FOUNDATION FOR ANESTHESIA EDUCATION AND RESEARCH

Medical Student Anesthesia Research Fellowship
2010 Host Departments and Projects

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Section B. Detailed Project Listings

Host Institution Name: The Children's Hospital of Philadelphia

Research Topic: Enteric astrogliosis and neurokinin-1 receptor activation in the persistent abdominal pain of pediatric AIDS.
Mentor(s): Lynnae Schwartz, M.D.
Student Role: Bench research assistance from methodology to data analysis with possible publication.

Research Topic: Isoflurane neurotoxicity in neonatal rats: effects on astroglia and neural progenitors.
Mentor(s): Lynnae Schwartz, M.D.
Student Role: Bench research assistance from methodology to data analysis with possible publication.

Research Topic: Role of immune-neural interactions in mediating pain during development.
Mentor(s): Gordon Barr, Ph.D.
Student Role: Bench research assistance from methodology to data analysis with possible publication.

Research Topic: Modulation of opiate induced analgesia, tolerance and dependence by the immune system during development.
Mentor(s): Gordon Barr, Ph.D.
Student Role: Bench research assistance from methodology to data analysis with possible publication.

Research Topic: Gene co-expression analysis in neural tissue during development.
Mentor(s): Gordon Barr, Ph.D.
Student Role: Bench research assistance from methodology to data analysis with possible publication.

Host Institution Name: Children's Memorial Hospital

Research Topic: Chronic Pain Management in Children" The Use of Mind Body Therapies, Biofeedback Mechanism for Pain Relief.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Research Topic: Development of a small volume sampling technique for Fentanyl pharmacokinetic, pharmacodynamic and pharmacogenetic analysis in preter and term neonates with and without cyanotic congenital heart disease.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Research Topic: Postoperative Pain Control in Children Undergoing Laparoscopic Appendenctomy: Comparison of Peripheral Nerve Blocks to Local Anesthetic Infiltration.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Research Topic: Pain Management in Children Undergoing Primary Cleft Palate Repair.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Research Topic: Transversus Abdominis Plane Blocks for Infants and Children for Postoperative Pain Control: Is it the Concentration or Volume of Local Anesthetic Solution that Improves Analgesia?
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Research Topic: Experience with the Transversus Abdominis Plane Block for Post-Operative Pain at Children's Memorial Hospital.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Part icipant

Research Topic: Regional Anesthesia Database: A Multi-Institutional Prospective Database to Record Potential Adverse Effects and Complications Associated with Regional Anesthesia in Children.
Mentor(s): Santhanam Suresh, MD, FAPP
Director, Pain Management Service & Research
Children's Memorial Hospital
Profesor of Anesthesiology and Pediatrics
Northwestern University's Feinberg School of Medicine
Student Role: Active Participant

Host Institution Name: Cleveland Clinic

Research Topic: Regional analgesia and recurrence of breast cancer after potentially curative surgery
Mentor(s): Daniel Sessler, MD
Student Role: Patient enrollment, measurements, data analysis

Research Topic: Dexmeditomidine and postoperative delerium
Mentor(s): Leif Saager, MD
Student Role: Patient enrollment, measurements, data analysis

Research Topic: PerfecTemp vs. forced-air for maintenance of intraoperative normothermia
Mentor(s): Daniel Sessler, MD
Student Role: Patient enrollment, measurements, data analysis

Host Institution Name: Columbia University

Research Topic: Airway GABAA receptors and reactive airway disease (basic)
Mentor(s): Charles Emala,M.D. Professor of Vice-Chair for Research
Student Role: assist with measuring airway smooth muscle contraction in vitro

Research Topic: Neurokinin and GABAB receptor signaling (basic)
Mentor(s): Charles Emala,M.D. Professor of Vice-Chair for Research
Student Role: assist with in vitro cell signaling experiments in airway smooth muscle and epithelial cells

Research Topic: Nicotinic agonists as analgesic drugs (basic and clinical)
Mentor(s): Pamela Flood,M.D. Associate Professor of Clinical Anesthesiology
Student Role: assist with cellular biochemistry (basic) or patient recruitment (clinical)

Research Topic: Determinants of post-operative cognitive dysfuntion (clinical)
Mentor(s): Eric Heyer, M.D.,Ph.D. Professor of Clinical Anesthesiology
Student Role: assist with patient recruitment and adminstration of neurocognitive tests

Research Topic: Acute kidney injury after liver ischemia-reperfusion injury (basic)
Mentor(s): H.T. Lee, M.D., Ph.D. Associate Professor and Vice-Chair for Laboratory Research
Student Role: assist with in vitro cell signaling experiments

Research Topic: Volatile anesthetics and lipid kinases (basic)
Mentor(s): H.T. Lee, M.D., Ph.D. Associate Professor and Vice-Chair for Laboratory Research
Student Role: assist with in vitro cell signaling experiments

Research Topic: Dexmedetomidine and radioconstrast nephropathy (basic)
Mentor(s): H.T. Lee, M.D., Ph.D. Associate Professor and Vice-Chair for Laboratory Research
Student Role: assist with in vitro cell signaling and mice experiments

Research Topic: Epidemiology of anesthesia-related morbidity and mortality (epidemiological)
Mentor(s): Guohau Li, M.D., Ph.D. Professor of Anesthesiology and Epidemiology
Student Role: assist with literature review, research design, data collection, and manuscript development

Research Topic: Anesthesia safety indicators (epidemiological)
Mentor(s): Guohau Li, M.D., Ph.D. Professor of Anesthesiology and Epidemiology
Student Role: pursuing an independent study under the supervision of established investigators and within ongoing research projects

Research Topic: Beta-adrenergic receptor genotype and preterm labor (basic and clinical)
Mentor(s): Richard Smiley, M.D., Ph.D. Professor of Clinical Anesthesiology and Obstetrics
Student Role: assist with patient recruitment and laboratory genotyping

Research Topic: Leptin transport and neuroendocrine signaling in pregnancy (basic and clinical)
Mentor(s): Richard Smiley, M.D., Ph.D. Professor of Clinical Anesthesiology and Obstetrics
Student Role: assist with patient recruitment and laboratory assay for neuropeptides

Research Topic: Beta-adrenergic receptor genotype and progress of labor (basic and clinical)
Mentor(s): Richard Smiley, M.D., Ph.D. Professor of Clinical Anesthesiology and Obstetrics and Pamela Flood, M.D. Associate Professor of Clinical Anesthesiology
Student Role: assist with patient recruitment and laboratory genotyping

Research Topic: Comparison of clonidine and fentanyl for later first stage labor analgesia (clinical RCT)
Mentor(s): Richard Smiley, M.D., Ph.D. Professor of Clinical Anesthesiology and Obstetrics
Student Role: assist with patient recruitment and clinical assessment

Research Topic: Time patterns of births and anesthetic interventions in labor and delivery suite (health services assessment/research)
Mentor(s): Richard Smiley, M.D., Ph.D. Professor of Clinical Anesthesiology and Obstetrics and Pamela Flood, M.D. Associate Professor of Clinical Anesthesiology
Student Role: data gathering and entry

Research Topic: Post-anesthesia emergence agitation and delirium in children (clinical)
Mentor(s): Lean Sun,M.D. Professor of Anesthesiology and Pediatrics
Student Role: assess children in the recovery room using validated emergence agitation scale

Research Topic: Pediatric anesthesia neurodevelopment assessment project (PANDA)
Mentor(s): Lean Sun,M.D. Professor of Anesthesiology and Pediatrics
Student Role: review medical records to identify eligible study subjects; develop and implement survey of pediatric anesthesia practice in participating children's hospital study site; participate in all other relevant aspects of project

Research Topic: Anesthesia and Alzheimer's disease biomarkers in humans (basic)
Mentor(s): Robert Whittington, M.D. Associate Professor of Clinical Anesthesiology
Student Role: assist with cellular biochemistry in mice

Research Topic: Anesthesia and neuropathogenic pathways associated with Alzheimer's disease (clinical)
Mentor(s): Robert Whittington, M.D. Associate Professor of Clinical Anesthesiology
Student Role: assist with patient recruitment and administration of neurocognitive tests

Research Topic: Research in Neuroscience: Various Projects
Mentor(s): Neil Harrison, Ph.D. Professor of Anesthesiolgy and Pharmacology, Vice-Chair for Neurobiology Research
Student Role: laboratory studies of the electrophysiology and molecular biology of GABAA channels

Research Topic: Comorbidities and Clinical Outcomes of Malignant Hyperthermia
Mentor(s): Guohua Li, MD, PhD (Professor of Anesthesiology and Epidemiology) and Lena S. Sun, MD (Professor of Anesthesiology)
Student Role: pursuing an independent study under the supervision of established investigators and within ongoing research projects

Research Topic: Benchmarking Intraoperative Parameters

Mentor(s): Guohua Li, MD, PhD (Professor of Anesthesiology and Epidemiology) and Mitchell Berman, MD, MS (Associate Professor of Anesthesiology)
Student Role: pursuing an independent study under the supervision of established investigators and within ongoing research projects

Research Topic: Measuring Severity of Postoperative Complications
Mentor(s): Guohua Li, MD, PhD (Professor of Anesthesiology and Epidemiology)
Student Role: pursuing an independent study under the supervision of established investigators and within ongoing research projects

Host Institution Name: Dartmouth Hitchcock Medical Center

Research Topic: Stress Cortisol: Effects on Circulating and Transmigrated Human Monocytes
Mentor(s): Mentor(s): Mark P. Yeager, MD Professor of Anesthesiology & Medicine
Student Role: Student Role: The student will conduct a research study to test the effect of a short intravenous infusion of cortisol on peripheral blood leukocyte activation and functional responses. This will involve both in vivo and in vitro work. Leukocytes will be taken from subjects' peripheral blood and following their transmigration from peripheral blood into experimentally induced skin blisters. Leukocytes will then be examined for both phenotypic and functional responsiveness to ex vivo stimulation with bacterial endotoxin

Research Topic: Anesthesia-Associated Neuroapoptosis in Neonatal Swine
Mentor(s): Simon C. Hillier M.B.,Ch.B. Professor of Anesthesiology
Student Role: There is a growing body of animal evidence suggesting that the administration of anesthetic drugs during critical periods of brain development is associated with widespread neuronal apoptosis. Although the human clinical significance remains uncertain, there are obvious potential implications for children and pregnant women that require anesthesia. Our laboratory has significant experience with a piglet model of neurotrauma and has utilized experimental techniques that have been modified to develop a porcine model of anesthetic-induced apoptosis.

Research Topic: Investigating the behavioral and psychological effects of providing sedation for Voiding Cystourethrograms in Children.
Mentor(s): Joseph P. Cravero, MD Professor of Anesthesiology
Student Role: We continue to look at the effects of pain and stress during procedures on the post-procedural behavior of children. At CHaD we provide sedation for VCUG's - many other institutions do not. Our current project involved obtaining an inventory of personality and stress state from family prior to starting the procedure. We obtain data on the nature of the child's emotional state during the procedure and follow up with post hospitalization behavior questionnaires 2 days and 2 weeks after surgery. We have partnered with an institution that gives no sedation for the same procedure and will be comparing our outcomes.

Host Institution Name: Emory University School of Medicine

Research Topic: Evaluation of patients with heparin induced thrombocytopenia (HIT)
Mentor(s): Jerrold H. Levy, M.D., Professor of Anesthesiology
Student Role: Patients with HIT are at greater risk for multiple complications including prothrombotic and other adverse effects. The student will follow outcomes of thrombocytopenia in intensive care unit (ICU) patients and follow antibody titers to PF4 as a marker for HIT and outcomes. The antibody result

will be quantified and outcomes quantified to levels as expressed as an absorbance values reflecting the relative titer. The validated Parsonnet risk score will be included in the different models to adjust for the effect of patient comorbidities. Students will also participate at specific times on ICU rounds to understand the importance and clinical relevance of these data collected.

Research Topic: Evaluation of postoperative hypertension
Mentor(s): Jerrold H. Levy, M.D., Professor of Anesthesiology
Student Role: Students will evaluate intensive care unit (ICU) patients who develop hypertension requiring therapy. Information to be obtained will include perioperative outcomes including blood pressure (BP) maximum (max) and minimum (min), ICU length of stay (LOS), therapeutic agents, transitioning, and outcomes. Adverse events, duration of therapy, and other pharmacoeconomic data will be collected Students will also participate at specific times on ICU rounds to understand the importance and clinical relevance of these data collected.

Research Topic: Stem cell transplantation therapy for brain disorders
Mentor(s): Ling Wei, M.D., Professor of Anesthesiology
Student Role: Students will learn cellular, molecular and animal techniques for basic and pre-clinical research. The lab is specialized in stem cell cultures, differentiation, and transplantation methods into animal models of ischemic stroke, neuropathic pain and mechanism of brain damage.

Research Topic: Mechanism and treatment of inflammatory/neuropathic pain in animal models
Mentor(s): Shan Ping Yu, M.D., Ph.D., Professor of Anesthesiology
Student Role: The investigation will study how NMDA receptor subunits can regulate pain and explore a novel treatment of inflammatory/neuropathic pain using erythropoietin. Students will have the opportunity to participate in animal and cell culture experiments. He or she will learn basic cellular and molecular techniques such as cell death assays and gene expression assays, and will perform animal behavior tests as well as pain measurements.

Research Topic: Retrospective review of hemostatic management in cardiac surgical patients
Mentor(s): Kenichi Tanaka, M.D., M.Sc., Associate Professor of Anesthesiology
Student Role: Data collection from medical records, basic analysis, modeling (if person has advanced skills in biochemistry or statistics)

Research Topic: The Molecular Mechanisms of General Anesthetics
Mentor(s): Andrew Jenkins, Ph.D., Assistant Professor of Anesthesiology and Pharmacology
Student Role: The successful applicant will learn the techniques of whole cell patch clamp electrophysiology, site directed mutagenesis and numerical modeling of stochastic processes. Having perfected these techniques, the student will use these methods to measure the effect of general anesthetics, other perioperative drugs and novel compounds on the function of native and mutant GABA(A) receptors. The goal will be to make a significant contribution to an ongoing research project and earn an authorship on a peer-reviewed article.

Research Topic: Depth of Anesthesia, Inflammatory Markers and Clinical Outcome in Cardiac Patients
Mentor(s): Chantal Kerssens, Ph.D., Assistant Professor of Anesthesiology
Student Role: The successful applicant will participate in perioperative clinical research and record anesthesia depth indicators including EEG bispectral index (BIS) in cardiac patients undergoing elective surgery. Anesthesia depth and other critical physiological variables will be related to the acute-phase inflammatory response by taking blood samples postoperatively and by examining the incidence of relevant clinical complications. The student will contribute significantly to all aspects of the study including data reduction, analysis, and academic presentations.

Host Institution Name: Massachusetts General Hospital, Department of Anesthesia, Critical Care, & Pain Medicine

Research Topic: Where do potent intravenous general anesthetics act on human GABA-A receptors? We use electrophysiology to study the actions of etomidate, propofol, and alphaxalone on their major molecular targets, GABA-A receptors. Cysteine mutations in putative drug binding sites are characterized for effects on GABA-A receptor function and anesthetic sensitivity, as well as for accessibility to cysteine-reactive probes. Cysteine protection is used to establish proximity of drugs to different amino acids.
Mentor(s): Associate Professor of Anaesthesia Stuart A. Forman, MD, PhD
Student Role: Students will work with the PI and postdocs. They will learn basic laboratory skills and methods for receptor expression and electrophysiological studies in Xenopus oocytes, with the aim of characterizing a new mutant receptor. Student will also read background literature related to the lab's research and participate in weekly laboratory meetings and journal clubs

Research Topic: The MGH Center for Translational Pain Research is a combined preclinical and clinical research facility devoted to studying pain mechanisms and exploring new pain therapies. Clinical research topics include 1) new therapies for chronic pain, 2) opioid-induced hyperalgesia, 3) quantitative sensory testing in clinical research and practice, 4) interactions between chronic pain and depression and opioid addiction, and 5) alternative medicine such as acupuncture. Preclinical research topics include 1) neural and molecular mechanisms of neuropathic pain, opioid tolerance and addiction, and opioid-induced hyperalgesia, 2) endogenous cannabinoids and neuropathic pain, 3) central glucocorticoid receptors and pain and opioid tolerance, and 5) peripheral and central mechanisms of burn injury-induced pain and radicular low back pain. The preclinical laboratory employs a variety of neuroscience research tools, including behavioral and pharmacological tools, autoradiography, ELISA, HPLC, patch clamping, cell culture, siRNA technique, Western blot, in situ hybridization, real-time PCR, EMSA. The potential candidate will have ample opportunities to participate in one of many preclinical or clinical research projects funded by multiple NIH grants.
Mentor(s): Associate Professor Jianren Mao, MD, PhD
Student Role: To learn state-of-the-art neuroscience research methodologies including molecular biology (e.g., real-time PCR, Wester blotting), pharmacology, electrophysiology (e.g., patch clamping), autoradiography (e.g., receptor binding assay), ELISA, protein kinase assay, animal behavioral testing and to learn basic clinical research skills including study design, data analysis, and regulatory issues.

Research Topic: 1. Studies of the role of nitric oxide and soluble guanylate cyclase in the molecular mechanisms regulating the changes in cardiac shape and function in response to hemodynamic challenge.
2. Studies of the role of bone morphogenetic proteins in cardiac development and the pathogenesis of pulmonary arterial hypertension.
Mentor(s): William Thomas Green Morton Professor of Anaesthesia Kenneth Bloch, MD
Student Role: Students participate in an intensive and focused research experience in cardiovascular biology and pathophysiology using genetically-modified mice and cutting-edge technologies ranging from echocardiography and physiology to molecular and cellular biochemistry.

Research Topic: My research focuses on elucidating the molecular mechanisms by which general anesthetics cause anesthesia and side effects. We locate anesthetic binding sites on receptors such as the GABAaR using agents that are both general anesthetics and photoaffinity labels. These covalently attach to their sites of action. We also study these binding sites using biophysical techniques such as x-ray crystallography, electron spin resonance spectroscopy and fluorescence.

Mentor(s): Mallinckrodt Professor of Pharmacology Keith W. Miller, D. Phil.
Student Role: Students will focus on a single problem commensurate with their skills. For example, they might employ biochemical techniques, such as proteolysis and HPLC, to characterize which region of the receptor binds anesthetics. Mass spectrometry is used to sequence these fragments.

Research Topic: Role of inhaled Nitric Oxide (NO) in Malaria
Role of cGMP pathway and other mediators in acute ischemia and vasomotor activity
Mentor(s): Jenney Professor of Anaesthesia Warren M. Zapol, MD
Student Role: To study a murine model of Plasmodia Berghei ANKA malaria . Especially the effect of inhaled nitric oxide to enhance survival. To define the mechanisms for this salutary effect including the paracidal and immunosuppressant nature of inhaled NO.

Research Topic: 1. To test the hypothesis that immobilization-induced muscle wasting results from decreased anabolic effects of insulin (insulin resistance). 2. To test the hypothesis that simple immobilization leads to inflammation and increased alpha7 acetylcholine receptor (alpha7AChR) expression and that alpha7AChR agonist will attenuate the inflammation and muscle wasting associated with immobilization.
Mentor(s): Anesthetist-in-Chief, Shriners Hospital for Children, Jeevendra Martyn, MD
Student Role: The student will participate in intensive and focused research experience in neuromuscular physiology and pharmacology. The projects will use signal transduction, biochemical pharmacology, in vivo muscle physiology and transgenic mouse models to test these hypotheses.

Research Topic: My research focuses on understanding how general anesthetics work and using that information to develop new anesthetic agents. This research project focuses on characterizing the pharmacological actions of an interesting, new I.V general anesthetic that we have developed in our laboratory. Such characterization includes measuring its anesthetic potency in animals, defining its actions on GABAA receptors using oocyte electrophysiology, defining its rate of metabolism using an in-vitro assay and in animals, and studying its affect on blood pressure and breathing
Mentor(s): Associate Professor of Anaesthesia Douglas E. Raines, MD
Student Role: Depending on the student's interest and experience, he/she will learn anesthetic pharmacology and the laboratory techniques needed to characterize this new compound in an enjoyable and productive setting.

Host Institution Name: Mayo Clinic

Research Topic: ***Sex Differences in Asthma***: Incidence, severity and complications of asthma differ between men and women. Asthma symptoms fluctuate with menstrual cycles and pregnancy, suggesting that sex steroids (estrogens, progesterone) modulate airway tone (bronchoconstriction vs. bronchodilation) in asthma.
In our laboratory, we are using human airway and lung tissues from male vs. female patients to test the hypothesis that estrogens facilitate bronchodilation and alleviate the effects of airway inflammation (i.e. estrogens are protective in women). To this end, we use real-time confocal microscopic imaging of fluorescently-tagged estrogen receptors, imaging of intracellular Ca^{2+} dyes, force measurement studies, biochemical and molecular biological techniques to determine cellular signaling mechanisms by which estrogens and inflammatory molecules interact to modulate airway tone.
Mentor: Y.S. Prakash, MD, PhD
Student Role: The student will be assigned an independent, focused project to study the mechanisms by which sex steroids can affect asthma. Working with the PI and his research team, the student will a) build/expand a solid knowledge base of airway structure and function, mechanisms of asthma, and how

sex steroids work; b) learn state-of-the-art fluorescence microscopic imaging techniques to study living cells and tissues, that will then be applied to study estrogen receptor signaling in human airway; c) apply advanced biochemistry and molecular biology techniques to study interactions between estrogens and inflammatory molecules. The relevance of such bench-based research to the clinical situation will be highlighted. Additional research experiences will include journal clubs, departmental seminars, and exposure to operating room environments. The expectation is that over a 10-12 week period, the student will accumulate sufficient data for presentation at a national meeting or contribute to a peer-reviewed manuscript.

Research Topic: ***Estrogen Modulation of Airway Epithelium***: In women, asthma symptoms fluctuate with menstrual cycles and pregnancy, suggesting that sex steroids (especially estrogens) modulate airway tone (bronchoconstriction vs. bronchodilation).

In our laboratory, we are exploring the hypothesis that estrogens enhance nitric oxide (NO) production in airway epithelium, thus facilitating bronchodilation. Using human airway and lung tissues from male vs. female patients and real-time microscopic fluorescence imaging of NO, as well as biochemical and molecular biological tools, we are exploring cellular signaling mechanisms by which estrogens and inflammatory molecules interact to modulate bronchodilation.

Mentor: Y.S. Prakash, MD, PhD

Student Role: The student will be assigned an independent, focused project to study how estrogens modulate NO signaling in human airway epithelial cells. Working with the PI and his research team, the student will a) build/expand a solid knowledge base of airway structure and function, mechanisms of asthma, and how sex steroids work; b) learn state-of-the-art fluorescence microscopic imaging techniques to study NO production in living cells, that will then be applied to study estrogen receptor signaling; c) apply advanced biochemistry and molecular biology techniques to study interactions between estrogens and inflammatory molecules in terms of NO signaling. The relevance of such bench-based research to the clinical situation will be highlighted. Additional research experiences will include journal clubs, departmental seminars, and exposure to operating room environments. The expectation is that over a 10-12 week period, the student will accumulate sufficient data for presentation at a national meeting or contribute to a peer-reviewed manuscript.

Research Topic: ***Mechanisms of Neonatal Lung Injury***: Preterm birth is associated with a host of problems with growth and maturation. In particular, exposure to high O2 levels (hyperoxia) at birth in order to maintain oxygen saturations results in neonatal lung injury that is further associated with a much higher incidence of reactive airway disease and childhood asthma. The mechanisms underlying such abnormal lung development and function (bronchopulmonary dysplasia) are still being investigated; however, it is clear that hyperoxia alters the structure and function of airway smooth muscle (ASM).

In our laboratory, we are using fetal and adult human ASM tissues and cells to determine the cellular mechanisms by which hyperoxia worsens smooth muscle signaling relevant to bronchoconstriction and bronchodilation. We hypothesize that hyperoxia alters neurotransmitter (e.g. neurokinins) and growth factor (e.g. neurotrophin) signaling that leads to enhanced airway contractility. To this end, we use real-time fluorescence imaging of intracellular Ca^{2+}, mitochondrial and other dyes, as well as biochemical and molecular biological techniques to determine cellular signaling mechanisms in fetal ASM cells altered by hyperoxia.

Mentor: Y.S. Prakash, MD, PhD

Student Role: The student will be assigned an independent, focused project to study fetal vs. adult human ASM cells that are exposed to normoxia vs. different levels of hyperoxia. Working with the PI and his research team, the student will a) build/expand a solid knowledge base of airway and lung development, and of neonatal lung injury; b) learn state-of-the-art fluorescence microscopic imaging techniques to study Ca^{2+} and other signaling molecules in living cells, that will then be applied to study hyperoxia effects; c) apply advanced biochemistry and molecular biology techniques to study hyperoxia

effects on ASM structure and function. The relevance of such bench-based research to the clinical situation of neonatal lung injury and bronchopulmonary dysplasia will be highlighted. Additional research experiences will include journal clubs, departmental seminars, and exposure to operating room environments. The expectation is that over a 10-12 week period, the student will accumulate sufficient data for presentation at a national meeting or contribute to a peer-reviewed manuscript.

Research Topic: ***Cigarette Smoke Effects on Airway Reactivity***: Smoking as well as secondhand smoke are known to worsen asthma, bronchitis and other airway diseases. In our laboratory, we are using human airway smooth muscle (ASM) tissues and cells from patients with known clinical histories (asthmatic, smokers etc.) to test the hypothesis that cigarette smoke exposure alters the production and signaling of key growth factors (called neurotrophins; e.g. nerve growth factor, brain-derived neurotrophic factor) that exacerbate airway reactivity and the effects of airway inflammation. We use advanced biochemical and molecular biology tools, real-time imaging of living cells, force measurement studies, and (where appropriate) mouse models of asthma and cigarette smoke exposure to examine mechanisms by which cigarette smoke affects ASM function.
Mentor: Y.S. Prakash, MD, PhD
Student Role: The student will be assigned an independent, focused project to study the effect of cigarette smoke on human ASM cells and tissues. Working with the PI and his research team, the student will a) build/expand a solid knowledge base of cigarette smoke exposures and their effect on airway function, asthma and other diseases; b) learn state-of-the-art fluorescence microscopic imaging techniques to study living cells and tissues, that will then be applied to study cigarette smoke effects in human airway; c) apply advanced biochemistry and molecular biology techniques to study interactions between cigarette smoke and growth factors (neurotrophins). Additional research experiences will include journal clubs, departmental seminars, and exposure to operating room environments. The expectation is that over a 10-12 week period, the student will accumulate sufficient data for presentation at a national meeting or contribute to a peer-reviewed manuscript.

Research Topic ***Mechanisms of Pulmonary Hypertension***: Pulmonary arterial hypertension (PAH) is a devastating disease with high morbidity and mortality. The mechanisms underlying PAH are being activel investigated.

In our laboratory, we are using human (patients with or without PAH) as well as mouse pulmonary artery endothelial cells and smooth muscle cells (ASM) to test the hypothesis that growth factors called neurotrophins (e.g. nerve growth factor; brain-derived neurotrophic factor) play a key role in the balance between pulmonary vasoconstriction (e.g. Ca^{2+} and other signaling pathways) and vasodilation (e.g. nitric oxide and prostacyclin pathways). We further believe that neurotrophins modulate the role of arginase in endothelial cells. To this end, we use real-time imaging of fluorescently-tagged neurotrophins and their receptors (Trk proteins), imaging of intracellular Ca^{2+}, NO and other parameters, force measurement studies, and biochemical and molecular biological techniques to determine underlying cellular signaling mechanisms in both human and mouse models.
Mentor Y.S. Prakash, MD, PhD
Student Role The student will be assigned an independent, focused project to study how neurotrophins modulate NO and prostacyclin signaling in human pulmonary artery endothelial cells. Working with the PI and his research team, the student will a) build a solid knowledge base of pulmonary artery structure and function, mechanisms of PAH, and neurotrophin signaling; b) learn state-of-the-art fluorescence microscopic imaging techniques to study NO production in living cells, that will then be applied to study neurotrophin effects; c) apply advanced biochemistry and molecular biology techniques to study interactions between neurotrophins and inflammatory molecules in terms of NO signaling. The relevance of such bench-based research to the clinical situation will be highlighted. Additional research experiences will include journal clubs, departmental seminars, and exposure to operating room environments. The

expectation is that over a 10-12 week period, the student will accumulate sufficient data for presentation at a national meeting or contribute to a peer-reviewed manuscript.

Host Institution Name: Medical College of Georgia

Research Topic: Nanomedicine: Correction of single gene disorders with nanoscale repair machines. This effort is part of the NIH Nanomedicine Roadmap Initiative and focuses on the design and testing of ZFN- and RAG-based prototypes of gene correction machines. We target the mutation of sickle cell anemia, a single gene β-hemoglobinopathy, because its molecular defect is well characterized and clinical cure of this devastating disease is limited to bone marrow transplantation. Once deployed to hematopoietic stem cells, these nanoscale machines are engineered to produce a double-stranded DNA break at the site of the sickle cell mutation. This will induce the cell's DNA repair machinery to "fill the defect" with sequence information from a healthy DNA repair template.
Mentor(s): Steffen E. Meiler, M.D., Associate Professor, Vice Chair of Research
Student Role: This exciting project will give the student the opportunity to interact with scientists from leading institutions (e.g. MIT, Caltech, Georgia Tech, Cold Spring Harbor, and others) during our monthly center videoconferences, to become familiar with the biology of hematopoietic stem cells and the principles of genetic engineering, and acquire in-depth knowledge about the clinical phenotype of sickle cell disease and its management in the operating room. The student will be guided by seasoned scientists in the laboratory, gain "hands-on" experience with various experimental assays and learn to assemble an effective research presentation.

