Fiscal Year:	FY 2020	**Task Last Updated:**	FY 03/09/2020
PI Name:	O'Connell-Rodwell, Caitlin Ph.D.		
Project Title:	The Effect of Microgravity on Neuronal Cytoskeletal and Intracellular Trafficking		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology		
Space Biology Cross-Element Discipline:	(1) Neurobiology		
Space Biology Special Category:	None		
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Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2016-17 Space Biology (ROSBio) NNH16ZTT001N-FG. App G: Flight and Ground Space Biology Research
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Flight Program:	ISS		
Flight Assignment:			
Key Personnel Changes/Previous PI:	March 2020: Not Applicable.		
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Task Description:	Crew members onboard the International Space Station (ISS) exhibit a range of microgravity induced physiological dysfunctions during extended missions (>1 month). Some of the most common effects of long-term microgravity exposure include immune system dysregulation, skeletal muscle atrophy, cardiovascular decline, bone loss, cognitive impairments, and decreased motor control. Unfortunately, the underlying etiology of microgravity induced dysfunction remains unclear. Decades of NASA research on ISS and shuttle missions have demonstrated that mammalian cell cultures exhibit altered morphology, proliferation, motility, differentiation, and often increased oxidative stress when exposed to the microgravity environment. Thus, physiological dysfunction at the tissue and systemic level is likely a result of altered cellular function, subcellular structural alterations, and intracellular communications. It has been well documented that the lack of gravity on-orbit has resulted in a cytoskeletal structural reorganization within a host of adherent mammalian cell cultures. Altered microtubule organization has enormous significance in the context of neurite outgrowth and neuronal intracellular communications. Intracellular effects may include the inability to clear aging and toxic proteins, a loss of trophic factor signaling, and compromised cellular energetics, resulting in axonopathies, synaptic loss, and eventual neuron death. Intracellular trafficking of vesicles is a fundamental subcellular process that can significantly alter cellular, tissue, and systemic processes if impaired in microgravity. Previous studies on Earth have demonstrated that disrupted intracellular communication contributes to abnormal physiological processes and that intracellular processes are sensitive to cytoskeletal organization. Thus, it is likely that microtubule reorganization in microgravity impairs neurite outgrowth, intra- and intercellular communications. However, the extent to which microgravity affects neuron microtubule structure dynamics remains unknown. We hypothesize that neuron microtubule organization is altered in microgravity which leads to inhibited neurite outgrowth and reduced intracellular vesicle trafficking which ultimately contributes to the cognitive impairments, motor control decline, and reduced neuroplasticity observed in microgravity. To characterize neuronal function in microgravity, we will quantify microtubule structure dynamics and intracellular vesicle trafficking utilizing the innovative Mobile SpaceLab (MoSL) platform to perform autonomous fluorescence microscopy and microfluidic delivery for the duration of a 4-week mission on-orbit. This investigation will seek to quantify vesicle transport, microtubule organization, neurite outgrowth, cell proliferation, differentiation, and motility with fluorescently labeled SH-SY5Y neuroblastoma cells. Ground control experiments with replicate hardware will be compared to the microgravity MoSL experiment. Preliminary results with the ground based MoSL facility demonstrate that microtubule structure and vesicle transport can be observed in real-time during long-term experimentation. This work will seek to 1) quantify the effect of microgravity on neuron microtubule organization and neurite outgrowth during differentiation, 2) quantify the effects of microgravity on intracellular vesicle trafficking within terminally differentiated neurons, and 3) delineate the effects of microtubule polymerization on neuronal structure and intracellular communication. This study will be the first of its kind to observe and quantify differentiating neuron function in microgravity on a minute to hour basis during a long-duration mission. This research has far reaching implications towards understanding the effects of microgravity on neuroplasticity, which may lead to future drug targets and therapeutic interventions to attenuate the deleterious effects of long-term microgravity exposure on human physiology.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The composition of the neuron’s cytoskeleton governs intracellular trafficking and synaptic function and any compromise of this structure that occurs due to microgravity exposure will directly affect overall nervous system function. The data from this study will inform the etiology of microgravity induced cognitive decline and/or motor control impairments to the ISS crew during long-term missions on ISS. This investigation has far reaching implications towards understanding the effects of microgravity on neuroplasticity which may lead to future drug targets and therapeutic interventions to attenuate the deleterious effects of long-term microgravity exposure on human physiology with the potential to treat common nervous system dysfunctions within the human population.
Task Progress:	The SCORPIO-V Team at HNu Photonics has successfully entered the Science Verification Testing (SVT) Phase I of the experiment integration of the Mobile SpaceLab-2 mission to differentiate neuroblastoma cells on ISS to understand the effects of microgravity on cytoskeletal organization and intracellular communications. To date, this mission has passed the Compliance and Science Requirements Reviews to advance to SVT experiments. Currently, the science is on schedule to meet a payload launch date for Space-X 21 transport to ISS. To date, the SVT Phase I results have defined: 1) the optimal neuroblastoma cell seeding density to effectively differentiate the cells over a 4 week experiment without over population, 2) the optimal medium formulations to promote healthy cell growth and proper differentiation, and 3) the appropriate media replacement interval to promote healthy cell growth in the absence of a 5% CO2 atmosphere. Ongoing SVT experiments include the optimization of nocodazole and taxol treatments, cell fixation methodology, and optimization of the fluorescence signal from the transfected neuroblastoma cell line. The upcoming milestones to be completed for the Mobile SpaceLab-2 mission in the next 6 months include SVT Phase I, SVT Phase II, Experiment Verification Test (EVT) Readiness Review, EVT, Selection for Flight Review, and the Flight Readiness Review.
Bibliography Type:	Description: (Last Updated:)