

Fiscal Year:	FY 2017	Task Last Updated:	FY 07/26/2016
PI Name:	Zanello, Susana Ph.D.		
Project Title:	A Gene Expression and Histologic Approach to the Study of Cerebrospinal Fluid Production and Outflow in Hindlimb Suspended Rats		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		TechPort:	No
Human Research Program Elements:	(1) HHC: Human Health Countermeasures		
Human Research Program Risks:	(1) SANS: Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	NOTE (January 2021): PI now at KBR/NASA JSC as of December 2020. Previously at imec USA from June 2019-November 2020; NASA JSC (KBRwyle) from August 2017 until spring 2019. Prior to August 2017, PI was with Universities Space Research Association.		
Project Type:	GROUND	Solicitation / Funding Source:	2013 HERO NNJ13ZSA002N-Crew Health (FLAGSHIP & NSBRI)
Start Date:	10/01/2015	End Date:	09/30/2018
No. of Post Docs:	1	No. of PhD Degrees:	0
No. of PhD Candidates:	0	No. of Master' Degrees:	0
No. of Master's Candidates:	0	No. of Bachelor's Degrees:	0
No. of Bachelor's Candidates:	0	Monitoring Center:	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Rivera, Adreana M.D. (Houston Methodist Hospital) Theriot, Corey Ph.D. (University of Texas Galveston) Chevez-Barrios, Patricia M.D. (The Methodist Hospital Research Institute)		
Grant/Contract No.:	NNX15AW48G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	<p>The etiology of the Visual Impairment and Intracranial Pressure (VIIP) syndrome is unknown. It is hypothesized that weightlessness-induced cephalad fluid shift, possibly associated with elevated intracranial pressure (ICP), may play a critical role. Cerebrospinal fluid (CSF) dynamics changes may be involved in the ICP increase. Leveraging on an existing hindlimb suspension (HS) analog in rats, we propose to study the molecular aspects of CSF production and outflow modulation as a result of HS in the tissues involved in these two processes of CSF dynamics, namely choroid plexus (CP) and arachnoid granulations (AG), respectively. On available tissue shared from the parent animal experiment (cohorts 3 and 4), we will perform differential gene expression profiling in the CP and AG of rats subjected to HS and their normal posture controls. In addition, we will compare the ultrastructure of the CP and AG and the histologic localization and distribution of putative targets implicated in CSF dynamics (aquaporins and cellular junction proteins) of the CP and the endothelial cell layer of the venous sinuses, in normal posture and in HR rats within each cohort. The research groups involved in this proposal have the necessary resources and techniques in place at their laboratories in order to maximize the likelihood of success in this project. An anticipated product of this study is the reduction of the uncertainty in the likelihood or consequence of the visual impairment risk by gaining a study tool (validated animal model) and knowledge on the molecular basis of the biological processes involved in CSF dynamics changes generated by HS.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	<p>By understanding the processes associated with fluid shift and its concomitant increase in intracranial pressure (ICP), we anticipate gaining clues as to ways to mitigate and reduce the impact of increased ICP in disease conditions like idiopathic intracranial hypertension, glaucoma, and traumatic brain injury.</p>
Task Progress:	<p>One of the responses to exposure to the microgravity spaceflight environment is a pronounced cephalic fluid shift. This project tests the hypothesis that this fluid shift is a causative factor in the ocular changes seen in astronauts during and following long-duration spaceflight. The study uses the well-documented rat hindlimb suspension (HLS) model to examine the relationship between cephalic fluid shifts and the regulation of intracranial (ICP) and intraocular (IOP) pressures as well as visual system structure and function. The experimental protocol uses HLS durations of 7, 14, 28, and 90 days. Subgroups of the 90-day animals are studied for recovery periods of 7, 14, 28, or 90 days. All HLS animals have age-matched cage controls. All animals have ad lib access to food and water. A 12:12 LD cycle is present. Eyes are collected at baseline, 7, 14, 28, and 90 days of HLS, and at 7, 14, 28, and 90 days of recovery, for histologic and gene expression evaluations. The study has started with the young adult male, young adult female, and old males cohorts. Comparing data between these cohorts will allow to determine if there is a gender and age difference in the responses. Following completion of these two groups, there will be one additional cohort exposed to elevated CO₂ levels similar to those experienced on ISS (International Space Station). This last group will allow to determine if a mild (~1%) hypercapnic environment plays a role in the cephalic shift response and possible development of VIIP (Vision Impairment and Intracranial Pressure).</p> <p>The continuation of this project entitled "A Gene Expression and Histologic Approach to the Study of Cerebrospinal Fluid Production and Outflow in Hindlimb Suspended Rats" addresses the mechanisms of production and resorption of cerebrospinal fluid in the brain at the molecular and histologic levels, and how these processes are affected by the fluid shift imposed by hindlimb suspension as a model of microgravity.</p> <p>This study depends on the availability of tissue samples from collaborators at University of California (UC) Davis. Due to the schedule of collections and delays in the conduction of the study at UC Davis, this project is delayed accordingly. We anticipate samples to be provided during FY17.</p>
Bibliography Type:	Description: (Last Updated: 09/04/2023)