Research Topic: Mechanisms of inhaled agents.
Annually 25 – 30 million patients are anesthetized in the United States; however, our understanding of how inhaled anesthetics achieve their desired (and adverse) effects is incomplete. To address this question, we decided to use a genetic approach to identify novel regulators of volatile anesthetic function in the model organism, Caenorhabditis elegans. We are currently screening ~ 17,000 genes of the C. elegans genome, employing state-of-the-art gene silencing methodology by RNA interference. Heretofore undiscovered genes are studied for their role in anesthetic effect by function and structure analysis. Methods applied include a feeding screen in C. elegans with ~17,000 E. coli/RNAi clones, computer-assisted mutant phenotype analysis, de-novo protein synthesis for novel genes, tissue expression studies by whole-mount immunohistochemistry and/or in vivo GFP-transgene imaging, construction of transgenic animals with dominant-negative and constitutively active gene constructs, classic genetics, focused gene arrays, proteomics, and others.
Mentor(s): Steffen E. Meiler, M.D., Associate Professor, Vice Chair of Research
Student Role: The student will be directly involved in many of the daily, practical tasks of this project, which according to interest and background will range from growing nematode populations, assisting in the RNAi feeding screen, conducting anesthetic assays and other pharmacological studies, participating in the quantification of mutant phenotypes, and more. Additionally, the student will acquire a general knowledge of current models of how different inhaled and intravenously administered anesthetic drugs are thought to achieve their effects. This theoretical background in combination with the research activities will be of tremendous value to the student in trying to develop an appreciation for the intended effects and short-comings of modern anesthetics during the clinical component of this fellowship.

Research Topic: Clinical and biological effects of nitric oxide on clinical severity of sickle cell disease. A major clinical symptom of patients with sickle cell disease (SCD), which affects 80,000 to 100,000 patients in the U.S., is vaso-occlusive painful crisis and those with crisis are often required to be hospitalized for treatments. Hydroxyurea has been used for treating both adult and pediatric patients with SCD, but at least one third to half of those patients are resistant to hydroxyurea therapy. Nitric oxide

(NO) has a diverse clinical and biological effects on clinical manifestations of SCD. For instance, inhalation of low concentrations of NO has been successfully used for treating patients with acute chest syndrome. Our previous in vivo and in vitro studies also show that inhalation of low dose NO augments oxygen affinity of sickle hemoglobin in SCD patients, which is largely attributable to inhibitory activities of NO in the polymerization of sickle hemoglobin under hypoxic conditions. Additionally, our recent clinical studies clearly demonstrate that NO decreases pain scores in SCD patients with vaso-occlusive painful crisis. High-level expression of fetal hemoglobin in SCD patients is associated with mild clinical manifestations. Our preliminary studies indicate that NO exhibits a strong inducing activity of fetal hemoglobin in erythroid cells, but the underlying mechanisms remain unknown. These clinical and experimental lines of evidence provide a rationale for the use of NO in the treatments of SCD patients. These projects are to investigate clinical and biological effects of NO in SCD and to establish NO as a novel therapeutics of this disorder.
Mentor(s): Tohru Ikuta, M.D. Ph.D., Associate Professor; Steffen E. Meiler, M.D., Associate Professor, Vice Chair of Research
Student Role: The student will acquire in-depth knowledge of the genetic basis and pathophysiology of sickle cell disease and learn of the special challenges that surgery and anesthesia pose to these patients. Additionally, the student will have the opportunity to participate in a myriad of experimental approaches ranging from physiology-based assays (such as intravital microscopy in genetic animal models) to assisting in advanced cell biology, molecular, biophysical, and hematological methods.

Host Institution Name: Medical College of Wisconsin

Research Topic: Anesthetic-Induced Cardioprotection
Mentor(s): Zeljko J. Bosnjak, PhD, Professor and Vice Chair for Research of Anesthesiology, Professor of Physiology
Student Role: Our laboratory has focused on the role of mitochondria in normal myocardial functions as well as in pathologies. One of the hypotheses is that a short exposure to volatile anesthetics provides protection for the heart against ischemic damage by preserving mitochondrial structure and function. This hypothesis is investigated in an interdisciplinary approach. We are using physiological, pharmacological and molecular techniques as well as proteomics to demonstrate that there are quantifiable alterations in protein expression, channel function and mitochondrial bioenergetics after their exposure to inhalational anesthetics. Here are some specific methodologies pertaining to the mitochondrial isolation and functional (bioenergetics) studies using isolated mitochondria:
Measurements of ATP synthesis: The rate of mitochondrial ATP synthesis is calculated and expressed as μmol ATP • min^{-1} • mg mitochondrial $protein^{-1}$ ATP concentration is expressed as nmol ATP • mg mitochondrial $protein^{-1}$.
Measurements of membrane potential: Mitochondrial membrane potential is determined spectrofluorometrically utilizing the dye Rhodamine 123. The maximal depolarization capacity of mitochondria can be determined after a challenge with carbonylcyanide-p-trifluoro-methoxylphenol hydrazone and Antimycin A, a combination of mitochondrial uncouplers.
Measurements of oxygen consumption: Oxygen consumption is measured polarographically with a Clark-type oxygen electrode in a water-jacketed chamber. The electron transport chain is examined using different site-specific substrates. All respiration rates are expressed as μmol of oxygen consumed mg $protein•L^{-1}•min^{-1}$.
Detection of reactive oxygen species: Mitochondrial reactive oxygen species are monitored with a fluorescent probe, dichlorohydro-fluorescein diacetate, which is oxidized in the presence of hydrogen peroxide to dichlorohydro-fluorescein.

Research Topic: Diabetes, Hyperglycemia, and Cardioprotection

Mentor(s): Judy R. Kersten, MD, Professor and Vice Chair of Anesthesiology, Professor of Pharmacology and Toxicology
Student Role: The student will be involved in all aspects of the project exploring the mechanisms whereby diabetes and hyperglycemia increase cardiovascular risk. Specifically, the student will be involved in: experimental design; conduct in vivo experiments; conduct in vitro experiments using Western blotting, immunoprecipitation, immunohistochemistry, real time PCR, and other techniques; analysis of data; scientific writing; oral presentation of results; interacting with scientists in other disciplines; and participation in journal club. The student will also have experience in the operating room observing patients with cardiovascular disease undergoing anesthesia and surgery, and will discuss the potential implications for translational research.

Research Topic: KATP Channels in Normal and Injured Sensory Transduction
Mentor(s): Constantine D. Sarantopoulos, MD, PhD, Associate Professor of Anesthesiology, Pharmacology, and Toxicology
Student Role: Student(s) participating in the project will be given the opportunity to get familiar, assist, and become involved in several aspects pertinent to the project. These include:

1) Understand the basic concepts of pain transduction and pathophysiology of neuropathic pain.
2) Assist in surgical techniques aiming at producing experimental neuropathic pain in rats; understand relevance to pain in humans.
3) Assist or independently conduct behavioral-sensory testing to confirm the presence of neuropathic pain in rats.
4) Train in techniques of dorsal root ganglia harvesting, neuronal dissociation, plating, and neuronal culturing.
5) Prepare special solutions for culturing neurons, as well as for identifying special membrane ionic currents.
6) Training and assisting in electrophysiological experiments using the patch-clamp technique.
7) Training and assisting in immunohistochemistry and molecular (RT-PCR) techniques.
8) Literature search, readings, and assist in paper writing and/or abstract presentation.

Research Topic: Role of Mitochondrial Function in Genetically Determined Resistance against Cardiac Ischemia-Reperfusion Injury
Mentor(s): Matthias Riess, MD, PhD, Assistant Professor of Anesthesiology
Student Role: Student(s) participating in the project will be given the opportunity for training and the participation in the planning, conducting, analyzing, and presenting of isolated heart experiments pertinent to the above topic.

Research Topic: Anesthetic Protection of Endothelial Function from Ischemia-Reperfusion Injury in Humans
Mentor(s): Thomas J. Ebert, MD, PhD, Professor of Anesthesiology
Student Role: Data acquisition during human studies in young volunteers and spreadsheeting and analysis of data.

Research Topic: Cardioprotection by Volatile Anesthetics
Mentor(s): David C. Warltier, MD, PhD, Professor and Chairman of Anesthesiology
Student Role: Student(s) in the laboratory participate actively in ongoing research programs investigating the mechanisms of anesthetic cardioprotection that are conducted using cell culture and animal models of ischemia and reperfusion injury. The student(s) will acquire skills in small animal surgical techniques, vascular and cardiac physiological nonitoring, and tissue and cell preparation for molecular (e.g. Western blotting, PCR) and biochemical analyses (e.g. ozone chemiluminescence). Student(s) will particpate actively in weekly laboratory meetings by giving periodic presentations of their

work. Student(s) are instructed on accurate data collection and are mentored in scientific technical writing skills. Student(s) interact on a daily basis with technical staff, visiting scientists, postdoctoral fellows, and junior faculty. The Anesthesiology Department annually hosts several world-renowned speakers for invited seminars for which all students and faculty are encouraged to attend.

Research Topic: Mitochondrial Cation Exchangers: Modeling Experimental Data
Mentor(s): David F. Stowe, MD, PhD, Professor of Anesthesiology and Physiology
Student Role: Conduct experiments in isolated cardiac mitochondria using specific cation dye spectrophotofluorimetry, assess changes in cation flux and the effect of cation exchange inhibitors, and help develop models of cation exchange that underlie mitochondrial bioenergetics.

Research Topic: Role of Calcium in the Cellular Mechanisms of Pain Following Nerve Injury
Mentor(s): Thomas A. Stekiel, MD, Associate Professor of Anesthesiology
Student Role: The student will have responsibility for planning protocols, generation of data, analysis and presentation of findings in a project involving measurement of rat pain behavior, rat surgery, cell dissociation, and recording of cellular events in sensory neurons, under my supervision.

Research Topic: Role of Calcium in the Cellular Mechanisms of Pain Following Nerve Injury
Mentor(s): Quinn Hogan, MD, Professor of Anesthesiology
Student Role: The student will have responsibility for planning protocols, generation of data, analysis, and presentation of findings in a project involving measurement of rat pain behavior, cell dissociation, and recording of cellular events in sensory neurons, under my supervision and the fellow.

Host Institution Name: Medical University of South Carolina

Research Topic: Locating Errors Through Networked Surveillance (LENS): The Society of Cardiovasculary Anesthesiologist Foundation FOCUS Initiative.
Mentor(s): James H Abernathy, MD, MPH, Assistant Professor, Chief, Division of Cardiothoracic Anesthesiology
Student Role: Data Collection and data analysis. Assist in manuscript preparation.

Research Topic: Assessment of midazolam, dexmedetomodine, and low-dose ketamine for sedation post cardiopulmonary bypass.
Mentor(s): James H Abernathy, MD, MPH, Assistant Professor, Chief, Division of Cardiothoracic Anesthesiology; Eric Nelson, DO, Instructor
Student Role: Enroll patients in a randomized trial. Assist in data collection and analysis. Assist in abstract and manuscript preparation.

Research Topic: The Ergonomics of OR design. How OR design can improve communication between multiple teams of caregivers.
Mentor(s): James H Abernathy, MD, MPH, Assistant Professor, Chief, Division of Cardiothoracic Anesthesiology
Student Role: Collect and analyze data about OR design using principles of human factors engineering. Assist in design and development of the OR of the future.

Research Topic: Improving human - machine interaction in the Cardiac Operating Room.
Mentor(s): James H Abernathy, MD, MPH, Assistant Professor, Chief, Division of Cardiothoracic Anesthesiology

Student Role: Collect and analyze data using principles of human factors engineering. Be involved in designing how the equipment in our ORs interact with the people. Assist in design and development of the OR of the future.

Research Topic: Does altering reaming technique decrease embolic load to the lungs? A study in orthopedic patients using Transesophageal Echocardiography.
Mentor(s): Matthew D McEvoy, MD, Assistant Professor, Vice Chair for Education; James H Abernathy, MD, MPH, Assistant Professor, Chief, Division of Cardiothoracic Anesthesiology
Student Role: Enroll patients in a randomized trial. Assist in data collection and analysis concerning TEE and blood gas values. Assist in abstract and manuscript preparation.

Research Topic: TMS Effects on Pain Perception
Mentor(s): Jeffrey J. Borckardt, PhD and Scott T. Reeves, MD, MBA
Student Role: The investigators are currently examining the effects of minimally invasive brain stimulation technologies including transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) on pain perception in a large cohort of healthy adult participants as well as in a cohort of patients with chronic neuropathic pain. These studies also involve functional MRI and diffusion tensor imagining experiments.

Students will get hands-on experience with experimentally-induced pain methodology including thermal pain threshold, pain tolerance and suprathreshold magnitude estimation procedures, mechanical pain threshold assessments and wind-up pain assessment methods. Students will get hands-on experience conducting functional MRI (fMRI) procedures using a pain evocation paradigm as well as conducting fMRI image analysis. Further, students will review the current research on the neurophysiological effects of electrical stimulation of the human cortex, learn and practice administration of cortical stimulation treatments, learn and practice cortical target location techniques, and implement TMS dosing strategy algorithms with the investigators.

Research Topic: TMS in the Management of Postoperative Pain
Mentor(s): Jeffrey J. Borckardt, PhD and Scott T. Reeves, MD, MBA
Student Role: The investigators are currently examining the effects of transcranial magnetic stimulation of the left prefrontal cortex on post-operative pain and opioid usage in a double-blind, sham-controlled clinical trial.

Students will review the current research on the neurophysiological effects of electrical stimulation of the human cortex, learn and practice administration of cortical stimulation treatments, learn and practice cortical target location techniques, and implement TMS dosing strategy algorithms with the investigators in the post-anesthesia care unit among a large cohort of patients immediately following bariatric surgery. Students will also be directly involved in collecting clinical pain and mood ratings from these patients as well as assessing side-effects and TMS-related post-operative complications during their post-operative hospital stays.

Research Topic: Randomized, Placebo-controlled Trial of the Effects of Dexmedetomidine and Gabapentin on PONV and acute pain in Bariatric Laparoscopic Surgical Patients (N=150)
Mentor(s): Matthew D. McEvoy, MD
Student Role: Data collection and data analysis and clinical participation in the anesthesia care team for these patients.

Research Topic: The Effect of Cognitive Aids on Performance During Simulated, High-Stakes Perioperative Events
Mentor(s): Matthew D. McEvoy, MD
Student Role: Participation in randomized educational trial, including enrolling subjects, collecting and analyzing data, running the simulator and acting as part of the standardized team, and abstract preparation.

Host Institution Name: Mount Sinai School of Medicine

Research Topic: Evaluations of outcomes relative to geriatric surgical patients
Mentor(s): Jeffrey Silverstein, MD
Student Role: Students will design and execute a project relative to their interests which may be small clinical studies or restrospective data reviews. Students will be expected to participate in some of the design and understand the regulatory requirements of their projects, although they will be ready to initiate upon arrival of the student.

Research Topic: Combined spinal-epidural analgesia vs. epidural analgesia
Mentor(s): Yaakov Beilin, MD
Student Role: Screening and recruiting patients and assisting with data collection and analysis.

There are two commonly used techniques for labor analgesia, epidural analgesia (epidural) and the combined spinal-epidural (CSE) technique. Epidural analgesia is the historical gold standard because of its efficacy and flexibility. There are a number of issues with labor epidural analgesia that have prompted some to seek alternative techniques. First, the time from epidural catheter placement until the patient is comfortable is variable, but depending on the local anesthetic, it can take up to 30 minutes. Other disadvantages of labor epidural analgesia include maternal hypotension, inadequate analgesia (15-20% of cases) and, even with the very dilute local anesthetic solutions, motor block. The CSE technique provides more rapid and intense analgesia than epidural analgesia and causes less lower extremity motor block. The use labor analgesia although popular (with > 90% of patients at MSH receiving one or the other) may lead to a change in obstetric outcome (cesarean delivery instead of a vaginal delivery) and may cause fetal heart rate abnormalities. The change in obstetric outcome (if true) may be related to the baby's head presenting in an abnormal position at the time of delivery. A recent non-randomized study demonstrated a greater incidence of occiput posterior positions (head facing up) with epidural analgesia than in those without anesthesia. There have been no such studies with the CSE technique and none comparing epidural to CSE. Additionally, fetal heart rate abnormalities following neuraxial anesthesia occur approximately 15% of the time although the vast majority do not change outcome. The incidence with CSE vs. epidural has not been adequately studied.

Research Topic: Real Time Monitoring for Cerebral Vasospasm using Bilateral processed EEG
Mentor(s): Stacie Deiner, MD
Student Role: The student will screen and recruit patients and assist with data collection and analysis.

Subarachnoid hemorrhage is a prevalent and morbid condition (45% -30 day mortality). One of the major causes of reduced cerebral blood blow (CBF) after the initial SAH is cerebral vasospasm. Early treatment of vasospasm (<2 hours) is necessary for improved neurologic outcome. Hence, there is significant interest in development of a monitor. The most common bedside diagnostic tool is transcranial Doppler (TCD) which is controversial given its low sensitivity and specificity. TCD is not a continuous monitor and is user dependent. Many centers rely on cerebral angiography for diagnosis of vasospasm; however angiographic spasm does not correlate with outcome. EEG can detect changes in cerebral blood flow

which precede clinical decline but is technically difficult to perform and not practical for continuous monitoring.
Processed EEG monitors have become somewhat popular in the operating room setting for assessment of depth of anesthesia. The recent introduction of bilateral 4 channel disposable probes presents to opportunity to use EEG as a non-invasive continuous monitor for vasospasm. In this proposal we present preliminary evidence for the feasibility of this idea. We propose a prospective observational study to assess real time changes in raw and processed EEG which we will correlate with clinical and radiologic evidence of vasospasm. Our primary clinical endpoint will be the determination of delayed cerebral ischemia. This modality could prove to be a significant clinical advantage for patients suffering from SAH. The data derived from this study will provide the basis for a prospective clinical trial.

Research Topic: Pilot study of topical eugenol and ketamine for neuropathic pain
Mentor(s): Marco Pappagallo, MD
Student Role: The student will screen and recruit patients and assist with data collection and analysis.

Eugenol is a local anesthetic widely used in dentistry for tooth pain. It is the main component of clove oil, comprising 85-90% of the essential oil. Eugenol is a phenylpropanoid with unknown mechanism of action, but proposed mechanisms include inhibition of voltage gated sodium channels and activation of transient receptor potential vanilloid subtype 1. The scientific literature cites eugenol as having an analgesic effect in an animal model of trigeminal neuralgia;
Topical ketamine is an agent with demonstrated analgesic effect in neuropathic pain. Ketamine is a noncompetitive antagonist at the NMDA receptor and its presumed mechanism of action is unrelated to voltage gated sodium channels and activation of transient receptor potential vanilloid subtype 1. No human studies have explored topical eugenol or a combination of eugenol and ketamine for neuropathic pain. Eugenol, eugenol and ketamine, and placebo will be used topically in this pilot study in a crossover fashion to explore the analgesic benefit of agents with presumed different mechanism of action.

Purpose of Study:
1. Explore patient pain response to topical eugenol and whether eugenol provides better analgesia than placebo
2. Explore whether topical ketamine in combination with eugenol provides better analgesia than placebo

Research Topic: Is cardiac mass associated with adverse outcomes after cardiac surgery?
Mentor(s): Gregory Fischer, MD
Student Role: The medical student will aid in acquiring measurements from the TEE clips as will as assist in the retrospective chart review.

Cardiac mass has been identified in the Framingham study as a highly sensitive predictor of adverse cardiovascular outcome. Yet, do date, this parameter has received little attention in perioperative medicine. We intent to retrospectively review all TEE exams performed in patients presenting to the Mount Sinai Hospital for cardiac surgery during the time period of 2008-2009. Cardiac mass will be calculated based on measurements obtained in the transgastric short axis mid-papillary view. A chart review will then be subsequently conducted recording all adverse events, ICU and hospital length of stay. Statistical analysis will search for an association between cardiac mass and adverse events.

Host Institution Name: Northwestern University's Feinberg School of Medicine

Research Topic: Clinical Pharmacology Applied to High Risk Surgical Patients
Mentor(s): Dhanesh K. Gupta, M.D., Michael J. Avram, Ph.D., and Tom C. Krejcie, M.D.
Student Role: The student will learn the fundamentals required to perform clinical and volunteer pharmacology research through involvement in a variety of ongoing clinical pharmacology studies investigating analgesia (opioids), hemodynamics (mannitol, remifentanil), glucose homeostasis (insulin), and cognitive function and brain function/neurologic function monitors (volatile anesthetics, propofol, opioids). The student will assist in collecting Pharmacokinetic-Pharmacodynamic (PK-PD) data in volunteers and surgical patients. The student will be introduced to the development of PK-PD models and the rational application of these models to the development of individualized dosing regimens for surgical patients. The student's activities during the research fellowship should lead to the student becoming a co-author on an abstract and subsequent publication.

Research Topic: Barriers to labor analgesia in the Hispanic and African American communities: the interaction between health literacy and patient analgesic decisions
Mentor(s): Paloma Toledo, M.D.
Student Role: Data collection, analysis, and preparation of abstracts and manuscripts

Host Institution Name: Oregon Health & Science University

Research Topic: Role of microglia in ischemic neuronal death,
Mentor(s): Ines Koerner, M.D., Ph.D. Assistant Professor
Student Role: Microglia are the brain's resident immune cells. They are activated after ischemic brain injury and likely contribute to ischemic injury and neuronal death. The project will use a system of primary cell cultures to examine the effect of activated microglia on neuronal injury after oxygen-glucose deprivation, which is an in-vitro model of ischemia. Specifically, we will investigate the role of the enzyme soluble epoxide hydrolase (sEH) for microglia-induced cell death. The student will prepare and maintain microglia and neuronal cultures, perform oxygen-glucose deprivation and cell death assays, and perform immunofluorescence staining and immunoblotting to analyze protein expression.

Research Topic: (1) A randomized controlled study of pain catastrophizing as a cause for systemic inflammation in women with chronic pain
Mentor(s): Beth Darnall, Ph.D., Assistant Professor
Student Role: This is an experimental study involving delivery of a catastrophizing stressor to the treatment group.

Research Topic: The effect of catastrophizing on labor outcomes in healthy nulliparous women
Mentor(s): Beth Darnall, Ph.D., Assistant Professor
Student Role: This is an observational study. Psychosocial variables are measured at baseline, immediately post-deliver (within 24 hours), and at 6-weeks post-partum. This study also involves medical chart review to gather labor outcomes data to determine presence of dystocia.

Research Topic:) A pilot study of home-based self-delivered mirror therapy for persons with phantom pain
Mentor(s): Beth Darnall, Ph.D., Assistant Professor
Student Role: This is a treatment outcome study. Pain and related variables are measured at baseline and post-treatment at months 1, 2, 3, and 6.

Research Topic: Pain-related interference in sexual functioning of women with non-pelvic chronic pain.
Mentor(s): Beth Darnall, Ph.D., Assistant Professor
Student Role: This study design is cross-sectional and involves chart review of patients at the Comprehensive Pain Center. The medical student would have the opportunity to also examine other variables of interest to them (e.g., sleep, work, relationships with others).

Research Topic: Role of P450 eicosanoids in ischemic stroke and subarachnoid hemorrhage-induced vasospasm
Mentor(s): Nabil J. Alkayed, MD, PhD, Professor of Anesthesiology
Student Role: The project is aimed at determining the role of P450 eicosanoids in cerebral blood flow regulation after ischemic and hemorrhagic strokes. The student will learn the mouse model of stroke and will assist in data acquisition and analysis.

Research Topic: Regulation of soluble epoxide hydrolase (sEH) expression and intracellular translocation after stroke
Mentor(s): Nabil J. Alkayed, MD, PhD, Professor of Anesthesiology
Student Role: The project involves preparing neuronal cell cultures, transfecting them with fluorescently tagged protein to track their intracellular movement. The student will assist in preparing cells and acquiring and analyzing images.

Research Topic: Mechanisms of the deleterious effects of hyperglycemia in cerebral ischemia
Mentor(s): Nabil J. Alkayed, MD, PhD, Professor of Anesthesiology
Student Role: The project is aimed at defining the mechanisms underlying the deleterious effects of hyperglycemia in ischemic stroke. The student will learn the mouse model of type 1 diabetes, and will learn and assist in carrying out ischemic stroke and in analyzing brain tissue in these mice after stroke.

Research Topic: Mechanisms of endothelial cell injury and protection from ischemic injury
Mentor(s): Nabil J. Alkayed, MD, PhD, Professor of Anesthesiology
Student Role: The project is aimed at elucidating the molecular mechanisms underlying endothelial cell damage after stroke and potential vasoprotective strategies. The student will learn how to prepare mouse brain endothelial cell culture, and how to analyze their response to ischemic injury induced by incubation under oxygen-glucose deprivation to simulate ischemia

Research Topic: Determination of the Effect of Nitrous Oxide Sedation on Intraocular Pressure (IOP) in Adults.
Mentor(s): Kirk Lalwani, MD, FRCA, Associate Professor, Departments of Anesthesiology and Pediatrics
Student Role: Determination of the Effect of Nitrous Oxide Sedation on Intraocular Pressure (IOP) in Adults.
Following our adult volunteer study last summer, we plan to study the effect of N2O on IOP in the older adult population presenting for eye surgery.
The student will be involved in IRB submission, patient recruitment, data collection, basic analysis, preparation and presentation of an abstract and poster at a national conference, followed by manuscript preparation for submission for peer-reviewed publication. It is anticipated that the student will become familiar with reference management, spreadsheet, and statistical analysis software during the project, and will present the poster at a national meeting.

Research Topic: Sleep-wake disturbances in adolescents with chronic pain
Mentor(s): Tonya Palermo, Ph.D

Student Role: The aim of this study is to characterize the type of sleep disturbances experienced by adolescents with chronic pain compared to healthy adolescents and to assess the impact of sleep disturbances on adolescent daily functioning and emotional status. Sleep is assessed using subjective survey measures and actigraphy. The student would enroll study participants, score and analyze sleep data.

Research Topic: Web-based cognitive-behavioral treatment of chronic pain in children
Mentor(s): Tonya Palermo, Ph.D
Student Role: The goal of this project is to develop and test the feasibility and efficacy of a web-based cognitive-behavioral treatment program for children and adolescents with chronic pain. This is a randomized controlled trial of an 8-week web-based treatment program in 72 children and adolescents with chronic pain (ages 11-17 years) who will either receive the web-based treatment or serve as no-treatment controls. The student would assist with beta testing of web site, and enroll study participants

Research Topic: Rodent Surgeries
Mentor(s): Stephanie J. Murphy, V.M.D., Ph.D., Diplomate, ACLAM, Associate Professor
Student Role: Student will learn how to handle mice and rats, perform rat anesthesia and minor surgeries such as gonadectomies and hormone implantations, and carry out peri-operative monitoring and care. Rodent surgeries can present unique challenges primarily due to their small size and provides excellent training for microsurgical manipulations. In addition to providing basic rat surgical support to our staff, fellows, and faculty, the student will be given a chance to perform sterile, survival surgery in mice as well as learn an experimental model of focal stroke in the rat involving occlusion of the middle cerebral artery. These are technically demanding studies requiring the use of a surgical microscope with the mice as well as placement of arterial and venous catheters and surgical preparation of cerebrovascular vessels in order to expose these rats to cerebral ischemia.

Research Topic: Genetically Engineered Mouse Colonies
Mentor(s): Stephanie J. Murphy, V.M.D., Ph.D., Diplomate, ACLAM, Associate Professor
Student Role: Project would involve managing and genotyping mice within the breeding colonies in the APOM department mouse breeding colonies. Our research program requires the use of transgenic and knockout mice to test our research hypotheses. Many of these animals are difficult to breed or require special care and have to be genotyped. The student will be trained to perform basic mouse health checks, mouse reproductive management and husbandry, mouse anesthesia, database entry, and tail tattooing and tail sampling for genotyping. The student will also be heavily involved with genotyping of several knockout mouse breeding colonies. This involved preparing DNA from tail samples, performing PCR with specific primers, and interpreting results in order to properly characterize mice born in our colonies and distribute them for use in various research projects.

Host Institution Name: Stanford University

Research Topic: Molecular Cardiac Physiology
Mentor(s): Andrew J. Patterson, MD, PhD, Associate Professor, Anesthesia
Student Role: The research in my laboratory focuses on the regulation of heart and blood vessel function. In addition to disease states like congestive heart failure, we are interested in the mechanisms by which sepsis impacts cardiovascular and renal function. The goal of the summer student project is to evaluate physiologic and molecular effects of vasopressin infusion during sepsis. Students will participate in experiments that involve microsurgical insertion of left ventricle catheters using genetically engineered mice with the goal of obtaining pressure volume measurements, laser Doppler assessments of tissue perfusion, and microarray gene expression analyses. They will learn to evaluate the results of

microarray studies using GeneSpring and Ingenuity Pathway Analysis software. Students will work with a research associate, undergraduate students from Stanford and other universities as well as Stanford Anesthesia residents and Critical Care Medicine Fellows.

Research Topic: Sympathetic neuron α2 adrenoceptor structure/function
Mentor(s): Timothy Angelotti, MD, PhD; Assistant Professor, Anesthesia
Student Role: My research efforts are focused on investigating the pharmacological and physiological interface of the autonomic nervous system with effector organs. Utilizing molecular, cellular, and electrophysiological techniques, the student and I will examine the function of a2 adrenergic receptors in sympathetic neurons cultured alone, or in the presence of other neurons, cardiac myocytes, or smooth muscle cells. Sympathetic neurons are isolated from various transgenic knock-out and knock-in mice, which have been designed to express altered adrenergic receptor subtypes (e.g. a2A/C, b1, b2). Using recombinant adenovirus constructs encoding additional wild-type, mutant, or chimeric adrenergic receptors, we are able to further modify the pharmacology and physiology of this system. Receptor binding, immunocytochemistry, single- cell analysis of neurotransmitter release, and standard molecular biology are the techniques that are employed to characterize this dynamic system. Development of this in vitro model of the sympathetic nervous system will allow us to better understand its role in sympathetically- mediated pain and in the stress response to surgery and critical illness.

