Fiscal Year:	FY 2024	**Task Last Updated:**	FY 09/18/2023
PI Name:	Lu, Xiaohong Ph.D.		
Project Title:	Develop a Novel Single-Cell Biodosimetry for Brain Genomic Instability and Neurodegeneration to Predict Clinical Health Outcomes in Human Spaceflight Crews		
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) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Neurobiology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
PI Email:	xiaohong.lu@lsuhs.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	3109803445
Organization Name:	LSU Health Shreveport		
PI Address 1:	1501 Kings Hwy		
PI Address 2:	BRI F5-22		
PI Web Page:			
City:	Shreveport	**State:**	LA
Zip Code:	71103	**Congressional District:**	4
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2018 Space Biology (ROSBio) NNH18ZTT001N-FG2. App D: Flight and Ground Space Biology Research
Start Date:	11/15/2020	**End Date:**	11/30/2024
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	1
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
Contact Monitor:	Griko, Yuri	**Contact Phone:**	650-604-0519
Contact Email:	Yuri.V.Griko@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 11/30/2024 per NSSC information (Ed., 11/15/23) NOTE: End date is 11/30/2023 (incorrectly listed in NSSC as 11/14/2021) per F. Hernandez/ARC (Ed., 7/27/21)		
Key Personnel Changes/Previous PI:	Per the PI, the list of Co-Investigators has changed. During the past reporting period, the team has been working with the newly established bioinformatics center at Louisiana State University for the project, and Dr. Cvek was not involved. Dr. Harrison has moved to a new position and will no longer serve on this project. (Ed., 9/17/23)		
COI Name (Institution):	Chancellor, Jeffery Ph.D. (Louisiana State University and A&M College)		
Grant/Contract No.:	80NSSC21K0273		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	As NASA plans future exploration missions to the Lunar and Martian surfaces, realistic ground-based analog studies and more predictive biodosimetry are needed to assess whether the space radiation poses a detrimental risk of brain genomic instability and neurodegeneration that leads to late-onset behavioral deterioration for spaceflight crews. Implementing a recently developed method of recreating the intravehicular (IVA) radiation environment expected on spaceflight vehicles and habitats and a novel genetic sensor, this proposal addresses Research Topic 3 – Animal Biology Studies in support of Human Space Exploration and Sub-topic AB1-A – Behavior and underlying neural function in Appendix D: Solicitation of Proposals for Flight and Ground Space Biology Research. We propose to determine how the space environment and sex affect brain genomic stability and consequent age-related brain structure and function changes. Our studies will support Human Space Exploration, by contributing the first biodosimetry for quantifying brain DNA instability and neurodegenerative changes to predict clinical health outcomes in human spaceflight crews and the utility of available ground-based analogs to realize basic mechanisms that can lead to the development of biologic counter-measures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our studies will support Human Space Exploration, by contributing the first biodosimetry for quantifying brain DNA instability and neurodegenerative changes to predict clinical health outcomes in human spaceflight crews and the utility of available ground-based analogs to realize basic mechanisms that can lead to the development of biologic counter-measures.
Task Progress:	1. To evaluate the age and sex-dependent long-term consequences of galactic cosmic radiation (GCR) exposure on sensorimotor, cognition, and emotion, we have completed the longitudinal behavioral analysis in mice irradiated at NASA Space Radiation Laboratory (NSRL) in two groups. Group 1 mice (6 months of age) were irradiated with 80 cGy moderated iron (3.2 cGy/min, High dose rate, "HDR") (n = 22) or non-irradiated control (n = 16). 2. Group 2 mice (6 months of age) were irradiated with 30 or 75 cGy moderated iron (0.75 cGy/min, Low dose rate, "LDR") (n = 12-17 per group), 30 or 75 cGy 5-ion simulated GCR (0.75 cGy/min "LDR") (n = 16, 15 respectively), or non-irradiated control (n = 17). A wide variety of behavioral analyses were monitored in two time points at 2-4 months of and 10-14 months after irradiation. 3. Dosimetry analysis is ongoing at Louisiana State University-Baton Rouge (LSU-BR) with preliminary data. 4. Preliminary findings from the behavioral analysis results: Mice exposed to 75-80 cGy radiation show persistent deficits in sensorimotor function, including spontaneous activity, with stronger deficits in female mice. Irradiated mice show acute deficits in challenged movement (increased average time to cross balance beam), and age-dependent progressive development of accelerating rotarod deficits. Group 1 mice show acute hypersensitivity to stimuli (decreased time to remove facial adhesive). Cognitive function: Female mice develop working memory deficits. Differences in search strategies among irradiated and control mice during the probe day challenge of a spatial memory test may indicate cognitive differences associated with risk-taking behavior. Social and emotion: Exposed to modulated beam exposure impaired social interaction in mice. 5. We finished the analysis of sensor labeling in mice irradiated with moderated iron or simulated GCR (5-ion). A robust increase in Probe with a viRal proxy for the Instability of DNA surveillance/repair in Somatic brain Mosaicism (PRISM) labeling following simulated GCR exposure at three doses indicates an increase in radiation-induced genomic instability in CamkIIa-Cre-expressing cortical pyramidal neurons. Exposure to 80 cGy modulated Fe radiation at 3.2 cGy/min increases PRISM labeling in C57BL/6 mice. Exposure to 75 cGy GCR sim or modulated iron (0.75 cGy/min) increases PRISM labeling in Gt(Rosa) mice. 6. We have completed an RNA sequencing (RNAseq) study of mice irradiated with modulated iron. The pathway analysis is ongoing. 7. Brain mapping of the genomic instability in the brain after irradiation is ongoing. The work is ongoing to determine neuronal genomic instability in different brain regions and at 12 and 24 months after irradiation. 8. Single-cell pathology analysis in sensor-labeled neurons already identified highly intriguing cell senescence, neuroinflammation, and disruption of protein homeostasis, suggesting accelerated brain aging. More pathology analysis is ongoing.
Bibliography Type:	Description: (Last Updated: 09/26/2024)