Summer Student Research Program
Project Description

FACULTY SPONSOR'S NAME AND DEGREE: *Steven W. Levison, PhD*
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PROJECT TITLE (200 Characters max):

Intranasal LIF Rx to improve neurological recovery from repeated intermittent hypoxic episodes in neonatal mice

HYPOTHESIS:

The goal of this project is to test the hypothesis that LIF is a regenerative cytokine and that the non-invasive, intranasal, administration of LIF can promote oligodendrocyte maturation and decrease the long-term burden of neurological deficits subsequent to a developmental brain injury.

PROJECT DESCRIPTION **(Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)**

Studies have found that exposing newborn mouse pups to repeated episodes of intermittent hypoxia impairs the maturation of the oligodendrocytes in the white matter of the brain, which is the same pathology seen in premature human infants who are born at very low birthweights. Presently there are no therapeutics available to stimulate white matter development in babies, and as a consequence up to 50% of infants born preterm have intellectual disabilities. We recently showed that administering intranasal LIF 3 days after a hypoxic-ischemic brain injury in perinatal mice (mimicking asphyxial injury in term human infants) reduced the extent of brain injury by ~60%, attenuated astrogliosis and microgliosis, improved white matter thickness and improved performance on sensorimotor tests at 2 weeks of recovery. Therefore, the goal of this research project will be to test the therapeutic efficacy of intranasal LIF in a dysmyelinating white matter mouse model of prematurity. These studies will be performed collaboratively with Dr. Vadim Ten's laboratory at RWJMS. The repeated intermitttent hypoxia episodes, intranasal LIF Rx and behavioral assays will most likely be performed in Dr. Ten's laboratory. Mouse brains or brain homogenates will then be transfered to the Levison laboratory for analyses. Samples will be compared for the extent of mylelination and oligodendrocyte development using both immunohistochemical markers as well as Western Blot analyses in LIF Rx vs. vehicle treated mice. We will correlate the results from the Western blots and immunofluorescence with the results of the behavioral tests. Upon completing these experiments, we expect to more completely understand whether LIF Rx will promote white matter development in a clinically relevent developmental brain injury model, substantiating LIF as a potential therapeutic to promote brain development in very prematurely born infants.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

1. Courtney Juliano, Sergey Sosunov, Zoya Niatsetskaya, Joseph A. Isler, Irina Utkina-Sosunova, Isaac Jang, Veniamin Ratner and Vadim Ten (2015). Mild intermittent hypoxemia in neonatal mice causes permanent neurofunctional deficit and white matter hypomyelination. Experimental Neurology, 264, Pages 33-42. PMID: 25476492 DOI: 10.1016/j.expneurol.2014.11.010.

2. Lin J, Niimi Y, Clausi MG, Kanal HD, Levison SW. Neuroregenerative and protective functions of Leukemia Inhibitory Factor in perinatal hypoxic-ischemic brain injury. Exp Neurol. 2020 Aug;330:113324. doi: 10.1016/j.expneurol.2020.113324. PMID: 32320698.

THIS PROJECT IS: ☐ **Clinical** ☒ **Laboratory** ☒ **Behavioral** ☐ **Other**

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THIS PROJECT IS CANCER-RELATED ☐
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☐
Please explain Heart, Lung, Blood relevance

THIS PROJECT INVOLVE RADIOISOTOPES? ☐

THIS PROJECT INVOLVES THE USE OF ANIMALS ☒
PENDING ☒ **APPROVED** ☐ **IACUC PROTOCOL #**

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS? ☐
PENDING ☐ **APPROVED** ☐ **IRB PROTOCOL # M**

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS	☐	ENTERING FRESHMAN	☐
SOPHMORES	☐	ALL STUDENTS	☒

THIS PROJECT IS WORK-STUDY: **Yes** ☐ **or** **No** ☒

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR FOR INTERESTED VOLUNTEERS: **Yes** ☐ **or** **No** ☒

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
The student will perform research activities within the Levison laboratory under Dr. Levison's supervision. The student will assist in generating histological sections of the brain, performing immunostaining on the tissue to evaluate white matter development and glial cell differentiation. In addition, the student will assist with analyzing the behavioral assays to assess whtie matter function. The student will correlate the results from the Western blots and immunofluorescence with the results of the behavioral tests to determine whether intranasal LIF Rx is beneficial.