Research Topic: Surviving Cerebral Ischemia
Mentor(s): Rona Giffard, MD, PhD, Professor, Anesthesia
Student Role: We study stroke in both surgical animal models and using brain cells. Students can participate in collecting data to characterize gene expression in brain with recovery after stroke, and help analyze the interaction of different brain cell types in response to stroke at the level of gene expression. Individual cell types are isolated from the brains of animals following stroke to understand their interactions. This will allow us to target therapies to individual cell types to protect the brain and reduce damaging effects. A second project a student could work on is understanding the contribution of inflammation and oxidative stress to stroke injury. Both astrocytes and microglia respond rapidly to injury and can have proinflammatory phenotypes. We need to study activation of these cell types through staining brain sections at different intervals following stroke, and then manipulate these phenotypes by altering gene expression in these cells. For the first project a student could learn to isolate RNA from the brain and learn about gene chip analysis. For the second project a student could learn immunohistochemical staining and techniques for changing gene expression in the brain. In both cases they could contribute to the development of a new potential treatment for stroke

Research Topic: Obstetric Anesthesia
Mentor(s): Brendan Carvalho, MD, Assistant Professor, Anesthesia
Student Role: The obstetric anesthesia group conducts clinical and translational research into various aspects of cesarean anesthesia and labor analgesia. We have completed a number of studies examining the role of extended-release epidural morphine and certain oral adjuvants including NSAIDs and COX-2 inhibitors for post-cesarean analgesia. We have determined ED50 and ED95 dosing requirements of local anesthetic for cesarean delivery and have conducted a number of studies investigating the efficacy of PCEA for labor analgesia. In addition we have demonstrated increased pain tolerance in pregnant patients compared to non-pregnant controls using quantitative sensory pain models. We have done research on the economics of obstetric anesthesia, patient perception of risk prior to cesarean delivery, coagulation changes following fluid loading and shivering during cesarean delivery. We have helped develop loss of resistance epidural syringe as well as a CSF and epidural pressure measurement device. We have many ongoing studies and a number of studies being developed. We are currently examining the role of cytokines in the development and maintenance of pain following cesarean delivery as well as determining the role of pharmacogenetics on labor pain and the response to opioids. We are also involved in simulator

training and offer a number of research opportunities in this area. A number of our faculty as well as two obstetric anesthesia fellows conduct the clinical and translational research. We have successfully helped undergraduate students, medical students, and residents complete research projects. Our past residents and fellows have gone on to academic careers or been very successful in private practice. One of the strengths of our group is our ability to collaborate with a variety of people in the institution. We have conducted projects in the past with Drs. Alex Macario (economics), Yasser El Sayed (fetal-maternal medicine), David Drover (pharmacokinetics and statistics), and Martin Angst (experimental pain).

Research Topic: Experimental clinical science to study (1) mechanisms of pain and inflammation in injured tissue, and (2) the pharmacology of opioids in pain and inflammation
Mentor(s): Martin Angst, MD; Associate Professor, Anesthesia
Student Role: The role will be identified on an individual basis and depends on a student's particular interest and current on-going research efforts.
Experimental settings: Research efforts including several collaborations take place in various settings. The core facility is the human pain laboratory, where mechanisms of pain and inflammation as well as interventions attenuating pain and modulating inflammation are studied in human biology under standardized and carefully controlled conditions. However, research is also undertaken in typical clinical settings such as the operating room, which can be viewed as a big laboratory offering real life models of pain and inflammation in tissue injured by surgery. Finally, collaborative efforts include work in animals allowing the use of more invasive methods not suitable for human research. An example of ongoing research efforts are our studies aiming at understanding the impact of opioids such as morphine on inflammatory processes in injured tissue. Some evidence suggests that the immune-modulating effects of opioids – typically given to alleviate pain – can impact wound healing and as such the risk for postoperative infections. We study this question in parallel in rodent models, human volunteers, and patients undergoing surgery. As such our research is truly translational.
Tools: Some of the key tools are:
(1) Psychophysical methods to measure clinical and experimentally induced pain. Experimental pain models at hand can mimic acute pain, pain associated with inflammation and pain due to sensitizing process within the central nervous system.
(2) Wound fluid and interstitial fluid samples from experimental lesions that are obtained with aid of micro-catheter techniques. Samples are assayed for biochemicals of interest such as the cytokines, neuro-trophic factors, or the prostanoids.
(3) Tissue biopsies are obtained for immunohistochemical analyses.
(4) Computer-controlled infusion algorithms are used to study the effects of drugs at steady-state pharmacokinetic conditions.

Other research areas: (1) Pharmacogenomic studies of opioids, (2) Bioinformatic approaches for pain biomarker discovery.

Research Topic: Mechanisms of pain
Mentor(s): David Clark, MD, PhD; Professor, Anesthesia
Student Role: Current projects being pursued in the Clark lab can generally be placed in one of two categories. One group of projects involves the investigation of the roles of cytokines, complement split products and other inflammatory mediators in incisional wounds. The laboratory has identified a number of novel inflammation-related molecules in the recent past. We are now attempting to determine which of these is related to inflammation in general versus nociception specifically. The interactions between analgesics and the inflammation-related molecules are of particular interest. The second group of projects involves the mechanistic exploration of opioid-induced hyperalgesia. Experiments from our lab have to this point demonstrated thermal hyperalgesia and mechanical allodynia in mice and rats after the cessation of opioid administration. This hyperalgesia has been partially characterized pharmacologically. Ongoing

studies seek to further elucidate the mechanism of this form of hyperalgesia as well as test methods for preventing or limiting its manifestation. We are currently using genetic, behavioral, immunohistochemical and biochemical methods.

Research Topic: Development of molecular approaches for the treatment of chronic pain
Mentor(s): David Yeomans, PhD; Associate Professor, Anesthesia
Student Role: Our main research focus is on the development of gene therapy methods for the treatment of chronic pain. Two of the primary problems in gene therapy have been the targeting of the right cells, and the duration of the desired effect. We have used a highly modified herpes simplex virus (the kind that causes cold sores) to carry analgesic genes into the pain-sensing neurons. Because herpes viruses stay naturally in these cells for the life of the host, we should obtain very long lasting analgesic effects using these treatments. Thus, we are making use of the natural proclivity of herpes for entering and staying in the very cells we are interested in. In this way, we target pain treatment to painful areas, and only painful areas. These new approaches to therapy could revolutionize the treatment of chronic pain. Students can directly participate in the laboratory in learning behavioral testing in rodent models for pain, as well as microscopy, histochemistry, virology, immunoassays, and other techniques

Research Topic: Mechanisms of action of central nervous system drugs
Mentor(s): Bruce MacIver, PhD; Associate Professor, Anesthesia (Research)
Student Role: The long-term goal of our research is to provide the physiological background information required for the rational design of safer and more effective anesthetics and analgesics. Synaptic Physiology Research: We investigate the cellular, synaptic and molecular mechanisms of action of central nervous system drugs; especially barbiturates, opiates, anesthetics, abused inhalants and other CNS depressants. Electrophysiological recording techniques and selective pharmacological probes are used to investigate the sites and mechanisms of action for CNS depressants. Most of our studies focus on the CA 1 area in rat hippocampal brain slices. Neurons in this brain area are depressed by anesthetics through a combination of pre-and postsynaptic actions on glutamate and GABA mediated neurotransmission.

EEG Research. The effects of pharmacological agents on EEG waves generated by the neocortex are being examined. EEG theta activity (4 to 12 Hz) is one of many rhythms, like alpha and delta (slow wave sleep) rhythms that are altered by CNS active drugs. Patch clamp and electrophysiological recording techniques are used to look at the effects of anesthetics on carbachol and bicuculline induced theta activity in neocortical brain slices. Anesthetic effects on brain slice micro-EEG activity are correlated to EEG effects seen in animals and humans during anesthesia. Effects on micro-EEG theta activity appear to involve actions at GABA and glutamate synapses, as well as effects on neuronal excitability. Theta activity can be recorded from specific regions of cortex in rat brain slices. Comparison of micro-EEG signals and intracellular recordings (whole cell) reveal that the low frequency theta waves (~ 8 Hz) were generated by synchronous synaptic potentials and discharge activity of cortical neurons. The discharge of each cortical neuron appears to contribute ~ 1.0 μV to the micro-EEG signal, so theta activity requires synchronous activity in ~ 100 neurons in each cortical location. Theta activity is known to be important for spatial mapping and may provide a 'binding' mechanism that contributes to the formation of memory in general. When selective populations of neurons are synchronously active they can interact in a 'Hebbian' manner to change the strength of synaptic inputs that are timed at the theta frequency. Theta activity is also known to be particularly sensitive to anesthetic agents at concentrations which block memory formation. Preliminary studies in our laboratory indicate that brain slice theta activity is also depressed by anesthetics and that this depression occurs with a profile similar to in vivo responses. Students would be directly involved in collecting and analyzing electrophysiology data from rodent brain slice models.

Research Topic: Pharmacokinetics and Pharmacodynamics
Mentor(s): David Drover, MD; Associate Professor, Anesthesia
Student Role: My research interest is in clinical research on the pharmacokinetics and pharmacodynamics of drugs. Medications studied are those commonly used for anesthesia and analgesia. Additionally, other drugs are studied if they have unique characteristics that require intensive or specialized monitoring. Particular effort is used to obtain quality real-time data from intensive pharmacokinetic/pharmacodynamic studies to enable mathematical modeling of drug effect on the human body. Mathematical modeling of data is mainly performed with NONMEM. Where possible, research projects use the electroencephalogram to quantitate pharmacodynamic effect and develop mathematical models to relate pharmacokinetics to pharmacodynamic response. The main interest of my research projects is to develop novel ways to model and describe clinical pharmacology relationships

Research Topic: Pain Neuroimaging, Systems Neuroscience, Clinical Pain Trials
Mentor(s): Sean Mackey, MD, PhD; Associate Professor, Anesthesia and Pain Management
Student Role: Dr. Mackey's lab (Stanford Systems Neuroscience and Pain Lab) is focused on using advanced imaging and psychophysical techniques to better understand the processing of pain in the brain and spinal cord. Dr. Mackey has pioneered novel techniques to perform neuroimaging of the human spinal cord and its response to acute and chronic pain. He has also developed innovative methods to permit subjects to directly view and control their own brain activity in real time using fMRI feedback. He is conducting multiple neuroimaging projects which would allow the interested student to participate at all phases of data collection, analysis and presentation. Additionally, he is conducting studies assessing outcomes in chronic pain utilizing validated outcomes measurements. These studies would be ideal for the student interested in epidemology or statistics. Finally, there are several pharmacologic studies investigating novel therapies for chronic neuropathic pain that would allow the student interested in clinical trials experience in study design, patient recruitment, study execution and data analysis. For more information on these projects, go to http://snapl.stanford.edu and http://paincenter.stanford.edu

Research Topic: Medical Acupuncture
Mentor(s): Brenda Golianu, MD; Assistant Professor, Anesthesia
Student Role: Research interests in the division of medical acupuncture involve the application of acupuncture techniques to medical problems that are inadequately addressed by current medical practice. Currently, that includes the use of acupuncture as an adjuvant in the treatment of cancer and the use of acupuncture in surgical patients. Additional projects include the use of acupuncture in decreasing opioid requirements in neonates after surgery, speeding recovery from surgery of critically ill infants electrical acupoint stimulation to decrease pain from heelstick, and use of acupuncture in improving outcomes in in vitro fertilization in adults. An interdisciplinary component to our program involves collaboration with physicians and researchers in other disciplines, including oncology, surgery, obstetrics and gynecology. Perioperative studies will compare nausea, vomiting, pain, antiemetic use, opiate use, and clinical outcomes in patients receiving acupuncture vs. control. Interested students may either join an existing project or construct a project of their own.

Research Topic: Experimental pulmonary hypertension
Mentor(s): Ronald Pearl, MD, PhD; Professor and Chair, Anesthesia
Student Role: My research examines mechanisms and therapy of experimental pulmonary hypertension. We use the combination of pneumonectomy and monocrotaline administration to produce proliferative pulmonary hypertension in mice and rats. We have examined the changes at a transcriptional and cellular level which result in pulmonary hypertension and the ability of vasodilator, immunosuppressive, and anti-proliferative therapies to prevent and/or reverse the pulmonary hypertension. Ongoing research is investigating the effects of specific genes on the development and reversal of pulmonary hypertension

Research Topic: Pediatric Cardiac Anesthesia
Mentor(s): Chandra Ramamoorthy, MBBS, FRCA; Professor, Anesthesia
Student Role: Loss of Cerebral Autoregulation during heart surgery in children with or without Cardiopulmonary bypass.

In the perioperative period, potential disruption of cerebral autoregulation with ensuing cerebral pressure passivity may contribute to neurological injury in children with complex heart disease. Near infrared spectroscopy (NIRS) is a non-invasive bedside technology that measures regional cerebral oxygenation (rSO2). NIRS can also identify infants with impaired cerebral autoregulation having concordance between mean arterial blood pressure (MAP) and rSO2. Such information may then support appropriate blood pressure management in these patients. Infants undergoing cardiac surgery may be at high risk for impaired cerebral autoregulation, which can also be readily detected using NIRS. NIRS measures of rSO2 provide a good estimate of cerebral blood flow.
Several studies using NIRS have shown loss of autoregulation in premature infants being significantly associated with mortality, severe intraventricular hemorrhage, and periventricular leukomalacia. These infants were more likely to have had periods of systemic hypotension. However studies of cerebral autoregulation in infants following cardiac surgery are limited.

rSO2 (cerebral oxygen saturation, triangle in figure) remains stable despite increases in MAP in this newborn (squares in figure).

In infants undergoing the Glenn procedure the superior vena cava is connected to the pulmonary artery, which is oxygenated and then returned to the left atrium via the pulmonary veins. Soon after surgery this results in increased cerebral venous pressure and potentially reduced cerebral blood flow. Thus by reducing flow, rSO2 decreases, and the SpO2 decreases. If the loss of autoregulation is not recognized the cerebral and then peripheral oxygen desaturation may remain untreated, contributing to potential adverse neurocognitive outcomes.

Hypoxia responsive genes in infants with cyanotic heart disease

It is well known that children with cyanotic heart disease have neurological adverse outcomes which is often thought related to surgery and cardiopulmponary bypass. Whether the chronic cyanosis itself has a role in these adverse outcomes is not well understood. Recently, when compared to their acyanotic cohorts, a group of neonates with arterial saturation 80% or lower, hypoxia responsive genes were expressed. It is unclear if during chronic cyanosis if there is ongoing tissue hypoxia and if these genes will be continued to be expressed, as these genes play an important role in tissue adaptation to hypoxia.

Hypoxia-responsive genes lead to different adaptive metabolic processes, such as autoregulation, glucose metabolism, cell survival and proliferation, angiogenesis, energy metabolism, and erythropoeisis. Hypoxia-inducible transcription factors (HIF) have been characterized as the most important regulators of O2-dependent gene transcription modulating oxygen and metabolic supply during hypoxia. HIF expression increases exponentially as cellular oxygen concentration falls. Numerous HIF target genes (e.g. EPO, VEGF, adrenomedullin) are activated, modifying oxygen and energy supply. However these have not been studied in patients with chronic cyanotic heart disease.

Methodology: Neonates and infants presenting for cardiac catheterization or surgery will be the subjects. Following IRB and parental approval, 1 cc of blood will be drawn from an indwelling venous line. Based on their peripheral oxygen saturation these subjects will be classified as cyanotic if the SpO2 is 80% or

less and acyanotic if higher. In the 1st phase we will identify the hypoxia responsive genes. This will require 11 patients/group. In the next phase we will look for hypoxia responsive genes from regional venous blood; the target organs are brain, heart and periphery. Microarray expression profiling will be performed with blood collected. Gene identification will be performed using DAVID (Database for Annotation, Visualization and Integrated Discovery) and the biologic relevance of changes in gene expression by exposure to chronic hypoxia will be described. RT-PCR will be used to confirm results obtained by microarray.

Significance: We will identify candidate genes whose expression in longitudinal studies could demonstrate their role in the patho-physiology of chronic cyanosis. The cerebral autoregulation dipped below the "critical threshold" of 40% on several occasions which were related to alterations in MAP (data not shown). We propose to study the changes in cerebral autoregulation before, during and after heart surgery in a cohort of infants undergoing the Glenn procedure with or without CPB. The cerebral oxygen saturation, arterial saturation and MAPS will be monitored after induction of anesthesia but before surgery, specific times during surgery and for 12 hours after surgery. Pressure passivity index (PPI) will be calculated as total time when there is concordance between rSO2 and MAP. (If autoregulation is present there will be discordance.) In this population we wish to determine when autoregulation is re-established and the interim factors that affect the return to autoregulation. This project has several important clinical implications. Establishing a sytematic time period following surgery when autoregulation is re-established, therapies can be suited to manage the vulnerable period. The role of osmotic diuretics such as such as Mannitol, in the early post operative periods when the cerebral venous pressure is high, can be evaluated. Ultimately by sustained improved cerebral oxygen saturation neurological outcomes in cyanotic children can be altered.

Research Topic: Factors causing prolonged post-surgical pain and prolonged opioid use
Mentor(s): Ian Carroll, MD, MS Instructor
Student Role: Chronic post-surgical pain as a result of nerve injury is a major complication of surgery. In short, virtually every surgery has a definite incidence of chronic neuropathic pain postoperatively. Following elective inguinal hernia repair 24% of patients experience pain 1 year postoperatively. 11% of patients experience moderate to severe pain. Similar numbers exist for other surgeries including: 13% of patients have chronic pain following knee replacement, 6% following cesarean section, 30-60% following thoracotomy, and as many as 50% following breast cancer surgery. We are collaborating with the thoracic, breast, general and orthopedic surgery divisions to measure the duration of post surgical pain. We hope to define for the first time a survival curve that describes the natural history of postsurgical pain. By changing our focus from elements influencing pain intensity to those influencing pain duration we hope to gain insight into factors influencing the incidence of delayed pain resolution, and chronic pain. We hope this work will allow us to identify those patients at highest risk of postoperative chronic pain so that they can be targeted in the future for early intervention and treatment. Data collection is currently ongoing in the pilot stage, and this project has provided opportunities for undergraduate students, medical students, and residents to contribute meaningfully in collecting data from patients, and analyzing results. Local collaborators include:

Sean Mackey	Pain Medicine
John Pollard	Anesthesia
Peter Barelka	Pain Medicine/ anesthesia
Stuart Goodman	Orthopedic surgery
George Yang	General Surgery
Fred Dirbas	Breast Surgery
Jessica Donnigton	Thoracic Surgery
Richard Whyte	Thoracic Surgery

Walter Cannon Thoracic Surgery
This work is exciting because little focus has been given to pain using duration as the primary endpoint. However, it is the chronicity of pain that results on its burden to society, We have excellent means of dealing with pain in the acute setting, but have much worse outcomes in the chronic setting. By focusing on pain duration, we hope to develop new insights into this problem. Ultimately, this research may help to answer the overriding question in pain medicine: Why following identical injuries is pain of short duration for most people but of extended or infinite duration for others?

Host Institution Name: SUNY Downstate Medical Center

Research Topic: The effect of diffusion of 4% lidocaine through the Medtronic EMG tube cuff on Nerve Integrity Monitor Response®
Mentor(s): Alexandru, Apostol, MD - Clinical Assistant Professor of Anesthesiology; Clinical Director of Anesthesiology
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: An investigation to evaluate the use of a Disposable Single –Needle Extra –Corporeal Hemo -filtration Circuit Intraoperatively in Management of fluid overload compare to Continuous Veno-Venous Hemofiltration (CVVH)
Mentor(s): Alexandru, Apostol, MD - Clinical Assistant Professor of Anesthesiology; Clinical Director of Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Correlation of complement activation and factors with delayed cerebral vasospasm and delayed
ischemic neurological deficits in aneurysmal subarachnoid hemorrhage patients
Mentor(s): Audree Bendo, MD – Professor of Anesthesiology; Residency Program Director; Director Neurosurgical Anesthesiology, Vice-Chair for Education; Ming Zhang, MD, PhD – Research Assistant Professor,
SUNY Downstate
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Temporal alterations in complement expression profiles are associated with increased mortality in septic shock
Mentor(s): Jean Charchaflieh, MD, MPH – Associate Professor of Clinical Anesthesiology; Director of Critical Care , Ming Zhang, MD, PhD - Research Assistant Professor, SUNY Downstate
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Efficacy and safety of drotrecogin alfa/xigris (activated) in adult patients with septic shock (Eli
Lilly & Co)
Mentor(s): Jean Charchaflieh, MD, MPH – Associate Professor of Clinical Anesthesiology; Director of Critical Care
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Ultrasound Imaging and Resident Diagnosis of Septic Shock/ hypotenisve patients
Mentor(s): Jean Charchaflieh, MD, MPH – Associate Professor of Clinical Anesthesiology; Director of Critical Care
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Development of novel amnesic agents using a strategy of blocking PKM activity
Mentor(s): James E Cottrell, MD – Distinguished Professor and Chairman, Department of Anesthesiology, Todd Sacktor - Professor of Physiology, Pharmacology, and Neurology
Student Role: Assist with laboratory investigations, data collection and analysis

Research Topic: Is there an increased benefit for ease of access during performance of neuraxial anesthesia amongst the variety of patient positioning?
Mentor(s): Dennis Dimaculangan, MD – Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Learning curves for the utilization of ultra-sound during regional anesthesia: learning curve for brachial plexus ultrasound imaging by anesthesia residents using the Cusum method
Mentor(s): Dennis Dimaculangan, MD – Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: The effect of periarticular injection of bupivacaine-ketorolac-epinephrine-morphine admixture,
in addition to continuous femoral nerve block, on rehabilitation and postoperative pain in patients undergoing
total knee replacement
Mentor(s): Dennis Dimaculangan, MD – Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Study comparing the effects of PCEA vs. periarticular single-shot injection (SSI) vs. continuous periarticular infiltration (CPI) of local anesthetic, on top of a standard multimodal postop pain management strategy, on pain and rehabilitation outcomes in patients undergoing total hip replacement surgery.
Mentor(s): Dennis Dimaculangan, MD – Clinical Assistant Professor of Anesthesiology
Student Role: Assist with patient recruitment, data collection and analysis.

Research Topic: Does epidural saline or selection of catheter type reduce complications of epidural catheter
insertion in combined spinal epidural analgesia for labor pain? A randomized double blind prospective case
control study
Mentor(s): Biswajit Ghosh, MD-Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Do Reading Processes, Vocabulary, Reading Comprehension, Reading Rate, Occupational
Stress, Demographics, Reading Title Exposure and Study Habits Correlate With Anesthesia In-Training Examination Scores?
Mentor(s): Julia Griffin, MD-Attending Anesthesiologist; Audree Bendo, MD – Professor of Anesthesiology;
Residency Program Director; Director Neurosurgical Anesthesiology; Vice-Chair for Education
Student Role: Assist with protocol implementation, patient recruiting, data collection and analysis

Research Topic: Global cerebral ischemia: examine the effect of lidocaine and sevoflurane preconditioning on

histology, immunocytochemistry and behavior following global cerebral ischemia
Mentor(s): Ira Kass, PhD-Professor, Department of Anesthesiology; James E Cottrell, MD – Distinguished Professor and Chairman, Department of Anesthesiology
Student Role: Assist with study implementation including laboratory investigations, data collection and analysis.

Research Topic: Acute brain slice: mechanisms by which anesthetics reduce hypoxic neuronal damage – to
examine the effects of anesthesia on electrophysiological, molecular biological and biochemical parameters
before, during and after hypoxia
Mentor(s): Ira Kass, PhD-Professor, Department of Anesthesiology; James E Cottrell, MD – Distinguished Professor and Chairman, Department of Anesthesiology
Student Role: Assist with laboratory investigations, data collection and analysis

Research Topic: Video glasses for use during inhalation induction in children
Mentor(s): Beklen Kerimoglu, MD – Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Looking for trends and/ or frequency of root cause analysis cases
Mentor(s): Ketan Shevde, MD – Clinical Professor of Anesthesiology, Director, Cardiothoracic Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Innate immunity responses to ischemic changes during cardiac surgery
Mentor(s): Ketan Shevde, MD – Clinical Professor of Anesthesiology, Director, Cardiothoracic Anesthesiology, Ming Zhang, MD, PhD – Research Assistant Professor, Department of Anesthesiology
Student Role: Assist with study implementation including IRB approval process, patient recruitment, data collection and analysis.

Research Topic: The Pharyngeal Ultrasound Guide-a new device extending the boundaries of the transesophageal echocardiography examination
Mentor(s): Ketan Shevde, MD – Clinical Professor of Anesthesiology and Director, Cardiothoracic Anesthesiology; Audree Bendo, MD – Professor of Anesthesiology; Residency Program Director; Director
Neurosurgical Anesthesiology, Vice-Chair for Education
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Effect of transfusion of PRBC and Cell saver Blood on Coagulation Parameters during cardiac
surgery
Mentor(s): Ketan Shevde, MD – Clinical Professor of Anesthesiology, Director, Cardiothoracic Anesthesiology
Namik Oliva, MD - Clinical Assistant Professor of Anesthesiology
Student Role: Assist with study implementation including IRB approval process, patient recruitment, data collection and analysis.

Research Topic: Pediatric Mask Induction: Do we still use or need Nitrous Oxide?
Mentor(s): Tigran Sukiasyan, MD - Attending Anesthesiologist

Student Role: Assist with study implementation including IRB approval process, patient recruitment, data
collection and analysis

Research Topic: The effect of mannitol on the tissue reperfusion injuries after cardiopulmonary bypass surgery
(Retrospective)
Mentor(s): Marina Svyatets, MD - Clinical Assistant Professor of Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Should ambulatory and same-day admission patients discontinue their angiotensin ace inhibitors medications preoperatively?
Mentor(s): Rebecca S. Twersky, MD – Professor of Anesthesiology, Vice-Chair for Research, Director, Ambulatory Anesthesia
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Smoking cessation in the perioperative period
Mentor(s): Rebecca S. Twersky, MD – Professor of Anesthesiology, Vice-Chair for Research, Director, Ambulatory Anesthesia
Student Role: Assist with protocol implementation, data collection and analysis

Research Topic: Complement Expression Profiles in Human Cord Blood
Mentor(s): Ming Zhang, MD, PhD – Research Assistant Professor, Department of Anesthesiology, Ivan Velickovic, MD-Staff Anesthesiologist, Director of Obstetric Anesthesiology
Student Role: Assist with protocol implementation, data collection and analysis

Host Institution Name: Thomas Jefferson University

Research Topic: Observational Study of Recurrent Hypoglycemia in Hospitalized Patients using a Continuous Glucose Monitoring System, IRB control #08D.334
Mentor(s): Jeffrey I Joseph, D.O., Director of Research, Associate Professor of Anesthesiology
Student Role: As key personnel, the student will assist with literature review, subject recruitment, glucose sensor insertion, data collection, data analysis and manuscript preparation.

Research Topic: Correlation Between Hyperglycemia and Glysouria in Surgical Patients, IRB control #08D.333
Mentor(s): Jeffrey I Joseph, D.O., Director of Research, Associate Professor of Anesthesiology
Student Role: As key personnel, the student will assist with literature review, subject recruitment, glucose sensor insertion, data collection, specimen testing, data analysis and manuscript preparation

Research Topic: Continuous Glucose Monitoring During Anesthesia, Surgery and ICU Care, IRB control #08D.430
Mentor(s): Jeffrey I Joseph, D.O., Director of Research, Associate Professor of Anesthesiology
Student Role: As key personnel, the student will assist with literature review, subject recruitment, glucose sensor insertion, data collection, specimen testing, data analysis and manuscript preparation

Research Topic: Cost Analysis of Mild, Moderate and Sever Hypoglycemia in a University Hospital
Mentor(s): Jeffrey I Joseph, D.O, Director of Research, Associate Professor of Anesthesiology

Student Role: As key personnel, the student will assist with literature review, subject recruitment, glucose sensor insertion, data collection, specimen testing, data analysis and manuscript preparation

Research Topic: Computer Models for Glucose and Insulin Dynamics in the Framework of Functional Data Analysis
Mentor(s): Brian Hipszer, Ph.D., APC Director of Biomedical Engineering, Assistant Professor of Anesthesiology
Student Role: As key personnel, the student will assist Dr Hipszer with computer simulations and modeling of human physiology, including the effects of surgical stress, catecholamines and steroids on glucose metabolism

Research Topic: An Observational Study using Continuous Glucose Monitoring to Correlate Changes in Blood Glucose Level with Coagulation and Ultrasound Evidence of Deep Vein Thrombosis in Patients undergoing Neurosurgery, IRB control #08D.313
Mentor(s): Boris Mraovic, M.D., APC Director of Clinical Trials, Assistant Professor of Anethesiology
Student Role: As key personnel, the student will assist with literature review, subject recruitment, glucose sensor insertion, data collection, specimen testing, data analysis and manuscript preparation.

Host Institution Name: University of Alabama at Birmingham

Research Topic: Relative Prevalence and severity of autonomic nervous system dysfunction in diabetic patients for retinal surgery
Mentor(s): Gwendolyn L. Boyd, MD, Professor & Chief Anesthesiology, Callahan Eye Foundation Hospital
Student Role: Perform ANS function testing, data colleciton, database management, statistical analysis, abstract and poster presentation.

