impressions of and feelings about resident autonomy in preoperative anesthesia planning. The student will be responsible for distribution of the survey, data collection and analysis, and survey revision as needed. The student will also prepare the survey for national distribution, which may include assisting the PI in securing permission for survey distribution from relevant Anesthesiology organizations and/or identifying Anesthesiology Residency Programs' point persons. If time permits, the student may be involved in national distribution of the survey.

Institution: University of Washington

Mentor: Monica Vavilala, MD

Project(s) Available:

1. Pediatric TBI guideline adherence and outcomes in Argentina. We are conducting an RCT of an implementation science based program called PEGASUS in Argentina in a mixed method analysis. The student will assist with conducting focus groups and key informant surveys of the 15 sites to examine preparedness, knowledge and attitudes of TBI Guidelines. The student will learn survey methods and focus group methodology and apply it to survey development. The student will be a part of the publication that ensues and participate in the INSIGHT program with seminars and observations that are provided (www.hiprc.org).
2. Clinician readiness to accept Artificial Intelligence technology in provision of anesthesia care. The aim is to examine knowledge, attitudes and beliefs of providers regarding data sciences and to determine if predictive algorithms will be accepted by providers to augment clinical care. In a mixed method analysis, the student will assist with conducting focus groups and key informant surveys of the 15 sites to examine preparedness, knowledge and attitudes of TBI Guidelines. The student will learn survey methods and focus group methodology and apply it to survey development. The student will be a part of the publication that ensues and participate in the INSIGHT program with seminars and observations that are provided (www.hiprc.org).

Institution: University of Wisconsin

Mentor: Misha Perouansky, MD

Project(s) Available: Anesthetic Effects on Mortality in a Drosophila Model of Polytrauma:

An ongoing collaboration between Misha Perouansky, MD (Dept. of Anesthesiology), and David Wassarman, PhD (Department of Genetics), investigates the effect of general anesthetics on the outcome of traumatic brain injury in a fruit fly model. Part of the project is oriented towards testing flies of various genetic backgrounds. In order to be able to compare anesthetic sensitivity between genetically different fly strains, we are developing robust behavioral measures of anesthetic depth.

Role of the student:

The student will test one or more strains of flies with respect to one or more behavioral measures. Testing of one strain with one drug can be accomplished within two to three weeks. In addition to conducting experiments, analyzing and graphically presenting the results, the student will be encouraged to familiarize her/himself with literature pertinent to models of anesthetic mechanisms, models of traumatic brain injury, non-canonical actions of anesthetic agents and with the potential of flies as genetically accessible models of human disease.

Institution: University of Wisconsin

Mentor: Robert Pearce, MD, PhD

Project(s) Available: Mechanisms of memory suppression under anesthesia:

An essential goal of anesthesia is to prevent intraoperative memories from being formed. We are investigating how anesthetic modulation of GABA receptors in interneurons of the hippocampus contributes to this effect. We are particularly interested in the role of GABA-A receptors that incorporate alpha5 subunits (alpha5-GABAARs), as these receptors are highly enriched in hippocampus and have been implicated in memory control as well as other cognitive processes. For the current project, we are eliminating alpha5-GABAARs from specific types of interneurons and measuring the impact on memory formation, as well as its modulation by etomidate.

Role of the student:

The FAER student will participate in experiments to measure the firing of hippocampal pyramidal neurons that fire in specific locations in an environment (termed 'place cells') using a head-mounted camera, in the absence and presence of anesthesia. Experiments will be conducted in wild type mice and in genetically modified mice. Specific tasks will be animal handling, data collection, analysis using specialized software that is already developed, and preparation of results for presentation for at least one type of genetic manipulation.

Institution: UT Southwestern Medical Center

Mentor: Philip Greilich, M.D., MSc, FASE

Project(s) Available:

Study Topic: Applying Implementation Science Principles to the OR-to-ICU Handoff Process

Overview: My most recent work has focused on applying the principles of human factors and ergonomics, system engineering and implementation science to the development of transdisciplinary teams designed to improve healthcare delivery and research. This work aligns frontline clinicians with senior institutional leadership and national medical societies and provides guidance to transdisciplinary unit-based safety teams. This work has resulted in a series of successful local and national projects. My work as a Patient Safety Officer has highlighted the need to build and deploy evidence about changing healthcare practice to improve quality and outcomes. This area of scholarship aims to facilitate the spread of evidence-based healthcare management.

