Fiscal Year:	FY 2021	**Task Last Updated:**	FY 08/13/2020
PI Name:	Cekanaviciute, Egle Ph.D.		
Project Title:	Astrocytes as Key Mediators of Central Nervous System Responses to Space Radiation		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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PI Organization Type:	NASA CENTER	**Phone:**	415-623-0033
Organization Name:	NASA Ames Research Center		
PI Address 1:	Space Biosciences Research Branch		
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City:	Moffett Field	**State:**	CA
Zip Code:	94035	**Congressional District:**	18
Comments:	NOTE: PI formerly at Universities Space Research Association at NASA Ames Research Center; became civil servant at NASA Ames in summer 2020.		
Project Type:	Ground	**Solicitation / Funding Source:**	2018 HERO 80JSC018N0001-Crew Health and Performance (FLAGSHIP, OMNIBUS). Appendix A-Flagship, Appendix B-Omnibus
Start Date:	10/17/2019	**End Date:**	09/30/2021
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
Contact Monitor:	Lewis, Laura	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2021 per F. Hernandez/ARC when PI became civil servant summer 2020 and project extended as internal project at NASA Ames; USRA grant 80NSSC20K0125 has official end date of 6/5/2020 (Ed., 9/2/2020)		
Key Personnel Changes/Previous PI:	NOTE (Ed., 9/2/2020): PI became civil servant at NASA Ames in summer 2020 ; project extended as internal project at NASA Ames and previous USRA grant 80NSSC20K0125 has official end date of 6/5/2020.		
COI Name (Institution):	Costes, Sylvain Ph.D. (NASA Ames Research Center)		
Grant/Contract No.:	Internal Project ; 80NSSC20K0125		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	One of the main risks of human deep space exploration is central nervous system (CNS) damage, which is associated with neuronal damage and neuroinflammation, caused by exposure to space radiation combined with microgravity, and can lead to cognitive and behavioral dysfunction. CNS responses to injuries are strongly regulated by astrocytes, which are a major glial cell type in the brain that has also been shown to control the blood-brain barrier permeability, essential neuronal functions, and inflammation; and thus could serve as a robust CNS-specific target for countermeasure development. Therefore, we propose to investigate the astrocytic regulation of neuronal health in response to simulated space radiation. We propose to utilize for the first time a novel high-throughput human tissue-on-a-chip model for 3D neuronal/astrocyte cultures. We will investigate the morphological and physiological outcomes as well as gene expression changes after simulated space radiation exposure (5-ion simulation of galactic cosmic rays, 500 mGy) and compare them to the responses to gamma radiation in order to establish the relative biological effectiveness. We will also evaluate the necessity and sufficiency of astrocytes in regulating radiation responses by establishing experimental models where astrocytes are either the only cell type that is irradiated, or the only cell type that escapes irradiation. Finally, we will test whether driving astrocytes more towards A1 (inflammation) or towards A2 (scarring) phenotypes may serve as countermeasures by reducing radiation-mediated neuronal damage. In summary, we will examine whether astrocytes are necessary and sufficient to protect neurons from damage induced by simulated space radiation and evaluate their effectiveness as a target for further countermeasure development. We will also provide a proof of concept for human tissue-on-a-chip use for studying space radiation effects on the CNS. Our proposal addresses the Part "B. Basic Investigations Opportunity for Investigators New to NASA" of the Appendix B. The new investigator (Principal Investigator) and experienced investigator (CoInvestigator/Institutional Principal Investigator) have combined expertise in space biology, neuroinflammation astrocyte functions, TGFbeta functions in regulating astrocyte phenotypes, and responses to particle radiation. Thus, we have the capacity to complete this 1-year project at NASA Ames and, given sufficient interest, could easily expand it to a) investigate the outcomes of combined exposures to microgravity, stress, and radiation, and b) design an in vivo follow-up study on astrocytic regulation of CNS responses to spaceflight stressors.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	So far, my research has demonstrated that astrocytes are particularly sensitive to ionizing radiation, especially particle radiation, by increasing neuroinflammation, oxidative stress, and blood-brain barrier permeability. It is important not only for deep space exploration, but also for understanding the outcomes of human central nervous system irradiation for therapeutic purposes, to treat brain cancer.
Task Progress:	The goal of this project was to investigate the role of astrocytes in regulating central nervous system (CNS) responses to deep space radiation: simulated galactic cosmic rays (GCRs). We have established a robust and reproducible model of human CNS-on-a-chip that includes blood-brain barrier components in addition to astrocytes. We used this model to discover that GCR components (e.g., 600 MeV/n Fe particles) selectively damage astrocytes and increase blood-brain barrier permeability in an astrocyte-specific manner. In addition, based on our X-ray irradiation experiments, radiation-mediated increase in blood-brain barrier permeability is associated with damage to endothelial cells and tight junctions, release of inflammatory cytokines, and increased oxidative stress. Our 5-ion simplified simulated GCR exposure experiments were canceled due to Covid-19; therefore, we have requested a costed extension to be able to finish this work once Covid-19 mediated shelter-in-place is over, and to perform additional experiments that aim to demonstrate the molecular and cellular correlates of responses to GCR irradiation, and also evaluate whether astrocytes could be targeted for radioprotection.
Bibliography Type:	Description: (Last Updated: 06/23/2023)