Brown University

2017 PLME SRA Package

Summer Research Assistantships are offered to PLME students and carry with them a stipend of $3,500.

How are SRAs Awarded?

- Students must submit an application for a specific research project.
- Student proposals/applications are reviewed by a committee comprised of PLME Advising Deans and Brown faculty.
- The SRA Committee gives favorable consideration to proposals with a well-delineated research program involving experimental methods and hypotheses that are appropriate to the student's educational and research background.

For additional information visit the PLME website: https://www.brown.edu/academics/medical/plme/current-students/enrichment-activities/research-opportunities/plme-summer-research-assistantship-soc
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Faculty Sponsor(s):

Faculty Sponsor email:  agshoulder@aol.com, abell@universityorthopedics.com

Proposed SRA 2017 Project Title:

Health Utility Assessment of Shoulder Arthroplasty

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Division of Shoulder and Elbow Surgery, Department of Orthopaedic Surgery

Research Location:

University Orthopedics office

Student researcher's qualifications & experience should include:

Experience with Microsoft Excel, basic biostatistics. Must be reliable and committed to biomedical project. Excellent communication skills a must.

What is your plan for mentoring a student researcher?

Direct interaction related to research project including planning of study, data acquisition, data analysis, manuscript preparation, weekly meetings following a curriculum focused on outcomes in orthopaedic surgery (shoulder specific.)

Project Description:

No project description provided.

Other Comments:

Student must have interest in pursuing residency and career in orthopaedic surgery.
Faculty Sponsor(s): Waeil Asaad, MD, PhD

Faculty Sponsor email: wael_asaad@brown.edu

Proposed SRA 2017 Project Title:

Neurophysiology of Movement Disorders and Deep Brain Stimulation

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Neurosurgery

Research Location:

RIH / Aldrich Labs

Student researcher's qualifications & experience should include:

- Strong interest in neurophysiology and behavior.
- Willingness to learn or experience with coding, signal processing and data analysis.
- Basic coursework in neuroscience.
- Desire to interact with patients both in the clinic and in the operating room.

What is your plan for mentoring a student researcher?

The student will collaborate with other lab members until s/he has gained sufficient skills and expertise to branch off on more independent projects. I will directly mentor the student, along with post-docs, graduate students and other lab members. We typically have lab meetings weekly, but additional meetings are often arranged ad-hoc to discuss ongoing work and research strategy. Previous PLME students have been very successful and have presenting their work at national meetings; we hope all new students progress to that point, and ultimately to peer-reviewed publication of their work.

Project Description:

Our lab seeks to understand the neurophysiological basis of disease, particularly movement disorders such as Parkinson's Disease and Essential tremor. Toward this goal, we record neuronal activity from patients undergoing deep brain stimulation while they perform cognitive and motor tasks, test their performance on these tasks extra-operatively and under various brain stimulation conditions, and are designing new protocols for closed loop and adaptive neuromodulation. Our lab is always interested in
motivated students who wish to learn about these disease, neurophysiology, and the technical aspects of neural signal processing and rigorous behavioral analysis. Current projects include: Motor adaptation and its modulation by VIM thalamus deep brain stimulation; Novel patterns of deep brain stimulation to eliminate tremor and preserve motor and speech function; Closed-loop deep brain stimulation for Parkinson's Disease; Connectivity analysis of deep brain stimulation targets using MRI tractography.

Other Comments:
Faculty Sponsor(s): Janette Baird, PhD

Faculty Sponsor email: janette_baird@brown.edu Proposed

SRA 2017 Project Title:

Opiates in Emergency Medicine

SRA Research Subject Area:

Clinical Medicine

Department Sponsor:

Janette Baird, PhD

Research Location:

Rhode Island Hospital

Student researcher's qualifications & experience should include:

Organized
Timely
Attention to detail
Good writing skills
Skilled in using Excel
Self motivated

What is your plan for mentoring a student researcher?

The student will conduct their research in the Anderson Emergency Department of the Rhode Island Hospital. All of the necessary equipment, office space, and access to records will be provided throughout the project. Additionally, they will have the opportunity to collaborate with other team members through weekly team meetings. The research project will be broken down into a manageable schedule and the student will be provided with a weekly, structured, research program. The student will be trained on the strategies to improve accuracy and minimize inconsistency in prospective study recruitment. They will be trained on how to identify the requisite information and we will set up explicit protocols to help identify which patients will be recruited and subject to analysis. Each variable will be explicitly defined and all questions will be answered to minimize misunderstanding the data variables. The first week of the project will be spent understanding the data collection form and the appropriate responses to each variable. During the weekly meetings, the data sheets will be reviewed, we will resolve disputes, and maintain consistency in chart selection and analysis.
**Project Description:**

No project description provided.