Student's Role: The student will be involved in the collection, organization, and storage of data related to Handoffs. He/She will be actively involved in interfacing with our collaborators around the nation who are key players in our Multicenter Handoff Initiative, including our human factor engineers at Embry-Riddle Aeronautical University. The student will be able to utilize their creativity and strategic thinking skills to help implement processes that complement clinician workflow. The student will also have the opportunity to present their project to faculty.

Institution: UT Southwestern Medical Center

Mentor: Ravi Joshi, M.D.

Project(s) Available:

Study Topic: Patient Blood Management – Impact of Transfusion Algorithm and Point-of-Care Testing on Blood Product Utilization and Outcomes in Cardiac Surgery.

Overview: Although transfusions are often considered lifesaving measures, increasing evidence has shown that blood transfusions are an independent risk factor for many adverse clinical outcomes including increased mortality, stroke, major adverse cardiac events (MACE), renal failure, and infection. This project will use data collected from a Blood Conservation and Hemostasis in Cardiac Surgery survey distributed to the members of the Society of Cardiovascular Anesthesiologists (SCA) to determine if the use of transfusion algorithms supported by point-of-care (POC) testing has a significant impact on blood utilization. Institutions that utilize transfusion algorithms with POC testing will be compared to those utilizing only one or none of these best practice interventions. The Society of Thoracic Surgery (STS) database will be used to examine the impact of these two best practices on blood transfusion and risk-adjusted clinical outcomes.

Student's Role: The student will be involved in the collection, organization, and storage of data from the Society of Cardiovascular Anesthesiologists blood management survey. In addition, the student will collect, organize, and store data from the STS database inquiry and searches. The student will also be involved in data analysis and presentation on preliminary results, possibly an abstract. He/She will meet routinely with Dr. Joshi, attend organizational meetings, collaborative research meetings, departmental grand rounds, and will be directed to online research resources.

Institution: Vanderbilt University Medical Center Program

Mentor: Edward Sherwood, MD, PhD

Project(s) Available: Augmentation of Innate Antimicrobial Immunity with Toll-like receptor (TLR) Agonists
Infection, especially with antibiotic resistant pathogens, is a common and important problem in perioperative and critically ill patients. This project will examine the ability of TLR ligands to improve host resistance to infection with common pathogens that exhibit a high incidence of antibiotic resistance (*Pseudomonas*, *Acinetobacter*, *Staphylococcus*).

The project assignment will be determined through discussion with the PI and based on the student's existing skills and experience. It is expected that students will gain independence and run their own experiments as their experience advances. However, we are committed to providing strong mentorship to assure a meaningful learning experience.

Students will gain experience with mouse models of infection with particular emphasis on systemic and local infection with *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Specific skills will include preparing, growing and quantifying bacterial cultures, inoculating mouse with bacteria, harvesting blood and tissues for quantitative bacterial culture, measurement of leukocyte recruitment into sites of infection using flow cytometry and measurement of cytokine production using ELISA and Bioplex assays.

Further experiments will include assessment of leukocyte metabolism using a Seahorse XFe96 metabolic flux analyzer and gene expression using qPCR, Western blotting and ELISA. The student will learn cell culture techniques, especially related to developing cultures of bone marrow-derived macrophages.

Students will participate in experimental design, data acquisition and data analysis. They will be required to present results at our weekly lab meeting and have a good understanding of the literature related to their project. Based on their contributions, students may serve as co-author on peer-reviewed publications generated through their work, a goal that several previous summer students have attained.

Institution: Vanderbilt University Medical Center Program

Mentor: Jonathan Wanderer, MD, MPhil

Project(s) Available: Understanding the Relationship between Patient Satisfaction and Formal Measurements of Care Quality

Anesthesiologist performance is being increasingly measured by government agencies, hospitals and at a departmental level, using a variety of sources of information. While the importance of patient satisfaction in health care is clear, and the necessity of developing care quality metrics is apparent, little work has been done to evaluate the relationship between patient satisfaction and care quality metrics in anesthesia. We hypothesize that patients who rank their satisfaction with anesthetic care highly also have correspondingly high objective measurements of care quality.