Research Topic: Functional Imaging of Pain
Mentor(s): Michael Froelich, MD, Associate Professor of Anesthesiology
Student Role: Research Assistant

Research Topic: Delineation of the Mechanisms of Nitrosothiol Formation from Nitric Oxide (NO) in Cells
Mentor(s): Jack R. Lancaster, PhD, Professor of Anesthesiology
Student Role:

Research Topic: Prevention and Treatment of Chlorine Gas Induced Injury to the Pulmonary System
Mentor(s): Sadis Matalon, PhD, Alice McNeal Professor and Vice Chairman for Research, Department of Anesthesiology; Professor of Cell Biology, Physiology and Biophysics & Microbiology; Director, Pulmonary Injury and Repair Center, School of Medicine; Professor of Environmental Health Sciences, School of Public Health, University of Alabama at Birmingham; Deputy Editor, American Journal of Respiratory Cell and Molecular Biology
Student Role: Chlorine (Cl2) is a moderately soluble, highly reactive oxidant gas, used extensively for water purification, manufacturing of Pharmaceuticals and chemicals and as a potent disinfectant. Persons exposed to chlorine gas, may experience mild symptoms for the first 6-24 hours (h). However, following this latency period, severe lung injury, characterized by protein-rich edema and the onset of hypoxemia may develop. Presently, the cellular and biochemical events leading to this injury have not been elucidated. We propose that reactive oxygen-chloride and nitrogen intermediates (RONS), formed by the interaction of C12 and its hydrolysis products with nitric oxide (NO), initiate self-propagating chain

reactions, the products of which damage alveolar epithelial cells decreasing their ability to produce and secrete surfactant, actively transport sodium (Na+) ions and maintain a tight, semi-permeable barrier. Thus, systemic administration of reactive species scavengers (such as ascorbate, N-acetyl-cysteine (NAC), and deferoxamine, as well as agents that augment surfactant levels, ion transport and paracellular resistance (such as albuterol (a long acting b-agonist), shortly after exposure to C12 will decrease lung injury, morbidity and mortality. This hypothesis is tested by exposing either confluent monolayers of rat alveolar type II (ATII) epithelial cells or rats to C12 (50-200 ppm for 30 min) and measure the following indices at 0.5, 6, 12 and 24 h post exposure: physiological and biochemical indices of lung function (including surfactant function and composition), ability of the lungs to transport ions in vivo and in vitro and clear pulmonary edema in vivo, levels of inflammatory cytokines in the rat alveolar space and in the plasma, arterial blood gases and pH, as well as levels of low reactive species scavengers (ascorbate, NAC) at 0.5, 6, 12, 24 and 48 h post exposure. These measurements will be repeated following intravenous injections of NAC, ascorbate and deferoxamine as well as albuterol, every 6 h post exposure for 48 h. The subject matter of this research is both timely and important: more than 25 million tons of chlorine is manufactured annually in the United States and the majority of this gas is transported by rail and can be used as a chemical weapon.

Research Topic: Mechanisms of ENaC Inhibition by Replicating Influenza Virus: Role of M2 Protein
Mentor(s): Sadis Matalon, PhD, Alice McNeal Professor and Vice Chairman for Research, Department of Anesthesiology; Professor of Cell Biology, Physiology and Biophysics & Microbiology; Director, Pulmonary Injury and Repair Center, School of Medicine; Professor of Environmental Health Sciences, School of Public Health, University of Alabama at Birmingham; Deputy Editor, American Journal of Respiratory Cell and Molecular Biology
Student Role: Influenza (flu) is a contagious respiratory illness caused by flu viruses, leading to about 36,000 deaths every year in the United States alone, with the potential for at least a ten fold increase in epidemic and pandemic scenarios. During attachment of flu viruses to epithelial cells, hemagglutinin, one of its surface proteins, binds to sialic acid residues, initiating a series of events leading to activation of PKC, which in turn, down-regulates the activity of amiloride sensitive epithelial Na+ channels (ENaC) of tracheal and alveolar cells. It has been thought that these events are responsible for flu-induced rhinorrhea and life-threatening alveolar edema in humans. However, events occurring during the attachment of influenza virus to epithelial cells are likely to be transient and relatively few cells will be initially affected. We propose that M2, a transmembrane protein that plays a critical role in viral replication, enhances intracellular production of reactive oxygen-nitrogen species (RONS) which (i) oxidize and nitrate ENaC; and (ii) activate PKC(. Both processes enhance ENaC ubiquitination and subsequent destruction by the proteasome or lysosome systems. These hypotheses will be tested by completing the following comprehensive in vitro and in vivo studies listed in four specific aims: (1) Identify regions and specific amino acids of the influenza strain A/Udorn/72 M2 proton (H+) channel responsible for ENaC down-regulation in Xenopus oocytes microinjected with 1-,2-, and 3-ENaC. (2) Identify the mechanisms by which M2 decreases ENaC protein levels and function. We propose that M2 enhances intracellular production of reactive oxygen-nitrogen species (RONS) which (i) oxidize and nitrate ENaC; and (ii) activate PKC(. Both processes enhance ENaC ubiquitination and subsequent destruction by the proteasome or lysosome systems (3) Identify the mechanisms by which M2 inhibits amiloride sensitive Na+ currents in human airway (H441) and rat alveolar type II (rATII) cells, expressing native ENaC and (4) Establish the contribution of M2 in the inhibition of lung fluid clearance of mice infected by replicating flu viruses and identify the mechanisms involved. The results of our studies may provide the rational basis for the development of new therapeutic strategies, against a highly conserved region of the viral genome to knockdown M2 expression, and thus broadly and effectively decrease flu induced pulmonary edema and rhinorrhea. Due to the public health impact of influenza, there is a strong need to investigate and develop therapies that address the host response to viral infection, which may contribute to the morbidity and mortality of pathogenic respiratory viruses. PUBLIC HEALTH RELEVANCE: The

results of our studies will provide the rational basis for the development of new therapeutic strategies, such as administration of agents to decrease M2 expression, and thus broadly and effectively decrease the flu-induced rhinorrhea, alveolar edema and hypoxemia. Due to the public health impact of influenza, there is a strong need to investigate and develop therapies that address the host response to viral infection, which may contribute to the morbidity and mortality of pathogenic respiratory viruses.

Research Topic: Urinary Bladder Pain
Mentor(s): Timothy J. Ness, MD, PhD, Professor of Anesthesiology
Student Role: Participation in ongoing studies in rodents related to the effect of neonatal inflammation and the susceptibility to stress. These are whole animal studies that utilize electrophysiological techniques, as well as neurochemical (Western Blot, Elisa) and immunohistochemical techniques.

Research Topic: Stress-Induced Bladder Hypersensitivity
Mentor(s): Meredith Robbins, PhD, Assistant Professor of Anesthesiology
Student Role: Using a urological pain model, we have demonstrated that exposure to experimental stressors magnifies physiological responses to previously innocuous stimuli via a stress-related neuropeptide-mediated mechanism. There appears to specifically be a role for the corticotrophin-releasing factor-2 (CRF2) receptor and its endogenous agonist, urocortin 2, in spinal processing of nociceptive information. A student working on this project would, under supervision, perform experiments utilizing molecular biology, immunohistochemical, behavioral or electrophysiological techniques to gain a better understanding of stress-induced hyperalgesia in a urological system by dissecting out the role of possible CRF-related neuropeptide modulators of pain sensation.

Research Topic: Reactivation of labor epidurals for post partum tubal ligation-success, efficiency and predicators
Mentor(s): Yasser Sakawi, MD, Associate Professor, Director Medical Student Elective in Anesthesiology
Student Role: Patient recruitment and data collection

Host Institution Name: University of California, Irvine

Research Topic: Impact of Ventilation Mode on the Ability of dynamic Parameters to Predict Fluid Responsiveness in Mechanically Ventilated Patients Under General Anesthesia
Mentor(s): Maxime Cannesson, MD, PhD, Associate Professor of Clinical Anesthesiology
Student Role: Data collection, data analysis, acquisition of the medical knowledge necessary to the understanding of the topic, presentation of the data to national meetings, participation in the redaction of the manuscript.

Research Topic: Closed-loop Controlled Fluid Optimization Based on Dynamic Parameters of Fluid Responsiveness
Mentor(s): Maxime Cannesson, MD, PhD, Associate Professor of Clinical Anesthesiology
Student Role: Data collection, data analysis, acquisition of the medical knowledge necessary to the understanding of the topic, presentation of the data to national meetings, participation in the redaction of the manuscript.

Research Topic: Decision Support System for hemodynamic Management During Cardiac Surgery: Impact on Residents' Decision Making Process
Mentor(s): Maxime Cannesson, MD, PhD, Associate Professor of Clinical Anesthesiology

Student Role: Data collection, data analysis, acquisition of the medical knowledge necessary to the understanding of the topic, presentation of the data to national meetings, participation in the redaction of the manuscript.

Research Topic: Goal-directed Fluid Optimization Based on Respiratory Variations in the Pulse Oximeter Plethysmographic Wave form during Moderate Risk Surgery
Mentor(s): Maxime Cannesson, MD, PhD, Associate Professor of Clinical Anesthesiology
Student Role: Data collection, data analysis, acquisition of the medical knowledge necessary to the understanding of the topic, presentation of the data to national meetings, participation in the redaction of the manuscript.

Research Topic: Goal-Directed Fluid Optimization Based on Respiratory Variations in the Arterial Pulse Pressure form during High Risk Surgery
Mentor(s): Maxime Cannesson, MD, PhD, Associate Professor of Clinical Anesthesiology
Student Role: Data collection, data analysis, acquisition of the medical knowledge necessary to the understanding of the topic, presentation of the data to national meetings, participation in the redaction of the manuscript.

Host Institution Name: University of California, San Francisco

Research Topic: Is Posttraumatic Stress Disorder a Risk Factor for Medical and Psychiatric Complications in the Perioperative Period?
Mentor(s): Marek Brzezinski, MD, PhD; Assistant Clinical Professor of Anesthesia
Student Role: Students will have an opportunity to participate in most aspects of an ongoing clinical research study. Students will be involved in participant enrollment, informed consent, questionnaire administration both preoperatively and postoperatively, data collection, and data analysis. Students will leave with a better understanding of construction and implementation of clinical research processes and human subjects' review. Students will also have exposure to psychological and ICU delirium assessment as well as mental health diagnoses and their impact on medical care. Student publication will be encouraged.

Research Topic: Pathophysiology of postoperative delirium and cognitive decline in older surgical patients.
Mentor(s): Jacqueline M. Leung, MD, MPH (Professor of Anesthesia & Perioperative Care), Sakura Kinjo, MD (Clinical Associate Professor of Anesthesia & Perioperative Care)
Student Role: The general expectation from the student's participation is to gain familiarity with clinical research design, critically review medical literature pertinent to the study goals, and participate in one or more aspects of the research activities such as data collection, patient interviews if appropriate, data analysis, presentation of results. Co-authorship in abstracts or papers are not required but highly encouraged

Research Topic: Roles of vascular remodeling in the pathophysiology of aneurysms. Our primary interest is to study the pathophysiology of intracranial and aortic aneurysms using novel animal models. Our goals are to identify the mechanisms for growth and rupture of aneurysms and to develop pharmacological therapies to prevent aneurysmal rupture.
Mentor(s): Tomoki Hashimoto, MD (Associate Professor in Residence)
Student Role: A student is expected to complete a small project that is a subset of a larger project in our lab. The student will conduct experiments on animals and tissues harvested from animals. Techniques will include animal surgery, tissue staining, and molecular biological assays.

Research Topic: Role of endothelial progenitor cells (EPCs) in neurological outcome of cerebral vascular malformation.
Mentor(s): Chanhung Lee, MD, PhD; Associate Professor of Anesthesia
Student Role: The general goal is to expose the student to the fundamentals of stem cell research in clinical studies. The student will learn the basics of cell culture and characteristics of EPCs. He/she may also learn how to analyse the results and prepare a manuscript. Co-authorship on a publication resulting from the student's activities during the fellowship period is highly encouraged.

Research Topic: Cerebrovascular physiology, genomics and vascular biology
Mentor(s): William L. Young, MD; Professor/Vice Chair of Department of Anesthesia
Helen Kim, PhD; Assistant Professor, Department of Anesthesia
Hua Su, MD; Associate Professor, Department of Anesthesia
Ludmila Pawlikowska, PhD; Assistant Professor, Department of Anesthesia
Student Role: Human studies include clinical studies of brain hemorrhage from vascular malformations. A major emphasis is on using genomic techniques to identify risk of poor outcome as well as disease susceptibility. There is emphasis on the contribution of vascular inflammation and various kinds of progenitor cells in mounting abnormal vascular remodeling. Other studies include use of cell and viral therapy to protect or resuscitate the brain from ischemic injury

The student would be expected to pick a project that is fairly well defined by ongoing studies and shepherd it through the fellowship period. The general goal is a broad exposure to clinical and translational neuroscience with an emphasis on cerebrovascular disease research in a multidisciplinary setting. A goal is to be a co-author on a publication resulting from the student's activities during the fellowship period.

Specific Projects would include (a) Genetic predictors and outcome in brain vascular malformations, Role: nat hx rankin analysis (b) Somatic mutation detection in brain AVM by massively high-throughput sequencing , Role: LCM tissue, Mentors: LP, HK); (c) Historical archived brain AVM tissue as a replication cohort for genetic association studies, Role: test nugen WGA kit, Mentors: LP, HK); (d) Integration of gene expression and SNP data for prioritizing SNPs for follow-up studies, Role: data analysis, Mentors: HK); (e) animal studies involving induction of vascular malformations in genetically altered mice using viral transduction of growth factors into brain in order to study lesion pathogenesis.

Research Topic: Basic science: Developmental neurotoxicity of anesthesia. Anesthesia makes neonatal rats dumb for life. We are trying to figure out why that is. We hypothesize that vulnerability to anesthetia corresponds to the period of time during which anesthesia excites (!) the neonatal rat brain. We will block the ion channel that is responsible for the excitatory action of anesthetics in the developing brain to assess if this can prevent anesthesia-induced long-term neurocognitive dysfunction.
Mentor(s): Greg Stratmann, MD, PhD; Associate Professor of Anesthesia
Jeff Sall, MD, PhD; Assistant Professor of Anesthesia
Student Role: 15% clinical anesthesia (general operating room, cardiac OR, pediatric cardiac OR). Participation in busy behavioral experiments during the summer from start to finish including data collection, statistical analysis using statistical package.
Presentation of data at lab meeting and at FAER student research conference at ASA 2010. Co-authorship of resulting manuscript.

Research Topic: Clinical research: Developmental neurotoxicity of anesthesia. Anesthesia makes neonatal rats dumb for life. We are trying to figure out if this happens in humans as well. We collaborate with the Center for Mind and Brain at UC Davis to study the long-term neurocognitive outcome of

anesthesia. We test children aged 6-10 that had 2h or more of anesthesia at 2 years or less for diseases that would not predispose them to neurocognitive decline. We are keenly interested in developing a web-based test battery.
Mentor(s): Greg Stratmann, MD, PhD; Associate Professor of Anesthesia
Jeff Sall, MD, PhD; Assistant Professor of Anesthesia
Student Role: 15% clinical anesthesia (general operating room, cardiac OR, pediatric cardiac OR). Participation in ongoing behavioral testing. Design, development and testing of web-based neurocognitive test battery. Presentation of data at lab meeting and at FAER student research conference at ASA 2010.

Host Institution Name: The University of Chicago

Research Topic: Molecular mechanisms of ischemic neuroprotection (basic science); Clinical studies of post-operative visual loss. The goals of the research are to examine the roles of mitochondrial KATP channels, and associated downstream mediators including PKC, NOS, oxygen free radicals, and mitogen-activated protein kinases in the development of endogenous tolerance to ischemia. In addition, experiments examine the use of stem cells to promote regeneration and novel molecular delivery after ischemia, and magnetic resonance imaging is used to evaluate metabolic function in the retina after ischemia. This research is supported by NIH grant RO1EY10343, Illinois Society for Prevention of Blindness, and the Dean's Research Advisory Committee.
Mentor(s): Steven Roth, MD; Professor of Anesthesia and Critical Care; Chief, Neuroanesthesia
Student Role: The student will participate in design of the study, will perform experiments, analyze data, present results to PI and to the lab group, and prepare a manuscript for publication.

Research Topic: Nicotinic Modulation of the Mesoaccumbens DA System
Our research is focused on determining the cellular mechanisms underlying the behavioral effects of nicotinic acetylcholine receptors (nAChRs) in the central nervous system. Nicotine addiction and nicotinic analgesia are the two main behavioral roles that we are currently investigating. To study these phenomena, we test the effects of nicotine on neuronal excitability in those areas of the nervous system that have been implicated in reward related behavior and pain signaling. We use electrophysiological methods in tissue slice preparations and cell culture. This research is supported by NIH Grant P01 DA19690
Mentor(s): Dan McGehee, PhD; Associate Professor of Anesthesia and Critical Care
Student Role: Students entering my laboratory would be exposed to and have the opportunity to conduct electrophysiological studies of neuronal excitability within the contexts outlined above. There would also be opportunities to examine the expression of nAChR subunit mRNA and protein using molecular, immunocytochemical, and biochemical assays.

Research Topic: Effect of Ginseng on Cisplatin-Induced Emesis
The goal of this project is to use the herbal anti-oxidant, American ginseng, to antagonize the oxidant events and to determine its potential in treating cisplatin-induced emesis. This research is supported by NIH grants R21 AT003255 and P01 AT004418
Mentor(s): Chun-Su Yuan, M.D., PhD; Cyrus Tang Professor of Anesthesia and Critical Care; Director, Tang Center
Student Role: The student will participate in design of the study, will perform experiments, analyze data, present results to PI and to the lab group, and prepare a manuscript for publicati

Research Topic: Optimizing the Sedation Regimen for “Awake” Fiberoptic Intubations

The goals of this series of studies are to: 1) compare the common sedation regimens for awake fiberoptic intubations using respiratory and hemodynamic parameters as the primary endpoints and patient and anesthesiologist satisfaction as secondary endpoints, 2) evaluate the "sticking points" in the airway during fiberoptic intubation, and 3) refine the list of physical characteristics that best predict difficulties with ventilation and/or intubation.
Mentor(s): David B. Glick, MD, MBA: Associate Professor of Anesthesia and Medical Director of the PACU.
Student Role: The student will be involved in study design, data acquisition, data analysis, presentation and manuscript preparation.

Research Topic: Exploring Technical Work Using Cognitive Artifacts
This research will analyze technical work processes involving cognitive artifacts in use at a major urban teaching hospital
Mentor(s): Richard Cook, MD; Associate Professor of Anesthesia and Critical Care; Director, Cognitive Technologies Laboratory
Student Role: The student will participate in design of the study, will perform experiments, analyze data, present results to PI and to the lab group, and prepare a manuscript for publication.

Research Topic: Molecular Mechanisms of Drug Addiction
The goal of this project is to evaluate the role of dopamine receptors or signaling molecules in mediating the long-term behavioral effects of drugs abuse and the relapse process of drug addiction. The resulting knowledge will help to develop treatment strategies to attenuate the development or facilitate the extinction of drug addiction. This research is supported by NIH grants DA25088 and DA17323.
Mentor(s): Ming Xu, Ph.D.; Professor of Anesthesia and Critical Care
Student Role: The student will participate in evaluating the hypothesis and designing feasible experiments, will perform experiments, analyze results, present data to the lab, and possibly prepare a manuscript for publication.

Host Institution Name: University of Cincinnati

Research Topic: Sympathetic sprouting in neuropathic pain
Mentor(s): Jun-Ming Zhang, MD, Msc, Professor of Anesthesiology & Director of Research; Judith A Stong, PhD, Research Associate Professor
Student Role: Making animal model of neuropathic pain, primary cell culture, PCR, immunohistochemical staining of sympathetic fibers, imaging analysis.

Research Topic: Neural and chemical basis of pathological pain
Mentor(s): Jun-Ming Zhang, MD, Msc, Professor of Anesthesiology & Director of Research; Judith A Stong, PhD, Research Associate Professor
Student Role: Participate in making animal model of low back pain, primary cell culture, real time PCR, animal behavioral testing, data analysis, PCR, western blotting.

Research Topic: Sphingosine 1-phosphate receptors and sensitization of sensory neurons
Mentor(s): Jun-Ming Zhang, MD, Msc, Professor of Anesthesiology & Director of Research; Judith A Stong, PhD, Research Associate Professor
Student Role: PParticipate in surgical procedures, behavioral testing, immunohistochemistry, data analysis.

Research Topic: Maturation of spinal nociceptive circuits

Mentor(s): Mark Baccei, PhD, Research Assistant Professor of Anesthesiology
Student Role: Making animal model of pain, animal behavioral testing, data collection/analysis.

Research Topic: Mechanisms of nociception induced by innocuous cold in trigeminal system
Mentor(s): Jianguo Gu, PhD, Professor of Anesthesiology
Student Role: Participate in calcium imaging, primary cell culture, data collection/analysis

Research Topic: Effects of SLC6A4, BDNF and Ecstasy Use on Brain Structure in Young Adults
Mentor(s): Judith A. Strong, PhD, Research Associate Professor
Student Role: Genotyping, PCR, data analysis.

Host Institution Name: University of Colorado Denver

Research Topic: The effect of statin lactones on skeletal muscle cells.
Mentor(s): Uwe Christians, MD, PhD, Professor
Student Role: This project will be part of an NIH sponsored project (NIH RO1 HL071805-03). The goal is to set up an in vitro muscle toxicity model. This model will be based on human cells in combination of state of the art proteomics and biochemical profiling technologies. This model will be set up using statins (HMG-CoA reductase inhibitors) as model drugs. The goal is (A) to evaluate which biochemical pathways in the muscle cells are affected by statins using an unbiased 'shotgun' approach and (B) to assess as to whether the statin acids or the more lipophilic statin lactones are more potent. The student will learn (A) how to plan complex project, (B) technologies such as cell culture, metabolic profiling (GC-MS, LC-MS) and proteomics (2D gels, LC-MS/iontrap and data base searches), (C) data and analysis and presentation of data in our Department's research seminar.

Research Topic: Drug metabolism and pharmacokinetics of the opioid sinomenine.
Mentor(s): Uwe Christians, MD, PhD, Professor
Student Role: Sinomenine is an opioid with anti-inflammatory and anti-pain activities that has been used in Southeast Asia in the treatment of rheumatic arthritis for 4000 years. Our recent work found that sinomenine is a prodrug and its main metabolite, nor-sinomenine, is ten-fold more potent than the parent drug. The student will establish an HPLC-MS assay to quantify sinomenine and its active metabolite, will study the enzyme kinetics of sinomenine metabolism using isolated human liver microsomes and will identify the cytochrome P450 enzymes involved in sinomenine metabolism using individually expressed and isolated cytochrome P450 enzymes, specific antibodies and specific chemical inhibitors.

Research Topic: The effects of sirolimus derivative eluted from coronary stents on smooth coronary muscle cells.
Mentor(s): Uwe Christians, MD, PhD, Professor
Student Role: After initial enthusiasm due to significantly decreased coronary restenosis rates compared with bare metal stents, it has now been realized that drug eluting stents have an increased risk for sometimes fatal late coronary thrombosis. It is the hypothesis of this project that drug doses currently coated on stents are toxic to the coronary muscle cells and instead of selectively inhibiting growth via mTOR, the mammalian target of rapamycin, lead to cell death. The student will be trained in the LC-MS analysis of sirolimus and its metabolites, in cell culture techniques as well as in standard proteomics and metabolomics methodologies. The student will evaluate the dose dependent effect of sirolimus and its metabolites on the metabolism and protein expression of human coronary muscle cells in culture.

Research Topic: The role of the biliary transporter c-MOAT (ABCC2) in the elimination of metabolites of the immunosuppressant cyclosporine.

Mentor(s): Uwe Christians, MD, PhD, Professor
Student Role: Cyclosporine has been the cornerstone of immunosuppressant drug regimens in solid organ transplantation for more than 2 decades. Cyclosporine is a substrate of cytochrome P4503A and is known to cause and to be the target of a multitude of pharmacokinetic drug-drug interactions. Interestingly, the role of active transporters in the elimination of cyclosporine is still poorly understood. There is evidence that active biliary transporters are the site of several cyclosporine drug-drug interactions. One of the most important transporters that seem to be involved in cyclosporine drug-drug interactions is c-MOAT. Interestingly, c-MOAT as an organic anion transporter has a preference for acids. The major metabolite of cyclosporine, AM1A, is a carboxylic acid and therefore may be involved. We will systematically study the effect of c-MOAT in a pharmacokinetic study using wild-type and c-MOAT-deficient rats. The student will carry out the study, will be involved in sample collection and will analyze the concentrations of cyclosporine and its metabolites in blood, urine, bile and hepatic tissue using HPLC/MS, will analyze the data using pharmacokinetics software (WinNonlin) and will prepare a presentation/ publication.

Research Topic: Extracellular adenosine signaling in myocardial ischemia
Mentor(s): Tobias Eckle, MD PhD, Assistant Professor
Student Role: Preliminary data indicate that extracellular adenosine signaling protects the heart from ischemia (Eckle et al. Circulation 2007 and 2008). Here, we will attempt to define the role of one of the four known adenosine receptors in cardioprotection.
The student will help to expose wildtype mice or gene-targed mice for individual adenosine receptors to myocardial ischemia. Additional studies will be performed using bone-marrow chimeric mice to study the contribution of myeloid versus cardiac tissues.

Research Topic: Period-1 in cardioprotection
Mentor(s): Tobias Eckle, MD PhD, Assistant Professor
Student Role: Previous studies suggest a role of metabolic adaptation in cardioprotection from ischemia (see for example Eckle et al. Circulation 2008). Here, we will pursue the role of period-1, a protein important in regulation of metabolic adaptation.
The student will use genetic and pharmacological approaches to address the role of period-1 in mouse models of myocardial ischemia and cardioprotection

Research Topic: Extracellular adenosine in lung protection
Mentor(s): Tobias Eckle, MD PhD, Assistant Professor
Student Role: Preliminary data from our laboratory indicate that during mechanical ventilation extracellular adenosine levels are enhanced and protect the lungs from acute injury (see Eckle et al. Journal of Clin. Invest. 2008, Eckle et al. Journal of Immunology 2007).
The student will learn how to induce acute lung injury in mice, using inhalation of LPS or mechanical ventilation. Using adenosine receptor "knockout" mice, the student will then identify the role of individual adenosine receptors in lung protection from ischemia

Research Topic: Novel approaches to prevent hepatic ischemia reperfusion injury
Mentor(s): Holger K. Eltzschig, MD PhD, Associate Professor
Student Role: Studies from our laboratory indicate that extracellular adenosine generation via the ecto-nucleotidase CD73 (an enzyme located on the outside of the cell membrane that converts AMP to adenosine) is important in liver protection from ischemia (see Hart et al. Gastroenterology 2008).
The student will learn how to induce hepatic ischemia in mice. This will be followed by studies of acute hepatic ischemia in gene-targeted mice for individual adenosine receptors to identify the contribution of extracellular adenosine signaling in liver protection from ischemia.

Research Topic: Neuronal guidance molecule netrin-1 as endogenous activator of adenosine receptors
Mentor(s): Holger K. Eltzschig, MD PhD, Associate Professor and Carol Aherne, PhD
Student Role: We recently identified the neuronal guidance molecule netrin-1 as hypoxia responsive gene (see Rosenberger et al. Nature Immunology 2008). Additional studies in different models indicate that netrin-1 attenuates inflammatory hypoxia via enhancing adenosine-dependent signaling pathways. The student will help with further characterizing the interaction of netrin-1 with the A2B adenosine receptor. Such studies will include in vitro assays of A2BAR activation through adenosine, e.g. my measurements of intracellular cyclic AMP (cAMP).

Research Topic: Novel approaches to reduce stretch-induced lung inflammation in mechanically ventilated patients
Mentor(s): Ana Fernandez Bustamante, MD PhD, Assistant Professor
Student Role: This clinical study will explore novel mechancial ventilation approaches in search of less stretch-induced inflammatory responses in the lung. This work will be performed in adult mechanically ventilated patients at UCH. The student will help with physiology data and sample collection, laboratory analysis (spectrophotometric and ELISA techniques), statistical analysis and interpretation of physiology and experimental data.

Research Topic: Stretch-induced lung injury
Mentor(s): Ana Fernandez Bustamante, MD PhD, Assistant Professor
Student Role: This research program will study the consequences of cyclic mechanical stretch in vitro and mechanical ventilation in vivo on gene transcription. Preliminary data indicate that inflammatory mediators are up-regulated by cyclic mechanical stretch in a time and stretch intensity-dependent manner. Further studies will be aimed to characterize this biological response and its potential translational applications for ventilator-induced lung injury. This work will be performed using in vitro models of human cells submitted to cyclic stretch and animal models submitted to mechanical ventilation (including a adult-sized ovine model).
The student will be working with real-time reverse transcriptase PCR techniques to define changes in gene expression with cyclic mechanical stretch. In addition, changes in transcript level of specific genes will be confirmed on a protein level using Western blot and ELISA analysis. For the in vivo relevance of these findings the student will help with analysis and interpretation of physiology data, as well as with laboratory analysis of animal samples.

Research Topic: Carbon Monoxide Screening in Preanesthetic Children using Masimo Pulse Oximetry to Measure Carboxyhemoglobin
Mentor(s): Robert H. Friesen, MD, Professor; Jeannie Zuk, PhD
Student Role: Exposure to environmental tobacco smoke (ETS) is associated with an increased risk of perianesthetic respiratory complications in children. A quantitative screening tool for ETS in children is desirable because historical screening is inaccurate and unreliable. This project will evaluate carboxyhemoglobin measured by pulse oximetry as a screening tool for exposure to ETS in preanesthetic children and correlate COHb values with urine or plasma cotinine (metabolic product of nicotine). The student will enroll subjects, perform measurements of COHb by pulse oximetry, and collect specimens in the Operating Room for cotinine analysis.