**Other Comments:**

Drug overdose is the leading cause of accidental death in Rhode Island. To decrease nonfatal and fatal drug overdoses and to educate prescribers about responsible prescribing practices, the Department of Health has launched an educational campaign, coupled with mandates regarding the management of patients in the Emergency Department. The goal of this study is to collect epidemiological information about the diagnoses that receive narcotics in the ED, the epidemiology of the patients that receive Narcan and the utility of the Suboxone program.
Faculty Sponsor(s): Ghada Bourjeily, MD

Faculty Sponsor email: ghada_bourjeily@brown.edu

Proposed SRA 2017 Project Title:

Sleep disordered breathing in special populations

SRA Research Subject Area:

Clinical Medicine

Department Sponsor:

ghada bourjeily

Research Location:

146 west river street in providence

Student researcher's qualifications & experience should include:

We hope to have a student with a respectful and happy personality who can engage research participants and referral sites and encourage research participation. Prior experience in clinical research would be ideal but we are also happy to train the student. Bilingual students preferred but not a pre-requisite. As the lab is off site and some of the tasks may require going to more off site places, a student needs to have transportation means.

What is your plan for mentoring a student researcher?

My mentoring style consists of initial meeting with student to establish strengths and needs of student and to agree on expectations, followed regular face to face contact to review progress, answer questions and give direction, with frequent communications by email or phone. For day to day training and follow up, the student will be paired with one of three coordinators and possibly a research assistant who can show the student the day to day operation of clinical research and for assigning tasks.

Project Description:

Our team investigates mechanistic pathways underlying sleep disordered breathing in pregnancy. Pregnancy predisposes to the development of sleep disordered breathing and the latter condition has been associated with adverse outcomes during pregnancy such as preeclampsia, gestational diabetes and others. It is also likely that sleep disordered breathing is associated with adverse outcomes in

Sleep disordered breathing in special populations][ Ghada Bourjeily, MD
newborns. Our program evaluates the association of OSA with placental function and the impact of positive airway pressure on placental function and morphology in women with obstructive sleep apnea - a condition in the spectrum of sleep disordered breathing-. In addition we are evaluating a model consisting of physiologic and anthropometric variables that predict the development of obstructive sleep apnea in pregnancy. A student may help with any of these studies and would have the opportunity to ask many questions outside of the main aims of the study that could prove to be quite stimulating and novel. Such questions would include the impact of a diagnosis of OSA early in pregnancy on the likelihood of insulin resistance, correlation of obstructive sleep apnea variables early in pregnancy with blood pressure measures -diurnal and nocturnal-, the correlation of clinical symptoms with respiratory variables obtained during sleep. Students will have the opportunity to learn various skills in the evaluation of the cardiovascular system, sleep and activity measures, body composition analyses etc..

Other Comments:
Faculty Sponsor(s): Yupeng Chen, PhD

Faculty Sponsor email: Yupeng_Chen@brown.edu

SRA 2017 Project Title:

Novel Nano-Therapeutics for the Treatment of Arthritis

Research Subject Area:

Biomedical Science

Department Sponsor:

Orthopaedics

Research Location:

Coro West, RIH

Student researcher’s qualifications & experience should include:
Basic knowledge in Biology or related fields, such as Materials Science, Chemistry or Bioengineering. Previous lab experience is a plus.

What is your plan for mentoring a student researcher?

The student will conduct cell and animal experiments to fabricate and characterize the therapeutic potentials of Nanopieces to deliver RNA for the diagnosis and treatment of arthritis. The student will learn a series of lab techniques, such as cell culture, nanomaterial fabrication, fluorescence microscopy, small animal imaging, PCR, etc. The student will also participate in the group meeting every week and he/she is welcome to discuss research and other topics with the PI and other lab members.

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Eunyoung Cho, ScD

Faculty Sponsor email: eunyoung_cho@brown.edu

Proposed SRA 2017 Project Title:

Diet and dermatological diseases

SRA Research Subject Area:

Behavioral Science

Department Sponsor:

Eunyoung Cho.

Research Location:

339 Eddy St (Dermatology Research Lab)

Student researcher's qualifications & experience should include:

Basic knowledge in biostatistics and/or epidemiology would be helpful but not required.

What is your plan for mentoring a student researcher?

The student will work on a review paper on diet and a dermatological disorder. He/she will conduct literature search of relevant scientific papers, summarize the findings in table format, and contribute to write the manuscript.