The student will be responsible for formulating a data analysis plan, identifying target variables to ascertain which covariates need to be adjusted for and selecting the formal measurements of care quality. After understanding these elements, the student will perform an analysis to determine how and if patient satisfaction is related to objective measures of care quality, as currently defined. No programming or computer skills are required as we have a highly functional engineering team which can provide ready access to electronic patient data. Statistical support is available through our team biostatistician should this be required.

Institution: Vanderbilt University Medical Center Program

Mentor: Matthias Riess, MD, PhD

Project(s) Available: Use of Copolymer-based Cell Membrane Stabilizers to Provide Cardiac Protection against Myocardial Infarction

Myocardial infarction remains a leading cause of morbidity and mortality world-wide. Although prevention has high priority, early reperfusion, i.e. reintroduction of blood flow, remains of utmost importance after myocardial

ischemia has occurred. Oxidative stress on reperfusion and concomitant molecular and metabolic changes, however, lead to significant injury in addition to the ischemic insult itself. Subsequent cellular dysfunctions largely contribute to ischemia/reperfusion (IR) injury and cell death. We have shown that copolymer-based cell membrane stabilizers (CCMS) improve in-vitro cellular viability when given at the start of reoxygenation following hypoxia, and improve recovery from IR injury in the in-vivo heart when given upon reperfusion. CCMS may represent an innovative therapy that can break the chain of deleterious cellular and molecular events set in motion by myocardial IR.

The student will actively participate in experiments to test the hypothesis that CCMS improve cellular viability and attenuate cytotoxicity using cultured coronary artery endothelial cells and cardiomyocytes in state-of-the-art in-vitro models of hypoxia/reoxygenation. On a daily basis, the student will work with a research assistant or doctoral student. The student will acquire all the necessary technical skills for the summer project, and will be mentored on data collection and analysis, as well as scientific writing. Subsequent local and/or national poster presentations are encouraged and strongly supported. This focused basic science research experience in a laboratory with a long tradition of mentoring FAER students will be complemented by frequent opportunities to shadow anesthesiologists in different clinical environments and simulations at a premier academic institution. For more information on the Riess lab visit: <https://ww2.mc.vanderbilt.edu/1anesthesiology/45920>.

Institution: Vanderbilt University Medical Center Program

Mentor: Robert Freundlich, MD, MS

Project(s) Available: Understanding the Relationship between Patient Satisfaction and Formal Measurements of Care Quality

Anesthesiologist performance is being increasingly measured by government agencies, hospitals and at a departmental level, using a variety of sources of information. While the importance of patient satisfaction in health care is clear, and the necessity of developing care quality metrics is apparent, little work has been done to evaluate the relationship between patient satisfaction and care quality metrics in anesthesia. We hypothesize that patients who rank their satisfaction with anesthetic care highly also have correspondingly high objective measurements of care quality.

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Institution: Vanderbilt University Medical Center Program

Mentor: Julia Bohannon, PhD

Project(s) Available:

Project Title: Enhancing Resistance to Infection after Burn Injury with Toll-like Receptor Agonists

Project Description: Severely burned patients are at significantly increased risk of acquiring deadly infections with opportunistic pathogens. This is due not only to the loss of the protective skin barrier, but also due to a number of injury-induced immune alterations that prevent the burned patient from developing a proper immune response to clear microbial infections. Prior work has demonstrated that multiple toll-like receptor (TLR) 4 agonists can prime the immune response in burn-injured animals, leading to enhanced innate immune responses and augmented resistance to a variety of clinically relevant infectious organisms (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida albicans*). The mechanisms responsible for augmentation of antimicrobial protection are unknown. The aims of this project are to 1) determine the signaling pathways initiated by TLR activation during priming that lead to augmented host immune responses, 2) determine the cellular and

molecular mechanisms that are altered by TLR agonists leading to enhanced antimicrobial functions, 3) determine whether other TLR agonists can mediate similar augmented resistance against infection.

Student Role: Students will gain experience in mouse models of burn injury with subsequent infection, tissue and blood harvesting, cell isolation techniques, flow cytometry, bacterial growth and plating, ELSIA, and cell culture. Students will be required to present their data at weekly lab meetings. Additional responsibilities will include coordination of personnel and supplies for experiments, performance of experiments, and care of the mouse colonies both before and during experiments. Students will be involved in management of data records, assistance with preparation of oral and poster presentations, as well as manuscript preparation, with the opportunity to serve as co-author on both meeting abstracts and manuscripts.

