Fiscal Year:	FY 2018	**Task Last Updated:**	FY 08/01/2018
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		
PI Email:	susana.b.zanello@nasa.gov	**Fax:**	FY
PI Organization Type:	NASA CENTER	**Phone:**	832-576-6059
Organization Name:	KBR/NASA Johnson Space Center		
PI Address 1:	Human Research Program Chief Scientist Office		
PI Address 2:			
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City:	Houston	**State:**	TX
Zip Code:	77058	**Congressional District:**	36
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:**	09/30/2019
No. of Post Docs:	0	**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
Contact Monitor:	Norsk, Peter	**Contact Phone:**	
Contact Email:	Peter.norsk@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2019 per HRP (Ed., 11/19/18)		
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:	The etiology of the Spaceflight-Associated Neuro-Ocular Syndrome (SANS) (formerly called Visual Impairment Intracranial Pressure) 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, 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. An anticipated product of this study is the reduction of the uncertainty in the likelihood or consequence of the SANS 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.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	By understanding the processes associated with fluid shift and its concomitant increase in intracranial pressure (ICP), we will gain clues to mitigate and reduce the impact of increased ICP in disease conditions like idiopathic intracranial hypertension and traumatic brain injury.
Task Progress:	A NASA-funded study using the hindlimb suspension (HS) analog in rats to model the physiological changes observed in the Spaceflight-Associated Neuro-Ocular Syndrome (SANS) was conducted. Animal experimentation has been completed, and sample and data analysis is ongoing. The project proposes to study the molecular bases of cerebrospinal fluid (CSF) production and outflow, and their modulation as a result of HS, bringing a molecular and histologic approach to investigate genome wide expression changes in the arachnoid granulations or villi (AG/AV) and choroid plexus (CP) of HS rats compared to rats in normal posture. To date, transmission electron microscopy (TEM) has been performed in coronal microsections of the brain containing the CP and AV, and laser capture microdissection of the CP and AV is being conducted in order to extract RNA from these specialized areas.
Bibliography Type:	Description: (Last Updated: 09/04/2023)
Articles in Peer-reviewed Journals	Zanello SB, Tadigotla V, Hurley J, Skog J, Stevens B, Calvillo E, Bershad E. "Inflammatory gene expression signatures in idiopathic intracranial hypertension: Possible implications in microgravity-induced ICP elevation." npj Microgravity. 2018 Jan 11;4(1):1. https://doi.org/10.1038/s41526-017-0036-6 ; PubMed PMID: 29354685; PubMed Central PMCID: PMC5764966 , Jan-2018
Articles in Peer-reviewed Journals	Cromwell RL, Scott JM, Downs M, Yarbough PO, Zanello SB, Ploutz-Snyder L. "Overview of the NASA 70-day Bed Rest Study." Med Sci Sports Exerc. 2018 Sep;50(9):1909-19. Epub 2018 Mar 22. https://doi.org/10.1249/MSS.0000000000001617 ; PubMed PMID: 29570535 , Sep-2018