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Daniel Dickstein, MD

Faculty Sponsor email: Daniel_Dickstein@Brown.edu

Proposed SRA 2017 Project Title:

Brain changes associated with neuropsychiatric illness

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Psychiatry

Research Location:

Bradley Hospital

Student researcher's qualifications & experience should include:

This SRA position is open to students with any of these skills or interests--and--depending on those skills and interests--might take slightly different twists in what aspect of research they are engaged in: (a) students interested in brain and/or behavioral mechanisms associated with neuropsychiatric illness with some skill with either SPSS, Excel, or basic unix programming would likely focus on analyzing imaging and/or behavioral data already collected from kids or adults; (b) students interested in computer science with programming and/or app development skills would focus on novel ways to assess patients' psychiatric symptoms.

What is your plan for mentoring a student researcher?

Mentorship is very important to me--as all students receive direct mentorship from me including supervised readings and meetings, as well as the chance for clinical shadowing as I see child, teen, and young adult patients with psychiatric disorders. Students will be part of our PediMIND program research team. To learn more about us, visit www.pedimind.org

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Elizabeth Harrington, PhD

Faculty Sponsor email: Elizabeth_harrington@brown.edu

Proposed SRA 2017 Project Title:

The role of NPR recycling in Acute Lung Injury (ALI)

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Medicine

Research Location:

Providence VA Medical Center, building 35

Student researcher's qualifications & experience should include:
The research would benefit from someone with course work in cell biology, biochemistry, and/or molecular biology. Also, the project may include use of rodent models of acute lung injury, so the researcher should be willing to participate in these types of research.

What is your plan for mentoring a student researcher?
The mentorship would include mentoring by:
i) myself, Elizabeth Harrington, PhD; ii) my colleague James Klinger, MD, iii) postdoctoral fellow, Ashok Kumar, PhD; and iv) assistance by research assistants, Julie Braza and Huetran Duong.
The student would meet formally with the group 1X per week, and meet daily with me as needed. In addition, hands on laboratory/ experimental assistance will be provided by Dr. Kumar, as well as by Julie and Huetran.
It would be anticipated that the student would participate in development of the project and experimental design as expertise grows. In addition, we host a series of seminars where the students hosted during the summer semester present their work to the group and receive feedback.

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Daphne Koinis Mitchell, PhD

Faculty Sponsor email: daphne_koinis-mitchell@brown.edu

Proposed SRA 2017 Project Title:

Disparities in Pediatric Asthma, Obesity, and Sleep Outcomes in Children

SRA Research Subject Area:

Behavioral Science

Department Sponsor:

Daphne Koinis Mitchell, PhD

Research Location:

Bradley Hasbro Research Center, RI Hospital

Student researcher's qualifications & experience should include:

Concentration in psychology, biological sciences, or public health. Completion of research methods and introductory statistics course preferred. Strong organizational and time management skills, excellent attention to detail, a thorough working knowledge of MS Office applications, comfort and experience interacting with children and parents from a variety of cultural backgrounds.

What is your plan for mentoring a student researcher?

The intern will meet with the primary faculty mentor, Dr. Koinis Mitchell regularly to develop an individual research project and to review progress with relevant literature review and data processing, and to synthesize this information within the context of the larger study. Ms. Sheryl Kopel (research associate, Department of Psychiatry and Human Behavior) will serve as a secondary mentor, providing day-to-day training and supervision of activities.

Project Description:

Other Comments:

Working within the Childhood Asthma Research lab, the research student will meet and interact with an interdisciplinary team of pediatric asthma researchers, including clinical psychologists, asthma specialists, obesity researchers, child development and education experts, as well as other trainees in
these areas. Interns will have the opportunity to assist with research participant recruitment and scheduling, orienting families to research protocols and conducting research visits, data entry, lab organization, and other tasks integral to research.
Faculty Sponsor(s): Wen-Qing Li, PhD

Faculty Sponsor email: wen-qing_li@brown.edu

Proposed SRA 2017 Project Title:

Epidemiology of atypical nevi

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Dermatology

Research Location:

339 Eddy Street, Providence, RI

Student researcher's qualifications & experience should include:

Students with knowledge/understanding in epidemiology or biostatistics and past research experiences are eligible. The independent ability to do the statistical analysis and the past experiencing in writing/publishing scientific papers would be ideal.

What is your plan for mentoring a student researcher?

The student will be working on cancer epidemiology, specifically on the epidemiological factors associated with atypical nevi, a melanoma precursor and risk factor. We have very good population resources well deposited and atypical nevi data collected. With my mentorship, student will propose hypothesis, do the study design, data analysis (with the help of our statistical programmer), and manuscript draft.