Institution: Washington University

Mentor: Ben Palanca, MD, PhD, MSc

Project(s) Available:

1. Inpatient PreOperative Sleep Quality in Cardiac Surgical Patients. Sleep satisfies a fundamental need for restoring mental and physiologic processes. Unfortunately, sleep quality is notoriously poor in the inpatient hospital setting with unclear implications for surgical recovery. The trainee will become an integral member of the Prognosticating Delirium Recovery Outcomes using Wakefulness and Sleep Electroencephalography, P-DROWSE, an R01-funded investigation on the relationships between postoperative delirium and EEG markers of sleep and wakefulness. (S)he will be involved in patient recruitment, data acquisition, and analyses of the EEG markers. The student will also have direct interactions with sleep technologists and sleep medicine physicians.
2. EEG Markers During the Recovery from Electroconvulsive Therapy. Electroconvulsive therapy (ECT) is an effective therapy for depression but requires the induction of generalized seizures through the electrical stimulation of the scalp. Electroencephalography (EEG) is typically employed to evaluate the initiation and cessation of seizure activity but the predictive measures of ECT efficacy and side effects are poorly characterized. A trainee with an analytical background will analyze EEG recorded during the recovery from ECT and ketamine anesthesia. These records will be compared to EEG recorded during sham ECT and ketamine anesthesia. The student will learn fundamentals of ECT and quantitative EEG analysis through custom-written MATLAB software. S(he) will have direct interactions with collaborating epileptologists and psychiatrists.
3. Functional and Structural Magnetic Resonance Imaging Markers Associated with Postoperative Delirium. Delirium after surgery is associated with poor clinical, functional, and cognitive outcomes. The neural substrates contributing to delirium remain unclear. Thirty-nine cardiac surgical patients underwent perioperative magnetic resonance imaging (MRI) and serial delirium assessments. A student with a prior background in MRI will evaluate relationships among diffusion tensor imaging and resting-state functional connectivity measures in these patients.

Institution: Washington University

Mentor: Michael Avidan, MBBCh, FCASA

Project(s) Available: Telemedicine Control Tower for the Operating Room: Navigating Informatics, Care and Safety (TECTONICS) R01 NR017916-01A1

Project Description

Perioperative morbidity and mortality is a public health priority. With the annual increase of surgical cases there is a need for research into the potential utility of a telemedicine-based control center for the operating room to assess risk, diagnose negative patient trajectories, implement evidence-based practices, and improve outcomes.

Student Role

The student's primary role will be to participate in the Anesthesiology Control Tower together with an attending anesthesiologist and a resident anesthesiologist. In this role, the student will learn about perioperative telemedicine, machine learning, randomized clinical research, and the clinical practice of anesthesia. The student will have a specific project related to determining if the Anesthesiology Control Tower can improve, through structured communications with anesthesiologists, fellows, residents and CRNAs, perioperative quality of care metrics including temperature, antibiotic redosing, mean arterial pressure, mean airway pressure with mechanical ventilation, blood glucose, anesthetic concentration, and efficient fresh gas flow.

This project has been ongoing for over five years and is continuously gaining momentum. Its feasibility is demonstrated by this successful track record, and by funding from NSF, AHRQ and the Washington University Faculty Practice Plan. Participation in TECTONICS is an exciting opportunity for a medical student to participate in a unique perioperative telemedicine experiment. Through their participation, they will gain insights into technological advances in healthcare and the modern practice of anesthesiology

Institution: Washington University

Mentor: Michael Montana, MD, PhD

Project(s) Available: Bilateral Pectoralis Nerve Block for Postoperative Pain Management in Pediatric Patients undergoing Cardiac Surgery - This project will be a double-blinded prospective pilot study of pectoralis nerve blocks for the treatment of postoperative pain in pediatric patients undergoing elective surgeries that require median sternotomy. The inclusion ages are 2-18 year olds and there is a target enrollment of 50 patients, 25 in each arm (placebo vs. treatment). Regional anesthesia for median sternotomy is understudied in general, and in pediatric patients specifically. Furthermore, many pediatric patients with congenital heart disease undergo multiple staged surgeries early in life, and are exposed repeatedly to sedatives and opioids. Given the risks of sedative habituation, tolerance, and withdrawal in children administered opioids, alternative approaches for analgesia are needed. The pediatric cardiac surgery group at our institution has enthusiasm for this project. A medical student team member would receive an opportunity for learning, and to be a primary team member (with appropriate mentorship) in multiple critical arenas, including IRB protocol drafting and submission, trial design, implementation of clinical studies/trials, collection of clinical research data, multimodal analgesia, cardiac anesthesia, cardiac surgery, and statistical analysis.