Research Topic: Protection from renal ischemia: Role of extracellular adenosine signaling
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Several studies implicate an important role of extracellular adenosine in tissue protection during conditions of limited oxygen availability. Based on these studies, we will utilize in vitro and in vivo models of renal hypoxia and preconditioning to understand A2BAR-dependent mechanisms of tissue protection during preconditioning. In addition, novel pharmacological approaches to diseases precipitated

by renal ischemia/hypoxia would be made, a medical problem contributing to morbidity and mortality of critically ill patients from different fields of medicine and surgery. The student will learn (i) to investigate renal function by inulin-clearance, (ii) to perform renal ischemia with or without ischemic preconditioning by the hanging weight system, (iii) to measure electrolytes, (iv), to perform metabolic cage investigations, (v) to perform RT-PCR and Western Plot analysis and (vi) immunohistochemistry. (Grenz A, Zhang H, Hermes M, Eckle T, Klingel K, Huang DY, Müller CE, Robson SC, Osswald H, Eltzschig HK. Contribution of E-NTPDase1 (CD39) to renal protection from ischemia-reperfusion injury. FASEB J 21 (11): 2863-2873, 2007.)

Research Topic: Neuronal Guidance Molecule Netrin-1 in Acute Kidney Ischemia
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Recent studies from our laboratory identified netrin-1 as novel mediator for attenuating hypoxia-associated inflammation of the kidneys, which involves the activation of extracellular adenosine receptors. Other studies demonstrated that netrin-1 expression is increased in renal tissues following ischemia. The student will learn (i) to induce renal ischemia in vivo by the hanging weight method, (ii) to conduct renal function tests in mice, (iii) to perform RT-PCR, Western, Immunohistochemistry of netrin and adenosine receptors in the kidney, and netrin determination in blood and urine, and (iv) to generate chimeric mice. (Grenz A, Eckle T, Faigle M, Laucher S, Thompson LF and Eltzschig HK. A2B adenosine receptor dampens hypoxia-induced vascular leak. Blood 111 (4): 2024-2035, 2008.)

Research Topic: Adenosine transporters during renal ischemia
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Once generated into the extracellular milieu, adenosine is rapidly cleared through passive uptake by nucleoside transporters, termed equilibrative nucleoside transporters (ENT). We hypothesize adenosine transport dampens inflammatory hypoxia of the kidney. The goal of these studies is to investigate kidney damage due to hypoxia in gene targeted mice for the ENT1 and ENT2. Moreover we will study the role of the ENT location in renal cells versus hematopoietic cells in chimeric mice. The student will learn (i) to plan a complex project, (ii) to investigate renal function (inulin-clearance, metabolic cage investigation) in in vivo studies, (iii) to perform renal ischemia, (iv) to measure adenosine re-uptake in cell cultures including siRNA studies in in vitro, (v) how to generate chimeric mice. (Grenz A, Osswald H, Eckle T, Yang D, Zhang H, Tran ZV, Klingel K, Ravid K, Eltzschig HK. The reno-vascular A2B adenosine receptor protects the kidney from ischemia. PLoS Medicine 24 (5): 968-986, 2008)

Research Topic: Evaluation of proline hydroxylation as a potential regulatory mechanism in hypoxia.
Mentor(s): Karen Jonscher, PhD, Assistant Professor
Student Role: Under normoxic conditions, proline amino acid residues in the protein hypoxia inducible factor (HIF) are hydroxylated, leading to HIF degradation by the proteasome. Under hypoxic conditions, HIF is not modified; it accumulates and induces gene transcription in a variety of signaling pathways. A bioinformatics screen of human and mouse proteomes reveals potentially hundreds of proteins containing motifs for proline hydroxylation. The goal of this project is to use targeted mass spectrometry to globally identify proline hydroxylation sites in a model of hypoxia. The student will help with generating the list of proteins and peptides to be targeted and will learn to develop multiple reaction monitoring methods for targeted proteomics, prepare samples, and analyze results.

Research Topic: Unraveling oxidative stress pathways in a mouse model of obesity
Mentor(s): Karen R. Jonscher, PhD, Assistant Professor
Student Role: We have recently shown that important metabolic proteins, particularly those involved in the TCA cycle, gluconeogenesis, glycolysis and oxidative phosphorylation, are preferentially modified by acetylation in a mouse model of obesity. Indeed, acetylation appears to be emerging as an important

regulator of cellular function. The goal of this project is to identify proteins modified by carbonyl oxidation in this model, as our prior results suggested potential impairment of oxidative stress defense pathways. The student will learn to immunoprecipitate proteins, perform gel electrophoresis and proteomics sample preparation, and will learn to use nanoscale liquid chromatography mass spectrometry to identify modified proteins. The student will also learn various database searching and data mining techniques.

Research Topic: Does TNF induce mitochondrial hypoxia and the ER stress response?
Mentor(s): Karen R. Jonscher, PhD, Assistant Professor
Student Role: We have previously identified changes in the expression of ER stress response proteins in a mouse model of Chrohn's disease, where the expression of TNF is virtually unregulated. These mice have systemic inflammatory phenotypes, including bowel ulcerations and rheumatoid arthritis. We hypothesize that TNF overexpression leads to mitochondrial hypoxia, resulting in upregulation of the ER stress response pathway and chronic inflammation. The goal of this project is to confirm our initial results using PCR and mass spectrometry. The student will learn proteomics sample preparation, and how to use nanoscale liquid chromatography mass spectrometry to identify modified proteins. The student will also learn various database searching and data mining techniques as well as qRT-PCR.

Research Topic: Biochemical properties of fetal membranes leading to rupture
Mentor(s): Karen R. Jonscher, PhD, Assistant Professor
Student Role: Fetal membranes are the only tissues in the body designed to break, but why some membranes rupture early, some on time, and some not at all is not well understood. In a collaborative effort to correlate biochemical and biomechanical properties (strength, elasticity, etc) of fetal membranes, we are quantifying the expression of several putative mediators of membrane rupture both near and far from the rupture site. The student will learn to prepare samples for proteomic analysis, will learn multiplexed ELISA for cytokine analysis, and will perform confirmatory Western blots.

Research Topic: Development of an LC-MS/MS assay for profiling of endothelial dysfunction markers.
Mentor(s): Jelena Klawitter, PhD, Assistant Professor
Student Role: This project involves as systematic review of the available literature, a systematic training program in modern mass spectrometry technologies, project planning, hands-on development and validation of LC-MS assays following current FDA guidances, analysis of the results and writing a report summarizing the results in preparation of a publication.

Research Topic: Perioperative antibiotic prophylaxis in colorectal surgery and obese patient
Mentor(s): Pierre Moine, M.D., Ph.D., Associate Professor
Student Role: Surgical site infections are the leading cause of postoperative morbidity and mortality after colorectal surgery and add significantly to the cost of care. It is therefore largely admitted that the use of antibiotic prophylaxis for patients undergoing colorectal surgery is imperative. Limited published data exist on appropriate antimicrobial dosing for prophylaxis. In USA, nearly one in every three adults is obese (body mass index (BMI) > 30 kg/m2) and nearly 1 in every 20 adults is morbidly obese (BMI > 40 kg/m2). If obesity is not a risk factor for postoperative mortality or major complications, obesity is an independent risk factor for overall morbidity owing to an increased incidence of minor complications, primarily wound infections. The incidence of would infection increases steadily with increasing BMI. This population poses a significant challenge to clinicians when considering antimicrobial dosing for prophylaxis and treatment of surgical site infection. The objective of this study is to analyze cefoxitin, cefotetan, cefazoline, ceftriaxone, and ertapenem pharmacokinetic and pharmacodynamic target attainments in obese patients using the recommended doses through population modeling and Monte Carlo simulations. Students will be involved in sample collection and will analyze the concentrations of

antimicrobial agents in blood and pericolonic fat tissue using HPLC, will analyze data using pharmacokinetics software , and assist in statistical analyis (Monte Carlo simulations).

Research Topic: Recognition of host immune activation by Streptococcus pneumoniae
Mentor(s): Pierre Moine, M.D., Ph.D., Associate Professor ; Natalie Serkova, Ph.D, Associate Professor ; Karen Jonscher, Ph.D, Assistant Professor
Student Role: Streptococcus pneumoniae remains a major causative agent of life-threatening human diseases accounting for over one million deaths annually worldwide. The molecular processes responsible for diseases and their severity are still incompletely understood. Given that there is accumulating evidence that the Th1 cytokine response is important for clearance of pneumococcal infections, our main hypothesis is that Th1 and/or Th2 cytokines might directly alter S. pneumoniae gene expression profiles. To that end, we will expose cultures of S. pneumoniae to human IL-2, IL-12, INF-a, TNF-a, IL-4, IL-6, IL-10, and IL-13, or to fresh human blood followed by differential genomic, proteomic and metabolomic analyses of the bacterial cells and media, or serum. We will then address the mechanistic details of cytokine binding with the determination of the biding site and specific signaling pathways that mediate these alterations. Students will process samples, will run genomic, proteomic, and metabolomic profiling analysis, and will be trained in data collection, analyses, interpretation, writing, and presentation.

Research Topic: Magnetic Resonance Imaging (MRI) to Determine Spinal Cord Injury and Inflammation.
Mentor(s): Natalie J. Serkova, PhD, Associate Professor
Student Role: In this project, MRI will be used to assess non-invasively time-dependent changes in the spinal cord of rats untreated and treated with IL10-releasing nanoparticles (to prevent spinal cord inflammation). The student will be involved in animal MRI including animal handling and anesthesia, acquisition of MR images, and MRI data analysis.

Research Topic: The effect of chronic hypoxia (altitude) on uteroplacental vascular remodeling in preeclampsia.
Mentor(s): Martha Tissot van Patot, Ph.D., Associate Professor
Student Role: The overall goal of the research is to determine the role of uterine artery smooth muscle and endothelial cells during normotensive and preeclamptic pregnancies. Hypoxia is used to induced changes in similar to those seen during preeclampsia. Students will learn some or all of the following: PCR, western blotting, immunohistochemistry, to work with transgenic animals and will be trained in data collection, analyses, interpretation, writing and presentation.

Research Topic: Mitochondrial adaptation to chronic hypoxia (altitude): physiologic and pathophysiologic responses during pregnancy.
Mentor(s): Martha Tissot van Patot, Ph.D., Associate Professor
Student Role: The goal of this research is to investigate the mechanisms by which mitochondria adapat or fail to adapt to chronic hypoxia during pregnancy. Students will learn methods in molecular biology, nuclear magnetic resonance, cell culture, laser microscopy and PCR. The student will be mentored by the principal investigator in methods of experimental design, data collection and interpretation, writing and presentation.

Research Topic: Induction of heat shock proteins by glutamine.
Mentor(s): Paul Wischmeyer, MD, Associate Professor
Student Role: The student will assist in planning animal studies, will assist in experiments, will collect and analyze samples (Western blot, PCR, 1H NMR), and will analyze and manage data.

Research Topic: Role of the A2B adenosine receptor in diabetic nephropathy
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Diabetic nephropathy is the leading cause of end-stage renal failure in most developed countries with a five-year mortality in these patients approaching 70%. Novel therapeutic approaches to prevent or at least treat diabetic nephropathy are presently an area of intense investigation. Extracellular adenosine represents an endogenous signaling molecule to balance inflammatory reactions under different pathophysiological conditions. Therefore, we aim towards characterizing the role of A2BAR signaling in diabetes-induced kidney disease and test the A2BAR agonist as a therapeutic target. The student will learn (i) to induce streptozotocin-induced diabetes mellitus, (ii) metabolic cage investigations in diabetic mice, (iii) renal function tests in diabetic mice, (iv) to investigate high glucose levels on cell function regarding ischemia and the role of adenosine in in vitro experiments, and (v) RT-PCR, Western, Immunohistochemistry.

Research Topic: From Bench to Bedside: Translating Adenosine Pathways into Patients Undergoing Liver or Kidney Transplantation
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Delayed graft function has been shown to impact long-term graft outcome and cause a significantly higher mortality rate among recipients. Interventions that ameliorate graft injury would therefore improve transplant recipient outcomes. We have previously shown that adenosine generation and signaling pathways attenuate kidney and liver injury associated with ischemia and reperfusion injury (IRI) in animal models. Treatment with a specific AR agonist attenuates ischemic organ damage and improves renal and liver function. Thus we hypothesize that similar pathways are present in human tissues. This clinical study is a first attempt to transfer our findings from bench to bedside and will lay a unique platform for relevant interactions between research and clinic.The student will learn (i) to plan a complex project, (ii) to perform molecular studies on human and murine tissue samples, (iii) to perform liver and kidney ischemia in the mouse, and (iv) how to organize a clinical study.

Research Topic: Development and validation of a novel protein biomarker multiplexing assay
Mentor(s): Jost Klawitter, PhD, Assistant Professor
Student Role: There are several advantages in using HPLC/MS based technology for the specific and quantitative analysis of proteins. The analysis of several protein/peptide biomarkers using conventional ELISA assays is often complicated due to the existence of several isoforms and posttranslational modifications. The antibodies used in ELISA are often non specific and crossreactivity results in inaccurate measurements.
The student will help to develop and validate an assay for the specific quantitative analysis of protein/peptide biomarkers using robotic immunocapture nano-HPLC-MS/MS technology.

Research Topic: Protection from renal ischemia: Role of extracellular adenosine signaling
Mentor(s):
Student Role: Several studies implicate an important role of extracellular adenosine in tissue protection during conditions of limited oxygen availability. Therefore, the goal of these studies is to identify and functionally characterize mechanisms of A2BAR-dependent tissue protection of the kidneys during ischemia. Furthermore we will define the tissue-specific localization of the renal A2BAR and its expressional responses to ischemia in vivo. Based on these studies, we will utilize in vitro models of renal hypoxia and preconditioning to understand A2BAR-dependent mechanisms of tissue protection during preconditioning. Finally, we will define strategies to target the A2BAR during renal ischemia in vivo. These experiments will facilitate significant progress on several fronts, including a more basic understanding of innate mechanisms of renal adaptation to ischemia/hypoxia. In addition, novel pharmacological approaches to diseases precipitated by renal ischemia/hypoxia would be made, a medical problem contributing to morbidity and mortality of critically ill patients from different fields of medicine

and surgery. The student will learn (i) to investigate renal function by inulin-clearance, (ii) to perform renal ischemia with or without ischemic preconditioning by the hanging weight system, (iii) to measure electrolytes, (iv), to perform metabolic cage investigations, (v) to perform RT-PCR and Western Plot analysis and (vi) immunohistochemistry. (Grenz A, Zhang H, Hermes M, Eckle T, Klingel K, Huang DY, Müller CE, Robson SC, Osswald H, Eltzschig HK. Contribution of E-NTPDase1 (CD39) to renal protection from ischemia-reperfusion injury. FASEB J 21 (11): 2863-2873, 2007.)

Research Topic: Adenosine transporters during renal ischemia
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Once generated into the extracellular milieu, adenosine is rapidly cleared through passive uptake by nucleoside transporters, termed equilibrative nucleoside transporters (ENT). As previous studies implicated extracellular adenosine in endogenous attenuation of intestinal inflammation following ischemia, we hypothesized adenosine transport in dampening inflammatory hypoxia of the kidney. The goal of these studies is to investigate kidney damage due to hypoxia in gene targeted mice for the ENT1 and ENT2. Furthermore we will localize these channels in renal epithelial cells and study adenosine uptake in in vivo studies. Moreover we will study the role of the ENT location in renal cells versus hematopoietic cells in chimeric mice. The student will learn (i) to plan a complex project, (ii) to investigate renal function (inulin-clearance, metabolic cage investigation) in in vivo studies, (iii) to perform renal ischemia, (iv) to measure adenosine re-uptake in cell cultures including siRNA studies in in vitro, (v) how to generate generic mice. (Grenz A, Osswald H, Eckle T, Yang D, Zhang H, Tran ZV, Klingel K, Ravid K, Eltzschig HK. The reno-vascular A2B adenosine receptor protects the kidney from ischemia. PLoS Medicine 24 (5): 968-986, 2008)

Research Topic: Neuronal Guidance Molecule Netrin-1 in Diabetic Nephropathy
Mentor(s): Almut Grenz, MD, PhD, Assistant Professor
Student Role: Despite optimal glucose management, up to 40% of patients with long standing type I or type II diabetes develop diabetic nephropathy. In fact, diabetic nephropathy is among the leading causes of morbidity and mortality in diabetic patients. Therefore, novel therapeutic approaches to attenuate diabetic nephropathy are an area of intense investigation. The goal of this study is to investigate the role of the neuronal guidance molecule netrin-1 in modulating renal inflammation during diabetic nephropathy. Previous studies demonstrated that netrin-1 is accumulated in the urine and urinary netrin-1 levels correlated with the degree of diabetic nephropathy. Other studies from our laboratory indicated that the treatment with endogenous netrin-1 attenuates renal inflammation and improves kidney function from diabetes, while gene-targeted mice for netrin-1 experience a more severe phenotype during diabetic nephropathy. Based on these studies, it is our hypothesis that Netrin-1 protects the kidneys from renal inflammation and dysfunction during diabetic nephropathy. The student will learn (i) to induce streptozotocin-induced diabetes mellitus, (ii) metabolic cage investigations in diabetic mice, (iii) renal function tests in diabetic mice, (iv) to investigate high glucose levels on cell function regarding ischemia and the role of adenosine in in vitro experiments, (v) RT-PCR, Western, Immunohistochemistry of netrin in the kidney and netrin determination in blood and urine. (Grenz A, Eckle T, Faigle M, Laucher S, Thompson LF and Eltzschig HK. A2B adenosine receptor dampens hypoxia-induced vascular leak. Blood 111 (4): 2024-2035, 2008.)

Research Topic: Stretch-induced lung injury
Mentor(s): Ana Fernandez Bustamante, MD PhD, Assistant Professor
Student Role: This research program will study the consequences of cyclic mechanical stretch in vitro and mechanical ventilation in vivo on gene transcription. Preliminary data indicate that inflammatory mediators are up-regulated by cyclic mechanical stretch in a time and stretch intensity-dependent manner. Further studies will be aimed to characterize this biological response and its potential translational applications for ventilator-induced lung injury. This work will be performed using in vitro models of

human cells submitted to cyclic stretch and animal models submitted to mechanical ventilation (including a adult-sized ovine model).
The student will be working with real-time reverse transcriptase PCR techniques to define changes in gene expression with cyclic mechanical stretch. In addition, changes in transcript level of specific genes will be confirmed on a protein level using Western blot and ELISA analysis. For the in vivo relevance of these findings the student will help with analysis and interpretation of physiology data, as well as with laboratory analysis of animal samples.

Research Topic: Extracellular adenosine signaling in myocardial ischemia
Mentor(s): Tobias Eckle, MD PhD
Student Role: Preliminary data indicate that extracellular adenosine signaling protects the heart from ischemia (Eckle et al. Circulation 2007 and 2008). Here, we will attempt to define the role of one of the four known adenosine receptors in cardioprotection.
The student will help to expose wildtype mice or gene-targed mice for individual adenosine receptors to myocardial ischemia. Additional studies will be performed using bone-marrow chimeric mice to study the contribution of myeloid versus cardiac tissues …

Research Topic: Period-1 in cardioprotection
Mentor(s): Tobias Eckle, MD PhD
Student Role: Previous studies suggest a role of metabolic adaptation in cardioprotection from ischemia (see for example Eckle et al. Circulation 2008). Here, we will pursue the role of period-1, a protein important in regulation of metabolic adaptation.
The student will use genetic and pharmacological approaches to address the role of period-1 in mouse models of myocardial ischemia and cardioprotection.

Research Topic: Extracellular adenosine in lung protection
Mentor(s): Tobias Eckle, MD PhD
Student Role: Preliminary data from our laboratory indicate that during mechanical ventilation extracellular adenosine levels are enhanced and protect the lungs from acute injury (see Eckle et al. Journal of Clin. Invest. 2008, Eckle et al. Journal of Immunology 2007).
The student will learn how to induce acute lung injury in mice, using inhalation of LPS or mechanical ventilation. Using adenosine receptor "knockout" mice, the student will then identify the role of individual adenosine receptors in lung protection from ischemia

Research Topic: Novel approaches to prevent hepatic ischemia reperfusion injury
Mentor(s): Holger K. Eltzschig, MD PhD
Student Role: Studies from our laboratory indicate that extracellular adenosine generation via the ecto-nucleotidase CD73 (an enzyme located on the outside of the cell membrane that converts AMP to adenosine) is important in liver protection from ischemia (see Hart et al. Gastroenterology 2008).
The student will learn how to induce hepatic ischemia in mice. This will be followed by studies of acute hepatic ischemia in gene-targeted mice for individual adenosine receptors to identify the contribution of extracellular adenosine signaling in liver protection from ischemia.

Research Topic: Neuronal guidance molecule netrin-1 as endogenous activator of adenosine receptors
Mentor(s): Holger K. Eltzschig, MD PhD and Carol Aherne, PhD
Student Role: We recently identified the neuronal guidance molecule netrin-1 as hypoxia responsive gene (see Rosenberger et al. Nature Immunology 2008). Additional studies in different models indicate that netrin-1 attenuates inflammatory hypoxia via enhancing adenosine-dependent signaling pathways.

The student will help with further characterizing the interaction of netrin-1 with the A2B adenosine receptor. Such studies will include in vitro assays of A2BAR activation through adenosine, e.g. my measurements of intracellular cyclic AMP (cAMP).

Research Topic: Magnetic Resonance Imaging (MRI) to Determine Spinal Cord Injury and Inflammation.
Mentor(s): Natalie J. Serkova, PhD, Associate Professor
Student Role: In this project, MRI will be used to assess non-invasively time-dependent changes in the spinal cord of rats untreated and treated with IL10-releasing nanoparticles (to prevent spinal cord inflammation). The student will be involved in animal MRI including animal handling and anesthesia, acquisition of MR images, and MRI data analysis.

Research Topic: Unraveling oxidative stress pathways in a mouse model of obesity
Mentor(s): Karen R. Jonscher, PhD
Student Role: We have recently shown that important metabolic proteins, particularly those involved in the TCA cycle, gluconeogenesis, glycolysis and oxidative phosphorylation, are preferentially modified by acetylation in a mouse model of obesity. Indeed, acetylation appears to be emerging as an important regulator of cellular function. The goal of this project is to identify proteins modified by carbonyl oxidation in this model, as our prior results suggested potential impairment of oxidative stress defense pathways. The student will learn to immunoprecipitate proteins, perform gel electrophoresis and proteomics sample preparation, and will learn to use nanoscale liquid chromatography mass spectrometry to identify modified proteins. The student will also learn various database searching and data mining techniques.

Research Topic: Does TNF induce mitochondrial hypoxia and the ER stress response?
Mentor(s): Karen R. Jonscher, PhD
Student Role: We have previously identified changes in the expression of ER stress response proteins in a mouse model of Chrohn's disease, where the expression of TNF is virtually unregulated. These mice have systemic inflammatory phenotypes, including bowel ulcerations and rheumatoid arthritis. We hypothesize that TNF overexpression leads to mitochondrial hypoxia, resulting in upregulation of the ER stress response pathway and chronic inflammation. The goal of this project is to confirm our initial results using PCR and mass spectrometry. The student will learn proteomics sample preparation, and how to use nanoscale liquid chromatography mass spectrometry to identify modified proteins. The student will also learn various database searching and data mining techniques as well as qRT-PCR.

Research Topic: Biochemical properties of fetal membranes leading to rupture
Mentor(s): Karen R. Jonscher, PhD
Student Role: Fetal membranes are the only tissues in the body designed to break, but why some membranes rupture early, some on time, and some not at all is not well understood. In a collaborative effort to correlate biochemical and biomechanical properties (strength, elasticity, etc) of fetal membranes, we are quantifying the expression of several putative mediators of membrane rupture both near and far from the rupture site. The student will learn to prepare samples for proteomic analysis, will learn multiplexed ELISA for cytokine analysis, and will perform confirmatory Western blots.

Research Topic: Recognition of host immune activation by Streptococcus pneumoniae
Mentor(s): Mentor(s): Pierre Moine, M.D., Ph.D., Associate Professor ; Natalie Serkova, Ph.D, Associate Professor ; Karen Jonscher, Ph.D, Assistant Professor
Student Role: Streptococcus pneumoniae remains a major causative agent of life-threatening human diseases accounting for over one million deaths annually worldwide. The molecular processes responsible for diseases and their severity are still incompletely understood. Given that there is

accumulating evidence that the Th1 cytokine response is important for clearance of pneumococcal infections, our main hypothesis is that Th1 and/or Th2 cytokines might directly alter S. pneumoniae gene expression profiles. To that end, we will expose cultures of S. pneumoniae to human IL-2, IL-12, INF-□, TNF-□, IL-4, IL-6, IL-10, and IL-13, or to fresh human blood followed by differential genomic, proteomic and metabolomic analyses of the bacterial cells and media, or serum. We will then address the mechanistic details of cytokine binding with the determination of the biding site and specific signaling pathways that mediate these alterations. Students will process samples, will run genomic, proteomic, and metabolomic profiling analysis, and will be trained in data collection, analyses, interpretation, writing, and presentation.

Host Institution Name: University of Florida

Research Topic:

Reperfusion Injury Following Liver Transplantation
Mentor(s): Nikolaus Gravenstein, M.D., the J. H. Modell, M.D. Professor of Anesthesiology; Mark Rice, M.D., Clinical Assistant Professor
Student Role: Data collection and compilation of data with respect to adverse physiological changes during liver transplantation (i.e., reperfusion syndrome) as assessed by blood potassium concentration changes, cardiac function via echocardiography, and temperature deviations as determined by invasive temperature monitoring of the graft and host, and forward looking infrared imaging of the graft surface.

Research Topic: Personality Assessment of Resident Applicants for Patient Safety Improvement
Mentor(s): Alexander S. Matveevskii, M.D., Ph.D., Assistant Professor
Student Role: Development and execution of personality inventory testing with creation of an electronic database of quality assurance data for anesthetized patients at Shands Hospital at the University of Florida.

Research Topic: Maternal-fetal monitoring - electrohysterography using optimal linear filtering
Mentor(s): Tammy Euliano, M.D., Associate Professor
Student Role: Patient enrollment, application of monitoring device, data entry, monitoring during labor

Research Topic: GABAA/Glycine Receptor-mediated Excitatory Adverse Effects of Sevoflurane (NINDS 1R21NS060862-01A1)
Mentor(s): Anatoly E. Martynyuk, Ph.D., Research Associate Professor; Christoph N. Seubert, Ph.D., M.D., Associate Professor
Student Role: Provision of sevoflurane-anesthesia for rat pups with acquisition and analysis of electroencephalography

Research Topic: Emergence of Glucose in Exhaled Breath
Mentor(s): Timothy E. Morey, M.D., Professor, Scott Wasdo, Ph.D., Research Assistant Professor, Donn M. Dennis, the J.S. Gravenstein Endowed Professor of Anesthesiology
Student Role: Collection of breath and blood specimens from human subjects after informed consent; data analysis of ion chromatograms; comparison of values using Bland Altman and Clark Error analysis

Research Topic: A Breath-based Medication Adherence Monitoring System for HIV/AIDS Therapies (NIMH 1R43MH081767-01)

Mentor(s): Richard Melker, Ph.D., M.D., Professor; Donn M. Dennis, the J.S. Gravenstein Endowed Professor of Anesthesiology
Student Role: Collection of human breath samples with measurement using a mini-gas chromatogram; analysis of data and comparison with directly observed therapy (DOT) values.

Research Topic: Analysis of NIS (National inpatient sample) database on the occurrence of acute kidney injury among patients with subarachnoid hemorrhage (SAH).
Mentor(s): Azra Bihorac, M.D., Assistant Professor, Joseph Layon, M.D. Professor
Student Role: Students will be involved in learning basics of SAS programming and analysis of large administrative database. Students will work with Drs. Bihorac and Scholds, a statistician, on learning how to manipulate data from NIS and how to perform analysis.

Research Topic: Assessment of microcirculatory changes in the patients with subarrachnoid hemorrhage (SAH) admitted to NICU.
Mentor(s): Azra Bihorac, M.D., Assistant Professor, Joseph Layon, M.D. Professor
Student Role: Students will learn to implement technique of bedside assessment of microcirculation with video microscopy an will be involved also in the clinical data collection. Some basics of the video imaging interpretation will be useful.

Research Topic: Nonvolatile Exhaled-Breath Biomarkers for Clinical Diagnostics.
Mentor(s): Alexander V Glushakov, Ph.D., Research Assistant Professor, Timothy E. Morey, M.D., Professor
Student Role: Collection of breath and blood specimens from human subjects after informed consent; quantitative detection of biomarkers using analytical spectroscopy techniques as well as biochemical and molecular biological methods; analysis of experimental data.

Research Topic: Retrospective analysis of cerebral oximetric findings and outcomes from Procedures involving deep hypothermic circulatory arrest
Mentor(s): Gregory Janelle, M.D., Associate Professor
Student Role: Assist with collection of perioperative data and organization of database, analysis, and compilation of results

Research Topic: Biochemical Markers of Traumatic Brain Injury (NINDS 5R01NS052831-03)
Mentor(s): Steven Robicsek, Ph.D., M.D.
Student Role: Assist in recruitment of patients suffering TBI, collection of specimens and data, compilation of databases and analysis.

Research Topic: Surface Acoustic Wave Technology for Sensing Propofol in Exhaled Breath
Mentor(s): Timothy E. Morey, MD, Professor, Donn M. Dennis, the J.S. Gravenstein Endowed Professor of Anesthesiology.
Student Role: Working veterinary anesthesiologists and engineers to field trial a portable, real time propofol sensor: collecting specimens, operating the instrument, compiling data, performing pharmacokinetic analysis, and other tasks.