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Emily McDonald, PhD

Faculty Sponsor email: emily_mcdonald@brown.edu

Proposed SRA 2017 Project Title:

The impact of helminthiasis on energy metabolism of the human placenta

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Pediatrics

Research Location:

Center for International Health Research, 55 Claverick

Student researcher's qualifications & experience should include:

This project will involve the use of primary human cell isolation and culture, as well as examination of hormone levels in human blood samples. Previous basic lab experience (e.g. pipetting, sterile culture techniques) is preferred, but not required.

What is your plan for mentoring a student researcher?

Our lab has previously shown that maternal infection with schistosomiasis during pregnancy results in an inflammatory environment within the placenta, detectable also in the cord blood of affected neonates. We have also shown that metabolic hormones of the fetus (i.e. leptin and adiponectin) are impacted by the intensity and number of co-infections with other helminthes the mother has during pregnancy. This project will examine the placental metabolic response to helminth infection through the use of primary culture of isolated human trophoblast cells, collected from the placenta at delivery. Trophoblast cells will be exposed in vitro to schistosome antigens and production of IGF-1, -2 and leptin will be measured. In addition, we will examine the signaling pathways elicited by antigen exposure, specifically with regards to IGF signaling within the trophoblast cells, as this may help delineate a mechanism(s) by which antigen exposure in utero impacts the metabolic capacity of the developing fetus. Completion of this project will allow the student to gain technical skills in sterile cell culture, primary cell isolation from human tissue, and a variety of common molecular biology laboratory techniques. The PI will work closely with the student in the interpretation of results and development of future directions. Presentation of results will be encouraged.
Project Description:

Our lab has previously shown that maternal infection with schistosomiasis during pregnancy results in an inflammatory environment within the placenta, detectable also in the cord blood of affected neonates. We have also shown that metabolic hormones of the fetus (i.e. leptin and adiponectin) are impacted by the intensity and number of co-infections with other helminthes the mother has during pregnancy. This project will examine the placental metabolic response to helminth infection through the use of primary culture of isolated human trophoblast cells, collected from the placenta at delivery. Trophoblast cells will be exposed in vitro to schistosome antigens and production of IGF-1, -2 and leptin will be measured. In addition, we will examine the signaling pathways elicited by antigen exposure, specifically with regards to IGF signaling within the trophoblast cells, as this may help delineate a mechanism(s) by which antigen exposure in utero impacts the metabolic capacity of the developing fetus. Completion of this project will allow the student to gain technical skills in sterile cell culture, primary cell isolation from human tissue, and a variety of common molecular biology laboratory techniques. The PI will work closely with the student in the interpretation of results and development of future directions. Presentation of results will be encouraged.

Other Comments:
Faculty Sponsor(s): Gyan Pareek MD

Faculty Sponsor email: gyan_pareek@brown.edu

Proposed SRA 2017 Project Title:

Nephrolithiasis Incidence, Care, Management, Treatment and Complications

SRA Research Subject Area:

Clinical Medicine

Department Sponsor:

Gyan Pareek MD

Research Location:

Minimally Invasive Urology Institute, The Miriam Hospital

Student researcher's qualifications & experience should include:

GPA 3.0
Good academic standing
Successfully completed a basic science course

What is your plan for mentoring a student researcher?
-Student will work with attending physician mentor to prepare and present a urologic case study with a complete review of the literature for grand rounds
-Student will meet with attending physician mentor weekly to discuss research project
-Student will work with attending physician mentor to compose manuscript for publication

Project Description:

Stone research will be lead by Dr. Pareek. Dr Pareek is the Director of the Minimally Invasive Urology fellowship at Alpert Medical School. Along with his other co-Directors at the Minimally Invasive Urology Institute (MIUI) at The Miriam Hospital, Dr. Pareek and colleagues are internationally recognized researchers and teachers. The MIUI provides opportunity for research in the areas of robotic surgery (prostate, kidney and bladder), kidney stone disease and benign prostate disease. Our Stone Research Project will involve the student learning and conducting research on kidney stone disease. Kidney stone disease afflicts up to 12% of the population. Research in the area of kidney stone prevention is critical to decrease the incidence of this disease. The Miriam Hospital/Brown has the only multi-disciplinary Nephrolithiasis Incidence, Care, Management, Treatment and Complications

Gyan Pareek MD
center for stone prevention in the region which is focused on research to prevent stone disease. At the moment there are several opportunities for students to get involved. Projects are: Proteonomics in Kidney Stone Disease, Kidney Stone Center data assessment and clinical projects (retrospective studies). The latter involve minimally invasive surgical methods and outcome studies based on these methods in the management of kidney stone disease. There will be opportunity to observe surgeries if the student desires. This is a unique opportunity at the MIUI at The Miriam Hospital. We have offices at the Hospital where the student can do research. Computer access as well as weekly meetings with investigator and program director (Chris Tucci) will be a requirement. There is FULL expectation that the experience leads to a publication in a high impact factor peer reviewed journal.