Institution: Washington University

Mentor: Joanna Abraham, PhD

Project(s) Available: ICU End-of-Rotation Transitions of Care- Transitions in care between resident physicians have become recognized as a common cause for medical errors due to frequent communication breakdown. Yet, with increasing restrictions to resident work hours, the number of patient handoffs have increased considerably. End-of-rotation or service transition in care between residents in ICUs are detrimental to patient care quality and safety. Early studies focusing on this particular transition of care suggest these patients experience increased length of stay and cost. Residents and other training physicians rotate through hospital rotations continuously around the world, yet little evidence is reported on what happens to their hospitalized patients during these transitions. We are planning to conduct an exploratory multi-site study with the following aims:

Aim 1: To determine mortality and lengths of stay for patients exposed to end-of-rotation transitions in care as compared with patients not exposed to end-of-rotation transitions in care.

Aim 2: To determine if residents undergoing end-of-rotation transition are experiencing burnout more frequently as compared with residents not undergoing care transition. We will also explore the current processes by which residents are transitioning care at the end-of-each rotation to determine workflow patterns that may be contributing to burnout.

Aim 3: To determine if the outcomes of patients undergoing end-of-rotation transitions are related to the degree of burnout their care team is experiencing.

Aim 4: To determine the type of resident to resident handoff most commonly performed in the ICU setting at end-of-rotation transitions.

The medical student will assist with the research tasks and also gain skills in the following:

- Data collection using mixed-methods
- Chart reviews and extraction
- Data analysis
- Literature review and synthesis for manuscript analysis.

Institution: Washington University

Mentor: Anne Drewry, MD, MSCI

Project(s) Available: Sepsis: Approximately 20 percent of septic patients present with hypothermia, rather than fever, at the onset of infection. These patients have twice the mortality of non-hypothermic patients, but there is limited data as to why these patients have worse outcomes. The objective of this group's research is to determine whether critically ill septic patients who present with hypothermia exhibit impaired immunity which prevents

pathogen clearance and increases susceptibility to opportunistic infections. We expect that our results will provide significant insight into the timing and pathogenesis of sepsis induced-immunosuppression.

We are performing a prospective clinical study to examine the immunological phenotypes of critically ill septic patients who present with and without hypothermia and to determine whether hypothermic septic patients have increased susceptibility to opportunistic infections and reactivation of latent viruses. We identify critically ill septic patients who present with and without hypothermia and measure cell surface receptor expression and cytokine secretion serially throughout the septic course. We also monitor the patients for acquisition of opportunistic infections and measure serial blood levels of commonly reactivated viruses.

The student involved in this project would help screen the patient censuses of the medical and surgical ICUs to identify appropriate patients for inclusion and would approach patients and families to obtain consent for participation. The student would also assist with data collection from the electronic medical record and enter data into an online data management system. The student would also have the opportunity to observe and/or participate in performing cytokine secretion assays in the research laboratory.

Institution: Washington University

Mentor: Simon Haroutounian, BSc.Pharm, MSc.Pharm, PhD

Project(s) Available:

