Fiscal Year:	FY 2017	**Task Last Updated:**	FY 09/26/2017
PI Name:	Bowles, Dawn Ph.D.		
Project Title:	Proteomic Signatures of Space Radiation Induced Cardiovascular Degeneration		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **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:	27710-0001	**Congressional District:**	4
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-RADIATION. Appendix D: Ground-Based Studies in Space Radiobiology
Start Date:	05/12/2016	**End Date:**	05/11/2020
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Abraham, Dennis M.D. (Duke University) Kidane, Yared Ph.D. (Wyle Laboratories, Inc.) Mao, Lan M.D. (Duke University) Dewhirst, Mark D.V.M., Ph.D. (Duke University) Moseley, Martin Ph.D. (Duke University)		
Grant/Contract No.:	NNX16AK20G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Radiation damage and the cell's attempt to repair it triggers a myriad of signal transduction pathways which alter gene, and ultimately, protein expression. Space radiation may affect biomolecules, cellular processes, and ultimately the cellular protein content (the proteome) differently than radiation present on Earth. Epidemiological analysis of terrestrial radiation exposure indicates that single high- or multiple low-dose radiation exposure can culminate in a wide array of cardiac injury and malfunction over time. Based on terrestrial data, it is believed that cardiovascular disorders may develop in astronauts from exposure to the space radiation environment. Indeed, a recent study by Yan et al. (2014), found that a single full body exposure to a low dose of proton or iron particle radiation, which somewhat mimics the space radiation environment, was sufficient to induce a significant, long term, negative effect on murine cardiovascular function. In this proposal, we take advantage of our expertise with bioinformatics analysis of cardiovascular proteomic data sets and murine cardiovascular physiology to evaluate the consequences of low dose, chronic space radiation, or mixed field space radiation on the dynamics of the cardiac proteome and to understand how the radiation induced changes relate to cardiovascular function. In doing so, we will extend Yan et al.'s work by identifying a proteomic signature that predicts the development of permanent cardiovascular degeneration from a single low dose space radiation exposure. Further, we seek to evaluate whether the proteomic signatures differ when mice experience repeated exposures of space-like radiation or mixed field space radiation. This information will lead to a mechanistic understanding of the altered cellular and molecular processes contributing to the development of cardiovascular dysfunction at the organ and organismal level in scenarios better mimicking the space radiation environment. This information is needed to predict, monitor, and prevent cardiac damage during long term space flight. Yan, X., et al., Cardiovascular risks associated with low dose ionizing particle radiation. PLoS One, 2014. 9(10): p. e110269.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Limited information is known regarding the impact of chronic low level radiation on cardiovascular molecular biology and function both terrestrially and during extended space exploration. Our research is expected to provide information in regards to terrestrial and astronaut heath. Innovative technologies that may arise from our studies may include novel biomarkers predictive of cardiovascular susceptibility to chronic low level radiation as well as countermeasures that may be employed both on Earth as well as during space exploration.
Task Progress:	Studies are ongoing. One trip to Brookhaven National Laboratory (BNL) was made in Nov 2016. Male C57B6 mice acquired from Jackson Laboratories were shipped to Duke University Medical Center where at 5 months of age they underwent transthoracic echocardiograms to establish baseline cardiac function. Parameters evaluated included (a) M-mode (done in both long and short axis), (b) Septal and posterior wall width in diastole, (c) End diastolic dimension and end systolic dimension, (d) aortic valve velocity, and (e) aortic ejection time (all measured and averaged over 3 consecutive beats). Echocardiogram images were also acquired for measurement of diastolic dysfunction and strain. Mice were shipped to the NASA Radiation Science Laboratory at Brookhaven National Laboratories where they were subjected to single fully body irradiation at 6 months of age under the following conditions: a) gamma (50cGy, 100cGy, 200cGy), b) 16O (15cGy, 25cGy, 50cGy/ 600 MeV/n), c) 56Fe (15cGy, 25cGy, 50cGy 1 GeV/n). All radiation groups included sham irradiated control animals. Studies of these mice are ongoing. Evaluations include: a) serial transthoracic echocardiograms capturing all above parameters, b) terminal pressure volume loop hemodynamic assessments, and c) mass spectrometry based proteomics assessments (quantitative, dynamic, and post-translational modification proteomics) of the cardiac proteome. A second trip to BNL will occur in April 2017. A larger group of mice will be administered the same radiation exposures. The exposures will be single fully body irradiation at 6 months of age under the following conditions: a) gamma (50cGy, 100cGy, 200cGy), b) 16O (15cGy, 25cGy, 50cGy/ 600 MeV/n), c) 56Fe (15cGy, 25cGy, 50cGy 1 GeV/n). All radiation groups include sham irradiated control animals. All animals will be monitored as described above. Evaluations include: a) serial transthoracic echocardiograms capturing all above parameters, b) terminal pressure volume loop hemodynamic assessments, and c) mass spectrometry based proteomics assessments (quantitative, dynamic, and post-translational modification proteomics) of the cardiac proteome.
Bibliography Type:	Description: (Last Updated: 03/11/2025)
Abstracts for Journals and Proceedings	Bishawi M, Isaac D, Abraham D, Mao L, Slaba T, Kidane Y, Kuchibhatla M, Thompson JS, Moseley MA, Dewhirst MW, Bowles DE. "Proteomic signatures of space radiation induced cardiovascular degeneration." Poster presentation at 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. 2017 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 23-26, 2017. , Feb-2017
Abstracts for Journals and Proceedings	Isaac D, Bishawi M, Mishra R, Watson M, Slaba T, Dewhirst MW, Joshi M, Wu H, Bowles DE. "Tissue biobanking to understand molecular signatures of space radiation induced tissue degeneration." Oral Presentation at ISBER 2017 Meeting, Toronto, Canada, May 9-12, 2017. ISBER 2017 Meeting, Toronto, Canada, May 9-12, 2017. , May-2017