Other Comments:
Faculty Sponsor(s): Joseph Renzulli, MD

Faculty Sponsor email: jrenzulli@lifespan.org

Proposed SRA 2017 Project Title:

**Prostate Cancer and Robotic Prostatectomy Care, Management, and Complications**

SRA Research Subject Area:

Clinical Medicine

Department Sponsor:

Joseph Renzulli MD

Research Location:

Minimally Invasive Urology Institute, The Miriam Hospital

Student researcher's qualifications & experience should include:

- GPA 3.0
- Good academic standing
- Successfully completed a basic science course

What is your plan for mentoring a student researcher?

- Student will work with attending physician mentor to prepare and present a urologic case study with a complete review of the literature for grand rounds
- Student will meet with attending physician mentor weekly to discuss research project
- Student will work with attending physician mentor to compose manuscript for publication

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Sharon Rounds, MD

Faculty Sponsor email: sharon_rounds@brown.edu

Proposed SRA 2017 Project Title:

Mechanism of Cigarette Smoke-Induced Endothelial Mitochondrial Dysfunction

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Pulmonary/Critical Care Medicine

Research Location:

Providence VAMC, Building 35

Student researcher’s qualifications & experience should include:

Experience in chemistry and biology laboratory techniques, including knowledge of sterile technique, western blotting, and basic microscopy

What is your plan for mentoring a student researcher?

I will meet with the student at least once per week to discuss experimental plans and data. I will assist the student in preparing a oral presentation of the project for the Laboratory group. The lab manager and technical staff will assist with day to day performance of experiments of teaching of laboratory techniques.

Project Description:

No project description provided.

Other Comments:
Faculty Sponsor(s): Jennifer Sanders, PhD

Faculty Sponsor email: Jennifer_Sanders@brown.edu

Proposed SRA 2017 Project Title:

Nutritional Regulation of Liver Mitochondrial Metabolism

In utero pathology often manifests as metabolic dysregulation during the perinatal period. This is particularly the case for infants born prematurely or underweight. ....

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Pediatrics

Research Location:

RIH-Multiphasic Building

Student researcher's qualifications & experience should include:

No prior research experience necessary. Highly motivated & dedicated student.

What is your plan for mentoring a student researcher?

Student will be directly mentored at the bench by a senior research assistant. Student will meet at least weekly with PI to formulate and discuss experimental plans, data and papers relevant to project. Student is expected to attend weekly lab meeting where he/she will discuss their research activities and receive feedback from members of the laboratory.

Project Description:

This project will utilize a model of normal fetal and newborn development in the rat combined with the well characterized IUGR model of maternal nutrient deprivation. Changes in mitochondrial biogenesis and function at key time points ranging from prenatal (E20) to the end of the first postnatal week will be assessed. Data relating to mitochondrial dynamics (fusion and fission), oxidative phosphorylation, composition (the mitochondrial proteome) and signaling (the mitochondrial phosphoproteome) will be generated using contemporary methods such as, microarray analysis, proteomics and Seahorse technology. These studies can be extended to the examine the effects of IUGR on mitochondrial biogenesis and function later in life.
Faculty Sponsor(s): Lori Scott-Sheldon, PhD

Faculty Sponsor email: lori_scott-sheldon@brown.edu

Proposed SRA 2017 Project Title:

Stress, Coping, and Chronic Illness

SRA Research Subject Area:

Behavioral Science

Department Sponsor:

Lori A. J. Scott-Sheldon, PhD

Research Location:

Centers for Behavioral and Preventive Medicine, The Miriam Hospital

Student researcher's qualifications & experience should include:

Applicants should have an interest in behavioral and social sciences with a quantitative background (statistics).

What is your plan for mentoring a student researcher?

The goals of this summer research assistantship will be to (1) acquire enhanced knowledge of stress management in the context of chronic illness and (2) develop skills in systematic reviewing and meta-analysis. These goals will be accomplished primarily through weekly meetings with the faculty sponsor. These meetings will involve directed readings, discussions, and didactic and interactive statistical training. The student will be provided with a supervised research experience in conducting systematic and comprehensive literature searches, extracting key information from primary-level data, and for advanced students, statistical analyses and interpretation of meta-analytic findings.

Project Description:

No project description provided.