1. Comparison of Somatosensory Profiles of Patients with Neuropathic Pain Due to Diabetic Peripheral Neuropathy vs Chemotherapy-induced Peripheral Neuropathy. Painful peripheral neuropathies are a common etiology for chronic neuropathic pain. Current therapeutics options, which are mainly pharmacological (tricyclic antidepressants, SNRIs, gabapentin, pregabalin, and opioids), provide only limited relief, and are associated with major adverse effects. There is a research effort to understand the particular characteristics of neuropathic pain conditions of different etiologies, in an attempt to develop targeted approaches. We recently completed two clinical trials (NCT 02394951 and NCT02363803), using identical psychophysical approaches to characterize patients with diabetic painful neuropathy (DPN) and chemotherapy-induced peripheral neuropathy (CIPN). The trainee will contribute to writing a paper which will compare the somatosensory profiles (collected as a battery of standardized quantitative sensory tests) and pain characteristics of patients with DPN and CIPN (using the already collected data).
2. Development of Brain-computer Interface Device for the Treatment of Upper Extremity Neuropathic Pain. In collaboration with Eric Leuthardt's laboratory in the Neurological Surgery department, we are initiating a study where patients with neuropathic pain in the upper extremity will be treated by a newly developed prototype device that delivers non-painful stimulation driven by individual patient electroencephalogram (EEG) output that is associated with pain relief. The trainee will be involved in subject recruitment and consent, subject training, data collection. Once the project is completed, the trainee will have the opportunity to contribute to data analysis and manuscript preparation.

Institution: Washington University

Mentor: Broc Burke, M.D., Ph.D.

Project(s) Available: Development and Validation of a Bedside Functional Connectivity Imaging System In Acute Stroke Recovery Using Diffuse Optical Tomography - Given the enormous impact of stroke on global health, the rapid evolution of stroke during acute recovery, and known stroke related functional connectivity (fc) disruptions demonstrated with fMRI, this study develops a bedside imaging technique utilizing Diffuse Optical Tomography (DOT) to measure clinically relevant fc changes in patients during acute ischemic stroke recovery (first 72 hours). A medical student team member would receive an opportunity for learning, and to be a primary team member



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(with appropriate mentorship) in clinical, technical, and administrative domains, including subject recruitment, image acquisition, image analysis, and IRB protocols.

Institution: Yale-New Haven Medical Center Program

Mentor: Laura E. Niklason, M.D., Ph.D.

Project(s) Available: Vascular Regenerative in vitro

This project studies the growth and remodeling of tissue engineered vessels that are cultured from differentiated vascular cells. The impact of discrete physical cues, growth factors, and cell source are studied for their impact on graft mechanics in vitro and host cell remodeling in vivo.

Students will perform experiments in cell biology, biochemistry, and molecular biology to study events involved in vascular regeneration from differentiated and precursor cells in vitro. Specifically, students will learn the mechanics of vascular smooth muscle cell culture, as well as characterization by immunostaining and RT-PCR. Students will screen differentiated and stem cell-derived smooth muscle cells for markers of differentiation.

Institution: Yale-New Haven Medical Center Program

Mentor: Robert Brian Schonberger, M.D., M.H.S.

Project(s) Available:

1) Integrating perioperative care into the treatment of poorly controlled cardiovascular risk-factors

Atherosclerotic cardiovascular disease (ASCVD) is common, treatable, and deadly. While comprehensive guidelines assist physicians in the diagnosis and management of ASCVD, numerous studies show that patients consistently suffer from ongoing and widespread diagnostic and treatment failures. We propose to use the surgical encounter as a pathway for identifying and addressing these failures.

Students will obtain training on accessing our local perioperative database in order to gain access to diagnostic histories of patients involved in Dr. Schonberger's clinical studies. Students will learn basics of informatics, observational research, and possible roles of anesthesiologists in ASCVD treatment.

2) Childhood Lead Poisoning and the Anesthesiologist

While many modifiable factors may influence long-term cognitive outcomes in children, exposures to anesthetics do not appear to be among them. In contrast, overwhelming evidence demonstrates the long-term morbidity incurred by children due to modifiable environmental lead exposures. This project seeks to describe the prevalence of undertreated childhood lead poisoning among patients presenting for pediatric surgery at a tertiary care medical center. It will provide the foundation for possible prospective interventional studies.

Institution: Yale-New Haven Medical Center Program

Mentor: Paul Heerdt, M.D., Ph.D.

Project(s) Available: Integrative models of cardiopulmonary dynamics: The goal of these studies is to develop methods for combining data generated by independent monitoring systems into a common platform and then use these data to build near real-time models of cardiac dynamics. The student's role will be to use existing data sets generated in the experimental laboratory, clinical operating rooms, ICU, and cardiac catheterization facility to test hypotheses related to novel analytic methods.

Institution: Yale-New Haven Medical Center Program

Mentor: Robert LaMotte, Ph.D.

