Fiscal Year:	FY 2019	**Task Last Updated:**	FY 03/20/2019
PI Name:	Edwards, John Ph.D.		
Project Title:	Countermeasures to Radiation Induced Cardiomyopathy		
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		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	j_edwards@nymc.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	914-594-4166
Organization Name:	New York Medical College		
PI Address 1:	Department of Physiology		
PI Address 2:	15 Dana Rd		
PI Web Page:			
City:	Valhalla	**State:**	NY
Zip Code:	10595-1554	**Congressional District:**	17
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2017-2018 HERO 80JSC017N0001-BPBA Topics in Biological, Physiological, and Behavioral Adaptations to Spaceflight. Appendix C
Start Date:	02/01/2019	**End Date:**	01/31/2021
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Simonsen, Lisa	**Contact Phone:**	
Contact Email:	lisa.c.simonsen@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Eisenberg, Carol Ph.D. (New York Medical College) Rota, Marcello Ph.D. (New York Medical College)		
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Task Description:	The present application seeks to study the long-term consequences of cosmic radiation exposure. Space travel increases solar particle radiation exposure which is significantly elevated once travel moves beyond low Earth orbit. This includes a combination of high-energy protons and heavy ions such as 56Fe, 28Si, and 16O. The adverse risk of radiation-induced heart failure is also evident as a long-term consequence of accidental radiation exposure or cancer treatment. Survivors of cancer are also at risk for other adverse health outcomes including abnormal pulmonary function, endocrine disorders, neurocognitive impairment, and osteoporosis. All of these organ systems are characterized by a low turnover of cells and it is likely that an accelerated cell death and/or the failure of regeneration by the pluripotent cells may be the underlying cause of organ failure. Although this application will focus on heart failure, our findings will have implications for many organ systems. Our preliminary studies observed degradation of cardiovascular function in a model of cosmic radiation (High-Linear Energy Transfer) exposure. Mice were exposed to 50 cGy (Fe56) at 3 months of age and then studied at 24 months of age. Degradation of cardiac function was evident by significant decreases in myocardial contractility and relaxation. Concomitant with this were significant changes in mitochondrial and stem/progenitor cell function. In the present ground based application, we propose to evaluate the impact of High-Linear Energy Transfer (LET); to identify the pathway to heart failure, and evaluate three distinct protocols as potential countermeasures. Hypothesis: Radiation-induced cardiomyopathy is the result of a cell specific failure. Cell specific failure is the result of an inability to maintain the balance of repair/replacement that ultimately leads to activation of degradation pathways and accelerated cell loss. This study will utilize both cultured cells as well as Swiss Webster mice to be randomly assigned to control or single heavy ion high-LET exposure groups. Phase 1 will use single exposures to high-LET exposure of 1) 56Fe (50 cGy) or 2) Proton (200 cGy). Phase 2 will utilize a mixed field exposure following the guidelines of the Human Exploration Research Opportunities (HERO) Announcement (80JSC017N0001-BPBA; Appendix C). All exposures will be performed at the NASA Space Radiation Laboratory at Brookhaven National Laboratory. We plan to study three distinct countermeasures including 1) MitoTempo, 2) Metformin, and 3) Lisinopril. MitoTempo is an antioxidant that partitions to the mitochondria. Metformin, an antidiabetic mainstay, has more recently been shown to have significant anticancer properties. Lisinopril, an inhibitor of the angiotensin system, has been shown to mitigate radiation injuries from Low-LET exposure. Evaluations will be made on several levels, to include 1) Determination of cardiovascular function, 2) Identification of cell specific failure, and 3) Intracellular determination of damage focusing on genomic and mitochondrial DNA damage. Cell failure in terms of metabolic failure, accelerated senescence, as well as DNA damage will be determined. A number of investigations in Space Biology are currently ongoing at New York Medical College (NYMC) and collaborations and sharing of resources will enhance the research products derived from funding this application. Radiation induced cardiomyopathies are observed months or years after exposure. The present application will separate the insult from the consequences. Our preliminary findings demonstrated significant degradation of cardiac function similar to the accelerated aging phenotype observed with chemotherapy. It may not be relevant that any single cell dies but that the balance of cell death and cell replacement is upset. Although focused on the heart, these investigations will have widespread application to other organ systems and collectively serve the long term health and well being of flight crews.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2019.
Bibliography Type:	Description: (Last Updated: 07/05/2023)