Host Institution Name: University of Iowa

Research Topic: Use of Alternative and Complementary Therapies in Pain Relief

Mentor(s): Christina Spofford, MD, PhD, Associate of Anesthesia, and Timothy Brennan, MD, PhD, Samir Gergis Professor of Anesthesia and Vice Chair for Research
Student Role: Under appropriate guidance, the student would learn how to perform a simple surgery on rats and test pain behaviors that are correlated with clinical pain responses in humans after surgery. They would then administer herbal supplements to the animal and measure pain behaviors after the incision. The overall goal is to determine if the compound studied alters pain behavior and could be used as a potential therapeutic in humans. With guidance, the student would collect all data, analyze the data, and write the manuscript.

Research Topic: Surgeon and Anesthesiologist Perceptions of Turnover Times
Mentor(s): Ruth Wachtel, PhD, Associate Professor of Anesthesia, and Franklin Dexter, MD, PhD, Professor of Anesthesia
Student Role: The student role is to organize responses from a survey filled out by surgeons and anesthesiologists, and to compare those results with data obtained from OpTime. The goal is to determine perceptions about the length of turnover times and to compare those perceptions with actual times.

Research Topic: Pain Mechanisms after Surgery
Mentor(s): Timothy Brennan, MD, PhD, Samir Gergis Professor of Anesthesia and Vice Chair for Research
Student Role: Pain management after surgery is one aspect of difficult to control acute pain for patients. We have developed experimental animal models of postoperative pain. Possible experiments include behavioral measures and pharmacologic treatments for incisional pain. For a summer project, a student could learn surgical techniques like spinal catheterization and spinal drug administration. Novel analgesic treatments and their long-term effects could be studied.

Research Topic: Peripheral Nerve Block Injection Pressures Using the Compressed Air Injection Technique: An In Vivo Study in Humans.
Mentor(s): John Laur, MD, Assistant Professor, Medical Director of the Ambulatory Surgery Center
Student Role: Performance of peripheral nerve blocks in animal experiments has demonstrated increased risk of persistent nreve injury after high injection pressures (>20 p.s.i.). Low injection pressures (<20 p.s.i.) were not associated with injury. Using the compressed air injection technique (Ban Tsui, MD-2008) affords a standard method of maintaining a "safe" pressure (<20 p.s.i.) during injection. We aim to measure injection pressures and peripheral nerve outcomes. The student shall obtain data, perform measurements, and assist with statistical analysis and final manuscript authorship.

Host Institution Name: University of Medicine & Dentistry of New Jersey-New Jersey Medical School

Research Topic: A Prosepective, Randomized Study to Determineif Isoflurane Induced Anesrthetic Preconditioning is Valuable in Reducing Postoperative Complications in Elective Liver Resection Liver Resections
Mentor(s): Yuriy Gubenko, MD
Student Role: The student will benefit from their participation in a structured cilinical research study. They will be exposed to Good Clinical Practice (GCP) which ensures the rights and safety of clinical trial subjects and the integrity of clinical data obtained during the conduct of a clinical trial. The student will have the opportunity to have a comprehensive review of the protocol and participate in subject-investigator interactions. They will assist in data collection, analysis and reporting.

Students will benefit from the experience of interviewing potential study subjects and reviewing the medical history to assess the individuals eligibility for inclusion into the study. This study takes palce in the Operating Room and the student will benefit from the experience of spending time in the Operating Room Suite.

A component of the study involves analysis of tissue assays and the student may have the opportunity to assist in the Basis Science Laboratory and learn techniques in that environment as well.

Research Topic: Cellular and molecular mechanisms of Propofol-mediated injury on diseased vessels
Mentor(s): Chunxiang Zhang, MD, PhD
Student Role: The student will benefit from their participation in a structured research study. This is a Basic Science Study conducted in a state of the art laboratory setting. They will be come familiar with Federal regulations regarding the design of procedures involving animals and the performance of same with revelance to human health. The student will have the opportunity to have a comprehensive review of the protocol, participate in laboratory staff-investigator interactions and assist in data collection, analysis and reporting.

The objective of this research project is to identify the cellular and molecular mechanisms of Propofol-mediated injury on diseased vessels. . The project will be performed by the following specific aims: Specific Aim 1 will determine the signaling molecules that are related to Propofol-induced injury on VSMCs in vitro. Specific Aim 2 will determine the roles of microRNAs in Propofol-induced injury on VSMCs in vitro. Specific Aim 3 will determine the effects of antioxidative reagents on Propofol-induced injury on VSMCs in vitro. Specific Aim 3 will verify the in vitro discoveries from Aim 1 to Aim 3 using balloon-injured rat carotid arteries in vivo.

Host Institution Name: University of Miami Miller School of Medicine

Research Topic:
A multi-disciplinary program is underway to evaluate the mechanism of susceptibility to Chronic Pain Syndromes (CPS). Our aim is to identify specific gene-environment interactions important in the pathogenesis of CPS in order to develop better diagnostics and treatments. Adequate treatment for CPS remains a major unmet need. We are using genetic models of susceptibility to peripheral nerve injury to identify the genes and biologic pathways responsible for CPS
Mentor(s): Drs. Eugene Fu, Associate Professor, Chief of the Division of Neuroanesthesiology; Salahhadin Abdi, MD Professor and Chief of Pain Management; Keith Candiotti, MD Associate Professor of Anesthesiology, Internal Medicine and Urology, and Roy C. Levitt, MD Professor of Anesthesiology Perioperative Medicine and Pain Management, Director of Translational Research
Student Role: Students will assist with in vitro and in vivo genetics studies of susceptibility to CPS, including the use of transgenic systems in evaluating the role of specific candidate genes in CPS. Students should become familiar with translational research methods including genomic methods applicable to common complex clinical problems.

Research Topic: Our laboratory is studying risk factors underlying susceptibility to tobacco related diseases including: cardiovascular disease, chronic kidney disease, metabolic syndrome, and lung disease. Adequate treatment for tobacco related disease remains a major unmet need. We are using genetic models of tobacco smoke susceptibility and tissue repair to identify the genes and biologic pathways responsible for end-organ pathology and differential repair. We are working closely with the Divisions of Cardiology, Pharmacology, and Hussman Institute of Human Genomics in this multidisciplinary program.

Mentor(s): Roy C. Levitt, MD Professor of Anesthesiology Perioperative Medicine and Pain Management, Director of Translational Research and Academic Affairs
Student Role: Students will assist with in vitro and in vivo genetics studies, including the genome-wide mapping of susceptibility genes, bioinformatics techniques, and the evaluation of the role of specific candidate genes. Students will become familiar with translational research methods including genomic methods applicable to common complex clinical problems.

Research Topic: The purpose of this trial is to test 2 standards of care with the hypothesis that in multi-system traumatic injury, initial resuscitation with Hextend will stabilize hemodynamics better than an equivalent volume of standard of care crystalloid fluids. With Hextend vs crystalloid, overall fluid requirements will be
reduced, extravasation will be reduced, and outcome will be improved
Mentor(s): Kenneth G. Proctor, PhD Professor of Anesthesiology and Surgery
Student Role: The student will enroll and consent patients, and assist trauma/critical care attending physicians and fellows administer test fluids

Research Topic: The purpose of this study is to develop new triage tool for trauma patients based on heart rate variability (HRV). We intend to prospectively measure EKG in trauma patients in two locations: in the prehospital (the field and during transport by helicopter) and in the hospital setting. In each case HRV will be measured for 5 min and is derived from the EKG signal. HRV, along with other routinely measured variables (blood pressure, respiratory rate, pulse oximetry, etc), will be correlated with injury severity and day of discharge. An algorithm will be constructed using multiple linear regression. We hypothesize that: 1) reduced HRV in the field correlates with bad outcome; 2) the specificity and efficiency of HRV as a screening tool can be improved by controlling factors such as heart rate, age, gender, respiratory rate, and pulse oxygen saturation; 3) an easy to interpret HRV index can be derived that can be used for trauma triage or diagnosis
Mentor(s): Kenneth G. Proctor, PhD Professor of Anesthesiology and Surgery
Student Role: The student will enroll and consent patients, and assist trauma/critical care attending physicians and fellows collect HRV data

Research Topic: The purpose of this study is to determine whether Arginine vasopressin (AVP) is safe and effective to maintain cerebral perfusion pressure (CPP) = 60 mm Hg in patients with traumatic brain injury (TBI). We have already defined risks and benefits of AVP therapy, relative to PE, in four different clinically relevant laboratory model. We now plan to evaluate this new therapy relative to the current evidence-based guideline for CPP management in TBI patients. The working hypothesis is that the risk/benefit profile for AVP is equal, or superior to, PE at equi-effective doses for the management of CPP following TBI. A corollary is that a higher CPP can be safely tolerated with AVP vs PE
Mentor(s): Kenneth G. Proctor, PhD Professor of Anesthesiology and Surgery
Student Role: The student will enroll and consent patients, and assist trauma/critical care attending physicians and fellows care for patients with TBI

Research Topic: The purpose of this study is to critically evaluate three issues related to the treatment of blast injury, we aim:
1: To comprehensively evaluate the structural and functional consequences in a LD50 animal model that simulates blast-induced neuro- and poly-trauma followed by resuscitation with crystalloid (according to standard civilian practice) or Hextend (HEX, 6% hetastarch solution in lactated buffer: according to current military doctrine).
2: To evaluate the causes, and effectiveness of a potential treatment, for trauma-induced coagulopathy
3: To evaluate prophylaxis against intracranial hypertension

4: To evaluate three of the most commonly used alternative anesthetic regimens on structural and functional changes in the cerebral circulation
Mentor(s): Kenneth G. Proctor, PhD Professor of Anesthesiology and Surgery
Student Role: The student will assist a research fellow to design experimental protocols, collect data, analyze and interpret results.

Research Topic: Participate in an ongoing project to study the role of a free radical scavenger; in attenuating chemotherapy induced peripheral neuropathic pain in rats.
Mentor(s): Salahadin Abdi, MD Professor Anesthesiology Preoperative Medicine and Pain Management
Student Role: : The student will learn to the methods and techniques used in behavioral pain research.
1. Proper care, use, and humane treatment of animals used in research.
2. To use different types of behavior instruments and techniques to investigate the effect of the above scavenger in reducing pain in rats.
3. How to collect basic behavioral data, how to analyze it and present it as a poster presentation

Research Topic: The Effects of Genomic Polymorphisms on Acute Pain. The focus of this study is to evaluate the effects of genetic polymorphisms on the pain behavior in patients after surgery-typically nephrectomies. The project has both clinical and basic science elements. Evaluations of markers such as IL-1, IL-6 and CYP2D6, and their polymorphisms, will be evaluated for their effects on pain scores and morphine consumption
Mentor(s): Keith Candiotti, MD Associate Professor of Anesthesiology, Internal Medicine and Urology
Student Role: Students can be involved in this project on different levels. Students will be able to follow patients clinically, assisting with enrollment and the collecting of blood and fluid samples for analysis. Additionally, students can participate in the laboratory section of the study by assisting with the preparation of samples and running of different genomic assays

Host Institution Name: Regents of the University of Michigan

Research Topic: Sex-Specific Risk Profiles and Outcomes of Perioperative Stroke
Mentor(s): George A. Mashour, M.D., PhD, Assistant Professor of Anesthesiology and Neurosurgery; Director of Neuroanesthesiology, University of Michigan Medical School
Student Role: Student will take a primary role in managing and analyzing a national surgical database to assess the incidence and risk factors of perioperative stroke. Student will assist in choosing the variables to be analyzed, based on an extensive review of the current literature on the subject. Student will work with the mentor and biostatistician to analyze the data and will assist in the preparation of a manuscript describing the research findings. Additionally, Student will have opportunities to complement research work in perioperative neurologic outcomes by "shadowing" the mentor in the neurosurgical operating rooms, as well as the neurosurgical intensive care unit.

Research Topic: The mechanism of action for perineural dexmedetomidine added to local anesthetic for sciatic nerve block in rat.
Mentor(s): Chad M. Brummett, M.D.
Director of Pain Research, Department of Anesthesiology; Clinical Lecturer of Anesthesiology
University of Michigan Medical School
Ralph Lydic, Ph.D.
Bert N. LaDu Professor of Anesthesiology Research; Professor of Anesthesiology and Professor
of Molecular and Integrative Physiology

University of Michigan Medical School
Student Role: The student will assist in all final revisions for the study design. He or she will assist in all surgeries and neurobehavioral monitoring. The student will maintain the study database and assist in statistical analysis, with support from senior statisticians. He or she will be the main author on all manuscripts and posters to come from this study, including figure preparation.

Host Institution Name: University of Pennsylvania School of Medicine Department of Anesthesiology & Critical Care

Research Topic: Anesthetic-induced apoptosis and endoplasmic reticulum calcium
Mentor(s): Huafeng Wei, MD, PhD; Assistant Professor
Student Role: The projects in my lab are testing the hypothesis that volatile anesthetics can induce neuronal apoptosis by abnormally releasing calcium from the intracellular calcium stores. The medical students will use cell culture and flurorescence miscroscope to determine changes of intracellular calcium concentration and cell demage by apoptosis after exposure to different volatile anesthetics or other intravenous anesthetics.

Research Topic: Effects of nociceptive stimuli on rCBF in neuroICU patients
Mentor(s): W. Andrew Kofke, M.D. Professor and Director of Neuro-ICU
Student Role: Using continuous rCBF technology student will evaluate effects of nociceptive stimuli such as suctioning, intubation, extubation, foley placement, chest PT, needle sticks, post op pain and the effect of opioids for pain on regional cerebral blood flow. A secondary aim will be to evaluate the role of cbf in the well known impact of nociception to increase icp. CBF observations in patients will be calibrated against XeCTCBF as part of a federally funded study designed to validate the new rCBF monitoring technology.

Research Topic: Anesthetic effects on amyloidogenic proteins
Mentor(s): Roderic G. Eckenhoff, MD, Vice Chair and Professor
Student Role: This project uses cell culture and flow-cytometry to measure effects of different volatile anesthetics on apoptosis in various types of cultured cells. The student will design and conduct assays, analyze and summarize data, and prepare initial abstracts and presentations for meetings.

Research Topic: Anesthesia and sleep neurobiology
Mentor(s): Max Kelz, MD, PhD; Assistant Professor
Student Role: The global hypothesis being tested in my laboratory is that volatile anesthetics exert their hypnotic properties via specific interactions with the neural circuits governing sleep and wakefulness. Ongoing projects use behavioral (righting reflex), physiological (processed EEG/EMG indices) or immunohistochemical (looking for sub-regions of brain whose activity is altered by anesthetics) approaches following pharmacologic or genetic manipulations in mice to determine whether our treatments have altered the organism's sensitivity to inhaled anesthetics. The student will choose to focus on one of these approaches, collect and analyze data and prepare abstracts.

Research Topic: Anesthetic enhancement of Alzheimer pathogenesis
Mentor(s): Roderic G. Eckenhoff, MD, Vice Chair and Professor
Student Role: This project involves the student in ongoing animal experimentation. Transgenic animals that develop Alzheimer-like pathology and behavior will be used to determine whether certain anesthetics accelerate the pathogenesis. This will involve hands-on rodent behavior testing, surgical procedures, and biochemistry. The student will focus on a particular aspect of this work, collect and analyze data, and prepare initial abstracts and presentations for meetings.

Research Topic: Gene therapy for transient neuroprotection.
Mentor(s): James G. Hecker, PhD, MD, Assistant Professor
Student Role: Non-viral gene delivery to the brain depends on the composition of lipids and their formulation with nucleic acids. Dr. Hecker's lab offers opportunities to learn gene delivery to cells, optimization of transfection methods, measurement techniques for analysis of transfection of GFP, luciferase, or Heat Shock Proteins, and to assist with delivery, expression, and in vivo imaging in rodents.

Research Topic: Protein targets of inhaled anesthetics
Mentor(s): Jonas J. Johansson, MD, PhD; Associate Professor
Student Role: This project involves the student in ongoing research of how volatile anesthetics bind to proteins. This may involve techniques like isothermal titration calorimetry, fluorescence spectroscopy, x-ray crystallography and photoaffinity labeling. The student will focus on a given approach, collect and analyze data and then prepare initial abstracts and presentations for meetings.

Research Topic : Targeted drug delivery
Mentor David M. Eckmann, PhD, MD; Associate Professor
Student Role: This project studies targeted drug delivery by exploiting ligand-receptor binding interactions between drug carriers and endothelial cells. Experimental goals include developing nanocarriers for vascular delivery to desired sites - target cells, or tissues. Experiments in cell culture and in rodent models allow tuning of ligand or gene delivery to specific cellular compartments. Recombinant fusion proteins, liposomes, polymer nanocarriers, monoclonal antibodies and other affinity ligands are design elements of drug delivery systems being tested. Targeted drug delivery may lead to improved treatment pain syndromes, cancer, cardiovascular, metabolic and genetic diseases, diabetes, inflammation and infectious diseases, among many others. The student will choose an ongoing project, assist in design, collect and analyze data, prepare abstracts, and present the project to the department.

Research Topic: Mechanisms of organ dysfunction in sepsis
Mentor(s): Clifford S. Deutschman, MD; Professor
Student Role: Our lab studies the effects of sepsis, or overwhelming inflammation, on gene transcription, signal transduction, cell viability and organ function. We use a model of sepsis induced by peritoneal infection in rats and mice. Current projects underway in his lab include 1) The effects of white cell mediators IL-6 and TNF on transcription, signal transduction and cell death in the liver, 2) the effects of adenoviral gene therapy to increase intra-pulmonic expression of the heat shock protein HSP-70 in septic rats on the development of lung injury, 3) altered mitochondrial cytochrome c oxidase activity as an etiology for failed energetics during sepsis, 4) alterations in neutrophil function and modulation of septic responses by the signal transducer dPKC. The student will join an ongoing project, and use state-of-the-art techniques in molecular and cell biology and also focus on outcome.

Research Topic: Perioperative outcomes and costs in high risk surgical patients
Mentor(s): Lee A. Fleisher, MD, Chair and Professor
Student Role: The student will perform retrospective chart reviews and analysis of large databases in selected populations such as bariatric surgery, endovascular stent placement, or obese surgery. They will help select a population and design abstraction instruments and develop the databases after literature reviews to help define predictive models and outcome definitions. If appropriate, they will work with economists or MBAs in the Department to outline the costs of care and adverse events and develop cost-effectiveness models for different interventions. They will be required to present their work at an internal conference and work with members of the Department to develop a manuscript.

Research Topic: Lung injury via Functional MRI

Mentor(s): Mauricio Cereda, MD; Assistant Professor
Student Role: Our group is investigating the use of functional MRI of the lung (using hyperpolarized ^{3}He) in acute lung injury due to sepsis. Existing data suggest that HP ^{3}He MRI of the lung can provide pathophysiological and topographical information that cannot be obtained with conventional imaging techniques. We believe that functional MRI has the potential to be a valuable diagnostic tool in patients with sepsis and that it will allow to better monitor the physiological response to mechanical ventilation and to other therapies.
We are using a murine model of septic acute lung injury obtained by cecal ligation and punctures. Animals then undergo MRI under mechanical ventilation at different times point, as we seek correlations between imaging data, histological appearance, and pulmonary function tests. Students will be involved with animal surgeries, ventilatory support, imaging procedures, data collection, and imaging analysis. The students will also help in abstract and manuscript preparation and will present the study to the department.

Research Topic: tPA and treatment of stroke
Mentor(s): William Armstead, PhD; Res. Assoc. Professor
Student Role: tPA is the only FDA approved treatment for stroke. However, the brief therapeutic window of tPA and the high incidence of post-treatment complications has constrained the clinical use of this potentially life saving drug. The medical student will use an anesthetized piglet model of stroke to determine the effects of this insult on cerebral blood flow, will collect CSF samples to perform biochemical assays, and will use immunohistochemistry and histopathology to determine mechanism and outcome in experiments designed to improve clinical outcome by separating the favorable and harmful activities of tPA.

Research Topic: Endogenous plasminogen activators contribute to impaired cerebral hemodynamics and tissue injury after traumatic brain injury
Mentor(s): William Armstead, PhD; Res. Assoc. Professor
Student Role: Endogenous plasminogen activators such as tPA enhance excitotoxic neuronal cell death through interactions with the NMDA glutamate receptor. In the context of the neurovascular unit, cerebral hemodynamics is thought to influence neuronal cell integrity after CNS ischemic events such as traumatic brain injury (TBI). The medical student will use an anesthetized piglet model of fluid percussion brain injury to determine the effects of this insult on cerebral blood flow, will collect CSF samples to perform biochemical assays, and will use immunohistochemical and histopathologic techniques to determine mechanism of neuronal cell death in experiments designed to identify new therapies to treat victims of TBI.

Research Topic: Lung function after surgery
Mentor(s): E. Andrew Ochroch, MD, MSCE; Associate Professor
Student Role: We are studying the effect of several perioperative interventions to try to maintain lung function after surgery. The student will become familiar with clinical research theory and practice. They will participate in Patient Oriented Research education, and become certified. They will become familiar with the development of a research protocol and the role of the IRB. Direct patient contact will involve performing pulmonary tests on patients preoperatively and postoperatively.

Research Topic: Genetics of Chronic Pain
Mentor(s): E. Andrew Ochroch, MD, MSCE; Associate Professor
Student Role: Students will be doing chart review and adding data to an existing database. The database is of patients who have undergone thoracic surgery. The students will participate in Patient Oriented Research education, and become certified. They will learning fundamental of clinical research including study design, data integrity and analysis.

Research Topic: Morbid Obesity: An Anesthetic Challenge
Mentor(s): Ashish Sinha, MD., Assist. Professor
Student Role: Student Role: We are evaluating the outcomes with different interventions in the care of the morbidly obese. We are doing this by looking at outcomes in different surgical procedures. For instance, do larger patients with ankle fractures have delayed discharges or longer operative times or more infections etc? The same question will be addressed to other surgical procedures in the OR. We have near complete data capture for all patients that pass through the OR. A student would collect and analyze data and prepare abstracts or other write ups and be given credit with authorship if appropriate.
Dr Sinha's group is also active in clinical trials of anesthetic drugs on patients. Current trials include pain drugs, anti-nausea and vomiting drugs, and drugs to decrease side effects of other 'necessary' drugs. Any student that joined us would be involved in patient recruitment and data collection exercises.
Another project involves the use of hyperbaric oxygen for decreasing post surgical neurocognitive deficit.

Research Topic: Leadership, Gender and Stereotypical Concordance during Trauma Resuscitation
Mentor(s): Maureen McCunn, MD., Assistant Professor
Student Role: Observe trauma resusitations from video recordings. Score communications between members of care team according to standardized tools.

Research Topic: The evaluation of the predictive value of the opioid risk tool for identification of patients at high risk for aberrant drug-related behavior.
Mentor(s): Michael Ashburn, M.D. Professor, Director of Pain Medicine
Student Role: This is a retrospective trial in about 300 patients who have provided outcomes data and who have received opioids for the treatment of their chronic pain. We hope to determine if the Opioid Risk Tool (ORT) score, obtained at the time of the initial evaluation, was effective in identifying those patients who went on to demonstrate aberrant drug-related behavior. The student will assist in data collection and analysis.

Host Institution Name: University of Pittsburgh/ University of Pittsburgh Medical Center

Research Topic: Genetics of Post-Mastectomy Pain
Mentor(s): Inna Belfer, M.D., Ph.D., Associate Professor of Anesthesiology
Molecular Epidemiology of Pain Program
Student Role: Clinical: Interviewing patients for pain assessment and quantitive sensory testing; Laboratory: DNA extraction and genotyping of pain candidate genes. Student can participate in either or both components.

Research Topic: Genetics of Labor Pain and Analgesia
Mentor(s): Inna Belfer, M.D., Ph.D., Associate Professor of Anesthesiology
Molecular Epidemiology of Pain Program
Student Role: Clinical: Interviewing patients for pain assessment and quantitive sensory testing; Laboratory: DNA extraction and genotyping of pain candidate genes. Student can participate in either or both components.

Research Topic: Data Mining in the North American Malignant Hyperthermia Registry
Mentor(s): Barbara W. Brandom, M.D., Professor of Anesthesiology
and Michael Young, M.S. Biostatistics
Student Role: Dr. Brandom's group maintains the North American Malignant Hyperthermia Registry. Trainees will participate in research projects involving de-identified data already acquired by the North

American Malignant Hyperthermia Registry (over 4,000 cases), in developing and executing projects based on contacting patients with the malignant hyperthermia (MH) susceptible or MH negative diagnosis, or on clinical research involving patients undergoing anesthesia in the operating room at Children's Hospital. Together with other members of the Anesthesia Pain Service at Children's Hospital, we will perform studies of the management of post-operative or chronic pain in pediatric patients.

In the next few years, Dr. Brandom will continue to expand the methods by which MH susceptible patients can document their physical condition. Research will focus on measures of muscular function that could document the sub-clinical chronic myopathy that is one of the manifestations of some mutations in the ryanodine receptor gene. Trainees will have the opportunities to collaborate with geneticists who can document these and other mutations that increase risk of anesthetic and other stress induced episodes of muscle injury.

Research Topic: A Comparison of Lidocaine Versus Ropivacaine for Bilateral Continuous Thoracic Paravertebral Nerve Blocks for Post-Bowel Surgery Analgesia
Mentor(s): Jacques E. Chelly, M.D., Ph.D., M.B.A., Professor of Anesthesiology and Orthopedic Surgery, Vice Chair of Clinical Research
Student Role: Data collection from patients, patient monitoring, and other clinical research duties.

Research Topic: Continuous Ropivacaine Infusion via Bilateral Paravertebral Catheters Versus Thoracic Epidural Catheters
Mentor(s): Jacques E. Chelly, M.D., Ph.D., M.B.A., Professor of Anesthesiology and Orthopedic Surgery, Vice Chair of Clinical Research
Student Role: Data collection from patients, patient monitoring, and other clinical research duties.

Research Topic: Mechanisms of Hypersensitivity Following Cutaneous or Visceral Organ Insult
Mentor(s): Gerald Gebhart, Ph.D., Professor of Anesthesiology & Director of the Pittsburgh Comprehensive Pain Center
Student Role: A principal focus of the Gebhart laboratory is investigation of the mechanisms of enhanced sensitivity to pain (hyperalgesia - a plastic change in the nervous system) that develops following tissue injury, a common example being sunburn.. Experimental approaches include: single sensory nerve fiber recording, patch clamp recording from identified nerve cell bodies in dorsal root ganglion, and procedures for quantification or localization of peptides, G protein-coupled receptors, immediate early genes and ion channels that play an important role in pain.

Research Topic: Noninvasive Study of Neuroreceptor Systems in the Living Brain
Mentor(s): Ferenc Gyulai, M.D., Associate Professor of Anesthesiology
Student Role: Dr. Gyulai studies anesthetic mechanisms in nonhuman primates and in humans. The first project takes advantage of recent developments in positron emission tomography (PET) that permits the study of neuroreceptor systems noninvasively in the living brain, and thus offers a means to define the neurophysiological basis of unconsciousness produced by general anesthetics. PET is used to study the effect of the general anesthetic isoflurane on the functional state of the $GABA_A$-receptor ($GABA_A$-R), as well as postsynaptic processes directly linked to the receptor, such as neuronal metabolism, in the intact, living brain. Abundant data obtained from *in vitro* and small animal models support that the $GABA_A$-R is an important target for general anesthetics, which potentiate the actions of GABA at the receptor complex. The relevance of this potentiation of receptor function, however, has not yet been explored. This is due to inherent limitations of previous experiments employing destructive techniques. In sharp contrast, using PET methodology and the benzodiazepine ligand ^{11}C-flumazenil (^{11}C-FMZ), Dr. Gyulai's group recently demonstrated in fully intact brain, that isoflurane dose-dependently, and specifically, enhances $GABA_A$-R ligand binding, indicating that modulation of $GABA_A$-R conformational state occurs. To determine whether ^{11}C-FMZ binding is a valid reflection of $GABA_A$-R functional state in the living

brain, experiments are underway to test the specific hypothesis in nonhuman primates that the $GABA_A$-R agonist muscimol enhances ^{11}C-FMZ binding in a dose-dependent manner, as has been shown in *in vitro* studies. To determine whether muscimol-related increase in $GABA_A$-R function translates into enhanced inhibitory transmission, the effect of increasing doses of muscimol on regional neuronal metabolism, ($rCMR_{glu}$) is measured by ^{18}F-deoxyglucose (^{18}F-DG) PET. Analogous muscimol-^{11}C-FMZ binding and muscimol- $rCMR_{glu}$ dose-response curves are also obtained in the presence of isoflurane, to test whether the anesthetic produces a left-shift of these dose-effect curves indicating an increase in agonist affinity for the receptor, as well as a decrease in regional neuronal metabolism due to enhanced $GABA_A$-R function, respectively. The experiments are expected to yield insights into the relationship between isoflurane's effect on the $GABA_A$-receptor alone, as well as the translation of this effect into enhanced inhibitory transmission in various brain regions in the intact, living brain.

Anesthetic mechanisms are also studied *in vivo* in the intact human and primate brain. Studies are in progress to test the specific hypothesis that isoflurane specifically increases $GABA_A$-R *apparent affinity* (K_d) for the ligand ^{11}C-FMZ, rather than *receptor density* (B_{max}) in humans, in a dose-dependent manner using PET. Furthermore, to assess the functional relevance of $GABA_A$-R effects, the association of this conformational change with enhanced GABAergic transmission leading to inhibition of neuronal activity, and decreased $rCMR_{glu}$ is tested. The $GABA_A$-R hypothesis would predict that general anesthetics produce quantitatively similar dose-dependent effects on $GABA_A$-R conformation, as well as on $rCMR_{glu}$. To test these hypotheses, alterations in B_{max} and apparent K_d of the $GABA_A$-R are measured in parallel with reductions in $rCMR_{glu}$, in the same subjects, in selected brain regions, by ^{11}C-FMZ and ^{18}F-DG PET, respectively, in the presence and absence of 1.0 and 2.0 MAC isoflurane. The isoflurane-related changes in B_{max} and apparent K_d of the $GABA_A$-R and $rCMR_{glu}$, measured in the same brain regions, are then correlated by least squares regression.

