Fiscal Year:	FY 2023	**Task Last Updated:**	FY 09/15/2022
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		
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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:**	11/30/2023
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
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Flight Program:			
Flight Assignment:	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:	n/a		
COI Name (Institution):	Cvek, Urska Sc.D. (Louisiana State University, Shreveport) Chancellor, Jeffery Ph.D. (Louisiana State University and A&M College) Harrison, Lynn Ph.D. (Louisiana State University)		
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:	In the past year, we have two beamline exposures at the NASA Space Radiation Laboratory (NSRL). We used two method to develop a realistic ground-based simulation of galactic cosmic radiation (GCR) exposure. We also further modified a genetic sensor to generate a quantitative ratiometric sensor with membrane-tethered fluorescence protein to report different levels of genomic instability and visualize neuropathology. The radiometric sensors were administered in transgenic mice to label specific groups of neurons that are highly vulnerable to neurodegeneration. A radiation mimic, Bleomycin, increased genetic labeling neurons with genomic instability in the mouse brains. Simulated GCR exposure (iron modulator) at 80 cGy robustly increased the sensor labeling across the whole brain. The ratio of genetic labeling also increased, suggesting the sensor can report different levels of genomic instability. The DNA repair of the double stand breaks was also impaired. Mice that received simulated GCR exposure at 80 cGy showed multiple behavioral deficits (sensorimotor, cognition, and emotion/sociability) with gender differences three months post-irradiation. Finally, we also established the method to quantify single-neuron pathology and neuroinflammation and the method of mapping brain genotoxic stress using deep learning augmented volume imaging after GCR exposure.
Bibliography Type:	Description: (Last Updated: 09/15/2022)
Articles in Peer-reviewed Journals	El-Saadi MW, Tian X, Grames M, Ren M, Keys K, Li H, Knott E, Yin H, Huang S, Lu X-H. "Tracing brain genotoxic stress in Parkinson's disease with a novel single-cell genetic sensor. " Science Advances. 2022 Apr 15;8(15). http://dx.doi.org/10.1126/sciadv.abd1700 , Apr-2022