Project(s) Available: Assessment of Pain Mechanisms

Peripheral nerve sensation of pain is complex, with multi-factorial influences such as co-stimuli, inflammation, and learning all impacting pain outcome. Our laboratory focuses on the basic mechanisms of pain signaling in peripheral and dorsal root ganglion neurons, to increase our understanding of acute and chronic pain syndromes. Student will participate in laboratory assessments of pain mechanisms in animals and humans, and study means of pain modulation. Specifically, our laboratory studies pain mechanisms in the dorsal root ganglion in a rat model

of acute pain. Students will learn analysis of electrophysiological signals and will compare those arising from naïve animals to those arising from animals undergoing various interventions to modulate neural response to painful stimuli.

Assessment of Mechanisms of Cutaneous Itch

Cutaneous itch is an under-studied phenomenon that is associated with substantial discomfort and morbidity in some cases. Our laboratory is working as part of a consortium of investigators to tease out basic events that occur in the sensation and transduction of cutaneous itch. Student will participate in human and basic biochemical studies of the mechanisms of sensation of itch, and in the modulation of pathologies resulting in chronic sensation of itch. Studies of cutaneous itch are performed in normal human volunteers, using targeted pruritic stimuli. Students will learn analysis of electrophysiological signals to pruritic stimuli, and will compare those arising from naïve individuals to those arising from subjects undergoing various interventions to modulate neural response to pruritic stimuli.

Institution: Yale-New Haven Medical Center Program

Mentor: Manuel Lopes Fontes, M.D.

Project(s) Available: Evaluation of safety and efficacy of antithrombin for preventing thrombosis in VAD patients. Antithrombin III is a natural anti-coagulant that works by activating endogenous heparin moieties to prevent the progression of the coagulation cascade. When complex with heparin, antithrombin III binds and inactivates both thrombin and factor Xa. This study will look at the efficacy of antithrombin III administration in the prevention of thrombosis in patients receiving ventricular assist devices (VADs). Antithrombin III is administered peri-operatively to patients enrolled in the study, and thrombotic events intra-operatively and post-operatively are tallied. Safety and effectiveness of the drug will be studied.

Students will participate in various aspects of the clinical research, including patient recruitment and consent, and evaluation of medical records. In addition, students will assist in data collection and collation, as well as analysis in collaboration with statistical experts. Data to be collected and analyzed will include hemodynamic data, quantification of transfusion volumes, measurements of PT, PTT, platelet count, and ACT. Comparison of coagulation parameters in patients receiving Antithrombin III, with those patients

Institution: Yale-New Haven Medical Center Program

Mentor: Robert LaGasse, M.D.

Project(s) Available: Peer-review model of quality of care in Anesthesia.

Measurement of performance and quality outcomes in Anesthesia is difficult and has not been implemented in most academic medical centers across the US. By quantifying quality of care and outcomes, we can provide guidance on how to improve physician care, and we can measure improvements over time and across centers. Medical students participating in this project will work with Dr. Lagasse on implementing a structured peer review model for subspecialty care in the Department of Anesthesiology, measure performance through statistical process control of adverse outcomes, analyze causal factors of adverse events, coordinate performance improvement through systematic changes, and quantify the effects of those system changes through continuous monitoring.

Institution: Yale-New Haven Medical Center Program

Mentor: Miriam Treggiari, M.D., Ph.D., M.P.H.

Project(s) Available:

Project 1: Pre-hospitalization sleep duration and quality in relation to subsequent postoperative complications. Poor sleep quality and short sleep duration have been associated with elevated risk for several complications; however, the relationship between sleep and surgical outcomes has not been well characterized. In this study, we

plan to assess the association between pre-operative sleep attributes and subsequent postoperative complications.

Project 2: Hospitalization induced sleep changes among older surgical patients

It is known that sleep quality is disrupted, and sleep architecture is altered after surgery. In this study, we will focus on elderly patients and determine changes in sleep quality, characteristics, and circadian dysregulation occur after surgery and the role of exposure to various anesthetics.

Medical students participating in either of these projects will work with Dr. Treggiari on recruiting participants and collecting preoperative and postoperative data on sleep characteristics and other risk factors. They will then collect and analyze the data with the goal of writing an abstract for submission to the ASA and then completing a full manuscript.