Fiscal Year:	FY 2023	**Task Last Updated:**	FY 03/07/2023
PI Name:	Robinson, Lucy Ph.D.		
Project Title:	Investigating Lunar Stress and Parkinson's Disease Using an Alpha Synuclein Yeast Model (PI: Robinson)		
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) Cell & Molecular Biology (2) Microbiology		
Space Biology Cross-Element Discipline:	(1) Neurobiology		
Space Biology Special Category:	None		
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Zip Code:	71130	**Congressional District:**	4
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2021 Space Biology NNH21ZDA001N-LEIA E.10. Lunar Explorer Instrument for Space Biology Applications
Start Date:	12/01/2021	**End Date:**	11/30/2023
No. of Post Docs:		**No. of PhD Degrees:**	
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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:			
Key Personnel Changes/Previous PI:	NOTE: Per NASA Ames Research Center, the former Principal Investigator (Lynn Harrison, Ph.D., Louisiana State University) has moved to a new position and will no longer serve as PI on this project. A former CoInvestigator on the project will serve as the new PI. The new PI is Lucy Robinson, Ph.D. of Louisiana State University. (Ed., 3/7/23)		
COI Name (Institution):	Shi, Runhua Ph.D. (Louisiana State University System) Tatchell, Kelly Ph.D. (Louisiana State University System) Chancellor, Jeffery Ph.D. (Louisiana State University, Baton Rouge)		
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Task Description:	Astronauts will be exposed to partial gravity and deep space high energy radiation when living on the surface of the moon. Ionizing radiation increases oxidative stress in cells, and persistent oxidative stress in neurons from repeated exposure to low dose high energy radiation could increase the risk of developing neurodegenerative disease. Experiments are therefore needed to determine whether lunar living conditions increase toxic forms of proteins known to be involved in neurodegeneration. Alpha-synuclein (SYN) and mutations of this protein are implicated in Parkinson's disease. One such familial mutation is A53T-SYN, which increases aggregate formation and toxicity of SYN. Toxic forms of SYN can also form in cells under oxidative stress. The objective of this proposal is to determine whether lunar radiation or the stress of exposure to one sixth the Earth's gravity increases the toxicity of SYN. Two aims are proposed: aim 1 is to test the experiment in the Biosensor hardware to prepare for a possible lunar lander mission in the future and aim 2 is to use ground-based studies to determine whether SYN or A53T-SYN toxicity is increased by simulated lunar radiation or simulated lunar gravity. The Biosensor hardware has been tested for toxicity studies using yeast and the expression of SYN in Saccharomyces cerevisiae is an established model of Parkinson's disease. Low SYN levels in yeast are not toxic, but high levels induce apoptosis and Reactive Oxidative Species (ROS) accumulation. We will generate wild-type and RAD51 deleted Saccharomyces cerevisiae strains that can be induced to express SYN or A53T-SYN at low levels by red light. RAD51 deleted yeast are more radiosensitive than wild-type yeast and will increase the sensitivity of detection of SYN toxicity generated by radiation/oxidative stress exposure. Genes known to reduce SYN toxicity in yeast include the gene encoding manganese superoxide dismutase (SOD2), an enzyme that detoxifies superoxide radicals in mitochondria. We will therefore also develop strains that overexpress SOD2 in combination with SYN to determine whether SYN toxicity can be rescued by quenching superoxide radicals. The Biosensor hardware can determine toxicity by the Alamar Blue viability assay, and growth by culture turbidity. We will use these assays in aims 1 and 2 to determine SYN toxicity as well as colony-forming ability in the ground-based studies in aim 2. In aim 2, simulated lunar gravity will be achieved using the random positioning machine (RPM 2.0) at Kennedy Space Center and simulated lunar radiation exposure will be performed at Brookhaven. Dr. Chancellor, a team member, has developed techniques to recreate the polyenergetic radiation spectrum for ground-based studies of galactic cosmic rays, and will use measurements scheduled to occur in early 2022 on the lunar surface to guide exposure of the cultures at Brookhaven in aim 2. From the work in this proposal, we will be able to study SYN toxicity. We hypothesize that expressing SYN or A53T-SYN in yeast will increase toxicity to simulated lunar radiation or simulated lunar gravity, and toxicity will be greater in yeast expressing A53T-SYN. Toxicity will be decreased by overexpressing SOD2, an enzyme known to protect against SYN toxicity. Understanding how the stresses of living on the moon can enhance SYN toxicity is significant to humans thriving in deep space as extended space missions on the moon could enhance neurodegeneration in astronauts. Knowing the risks will allow NASA to establish countermeasures to protect astronauts on future deep space missions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This will be the first time that a yeast model of Parkinson's disease will be used to study the effect of lunar gravity and the lunar radiation environment on aggregation of a protein implicated in Parkinson's disease. This could have implications for risk assessment of neurodegeneration for astronauts living on the Moon. These experiments will provide the ground-based studies needed to justify performing experiments on the Moon. They will open up this field of research to other space biologists so the risk of neurodegeneration can be assessed in animals on the Moon. Without knowing how lunar living stress conditions alter brain physiology, it is not possible to design necessary countermeasures to keep our astronauts safe. Understanding the effects of alpha synuclein on irradiated cells will also have implications for radiotherapy patients that receive radiation to the brain. Experiments include initial tests with gamma radiation.
Task Progress:	New Project for FY2023.
Bibliography Type:	Description: (Last Updated:)