Fiscal Year:	FY 2019	**Task Last Updated:**	FY 04/26/2019
PI Name:	Jacob, Naduparambil K Ph.D.		
Project Title:	Predictive Biomarkers for Space Radiation Induced Cancer and Cardiovascular Injury Risk Assessment		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **Cancer**:Risk of Radiation Carcinogenesis (2) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	43210	**Congressional District:**	3
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2017 HERO 80JSC017N0001-Crew Health and Performance (FLAGSHIP1, OMNIBUS). Appendix A-Flagship1, Appendix B-Omnibus
Start Date:	07/02/2018	**End Date:**	07/01/2020
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Lee, Peter M.D., Ph.D. (Ohio State University)		
Grant/Contract No.:	80NSSC18K1691		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	To reduce the uncertainty in estimates of cancer and cardiovascular risks from space radiation, we will evaluate changes in molecular biomarkers in rodents and rabbits exposed to ions relevant to exposures of astronauts in the space environment. Serum, heart, liver, and lung tissues collected from exposed animals and matching controls will be used for biomarker discovery following systems-biology approaches. The study will use modern analytic technologies and rigorous statistics for assessing changes in expression of microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and messenger RNAs (mRNAs) associated with clinical endpoints for mechanistic understanding of disease initiation and progression. Analysis of samples from patients receiving radiation therapy and organ targeted and organ protected low-linear energy transfer (LET) irradiation model studies have shown changes in circulating miRNAs originating from organ systems as a function of dose and time, correlating with disease states. Archived cardiac specimens from rabbits and rats previously exposed to 0.5 Gy Proton or Oxygen ions with respective sham controls will be used for discovery and validation of space radiation-induced cardiovascular diseases. Changes in miRNAs mechanistically connected to inflammation and pathological changes using clinical, imaging, and biochemical endpoints of cardiovascular diseases will be evaluated. miRNAs and lncRNAs in lung, liver, and serum collected from mice exposed to 0.2 Gy Silicon ions will be compared with sham controls of changes in cancer endpoints. The availability of specimens (archived or upcoming sacrifices) from on-going or completed Carcinogenesis NASA Specialized Center of Research (NSCOR) and National Space Biomedical Research Institute (NSBRI) for Space Radiation Research studies focusing on cardiovascular diseases are ensured. Our project is cost-effective and unique because we will use samples both for developing cancer and cardiovascular risk assessment. Cellular and molecular mechanisms involved in space radiation-induced cardiovascular disease, lung, and liver cancer will be studied, which will significantly contribute to the testing of and validating effective countermeasures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The goal is to develop blood test for early detection of delayed cardiovascular complications resulting from high-LET radiation exposure to astronauts during long duration space travel.
Task Progress:	Longer space mission results in an unavoidable exposure of space radiation to astronauts that may create potential health risks including late occurring cardiovascular diseases and cancers. In order to identify biomarkers with potential to provide early readout of cardiovascular injury and risk assessment, specimens available thorough tissue sharing program were evaluated for changes in the expression of microRNAs. We hypothesized that space radiation-dependent DNA damage response and chronic inflammation will result in alteration of evolutionarily and functionally conserved microRNAs and as a readout of genetic/epigenetic reprogramming associated with initiation and progression of diseases. In the first year of the award, we focused on qualitative and quantitative analysis of microRNAs in cardiac tissue collected one year after the exposure of male Long Evans rats and New Zealand White rabbits to a single dose of 0.5 Gy proton (250 MeV) or 0.5 Gy oxygen ions (600 MeV/n). For discovery of biomarkers that are altered as a function of time after exposure to space radiation: An unbiased amplification-free hybridization based direct digital counting method was used for profiling, which allowed the evaluation of relative changes in up to 800 miRNAs. Robustness of the responses of candidate biomarkers identified from nanoString profiling was validated by a quantitative real-time PCR based approaches. Moreover, some of the responding molecules identified are known to modulate chronic inflammation and progressive diseases providing a potential link to molecular processes associated with delayed fibrosis and hypertrophy. The discovery and validation of biomarkers conserved in multiple animal models are predicted to help develop benchmarks for both risk assessment and evaluation of efficacy of countermeasures.
Bibliography Type:	Description: (Last Updated: 06/02/2023)
Abstracts for Journals and Proceedings	Jacob N, Liu J, Bhayana S, Yadav M, Lee P, Boerma M, Sridharan V. "MicroRNA Biomarkers of Radiation-induced Cardiovascular Injury." Radiation Health Effects. 2019 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. 2019 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. Poster #19193. , Jan-2019