RESEARCH OPPORTUNITY PROGRAM
299Y/399Y PROJECT DESCRIPTIONS 2019-2020
FALL/WINTER

Name and Title:  Dr. Padmaja Subbarao
Department:  Physiology

TITLE OF RESEARCH PROJECT:  Utility of Pulmonary Function Testing to Assess Preschool Asthma

Number of 299Y Spots:  1  Number of 399Y Spots:  1

OBJECTIVES AND METHODOLOGY:
Asthma is a common respiratory illness that is often diagnosed based on the presence of clinical symptoms. Clinical symptoms of asthma are incredibly variable. They may present themselves due to endogenous or exogenous stimuli, with varying numbers of episodes, and with different degrees of severity. Therefore, the clinical diagnosis of asthma is difficult to objectively obtain due to the variability of symptoms. Another challenge for defining and diagnosing asthma is the absence of a single cause, as asthma often involves complex gene-environment interactions. Pulmonary function testing is often used to provide a more objective and accurate diagnosis of respiratory illnesses. Our laboratory’s focus is on determining which lung function tests and outcome measures, provide the most useful information to aid physicians in diagnosing asthma in the pediatric population.

The student’s objectives will be to:
(1) aid in the preparation for and conduct of research study visits
(2) assist with the conduct and analysis of pulmonary function tests and
(3) assist in the preparation of a manuscript that explores the factors that predict the development and severity of asthma.

The following methodologies may be used during the student’s term:
(1) Physiological Tests: Multiple Breath Washout, Spirometry, Methacholine Challenge, Airway Oscillometry, Exhaled Nitric Oxide
(2) Various statistical analyses

DESCRIPTION OF STUDENT PARTICIPATION:
The ROP student will assist with the preparation for and conduct of research study visits. The student will gain skills by assisting with and analyzing pulmonary function tests, acquiring anthropometric measurements and collecting and processing samples. The student will also work with research study staff to develop a research proposal and assist in the preparation of a research manuscript. The student will be expected to provide biweekly updates of their research progress and do an oral presentation of their research findings. The student will be supported by a local interdisciplinary research team made up of research assistants, coordinators and managers as well as respiratory therapists, biostatisticians and other students.
MARKING SCHEME (assignments with weight and due date):

2. Oral Presentation – Due Nov 2019 – 15% of grade
3. Poster Presentation in Undergraduate Research Forum– March 2020 – 10% of grade
4. Participation in biweekly meetings by March 31 2020 – 20% of grade
5. Laboratory Performance – by April 2020 – 20% of grade
6. Final Report – Due April 2020 – 20% of grade
Name and Title: Dr. Haibo Zhang
Department: Anesthesia/Medicine/Physiology

TITLE OF RESEARCH PROJECT: Lung Regeneration in Acute Respiratory Distress Syndrome (ARDS)

Number of 299Y Spots: 1 Number of 399Y Spots: 1

OBJECTIVES AND METHODOLOGY:
Investigate the cellular and molecular mechanisms of lung repair and regeneration using in vitro and in vivo models of acute and chronic lung injury in mice and rabbits.

The 2 main types of lung cells that make up the alveolar space, which is essential for gas exchange function of the lung, are known as alveolar type I (AEI) and alveolar type II (AEII) epithelial cells. AEI are cells that covers 95% of the alveolar surface area and form the air-blood barrier between the lung and blood vessel. AEII are secretory epithelial cells with the ability to release proteins, known as surfactant proteins that prevent lung collapse due to surface tension.

Recently, studies have found that AEII also function as the stem cells in adult lungs (1). Under quiescent and normal conditions, AEII have a slow growth and proliferation rate. After lung injury, AEII are able to multiply and transition to become AEI cells (2), suggesting AEII cells have regeneration properties. Indeed, the lung is capable of regeneration and has been shown to be induced by increased breathing tension (3), such as deep breathing.

The proposed study is a proof-of-concept to assess the potential role of AEII as a therapeutic agent in treating ARDS. We will assess the therapeutic potentials of endogenous and exogenous AEII cells through 2 models: a) increased breathing tension by continuous positive airway pressure (CPAP) and b) administration of isolated AEII from donor mice, respectively. In the exogenously administered AEII model, fibroblasts will also be co-administered to improve AEII's survival and proliferation.

DESCRIPTION OF STUDENT PARTICIPATION:
Assist graduate students and post-doctoral fellow in their on-going research projects and are encouraged to conduct independent studies if required. Join the weekly lab meeting and other academic activities associated with the Critical Care Medicine and Physiology. Students will participate in weekly lab meetings and complete any project specific training such as animal handling courses, tissue culture room training and histology training.
in addition to mandatory biosafety training courses. The student will be given a lab book to document all of their experiments and to track their progress.

MARKING SCHEME (assignments with weight and due date):

10%  2 - page report November 1, 2019
15%  lab mark December 6, 2019
30%  final report, April 6, 2020
10%  participation in weekly journal clubs/lab meetings
10%  oral presentation March 2020 (mark due April 6, 2020)
15%  lab mark April 6, 2020
10%  final data and lab book April 6, 2020
Name and Title: Shuzo Sugita, Ph.D., Professor
Department: Physiology

TITLE OF RESEARCH PROJECT: Genetic analysis of synaptic transmission in C. elegans

Number of 299Y Spots: 2
Number of 399Y Spots: 2

OBJECTIVES AND METHODOLOGY:
Synaptic transmission is essential for neuronal communication in the brain. At synapses, electrical activity in the presynaptic neuron triggers rapid release of neurotransmitters in a Ca$^{2+}$-dependent manner. The neuronal SNARE complex, consisting of syntaxin-1, SNAP-25, and synaptobrevin/VAMP-2, plays a central role in mediating neurotransmitter release through membrane fusion/exocytosis. This process is regulated by key proteins such as Munc18-1, Munc13, complexin, synaptotagmin and Tomosyn. However, the precise regulatory mechanisms of exocytosis remain largely unclear.

Importantly, molecular mechanisms controlling synaptic transmitter exocytosis are highly conserved from C. elegans to humans. Using C. elegans as our model system, we will investigate the mechanisms of transmitter release.

DESCRIPTION OF STUDENT PARTICIPATION:
Students will learn how to modify the genome of C. elegans using CRISPR/Cas9 system and generate synaptic release mutants. They will also learn how to cross the mutant strains to generate double and triple mutants. Finally, they will learn how to analyze the phenotypes of resulting mutants using behavioral and pharmacological assays.

MARKING SCHEME (assignments with weight and due date):
1) The written proposal including Background literature review, Aims and Hypotheses: 10%
2) Participation in the Journal Club of the lab: 10%
3) Lab research work: 20%
4) Final presentation: 20%
5) The written final report: 40%