Other Comments:

The Centers for Behavioral and Preventive Medicine is located in the CORO Building, One Hoppin Street, Providence, RI.
Faculty Sponsor(s): Barbara Stonestreet, MD

Faculty Sponsor email: bstonestreet@wihri.org

Proposed SRA 2017 Project Title:

Neuroprotection in the fetus and neonate.

SRA Research Subject Area:

Behavioral Science

Department Sponsor:

Pediatrics

Research Location:

Kilguss lab 200 Chestnut Street and Stonestreet 3rd floor lab in Biomed at Brown

Student researcher’s qualifications & experience should include:

Some research experience would be good but not required; biology and neuroscience courses preferable

What is your plan for mentoring a student researcher?

I will mentor along with my MD PhD in the lab

Project Description:

Hypoxia-ischemia (HI) is the leading cause of neurodevelopmental morbidities in preterm and full term infants. The only therapeutic strategy to treat HI encephalopathy (HIE) is hypothermia for full term infants, which is only partially protective, and treatment does not exist for HI exposed preterm infants except for supportive care. Based upon the Stroke Therapy Academic Industry Roundtable (STAIR) criteria, sufficient dose-response and therapeutic time windows, adequate histological and behavioral outcomes, and understanding mechanism(s) of action for neuroprotectants are necessary for preclinical drug development to facilitate translation of neuroprotective strategies from animals to humans. The basis of this proposal is the identification of novel immunomodulatory proteins, Inter-alpha Inhibitor Proteins (IAIPs) that are currently in development as effective therapeutic agents in systemic inflammation/shock syndromes. IAIPs are novel anti-inflammatory molecules that broadly inhibit destructive serine proteases, robustly block pro-inflammatory cytokines, augment anti-inflammatory cytokine production, and block complement activation during systemic inflammation. Our exciting
preliminary studies using the blood derived IAIPs suggest IAIPs have remarkable neuroprotective properties in HI-neonatal rats. However, information regarding mechanism(s) of neuroprotective efficacy of IAIPs on HI-brain injury in neonates have not been elucidated. The purpose of this proposal is to fill this gap of knowledge: (1) To determine the optimal dose-response and therapeutic time windows for IAIPs in neonatal rats; (2) To assess short/long term neurobehavioral outcomes, and establish the greatest neuroprotective efficacy using optimal doses and time windows for IAIPs administration in neonates; (3) To examine molecular mechanism(s) of IAIPs (neuroinflammation/apoptosis) and targets (pro-inflammatory cytokines) on HI brain injury. The well-characterized Rice-Vannucci neonatal HI model will be used. The neuroprotective efficacy with various doses and time windows of IAIP treatment will be determined by comparing brain injury (Luxol fast blue/H&E), apoptosis, neuronal injury (Fluoro Jade B), and brain inflammation (cytokine production), astrogliosis, microglia activation, oligodendrocyte injury, etc. Short/long-term behavioral outcomes will be determined at different stages of brain development. The mechanism(s) of action and molecular targets of IAIPs will also be examined using primary neuronal cell co-cultures with and without exposure to oxygen-glucose deprivation (OGD). Mechanism(s) will be studied by determining neuroinflammation and apoptosis, along with neuronal/glial and microglial interactions. IAIP targeted pro-inflammatory cytokines will be determined by a Bio-Plex™ cytokine assay. The current proposal will establish drug efficacy, optimal dose-responses and time windows, with which IAIPs attenuate HI brain injury, reduce neuronal/glial cell death, and improve short/long term behavioral performance in neonatal HI rats. Results should yield novel preclinical information to accelerate IAIPs use as neuroprotective agents to treat HI-related brain injury in human premature and full term infants.

Other Comments:

Hypoxia-ischemia (HI) is the leading cause of neurodevelopmental morbidities in preterm and full term infants. The only therapeutic strategy to treat HI encephalopathy (HIE) is hypothermia for full term infants, which is only partially protective, and treatment does not exist for HI exposed preterm infants except for supportive care. Based upon the Stroke Therapy Academic Industry Roundtable (STAIR) criteria, sufficient dose-response and therapeutic time windows, adequate histological and behavioral outcomes, and understanding mechanism(s) of action for neuroprotectants are necessary for preclinical drug development to facilitate translation of neuroprotective strategies from animals to humans. The basis of this proposal is the identification of novel immunomodulatory proteins, Inter-alpha Inhibitor Proteins (IAIPs) that are currently in development as effective therapeutic agents in systemic inflammation/shock syndromes. IAIPs are novel anti-inflammatory molecules that broadly inhibit destructive serine proteases, robustly block pro-inflammatory cytokines, augment anti-inflammatory cytokine production, and block complement activation during systemic inflammation. Our exciting preliminary studies using the blood derived IAIPs suggest IAIPs have remarkable neuroprotective properties in HI-neonatal rats. However, information regarding mechanism(s) of neuroprotective efficacy of IAIPs on HI-brain injury in neonates has not been elucidated. The purpose of this proposal is to fill this gap of knowledge: (1) To determine the optimal dose-response and therapeutic time windows for IAIPs in neonatal rats; (2) To assess short/long term neurobehavioral outcomes, and establish the greatest neuroprotective efficacy using optimal doses and time windows for IAIPs administration in neonates; (3) To examine molecular mechanism(s) of IAIPs (neuroinflammation/apoptosis) and targets (pro-inflammatory cytokines) on HI brain injury. The well-characterized Rice-Vannucci neonatal HI...
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Faculty Sponsor(s): Edward Stopa, MD