Research Topic: Role of GABAa Receptors in Anesthetic Action
Mentor(s): Gregg E. Homanics, Ph.D., Professor of Anesthesiology
Student Role: Research in Dr. Homanics laboratory applies genetic dissection of putative molecular targets of inhaled anesthetics to explain the neurophysiologic basis of their actions. Knockin mice with alterations in specific GABAA-R and glycine receptor subunit genes will be created, characterized, and tested. These novel mice will be analyzed with tests spanning molecular, cellular, and behavioral levels. Such a multi-level approach allows a determination of the relevance of a specific drug target (receptor) as a mediator of a specific phenotype (e.g., amnesia).

Techniques student may learn: Molecular biology: recombinant DNA procedures, PCR, Southern blotting, vector construction. Cell culture: embryonic stem cell culture, electroporation, drug selection of clonal cell lines. Animal analysis: whole animal drug responses, behavioral characterization.

Research Topic: The Effect of Microglial Activation on Neurologic Outcome after Deep Hypothermic Circulatory Arrest in Rats
Mentor(s): Patrick M. Kochanek, M.D. Professor of Critical Care Medicine & Director of the Safar Center for Resuscitation Research
Tomas Drabek, M.D., Visiting Assistant Professor of Anesthesiology
Student Role: The role of the student would be assisting during rodent experiments involving cardiopulmonary bypass, assessment of neurobehavioral outcome after deep hypothermic circulatory arrest, evaluation of neurohistochemistry, and magnetic resonance imaging (in cooperation with Carnegie Mellon University).

Research Topic: The Genetics of Pain (in rodents)
Mentor(s): William R. Lariviere, Ph.D., Assistant Professor of Anesthesiology

Student Role: Dr. Lariviere's group is determining the genetics of heritable variability in several pain traits in mice and rats, including inflammatory and neuropathic hypersensitivity. Advanced biostatistics is used to understand which genetic mechanisms are involved in the traits, and in which tissues. Novel genetic targets are then tested with molecular and behavioral methods to ascertain which of the mechanisms are indeed involved.

Students would become familiar with the common behavioral pain tests that we use in the lab, the online biostatistical archives and tools that we use to go from the behavioral traits to the underlying genetic mechanisms, and common molecular and neuropharmacological techniques (drug admin methods) applied to the pain tests.

Research Topic: Creating a Human Patient Simulation of a Clinical Scenario
Mentor(s): William McIvor, M.D., Assistant Professor of Anesthesiology
Student Role: Students working on these projects, under Dr. McIvor's supervision, pick a clinical scenario to program and test that lends itself well to the current fidelity and capabilities of our human patient simulator. Past projects have included scenarios simulating congestive heart failure, acute uncal herniation, diabetic ketoacidosis, and managing patients with or without comorbidities having inductions of general endotracheal anesthesia. Students do a literature review to determine treatment recommendations and published descriptions of the associated vital signs. They then interview local experts (neuro, OB, cardiac anesthesiologists, or whoever is most appropriate) to get their recommendations for the likely vital sign changes seen and treatment interventions, and insight into the pathophysiology being emulated. They then work with Dr. McIvor to program our simulator, the Laerdal SimMan. After honing the program to Dr. McIvor's satisfaction the students arrange to test their scenario with local experts who comment on its validity and fidelity. Students can also participate in designing and carrying out experiments which examine experts' performance during human-patient simulations as a function of conditions associated with the simulation, like fidelity, location, and familiarity with the surroundings.

Research Topic: Cellular Ca^{2+} Homeostasis in Skeletal Muscle and its Relationship to Malignant Hyperthermia
Mentor(s): Jerome Parness, M.D., Professor of Anesthesiology
Student Role: The major area of research in the Parness laboratory surrounds the regulation of intracellular Ca^{2+} release in skeletal muscle as it relates to excitation-contraction coupling. The skeletal muscle sarcoplasmic reticulum (SR) calcium release channel is the ryanodine receptor (RyR1), a homo-tetrameric ion channel, each subunit of 565kDa molecular mass. RyR1 is associated with many SR proteins, but the identity and function of only a few of these are known. A single amino acid change at position 615 of RyR1 in pigs results in a sensitivity to volatile anesthetics comparable to a similar, if not identical, rare, pharmacogenetic syndrome in humans known as malignant hyperthermia (MH). An affected individual exposed to volatile anesthetics responds by releasing massive amounts of intracellular Ca^{2+} in skeletal muscle which stimulates both muscle contraction and various Ca^{2+} dependent metabolic processes resulting in elevated body temperatures and death. Dantrolene, a hydantoin derivative and the only specific therapy for MH, inhibits the release of intracellular Ca^{2+} from SR, presumably by affecting ryanodine receptor/Ca^{2+} channel function. The Parness lab uses dantrolene to help pick apart the regulation of the ryanodine receptor, and attempts to identify the molecular target(s) of dantrolene.

The trainees in Dr. Parness's laboratory will be introduced to the field of cellular Ca^{2+} homeostasis as it relates to the pharmacogenetic syndrome Malignant Hyperthermia (MH), an autosomal dominant syndrome of the hypermetabolic response of skeletal muscle to volatile anesthetics, and the mechanism of action of dantrolene, the drug that truncates this hypermetabolism. The trainees will learn the techniques related to understanding the process of excitation-contraction coupling and Ca^{2+} release in skeletal muscle. These include: skeletal muscle organelle isolation and gradient centrifugation, membrane protein purification, radioligand binding techniques and analysis, cell culture, cDNA purification, mutational

analysis, PCR, transfection, and Ca fluorescence microscopy. The trainees are expected to learn hypothesis generation, experimental design, the importance of controls, and techniques of data analysis.

Research Topic: Molecular Mechanisms of General Anesthesia: an Experimental Approach
Mentor(s): Pei Tang, Ph.D., Associate Professor of Anesthesiology
Student Role: Dr. Tang's major research interests include the determination of sequence-, structure-, and dynamics-function relationships of proteins (particularly those proteins in the central nervous system) and the investigation of the interactions between proteins and low-affinity drugs at the atomic resolution. The ultimate goal is to achieve rational designs of safer drugs with minimal side effects. Both experimental and theoretical approaches are taken in her laboratory to predict protein structures and to understand the molecular mechanisms of complex biological processes, with a strong emphasis on the molecular mechanisms of general anesthesia. Computational sequence analysis, homology modeling, and molecular dynamics simulations are combined with the state-of-the-art experimental tools, particularly multidimensional NMR spectroscopy, to validate theoretical predictions and to provide protein structural and dynamical information. Dr. Tang's research emphasis lies on elucidating the collective mechanisms of protein-protein, protein-membrane, and protein-ligand interactions in ion channels, particularly the neurotransmitter-gated receptors.

Students will receive training in both experimental and theoretical approaches to biomedical research. Experimentally, they will gain hands-on experience in our state-of-the-art instruments, including recently installed high-field NMR spectrometers, to (1) determine high resolution structures of proteins that have been recognized as potential anesthetic targets; (2) characterize interaction sites of anesthetic drugs on proteins and the impact of anesthetic interaction to protein structure and dynamics; (3) evaluate potential factors that contribute to protein aggregations and the aggregation related diseases.

Research Topic: Molecular Mechanisms of General Anesthesia: a Computational Approach
Mentor(s): Pei Tang, Ph.D., Associate Professor of Anesthesiology
Student Role: Students will receive training in both experimental and theoretical approaches to biomedical research. The theoretical approach will expose them to the computational facility at Pittsburgh Supercomputer Center and learn various computation methods, including (1) parameterizations of drug molecules for further use in molecular dynamics simulations; (2) all-atom molecular dynamics simulations of proteins in the absence and presence of anesthetic drugs; (3) the steered molecular dynamics (SMD) simulations to study anesthetic effects on ion permeation in ion channels; (4) simulations of collective protein motions using coarse-grained models.

Research Topic: The Interplay of Oxidants with Nitric Oxide in the Pathogenesis and Pathophysiology of Vascular Dysfunction
Mentor(s): Margaret Tarpey, M.D., Visiting Professor of Anesthesiology
Student Role: Dr. Tarpey's research is centered on the interplay of oxidants with nitric oxide in the pathogenesis and pathophysiology of vascular dysfunction, including hypertension and atherosclerosis. Our laboratory is particularly interested in the involvement of the enzyme, xanthine oxidoreductase in elevated steady state production of superoxide and hydrogen peroxide in diseased vascular tissue. Recent studies have demonstrated that moderate hypoxemia significantly enhances the expression and activity of xanthine oxidoreductase. The implication for enhanced vascular dysfunction in patients with hypoxemia secondary to cardiopulmonary disease is actively being explored. An additional focus of research endeavors is the development of site-directed antioxidants to ameliorate local production of oxidants. Finally, the laboratory directs significant effort to methods of accurate detection of these evanescent reactive species, particularly within a biologic or clinical milieu. Trainees will have the opportunity to study these questions from a variety of experimental approaches, such as kinetic modeling of enzyme inhibition, molecular and cellular biology studies of vascular cells in tissue culture, as well as organ physiology approaches and translational studies in patients with heart failure. Such investigations, aimed

at better understanding of the chemical, biochemical and cellular genesis of vascular dysfunction will provide opportunities to develop targeted therapies for the increasing number of patients with cardiovascular disease.

Research Topic: Asleep-Awake-Asleep Craniotomies and Anesthetic Morbidity and Mortality according to Technique
Mentor(s): Edward Teeple, M.D., Department of Anesthesiology, UPMC Shadyside Hospital
Sharad Khetarpal, M.D., Department of Anesthesiology, UPMC Shadyside Hospital
Arlen Mintz, M.D., Department of Neurosurgery, UPMC Shadyside and Presbyterian Hospitals
Student Role: Project Goal: To collect data from a series of awake and general anesthesia craniotomies to compare the incidents of problems, complications, and benefits of the two techniques.

Methods: A list of patients already exists. An excel sheet will be designed now for use with data collection for this study. The data will be statistically analyzed for significant differences.

Background: A meta analysis of a group of papers describing different methods of anesthesia for awake craniotomies already exists. This project would look at outcomes after applying a new inclusion exclusion criteria grid for these patients. This clinically significant project would be a good learning experience for the student.

Research Topic: Ultrasound-Guided Transversus Abdominis Plane Block for Post-Cesarean Section Analgesia
Mentor(s): Manuel C. Vallejo, M.D., Associate Professor, Director of Obstetric Anesthesia at Magee-Women's Hospital
Student Role: The medical student will help in the recruitment of patients, enter data and write an abstract for presentation at a national meeting.

Research Topic: Modification of Shear Induced Hemolysis by Anesthetic Agents
Mentor(s): Jonathan Waters, M.D., Visiting Associate Professor & Chief of Anesthesiology at Magee Women's Hospital
Student Role: Patient consenting, blood drawing, inducing hemolysis utilizing a validated shear model, blood centrifugation, measurement of hemolysis through spectrophotometry

Research Topic: Inherited Coagulation Dysfunction in Women Who Have Had a Postpartum Hemorrhage
Mentor(s): Jonathan Waters, M.D., Visiting Associate Professor & Chief of Anesthesiology at Magee Women's Hospital
Student Role: Patient consenting, blood drawing, data collection activities

Research Topic: Peripheral Nerve Blocks With Multimodal Analgesics
Mentor(s): Brian Williams, M.D., M.B.A., Associate Professor of Anesthesiology
Student Role: Dr. Brian Williams aims to develop appropriate animal models (rat) addressing the multimodal analgesic nerve block, in order to further advance opioid-sparing analgesia, and aim to reduce patient dependence on opioid analgesics as the primary mechanism of analgesia in the first week(s) after orthopedic surgery. Continuous nerve blocks have helped to reduce opioid requirements, but are technically complicated and subspecialized, while local anesthetics can produce unwanted motor block that may lead to the injury of an insensate extremity. This current study is designed to develop multimodal single-injection nerve blocks, in order to provide (i) sustained pain relief after surgery, (ii) reduced motor block, and (iii) reduced opioid requirements. The applicant student would have roles that would include rat habituation and training, nociceptive and locomotive behavioral testing, and data collation.

Research Topic: Volatile Anesthetic Interactions with Membrane Proteins
Mentor(s): Yan Xu, Ph.D., Professor of Anesthesiology and Vice Chair of Basic Sciences
Student Role: Experimental and theoretical approaches are combined to study how low affinity neurological agents, particularly general anesthetics and alcohols, exert their effects on the central nervous system at the molecular level. The goal is to understand the molecular mechanisms of general anesthesia.

Trainees in Dr. Xu's laboratory have the opportunity to learn a variety of modern techniques, including expression and purification of membrane proteins, immunohistochemistry, high-resolution nuclear magnetic resonance imaging and spectroscopy, imaging reconstruction, 3-D protein structure calculation, and molecular dynamics simulations

Research Topic: Membrane Protein Structural and Dynamical Studies by NMR
Mentor(s): Yan Xu, Ph.D., Professor of Anesthesiology and Vice Chair of Basic Sciences
Student Role: NMR is used to determine the transmembrane domain structures of the human glycine receptor, which is the primary inhibitory receptor in the spinal cord and brainstem and responsible for a wide range of diseases. The long-term goal is to provide the structural basis for novel design of drugs that are disease specific and devoid of side effects.

Trainees in Dr. Xu's laboratory have the opportunity to learn a variety of modern techniques, including expression and purification of membrane proteins, immunohistochemistry, high-resolution nuclear magnetic resonance imaging and spectroscopy, imaging reconstruction, 3-D protein structure calculation, and molecular dynamics simulations

Research Topic: Gene and Stem Cell Therapy for Brain Protection and Revitalization After Cardiac Arrest and Resuscitation
Mentor(s): Yan Xu, Ph.D., Professor of Anesthesiology and Vice Chair of Basic Sciences
Student Role: New gene therapy strategies are being developed to target reperfusion injury after cardiac arrest and resuscitation. Recently, Dr. Xu's group combined gene therapy with stem cell therapy using a non-controversial source of stem cells, in an effort to stop and reverse the neuronal loss and to rebuild neuronal circuitry after reperfusion from prolonged cardiac arrest or stroke.

Trainees in Dr. Xu's laboratory have the opportunity to learn stem cell transplantation, Various stroke models, high-resolution magnetic resonance imaging (MRI), image reconstruction, and confocal microscopy.

Host Institution Name: University of Rochester Medical Center

Research Topic: The bioactivation of nitrite by mitochondria in cardiac ischemia It is well known that nitrite (NO_2^-) is carried in the bloodstream, and can be converted to bioactive nitric oxide by a variety of mechanisms, under hypoxic conditions. In addition, nitrite is now entering clinical trials as a cardioprotective agent for the prevention of myocardial infarction. What is less clear is the role of mitochondria in this process. Several proteins within the mitochondrion have been proposed to exhibit nitrite reductase activity, and this project will aim at delineating the relative importance of these pathways, as well as identifying potentially novel nitrite reductases. In addition the project will look at the downstream mitochondrial signaling effects of nitrite-derived reactive nitrogen species, with an aim of finding novel targets for NO-mediated post-translational protein modifications (e.g. S-nitrosation).
Mentor(s): Paul S. Brookes, PhD. Associate Professor of Anesthesiology
Student Role: Student would learn several lab' skills including animal models of cardiac ischemia, isolation of mitochondria, and a variety of biochemical measurements of nitric oxide metabolites. Student would be expected to generate sufficient data to submit an abstract to a scientific meeting and to present his/her research to the department in a seminar style presentation.

Research Topic: To elucidate functional significance of mitochondrial dynamics. My lab studies the regulation of shape/morphology, of the cellular organelle mitochondrion (i.e. "mitochondrial dynamics"). Our previous studies have identified the protein machinery that regulates mitochondrial dynamics, via the processes of fusion and fission. The functional importance of changes in mitochondrial shape is less clear however. This project will employ various stimulations to cells (both physiological signals and pathologic perturbations) and analyze mitochondrial morphology and cellular functions to define the cause-and-effect relationship, and the participating signaling processes. Multiple molecular reagents, techniques, and model systems are available for this research.
Mentor(s): Yisang Yoon, PhD. Assistant Professor of Anesthesiology
Student Role: The student will be involved in cell culture, design of experiments, preparation and testing of specific molecular reagents (i.e. recombinant DNA technology), as well as the collection of data on mitochondrial morphology using fluorescence microscopy. The student will be expected to keep accurate lab records, and to present their work at lab meetings.

Research Topic: Neuroprotective effects of curcumin in a cell model of Alzheimer disease.It has recently been reported that curcumin may be neuroprotective, in part by reducing protein aggregation. We have recently found that a form of tau that is found in Alzheimer disease brain sensitizes neurons to cell death, and this is likely due in part to its oligomerization, altering protein-protein interactions. Further, we found the expression of this mutant tau compromises mitochondrial structure and function and this is likely due to the pathological conformation of the mutant tau. The focus of this study will be to determine if curcumin can protect neurons expressing this mutant form of tau against cell death and if so, is it due to its effects on the conformation of tau or on mitochondrial function, or both. This is an important project because curcumin and its derivatives are already being considered as therapeutics for the treatment of neurodegenerative conditions and limited clinical trials are already underway. Therefore curcumin can be considered a promising therapeutic for the treatment of Alzheimer disease.
Mentor(s): Gail V. W. Johnson, PhD. Professor of Anesthesiology
Student Role: The student would learn cell culture, immunoblotting, immunocytochemistry, and chemiluminescent oligomerization assays. In addition, the student will also learn how to measure mitochondrial status both biochemical and by using microscopic approaches.

Host Institution Name: University of Texas M.D. Anderson Cancer Center

Research Topic: Retrospective evaluation of percutaneous cement procedures
Mentor(s): Allen Burton, M.D.
Student Role: Through this data review, we expect to describe the types of vertebral fractures and tumor vs. osteoporosis) seen in M.D. Anderson's Pain Management Practice. Patient charts will be reviewed for the time period Jan 2001 to May 2008 to identify patients who have undergone percutaneous vertebral cement procedures. It is expected that this review will identify approximately 410 patients. The following data points will be collected retrospectively through the course of this study:

1) Patient demographics, such as age, sex, co-morbid medical conditions, cancer diagnosis and fracture diagnosis.
2) Outcomes related to procedure(s) to include: short-term pain relief and long-term pain relief, refracture rate, medication consumption, quality of life measurements and complication rates in vertebral fractures in M. D. Anderson's patient population.

Research Topic: Mechanisms of Chemotherapy-Induced Peripheral Neuropathy
Mentor(s): Patrick M. Dougherty, Ph.D.

Student Role: It is well known among cancer care providers that the most common cause of pain in cancer patients arises not from the disease but from the disease treatments. For example, painful neuropathy is the principal dose-limiting factor in chemotherapy with Vincristine, Taxol and Cisplatin. This neuropathy not only produces distress in cancer patients but also limits the effectiveness of their therapy thereby impacting on survival. Chemotherapy-induced pain is also refractory to treatment and often persists in cancer survivors limiting quality of life, rehabilitation and the return to productivity. In that these drugs are the treatment of choice for a multitude of lymphoid and solid tumors, hundreds of thousands of patients each year are affected. The long-term goal of this project is to determine the mechanism of chemotherapy-induced pain and identify potential therapeutic interventions for its relief and prevention. This project is composed of both **clinical** and **basic science** projects.

1. The clinical project involves psychophysical testing in patients who are undergoing or have undergone chemotherapy with Cisplatin, Taxol, Vincristine, or Bortezomib. Specific modalities of sensation are conveyed to the spinal cord in specific subsets of primary afferent fibers. The function of these fiber types can therefore be assessed by applying well-defined stimuli to the skin and quantifying the intensity of stimulation required to provoke reports of sensation in patients. Significant changes in the intensity required to provoke given sensations will indicate dysfunction in specific primary afferent fiber types. In some patients blood levels of pro-inflammatory cytokines will be measured and/or skin biopsies will be collected. A student participating in this project will assist in the psychophysical testing and sample collections from patients who are undergoing or have undergone cancer chemotherapy.

2. The basic science project is geared toward modeling chemotherapy neuropathy in rodents. Rats develop hypersensitivity to mechanical stimulation following 5 to 10 days of treatment with Vincristine, Taxol or Cisplatin. Neurophysiological, immunocytochemical, and biochemical studies are used to define the underlying mechanisms. A student participating in this project will learn how to conduct behavioral analysis of pain sensation in rats, surgical preparation of rats for neurophysiological recording, and the basics of neurophysiological analysis of spinal dorsal horn neurons.

Research Topic: Dorsal Horn Mechanisms of Somatosensory and Pain Encoding
Mentor(s): Patrick M. Dougherty, Ph.D.
Student Role: Hundreds of thousands of patients each year develop chronic pain and hyperalgesia that cannot be adequately managed due to our limited understanding of functional organization in the spinal dorsal horn. This project is composed of a series of interrelated intracellular neurophysiological studies in intact animals and in reduced spinal cord-dorsal root-dorsal root ganglion-preparations with follow-up immunohistochemical analysis of the subject tissues as a means to advance our understanding of spinal mechanisms of somatosensory and pain encoding.

Students participating in this project will assist in conducting whole-cell patch clamp neurophysiological studies of dorsal horn neurons from either intact anesthetized adult rats or using *in vitro* isolated spinal cord preparations from neonatal or young adult rats.

Research Topic: Proteomic Approaches to Opioid Tolerance and Addiction
Mentor(s): Howard B. Gutstein, M.D.
Student Role: The primary focus of our research is to understand the molecular mechanisms underlying the development of opioid tolerance and dependence and the interactions of pain and analgesic signaling. We employ a multidisciplinary approach to understand these problems using cutting-edge techniques. After demonstrating clinical and physiological relevance in animal behavioral studies, we dissect mechanisms underlying opioid tolerance, physical dependence, and pain. Since these are very complex phenomena, involving the interaction of genetic, environmental, and social factors, we have turned to the emerging field of proteomics in an effort to determine in the broadest possible fashion which changes in

cellular signaling are responsible for the adaptations causing opioid tolerance and chronic pain. Combining the techniques of laser-capture microdissection to analyze neurons expressing specific markers, 2-dimensional gel electrophoresis to separate proteins, and high-throughput mass spectrometry for protein identification permits us to address this issue with a power never before imagined.

The overall goal of these projects is to develop more effective therapies for treating chronic pain without causing the devastating side effects of tolerance, dependence, and addiction. Trainees gain experience integrating molecular, genetic, neuroanatomic, biochemical, and behavioral techniques to explore important neurobiological questions from many perspectives. Close relations with clinical colleagues in the pain clinic provide opportunities to translate our basic findings into clinical practice and eventually see the direct application of our efforts.

A tutorial in our laboratory would introduce students to concepts in addiction, pain mechanisms and opioid pharmacology. Students would employ a wide range of integrative techniques to explore these important neurobiological questions from many perspectives. Experience can be gained with techniques such as in situ hybridization, immunocytochemistry, cell culture and transfection, 2-D gel electrophoresis, mass spectrometry, image analysis, and behavioral studies on rats and mice.

Research Topic: Central Control of Autonomic Function
Mentor(s): Dei-Pei Li, M.D.
Student Role: The major goal of the ongoing project is to determine the neural and hormonal mechanisms involved in the central control of autonomic function in normal and disease conditions such as hypertension and heart failure.

- A combination of techniques including retrogradely tracing and whole cell patch-clamp recordings is used to study the projection neurons in the hypothalamic or brainstem slices;
- We also use techniques of microinjection of drugs into the central nucleus and recording cardiovascular parameters to study central control of cardiovascular function in normotensive and hypertensive rats;
- Also, we may also perform immunocytochemistry and Western blots to test the alteration of receptor proteins in hypertensive rats;

Students involved in the ongoing project will gain knowledge of neural and hormonal control of circulation and neurotransmission of the central nervous system. They will learn techniques of general experimental preparation, the principal of performing experiment, basis of scientific study design.

Research Topic: Demographic and Clinical Determinants of Having Do Not Resuscitate (DNR) Orders or Life Support Therapy Withdrawal (LSTW) in the Intensive Care Unit (ICU) of a Comprehensive Cancer Center.
Mentor(s): Joe Nates, M.D.
Student Role: The objective of this study is to describe the demographic and clinical determinants of having a DNR order in a group of adults with cancer admitted to the ICU of a Comprehensive Cancer Center. A secondary aim is to characterize the patients who died in the unit and went into the process of Life Support Therapy Withdrawal (LSTW).

The project is of high importance because characterizing the patients with DNR orders is the first step to describe the process of getting a DNR order. This study will help to understand the preferences and needs of our patients regardless of end-of-life issues. Moreover characterizing the patients who went into LSTW will help clinicians to identify better the transition from implementing aggressive life supportive therapies to providing comfort and respecting a patient's advance planning.

Research Topic: Unconventional Methods or Respiratory Support in Patients with Cancer and Influenza A H1N1.

Mentor(s): Joe Nates, M.D.
Student Role: The global healthcare organizations attention is focused on the latest threat to world health, the influenza pandemic of the century which was announced by the World Health Organization on June 11, 2009. Several countries have been already affected by the influenza epidemic with reports starting to appear in major journals such as the New England Journal of Medicine and the Journal of the American Medical Association.

The objective of this study is to describe the characteristics, treatment and outcomes of patients with cancer who develop critical illness from confirmed or suspected influenza A (H1N1). The study will be crucial to set baseline data on how this pandemic disease affects patients with cancer and to provide information for early detection of the disease.

Research Topic: Patient Satisfaction with Visitation Schedules in the Intensive Care Unit.
Mentor(s): Joe Nates, M.D.
Student Role: Patient satisfaction is an important element to measure quality of care. The Intensive Care Unit is a specialized area of the hospital where medical care is provided in an environment of fast change of care needs of our patients and where the their families are not allowed to stay for long periods of time. We recently changed our visitation policy allowing visitants for longer periods of time and by using an anonymous survey we expect to understand patients' and health care providers' opinions regardless this new policy.

Research Topic: Acute Chronic Pain
Mentor(s): Hui-Lin Pan, M.D., Ph.D.
Student Role: One of the major interests of our laboratory is to determine how pain information is regulated in the spinal dorsal horn and how spinally administered analgesics work in acute and chronic pain. We use the following complementary approaches in our studies:

1. Whole cell patch-clamp recordings in the spinal cord slices to determine the state of synaptic transmission;
2. Immunocytochemistry and Western blots to define the location of proteins and quantify their changes in various pain models;
3. Genetic techniques such as siRNAs and RT-PCR are also used to manipulate gene expressions and examine their relation to phenotypic changes in the spinal cord.

Students will participate in the ongoing projects and will be closely supervised by the senior postdoctoral fellows and faculty members. They will learn the general surgical preparation, the principal of the experimental techniques and gain some hand-on experience in the study design and the experiments.

Research Topic: Mechanisms of Opioid Tolerance and Addiction
Mentor(s): Zhizhong Z. Pan, Ph.D.
Student Role: Currently, opioid-based drugs are still the most effective and widely used analgesics for moderate to severe pain and cancer pain. However, repeated use of opioid drugs required for chronic pain conditions induces analgesic tolerance, physical dependence and drug addiction, which significantly limit the analgesic efficacy and prolonged use of opioid analgesics, leaving millions of chronic pain patients under-treated. As other more effective non-opioid analgesics will not emerge to replace opioid drugs in the foreseeable future, improving the current opioid therapies for chronic pain is a critical and achievable goal. Opioid research over the past several decades has extensively advanced our understanding of how opioids produce analgesia in the central nervous system. Recent animal studies focus on what adaptive changes chronic opioids produce in central pain-modulating and addiction-related circuits and how those changes lead to behavioral tolerance and drug addiction. New insights from these animal studies will

provide a pharmacological basis for improvements of opioid therapies for chronic pain by circumventing the problems of tolerance and reducing the risk of opioid addiction.

Research in this laboratory is animal-based, involving rat models of analgesic tolerance and opioid addiction. Multiple approaches at molecular, cellular and behavioral levels are used to identify chronic opioid-induced adaptations at opioid receptors, signal transduction pathways and synaptic networks in the brain. Based on new research findings, a variety of compounds and pharmacological strategies are tested in the animal models for their effectiveness in reducing analgesic tolerance to chronic opioids and preventing drug addiction.

Students participating in this program will conceptually gain frontier knowledge on analgesic functions and reinforcement effects of different types of opioid receptors and the underlying molecular and cellular mechanisms in acute and chronic conditions. Technically, those students will learn small animal surgeries, creation of small animal models of opioid tolerance and addiction, basic molecular methods for real-time RT-PCR and Western blotting, basics of whole-cell patch-clamp recording *in vitro* and various behavioral tests for assessment of opioid tolerance and addiction in the animal models. Short-term research projects are available to investigate the analgesic efficacy, chronic tolerance and functional interactions of laboratory and clinical opioid or non-opioid compounds with differential pharmacological profiles for opioid receptors.

Research Topic: The Role of Glutamate Transporters in Spinal Pain Mechanisms
Mentor(s): Han-Rong Weng, M.D., Ph.D.
Student Role: Sensitization of *postsynaptic* neurotransmission via glutamate receptors on spinal neurons has emerged as one of the key events underlying chronic pain and hyperalgesia and many insights to potential new therapies have been identified as a consequence of this work. However, the role that glutamate transporters, the system used to terminate excitatory neurotransmission, plays in regulating normal spinal sensory processing and the role that dysfunction in this system might play in acute and chronic pain states has gone largely unexplored. Three subtypes of glutamate transporters are normally expressed in cells of the spinal cord, two (GLAST and GLT-1) in astrocytes and one (EAAC1) in neurons, any or all of which might provide targets for new pain treatments. Students participating in this project will assist in a series of inter-related behavioral, neurophysiological and immunocytochemical studies in rats.

