Fiscal Year:	FY 2022	**Task Last Updated:**	FY 09/15/2021
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:**	11/30/2023
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
Contact Email:	Yuri.V.Griko@nasa.gov		
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:	• Constructed AAV-G22-Cre PRISM (adeno-associated viral) vectors and packaged in the neurotropic AAV-PhB.eB serotype with high titer and purity for non-invasive in vivo application (intravenous injection) in mice. • We have determined the dose-response curve and the baseline dose of AAV-G22-Cre PRISM to report the spontaneous DNA damage response in the mouse brain. We tested the gene dosage dependency of the genetic sensor with G22 repeats. We examined 6 different doses (5x1011, 1x1011, 5x1010, 1x1010, 0.5x1010 VG/mouse) in vivo. We have determined the best titer/dosage of 1x1010 VG/mouse for in vivo application. • We acquired Th-Cre, CamKII-Cre, D1-Cre, D2-Cre, Aai9 mouse breeding pairs from the Jackson Laboratory (JAX). We have been breeding these mice in C57BL/6J background. We already accumulated a sufficient number of mice for the simulated space radiation exposure at the NASA Space Radiation Laboratory (NSRL) this October 2021. • We successfully constructed the genetic sensor (biodosimetry) of neuronal genomic instability and validated the Cre dependency in vitro. These sensors will be used to determine space radiation-induced neuronal genomic instability in the most vulnerable neuronal cell types in multiple neurodegenerative disorders. • We generated a quantitative ratiometric sensor: AAV-G34/G22/G13- mScarlet/fWasabi/fBFP PRISM vector and packaged it in AAV-PhB.eB serotype in high titer and purity for non-invasive in vivo application (intravenous injection) in mice. • Intravenous systemic administration of AAV-G34/ G13- mScarlet/ fBFP PRISM sensor in different Cre driver lines (Drd1a. Drd2, TH Cre, CamkII Cre lines) was performed and we successfully labeled major neuronal cell types vulnerable to neurodegeneration, striatal medium spiny neurons, nigral dopamine neurons, hippocampal and cortical pyramidal neurons. • Developed assays to quantify and confirm the mechanism of action of Dn to induce neuronal genomic instability using T7E1, Next Generation Sequencing (NGS), and capillary electrophoresis. • We have made significant progress in optimizing the volume imaging of the iDISCO cleared mouse brains labeled with the genetic sensor of neuronal genomic instability. • We have demonstrated that radiation mimic, Bleomycin, can increase AAV-G22-Cre dependent expression of AAV-G34/ G13- mScarlet/ fBFP PRISM sensor (systemic administration) genetic labelling in the mouse brains. • We have scheduled and are ready for our first beamline exposures on 10/29-10/20/2021.
Bibliography Type:	Description: (Last Updated: 09/15/2022)
Abstracts for Journals and Proceedings	Knott EL, El-Saadi MW, Tian X, Chancellor J, Harrison L, Lu X-H. "A novel genetic biodosimetry of neuronal DNA damage response permits the risk assessment of space radiation-induced cognitive decline and neurodegeneration." Oral presentation at 37th Annual Meeting of the American Society for Gravitational and Space Research, Baltimore, MD, November 3-6, 2021. Abstracts. 37th Annual Meeting of the American Society for Gravitational and Space Research, Baltimore, MD, November 3-6, 2021. , Nov-2021
Abstracts for Journals and Proceedings	Knott EL, El-Saadi MW, Tian X, Chancellor J, Harrison L, Lu X-H. "A novel genetic biodosimetry of neuronal DNA damage response permits the risk assessment of space radiation-induced cognitive decline and neurodegeneration." Online and poster presentation at Neuroscience 2021 (Society for Neuroscience Annual Meeting), Virtual, November 8-11, 2021. Abstracts. Neuroscience 2021 (Society for Neuroscience Annual Meeting), Virtual, November 8-11, 2021. , Nov-2021