Faculty Sponsor email: estopa@lifespan.org

Proposed SRA 2017 Project Title:

Blood Brain Barrier Dysfunction in Alzheimer's Disease

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Pathology

Research Location:

RIH POB 322

Student researcher's qualifications & experience should include:

An interest in neurodegenerative disease.
Willingness to continue project to publication after the summer rotation has been completed

What is your plan for mentoring a student researcher?

Daily meeting with research mentor to discuss progress.

Project Description:

APOE4 is the only genetic risk factor for the late onset sporadic form of Alzheimer's disease (AD) affecting the majority of dementia patients. How APOE4 mediates its harmful effects remains to be elucidated. Mouse models of AD were utilized to demonstrate that apolipoprotein E4 increases cyclophilin A in microvascular pericytes damaging endothelial tight junctions and eroding the basement membrane of the neurovascular unit that forms the blood brain barrier (BBB) (PMCID: 4047116). In previous investigations we have shown that agrin, a proteoglycan essential to blood tissue barriers and a key component of the cerebral microvascular basement membrane, becomes fragmented and lost in AD patients. We hypothesized that the BBB would leak in AD and became the first to demonstrate that the normally excluded serum protein prothrombin increased as a function of both AD severity and APOE 4 genotype status. Using transgenic mice, we showed that the long amino terminus (LN) isoform of agrin was critical for microvascular damage in AD and that loss of LN agrin in a conditional knockout decreased aquaporin 4, a major water channel protein of the BBB. In Specific Aim 1, we will perform a
morphologic (quantitative immunohistochemistry) and biochemical (western, ELISA and qPCR) dissection of the BBB by examining cyclophilin A in control and AD patients who vary in disease severity and APOE genotype. We will look at matrix metalloproteinase 9 (increased by cyclophilin A) and components of the neurovascular unit including endothelial tight junctions (occludin and claudin 5), basement membrane (agrin) and astrocytic foot processes (aquaporin 4). Since transgenic mouse models are not always translatable to human disease, it is essential to confirm and characterize the effects of cyclophilin A in AD patients. We have hypothesized that loss of aquaporin 4 may cause a shift in the normal distribution of water across the BBB that may be detectable by MRI in living AD patients. In Specific Aim 2 we will measure water exchange and gadolinium-based contrast extravasation rates across the BBB utilizing intravascular steady-state (IVSS) and dynamic contrast enhanced (DCE) MRI techniques, respectively. Estimates of water exchange rates and contrast agent extravasation rates in patients with mild cognitive impairment, Alzheimer's disease, and age-matched controls with differing APOE genotypes will be compared. This novel approach may be used to confirm the diagnosis of AD and to follow treatment effectiveness. Data derived from the proposed studies could lead to novel therapeutic interventions aimed at stabilizing and preventing breakdown of the BBB. FDA approved inhibitors of the cyclophilins already exist and novel inhibitors that lack immunosuppressive effects are being considered for the treatment of other cyclophilin-related inflammatory diseases.

Other Comments:
Faculty Sponsor(s): Albert S. Woo, MD

Faculty Sponsor email: Albert.Woo@lifespan.org

Proposed SRA 2017 Project Title:

Evaluation of Craniofacial Deformities Utilizing 3D Imaging

SRA Research Subject Area:

Clinical Medicine

Department Sponsor:

Albert S. Woo, MD

Research Location:

RIH, MOC 180

Student researcher's qualifications & experience should include:

Student should be committed to working full time during the 10 week elective period. Familiarity with statistical analyses of clinical data would be beneficial. No previous experience with clinical imaging is necessary.

What is your plan for mentoring a student researcher?