Host Institution Name: The University of Utah

Research Topic: Case control study of risk factors for surgical site infection in primary total hip replacement.
Mentor(s): Harriet W. Hopf, MD, Professor of Anesthestiology
Student Role: The student will be responsible, with supervision, for identifying subjects from the database, reviewing charts and entering data, analyzing the data, and preparing the manuscript.

Research Topic: Prospective observational clinical study of the effect of preoperative yogurt consumption on surgical site infection.
Mentor(s): Harriet W. Hopf, MD, Professor of Anesthestiology
Student Role: The student will be responsible, with supervision, for identifying and enrolling subjects, including informed consent; collecting data in the pre-op clinic on yogurt consumption history and other variables; daily postoperative wound evaluation; data entry and analysis; and manuscript preparation.

Research Topic: Randomized controlled trial of the efficacy of an antimicrobial skin barrier foam protectant for reducing hand contamination and skin irritation in anesthesia providers..
Mentor(s): Harriet W. Hopf, MD, Professor of Anesthestiology
Student Role: The student will be responsible, with supervision, for identifying and enrolling subjects, including informed consent; ensuring that protocol is followed by the enrolled anesthesia providers; collecting samples for culture; assessing hand irritation; administering the satisfaction questionnaire; data entry and analysis; and manuscript preparation.

Research Topic: Fibromyalgia: Activation therapy. Weight management for Fibromyalgia
Mentor(s): Akiko Okifuji PhD, Professor of Anesthesiology
Student Role: Observing and learning clinical research processes, data entry and management, literature review.

Research Topic: Blood-based biomarkers distinguishing Chronic Fatigue Syndrome from Healthy Controls and Other Fatigue Disorders. Chronic fatigue syndrome (CFS) is a health problem affecting from 400,000 to 900,000 adults in the USA. It is so debilitating that fully 25% of sufferers are classified as disabled or unable to be employed, with severe economic consequences to the patient's family and to our nation's taxpayers. CFS is characterized by severe fatigue that does not resolve after rest and has lasted from at least 6 months up to many years, and by other chronic symptoms such as deep muscle pain and worsening of symptoms 24 hours or more after exercise. We firmly believe that CFS involves multisystem dysregulation, including the brain, immune and sympathetic nervous systems. Unique to our approach, however, is inclusion of examination of a recently discovered sensory pathway that has not previously been studied in CFS patients, but has been shown in animal models to be active during postexertional fatigue, inflammation and other manipulations inducing deep muscle hyperalgesia. Consistent and mounting evidence in animal models from Dr. Alan Light's lab and others indicates that the recently identified Acid Sensing Ion Channel-3 (ASIC3) may be the functional molecular receptor for enhanced myalgic pain, and that ASIC3 working in concert with other ion channel receptors, including Purinergic 2X Receptors (P2X4 and P2X5), act together to signal myalgia and fatigue. Dr. Kathleen Light's research has recently linked beta-adrenergic receptor activity to enhanced myalgic pain in Fibromyalgia.
We hypothesized that CFS patients have enhanced vulnerability to fatigue and muscle pain in part because, in these patients, this ion channel based sensory system is dysregulated in the direction of exaggerated sensitivity. Funded by an NIH R21 grant, our research team jointly led by both Drs. Light was the first to complete clinical research showing dysregulation in post-exercise ASIC3, P2X4 and P2X5 ion channel receptors (and also in alpha- and beta-adrenergic receptors) in patients with CFS compared with healthy individuals. Supported by a new grant from the CFIDS Association, we now plan to extend these findings in an effort to determine whether receptor expression of these ion channel receptors on leukocytes, alone or combined with adrenergic receptor expression and measures of pro- and anti-inflammatory cytokine response, can serve as blood sample-based biomarkers for CFS. At present, there is no objective biomarker for CFS, which is greatly needed to aid diagnosis and treatment. This study will serve as the initial effort to use these measures to develop safe and unbiased blood-based biomarkers for CFS.
Mentor(s): Kathleen C. Light and Alan R. Light (Co-Principal Investigators)
Student Role: The student will serve as a Research Assistant, acquiring skills in laboratory techniques such as real-time quantitative PCR to assess gene expression, in exercise testing of patient populations, and in data entry and analysis.

Research Topic: Does isoflurane anesthesia have an antidepressant effect equivalent to that of electroconvulsive therapy (ECT)? Do other anesthetics (e.g. ketamine, propofol) have similar effects? If so by what mechanisms and how can such therapy be optimized? Preliminary clinical studies suggest that

isoflurane has an antidepressant effect at least as effective as ECT without associated cognitive decline. Nevertheless the mechanism is little understood as are optimal dosing and treatment strategies. Pilot work in our laboratory used a mouse model to confirm this antidepressant effect and suggests a novel central nervous system mechanism. This ongoing preclinical project is working to further elucidate mechanisms involved in this treatment as well as optimize therapy to facilitate successful clinical trial and implementation.
Mentor(s): Scott C. Tadler, MD
Student Role: The medical student could participate in all phases of experimentation including: literature review, successful experimental design and implementation to include: mouse behavioral studies, tissue procurement and dissection, preparation of and assay for gene expression using real time polymerase chain reaction, imaging modalities, data analysis, interpretation, manuscript preparation and presentation. This exciting project involves collaboration with Drs. Alan and Kathleen Light as well as members of the Department of Neurology.

Research Topic: Does esmolol have analgesic effects? If so, at what dose and how is it best administered? Are there any potential adverse effects of such practice? Preliminary studies in humans suggest that esmolol has an analgesic effect. Pain scores when compared with traditional opioid based anesthesia demonstrate similar pain scores after laparoscopic cholecystectomy as well as open abdominal hysterectomy, less post-operative opioid use as well as significantly less nausea and vomiting. The mechanism of such an effect as well as optimal dosing and any potential adverse effects has not been studied. At our institution, we are undertaking to evaluate the effect of low and moderate dose intraoperative esmolol infusion on post op pain scores, opioid utilization, nausea/vomiting and other adverse effects such as surgical site infection rates for patients undergoing total hip arthoplasty. Moreover, in our laboratory, we are beginning to examine effects at the peripheral nerve and dorsal root ganglion level which may account for such an effect.
Mentor(s): Scott C. Tadler, MD
Student Role: The medical student could participate in all phases of experimentation including: literature review, successful experimental design and implementation to include: patient enrollment and preparation, staff education, pre-procedure patient evaluation, randomization, data collection (pain scores, evaluation of opioid utilization), data analysis, interpretation, manuscript preparation and presentation. This project involves collaboration with Drs Kathleen Light, Harriet Hopf as well as members of the acute pain service at our institution.

Research Topic: Clinical Evaluation of a Rebreathing Mask to Facilitate Recovery from Anesthesia. There is a much higher chance of an adverse clinical event occurring during recovery from anesthesia than in the operating room. Airway obstruction is the most frequent complication. We developed a charcoal filled rebreathing mask that accelerates the rate of removal of anesthetic vapors and shortens anesthesia recovery time. Patients quickly regain normal cognitive function, homodynamic normalcy and reflexes to that allow for airway protection from secretions and obstruction. We will conduct a clinical trial with 44 patients, measuring their rate of recovery and the incidence of critical events during the first 24 hours after surgery. If successful, the charcoal filled rebreathing mask has the potential to shorten the patients stay in the post anesthesia care unit by 20 min and reduce the risk of a critical event occurring by 60%.
Mentor(s): Dwayne Westenskow, PhD
Student Role: The medical student will manage a clinical trial with 44 patients, measuring the patient's rate of recovery and the incidence of critical events during the first 24 hours after surgery. The student will prepare the data collection forms and will collect data from patients during their recovery from anesthesia. The student will prepare an abstract for presentation at a national anesthesia meeting.

Research Topic: User Interface to Prevent Intravenous Infusion Pump Errors. The unintentional administration of incorrect medication doses through intravenous infusion pumps causes the most dangerous and the most frequent errors occurring in hospitals. A primary factor in the misuse of infusion pumps is the complicated and unintuitive nature of the user interface. We have developed a new interface that uses a large touch-screen on the anesthesia workstation. With the pump interface next to trend plots of blood pressure, heart rate and processed EEG, changes in drug delivery will be better informed and more rational. We use wireless technology to remotely control infusion pumps located next to the patient. A small display panel on the pump shows the drug name, infusion rate and time until empty. The user can program the pump through this small display should the wireless connection fail. We plan to compare the usability of our new remotely controlled infusion pump with a commercially available infusion pump in a simulated operating environment. These simulations will identify potential sources of error introduced with a remote pump, identify means to eliminate these errors and document an improvement in overall human performance for the remote pump interface. If successful a major source of error in the operating room will be reduced and patient safety will improve.
Mentor(s): Dwayne Westenskow, PhD
Student Role: The medial student will help manage the testing of the new infusion pump in a simulated operating room environment. The student will collect data on human performance during the simulations. The student will prepare an abstract for presentation at a national anesthesia meeting.

Host Institution Name: University of Washington

Research Topic: Cardiac metabolism in myocardial ischemia
Mentor(s): Rong Tian, MD, PhD, Professor of Anesthesiology and Pain Medicine
Student Role: participate in a project using transgnic animal models to delineate the molecular mechanisms by which metabolic modulations contribute to cardiac protection during ischemia and reperfusion.

Research Topic: Mitochondrial dysfunction in heart diseases
Mentor(s): Rong Tian, MD, PhD, Professor of Anesthesiology and Pain Medicine
Student Role: determine mitochondrial function in animal models of heart failure and investigate the molecular mechanisms leading to mitochondrial dysfunction during cardiac stresses.

Research Topic: AMPK signaling in cardiac development and hypertrophy
Mentor(s): Rong Tian, MD, PhD, Professor of Anesthesiology and Pain Medicine
Student Role: assist in the study of isoform specific function of AMPK in the heart using conditional gene deletion models.

Research Topic: NMR spectroscopy and imaging of the heart
Mentor(s): Rong Tian, MD, PhD, Professor of Anesthesiology and Pain Medicine
Student Role: participate the technology development of localized NMR imaging of the mouse heart during acute and chronic stresses.

Research Topic: Metabolomics analysis by NMR
Mentor(s): Rong Tian, MD, PhD, Professor of Anesthesiology and Pain Medicine
Student Role: analyze metabolite profiles of clinical and experimental samples using high resolution NMR spectroscopy and link the results to genomic analysis and/or clinical outcomes

Research Topic: Endocannabinoid modulation of itching
Mentor(s): Gregory Terman, MD, Phd, Professor of Anesthesiology and Pain Medicine

Student Role: Student would learn to give intrathecal injections to mice and rats and videotape and score itching and other motor behaviors to evaluate spinal mechanisms of itch.

Research Topic: Mechanisms of opiate prescription deaths
Mentor(s): Gregory Terman, MD, Phd, Professor of Anesthesiology and Pain Medicine
Student Role: Student would learn how to give subcutaneous injections to mice and rats and study the development of tolerance to the pain relieving, sedating and respiratory depressant effect of opiates.

Research Topic: Regional Anesthesia Outcomes in Children
Mentor(s): Sean Flack, MBChb FCA, Assistant Professor of Anestesiology and Pain Medicine
Student Role: Work with mentor to identify topic of interest in pediatric regional anesthesia, followed by interrogation of a national, multicenter database (Pediatric Regional Anesthesia Network). Project examples include efficacy and safety of epidurals in children, complication rates of peripheral nerve blocks in children, etc.

Research Topic: Time from Admission to Surgery for Trauma Patients Affecting Outcome
Mentor(s): Andreas Grabinsky, MD, Assistant Professor of Anesthesiology and Pain Medicine
Student Role: Participate in a retrsopective data analyis and chart review of trauma patients to determine the influence of time from admission to surgery on patient outcome.

Research Topic: Review of cases with extreme blood transfusion in trauma patients
Mentor(s): Andreas Grabinsky, MD, Assistant Professor of Anesthesiology and Pain Medicine
Student Role: Participate in the morbidity and mortality review of selected cases in which trauma patients received unusual high transfusion amounts of different blood products.

Research Topic: Review of paramedic student performance and skills in airway management
Mentor(s): Andreas Grabinsky, MD, Assistant Professor of Anesthesiology and Pain Medicine
Student Role: Participate in the application and evaluation of written and practical tests of paramedic students airway skills and the influence of different training methods.

Research Topic: Retrospective review of incidence and nature of adverse events followin pediatric sedation/anesthesia outside the operating room in a pediatric trauma and burn center
Mentor(s): Ramesh Ramaiah, MD, Acting Asst Professor of Anesthesiology and Pain Medicine
Student Role: Collection of data from the electronic records, data analysis and preparation of manuscript

Research Topic: Trends in anesthesia malpractice claims using the ASA Closed Claims Project Database
Mentor(s): Karen B. Domino, MD, MPH (Professor and Vice Chair for Clinical Research); Karen L. Posner, PhD (Research Professor, Laura Cheney Professor of Anesthesia Patient Safety)
Student Role: In consultation with mentors, choose focused clinical or liability issue for study, conduct literature review, identify important factors from the database to include in a statistical analysis, review malpractice claim narrative summaries to identify additional factors to analyze, write and present scientific abstract of project results.

Host Institution Name: University of Wisconsin-Madison, School of Medicine and Public Health

Research Topic: Spinal Plasticity and Neuropathic Pain (basic)
Mentor(s): Vjekoslav Miletic, PhD, Professor

Student Role: The processing of sensory information in the spinal dorsal horn may undergo significant changes following peripheral nerve injury to ultimately lead to the development of neuropathic pain. We are using a rat model of neuropathic pain to investigate the potential critical contribution of several genes and proteins to this spinal plasticity. The student would participate in multiple phases of data collection and analysis, including surgical preparation and behavioral assessment of the experimental animals and the detection of changes in gene expression by RT-PCR and protein levels by immunoblot procedures.

Research Topic: Fluoropolymer-Based Emulsions for the Intravenous Delivery of Fluorinated Anesthetics (basic)
Mentor(s): Robert A. Pearce, M.D., Ph.D., Professor
Student Role: Although sevoflurane and other fluorinated anesthetics are traditionally delivered by inhalation, there are potential advantages to delivery by the intravenous route. This project examines the anesthetic characteristics of novel formulations of sevoflurane, using in vitro and in vivo techniques. The student will participate in the design, conduct, and analysis of these studies.

Research Topic: Evaluating how General Anesthetics Alter Sensory Perception and Neural Coding in Auditory Cortex (basic)
Mentor(s): Matthew Banks, M.D., Associate Professor
Student Role: Ongoing research in our lab seeks to understand how neural activity patterns in auditory cortex relate to sensory processing in rats. Specifically, we are using general anesthetics as tools to disrupt cortical activity in auditory cortex and asking how these changes in activity relate to changes in performance on sensory discrimination tasks. We are addressing these questions using chronic multielectrode recordings from auditory cortex of rats trained to discriminate acoustic stimuli based on their frequency content. The student will be involved in all aspects of the research, including surgical implants of cortical electrode arrays, behavioral training of implanted rats, electrophysiological recordings from rats and data analysis.

Research Topic: Mechanisms of general anesthetic-induced amnesia (basic)
Mentor(s): Misha Perouansky, M.D., Professor
Student Role: The purpose of these in-vivo animal experiments is to characterize the effects of general anesthetics on central nervous system network activity underlying learning and memory. The student will participate in behavioral experiments (in selected cases together with micro-EEG recordings from the hippocampus using implanted electrodes) with genetically modified mice. The degree and nature of involvement (planning, conducting behavioral experiments, genotyping, electrode implantation, data collection, and data analysis) will depend on the interests and time commitment of the student.

Research Topic: Opioid receptors function and regulation in acute and chronic pain (basic)
Mentor(s): Thomas McDowell, M.D., Ph.D., Associate Professor
Student Role: We are interested in the function and regulation of opioid receptors in primary nociceptors in acute and chronic pain states. Ongoing projects include investigations into the interactions between growth factor receptors and opioid receptors, the mechanisms of opioid receptor desensitization and internalization, and the development of opioid tolerance. Students will help plan experiments, assist with animal surgeries, perform patch clamp recordings from isolated neurons, conduct behavioral tests of nociception in rats and measure changes in opioid receptor expression and trafficking.

Research Topic: Lymphocyte apoptosis in sepsis (basic)
Mentor(s): Jay Yang, MD, PhD, MSEE, Professor
Student Role: Early lymphocyte apoptosis and subsequent inability to fight off the infection is one cause of the high mortality from sepsis. This laboratory project looks at whether preventing lymphocyte apoptosis through molecular biological techniques can enhance survival in sepsis. The student will be

exposed to modern cellular/ molecular biological techniques including creation of engineered viral-vectors, assessment of apoptosis in primary lymphocytes, and the whole animal cecal-ligation-puncture model of murine sepsis.

Research Topic: Membrane metalloproteinase-9 as a biomarker for severe thoracic aneurysm (basic & clinical)
Mentor(s): Martha Wynn, MD, Associate Professor; Jay Yang, MD, PhD, MSEE, Professor
Student Role: MMP-9 is an enzyme known to attack the mechanical support of the aorta. This project looks at the funcitonal consequences (i.e. enzyme function and promoter activity) of the MMP-9 genetic alleles and use this information as a basis for determining whether MMP-9 genetic allele can serve as a biomarker for this disease in humans. The student will be exposed to molecular biology, enzyme function assay, and MMP-9 gene sequencing from human blood samples.

Research Topic: Pre- and Post-operative use of vasopressors (clinical)
Mentor(s): Scott Springman, MD, Professor
Student Role: Electronic medical records (EMR) provide unprecedented opportunity to evaluate clinical practice patterns. Although the use of vasopressors is familiar to all anesthesiologists, the actual usage in clinical practice vary between individuals and between institutions. We wish to document the pre and post -surgical usage of this class of drugs through data-mining of our EMR. Student involvement will be in record review and data collection.

Host Institution Name: Vanderbilt University – Department of Anesthesiology

Research Topic: Investigations into regulated drug transport in cardiac tissue
Mentor(s): Sabina Kupershmidt, PhD- Associate Research Professor
Student Role: drug transport assays cell culture, recombinant DNA work, data analysis

Research Topic: Non-routine events during perioperative care
Mentor(s): Matthew B. Weinger MD, Professor Anesthesiology
Jason Slagle PhD, Assistant Professor Anesthesiology
Student Role: Data collection and analysis

Research Topic: The effects of individual clinician and team workload on surgical quality and outcomes
Mentor(s): Matthew B. Weinger MD, Professor Anesthesiology
Jason Slagle PhD, Assistant Professor Anesthesiology
Student Role: Data collection and analysis

Research Topic: Simulation modeling of perioperative patient flow: Impact on quality and efficiency

Mentor(s): Dan France, PhD, MPH Assistant Professor Anesthesiology, Biomedical Engineering, Emergency Medicine, Matthew B. Weinger MD, Professor Anesthesiology
Student Role: Data collection, Computer modeling and analysis

Research Topic: Perioperative handoffs, communication, and coordination
Mentor(s): Matthew B. Weinger MD, Professor Anesthesiology, Jason Slagle PhD, Assistant Professor Anesthesiology, Dan France PhD, MPH Assistant Professor Anesthesiology, Biomedical **Engineering,** Emergency Medicine , Anne Miller, RN, PhD
Student Role: Data collection and analysis

Research Topic: Small-molecule binding sites in G protein-gated inward rectifying potassium (GIRK) channels
Mentor: Jerod Denton, Ph.D.
Student's Role: Employ molecular biology and two-electrode voltage clamp electrophysiology to map small-molecule binding sites in GIRK potassium channels.

Research Topic: Effectiveness of parent controlled analgesia
Mentor(s): JK Deshpande, MD Professor of Anesthesiology and Pediatrics, Anesthesiologist- In -Chief and Stephen Hays, MD Associate professor of Anesthesiology and Pediatrics
Student Role: student PI - a) participate in formalizing study design b) interview parents/patients and staff c) analyze data d) generate draft manuscript/report of study findings for presentation and publication

Research Topic: improving patient safety: near miss events in a pediatric perioperative unit
Mentor(s): JK Deshpande,MD Professor of Anesthesiology and Pediatrics, Ira Landsman, MD, Associate Professor of Anesthesiology Matt Weinger MD Professor of Anesthesiology
Student Role: a) participate in study design b) collate incident reports from the hospital's event reporting system c) analyze reports to identify themes and areas of possible improvement d) participate in designing interventional study aimed at reducing occurrence of patient events/incidents

Research Topic: Quality improvement project – quality of life in children after surgery
Mentor(s): JK Deshpande, MD Professor of Anesthesiology and Pediatriscs, Ira Landsman, MD, Associate Professor of Anesthesiology
Student Role : student PI - a) participate in formalizing study design b) interview parents/patients and staff c) analyze data d) generate draft manuscript/report of study findings for presentation and publication

Research Topic: increasing success of intravenous access by use of Ultrasound
Mentor(s): JK Deshpande, MD Professor of Anesthesiology and Pediatriscs, Ira Landsman, MD, Associate Professor of Anesthesiology
Student Role: Participate in formalizing study design. b) Data gathering and analysis c) generate draft manuscript and report of study findings for presentation and publication

Research Topic: Improving delivery of perioperative CPR
Mentor(s): JK Deshpande, MD Professor of Anesthesiology and Pediatriscs, Ira Landsman, MD, Associate Professor of Anesthesiology
Student Role: Participate in formalizing study design. b) Data gathering and analysis c) generate draft manuscript and report of study findings for presentation and publication

Research Topic: Determining risk factor for delirium
Mentor(s): Pratik Pandharipande MD, Associate Professor of Anesthesiology
Student Role: data collection and analysis

Host Institution Name: Washington University

Research Topic: Barnes-Jewish Apnea Prevalence in Every Admission Study (B-JAPNEAS)
Mentor(s): Michael Avidan, MD, Associate Professor of Anesthesiology, Cardiothoracic Division Chief

Student Role: Involvement in epidemiological screening program for obstructive sleep apnea (OSA) with the Berlin Questionnaire and the Flemons' Index. Students will learn about data entry and analysis,

and will have the opportunity to gain experience with software, such as Microsoft Access and SPSS. Students will have the opportunity to participate in writing scientific manuscripts.

Research Topic: BIS or Anesthesia Gas to Reduce Explicit Recall (BAG-RECALL); a 6000 patient multi-center study
Mentor(s): Michael Avidan, MD, Associate Professor of Anesthesiology, Cardiothoracic Division Chief
Student Role: Students will learn about the complication of awareness during anesthesia with subsequent explicit recall. Students will help to implement protocols designed to decrease the likelihood of this complication. They will learn about key concepts of anesthesia as well as electroencephalogram features of general anesthesia. They will be actively involved in practical aspects of the research: in recruiting patients to the study, in conducting the study in the operating rooms, and in administering questionnaires to patients who participate in the study. Students will be expected to present a PowerPoint presentation to the research team, and will have the opportunity to provide input to a scientific manuscript. Details of the study can be found at the following site:
http://www.clinicaltrials.gov/ct2/show/NCT00682825

Research Topic: A Simulation-Based Curriculum for Cardiovascular Physiology
Mentor(s): David J. Murray, Carol B. and Jerome T. Loeb Professor of Medicine, Director, Howard and Joyce Wood Simulation Center and Anesthesiologist-in Chief, Division of Pediatric Anesthesiology
Student Role: Students will design a set of four simulation-based Cardiovascular Physiology exercises for 1st year medical students. Many of the concepts taught in 1st year Physiology and Pharmacology require clinical correlation to reinforce concepts and provide medical students with a framework to build upon in clinical patient care settings. The goal of this research project is to use medical students who have just completed these courses to design more effective experiences using a simulation laboratory. Electromechanical mannequins with software interfaces and programming ability provide a means for students to model cardiac and respiratory physiologic variables in order to determine their impact on a simulated 'patient' . The student will establish the laboratory procedures that would demonstrate specific physiology concepts as these principles apply to clinical settings.

Research Topic: A Simulation-Based Curriculum for Respiratory Physiology
Mentor(s): David J. Murray, Carol B. and Jerome T. Loeb Professor of Medicine, Director, Howard and Joyce Wood Simulation Center Anesthesiologist-in Chief, Division of Pediatric Anesthesiology
Student Role: Students will design a set of simulation-based Respiratory Physiology exercises for 1st year medical students. Many of the concepts taught in 1st year Physiology and Pharmacology require clinical correlation to reinforce concepts and provide medical students with a framework to build upon in clinical patient care settings. The goal of this research project is to use medical students who have just completed these courses to design more effective experiences using a simulation laboratory. Electromechanical mannequins with software interfaces and programming ability provide a means for students to model cardiac and respiratory physiologic variables in order to determine their impact on a simulated 'patient' . The student will establish the laboratory procedures that would be conducted to demonstrate specific physiology concepts as these principles apply to clinical settings.

Research Topic: The VISION Study
Mentor(s): Peter Nagele, MD, Assistant Professor of Anesthesiology
Student Role: Our group has several exciting clinical and translational research projects in the field of personalized medicine, pharmacogenomics and perioperative outcomes. Specifically we are interested in perioperative myocardial infarction and we are a study site of one of the largest outcomes studies ever done in perioperative medicine – the VISION study with 40,000 patients worldwide. Medical students would be involved in all aspects of the research projects depending on their interest. Dr. Nagele has been a FAER mentor for medical students in 2008. Dr. Peter Nagele has been awarded a K23 Mentored

Patient-Oriented Research Career Development Award from the NIGMS for his project titled "Pharmacogenetics: Nitrous oxide and anesthetic outcomes"

Research Topic: Pharmacogenetics of Adverse Outcomes after Nitrous Oxide Anesthesia
Mentor(s): Peter Nagele, MD, Assistant Professor of Anesthesiology
Student Role: Being actively involved in the clinical trial, screening and enrolling study patients, following them throughout surgery and their postoperative period, collect research data, learn how clinical research works in a large clinical trial.

Research Topic: Define the mechanisms whereby certain genes control hypoxic cellular injury and adaptation.
Mentor(s): Charles Michael Crowder, M.D., Ph.D., Associate Professor of Anesthesiology
Student Role: Utilizing C. elegans as the primary model organism, the student will perform molecular genetic and cell biological experiments examining the role of protein homeostasis in hypoxic cellular injury. Various methods including genetic crosses, DNA construct building, fluorescent microscopy, and metabolic measurements will be used by the student in these projects. Being intimately involved in this ongoing research the student will gain valuable incite in the basic application of science to medicine

Research Topic: Mechanism of ritonavir changes in methadone pharmacokinetics and pharmacodynamics: studying Methadone metabolism and clearance
Mentor(s): Evan Kharasch, MD, PhD, Professor of Anesthesiology, Division Chief of Clinical and Translational Research
Student Role: Participate in laboratory experiments designed to evaluate the human cellular transporters and enzymes at the blood-brain barrier, intestine, liver and/or kidney; performing exkperiments to determine which enzymes are responsible for tissue influx and efflux, thus determining the onset and elimination of opioid effects.

Host Institution Name: Yale University

Research Topic: Vascular Regeneration in Vitro
Mentor(s): Laura E Niklason MD, PhD - Professor & Vice-Chair, Anesthesiology
Student Role: Perform experiments in cell biology, biochemistry, and molecular biology to study events involved in vascular regeneration from differentiated and precursor cells in vitro.

Research Topic: Lung Epithelial Regeneration
Mentor(s): Laura E Niklason MD, PhD - Professor & Vice-Chair, Anesthesiology
Student Role: Participate in epithelial cell culture on biomimetic lung scaffolds, within bioreactors that mimic fetal breathing movement in vitro.

Research Topic: Noninvasive Monitoring of Cardiovascular Waveforms
Mentor(s): David Silverman MD - Professor & Director of Departmental Clinical Research; & Kirk Shelley MD, PhD - Professor in Anesthesiology
Student Role: Participate actively in studies of autonomic reactivity in patients and controls, as well as the non-invasive assessment of intravascular volume status.

Research Topic: Noninvasive Monitoring of Periooperative Stress Response
Mentor(s): David Silverman MD - Professor & Director of Departmental Clinical Research

Student Role: Participate in studies monitoring the stress response, and attempt to modulate this response with interventions such as high-dose statin therapy.

Research Topic: Investigation of role of immune response in chronic pain
Mentor(s): Chao Ma PhD - Assistant Professor of Anesthesiology
Student Role: Assist with rodent experiments and cellular preparations of chronic pain models, and use biochemical and molecular techniques to identify the role of immune complexes in neural transmission.

Research Topic: Assessment of Pain Mechanisms
Mentor(s): Robert LaMotte PhD - Professor of Anesthesiology
Student Role: Participate in laboratory assessments of pain mechanisms in animals and humans, and study means of pain modulation.

Research Topic: Assessment of mechanisms of cutaneous itch
Mentor(s): Robert LaMotte PhD - Professor of Anesthesiology
Student Role: 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.

Research Topic: Perioperative applications of Alternative Medicine
Mentor(s): Shu-Ming Wang MD - Associate Professor of Anesthesiology
Student Role: Participate in studies which assess the application of acupuncture, hypnosis and other means to relieve periooperative pain and anxiety.

Research Topic: fMRI Imaging of impact of general anesthetics
Mentor(s): Ramachandran Ramani MD - Associate Professor of Anesthesiology
Student Role: Participate in studies of human and rodent exposure to general anesthestics, assist with analysis of data and images obtained from function magnetic resonance measurements of blood flow and metabolic activity.

Research Topic: Studies of Neuroscience of Alcoholism
Mentor(s): Albert Perrino MD - Professor of Anesthesiology
Student Role: Participate in clinical studies of alcholic patients within the VA medical system, assist with imaging of brains of affected patients to understand neurocognitive abnormalities.