The student will meet with me initially to finalize the specifics of the research plan. He/she will be expected to conduct a literature search of the topic material. Given the short time allotted, IRB approval will have been received prior to the student starting - however, CITI training and certification with the IRB will be necessary to be involved on any research level. The student will be directly supervised by my research coordinator, who will be present full time in the lab setting. I will be meeting with the lab on a weekly basis (at minimum), although I will be available to address any questions or issues that cannot be managed by the coordinator. Students will be expected to complete the project during the allotted time and submit an abstract to a national meeting. If accepted, they will be asked to present their research on a national level and also to submit a research paper for publication of their work. All necessary assistance will be provided to bring each project to fruition.
Project Description:

Students will be offered a number of topics associated with evaluation of specific craniofacial deformities. Most common topics include: elucidation of specific patterns of craniofacial abnormalities; evaluation of postoperative surgical results based on pre- and post-operative imaging. Students will then be trained to collect all data based on the imaging database at RI Hospital and to analyze them for pertinent information utilizing 3Dimensional imaging platforms (i.e. Analyze, TerraRecon and/or Mimics). These data will be recorded in a spreadsheet/database for evaluation. They will be assisted in statistical analyses by our resident statistician/lab coordinator. These data will then be used to draw appropriate conclusions regarding the original hypothesis being tested.

Occasionally, some students have completed projects early. Such individuals are then offered a second project, should they desire to do so. I have roughly a decade of experience with having students in my lab utilizing this same protocol, which has been very successful. Most students have presented their work nationally and published first author papers as a result of their efforts. A listing of these individuals and projects can be made available upon request.
Faculty Sponsor(s): Wenteian Yang, MD, PhD

Faculty Sponsor email: wentian_yang@brown.edu

Proposed SRA 2017 Project Title:

Mobilizing Cartilage Stem Cell for Cartilage Antidegeneration

SRA Research Subject Area:

Biomedical Science

Department Sponsor:

Orthopaedics

Research Location:

Coro West 4th floor

Student researcher's qualifications & experience should include:

Students with previous lab experience, such as cell culture, PCR and Western blotting, are preferred.

What is your plan for mentoring a student researcher?

I will meet the student on a weekly basis to go over the experiment design and discuss data interpretation.

Project Description:

Other Comments:
Faculty Sponsor(s): Shirley Yen, Phd

Faculty Sponsor email: Shirley_Yen_PhD@Brown.edu

Proposed SRA 2017 Project Title:

**Early phenomenology of borderline personality disorder**

SRA Research Subject Area:

Behavioral Science

Department Sponsor:

Steven Rasmussen

Research Location:

Butler Hospital

Student researcher's qualifications & experience should include:
The student should have an interest in psychiatry research, particularly the interface between borderline personality disorder and bipolar disorder. As all data has been collected and the project is primarily secondary data analyses, qualifications include basic familiarity with SPSS and pubmed.

What is your plan for mentoring a student researcher?

I have successfully mentored PLME students in the past; the goal of our work should be to lay a foundation for an honors thesis for the student and/or a published manuscript with student as a co-author. I will meet with the student researcher on a weekly basis or more often as needed, to guide the development of this proposal. In addition, the student participates in weekly lab meetings to gain familiarity with these disorder, and to learn how to used more advanced statistical analyses.

Project Description:

We seek to determine the prevalence and prospective effects of emergent Borderline Personality symptomatology in a sample of bipolar disorder youth that have been followed in a 10-year, multi-site, naturalistic, longitudinal study. High rates of Borderline Personality Disorder have been reported in adults with Bipolar Disorder, yet separation of the two is clouded by overlapping symptoms. However, distinctions between Bipolar disorder and Borderline Personality Disorder are essential for clarity of treatment. All existing studies regarding this issue evaluated personality and Bipolar Disorder concurrently during adulthood, after the critical risk window of onset for both disorders has passed. The...
Course and Outcome of Bipolar Youth study has prospectively assessed these disorders from age 18 forward in a cohort that already has Bipolar Disorder, yielding important new data on the stability of these classifications over time. This will allow for identification of early illness characteristics that predict the emergence of Borderline Personality Disorder, and conversely, document the impact of Borderline symptomatology on the course of Bipolar Disorder. Specifically, we seek to examine whether those with childhood-onset BP are more likely to develop Borderline Personality Disorder compared to subjects with adolescent-onset BP, even after controlling for history of sexual and physical abuse; whether subjects with Borderline Personality Disorder will have more cumulative time spent ill and more recurrences of mood episodes during follow-up, compared to subjects without comorbid Borderline Personality Disorder; whether prospective follow-up will confirm that Bipolar and Borderline Personality Disorder are distinct disorders as evidenced by different course trajectories.

Other Comments:

Early phenomenology of borderline personality disorder][ Shirley Yen, Phd