Fiscal Year:	FY 2020	**Task Last Updated:**	FY 12/07/2020
PI Name:	Fornace, Albert M.D.		
Project Title:	Space Radiation-Induced Persistent Estrogenic Response and Risk of Breast Cancer Development		
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		
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Zip Code:	20007-2126	**Congressional District:**	1
Comments:	http://www9.georgetown.edu/		
Project Type:	GROUND	**Solicitation / Funding Source:**	2018 HERO 80JSC018N0001-Crew Health and Performance (FLAGSHIP, OMNIBUS). Appendix A-Flagship, Appendix B-Omnibus
Start Date:	01/02/2020	**End Date:**	01/01/2024
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
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Ed. note December 2020: Original Principal Investigator was Kamal Datta, M.D., who is now affiliated with NIH, as of early 2019. PI changed to Albert Fornace, M.D., before grant was awarded.		
COI Name (Institution):	Brenner, David Ph.D. (Columbia University) Johnson, Michael Ph.D. (Georgetown University) Li, Xin Ph.D. (Georgetown University) Suman, Shubhankar Ph.D. (Georgetown University)		
Grant/Contract No.:	80NSSC19K1649		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Breast cancer is the most common malignancy in women worldwide and it is predicted that in the USA, 1 in 8 women will develop invasive breast cancer in her lifetime. Given that there is already high incidence of breast cancer in general population and even low doses of radiation have been established as a breast cancer risk factor, an even small increase in breast cancer after space radiation will have significant impact on health of women astronauts undertaking long duration space missions. Since space radiation is characteristically different than typical terrestrial radiation (gamma-rays and x-rays), it is expected that women astronauts will have higher risk of breast cancer relative to women on Earth. Also, deep space missions such as return trips from Mars due to their long time span have the risk of women astronauts being diagnosed with new mass in breast even during space travel. However, currently, there is large uncertainty in both temporal and spatial breast cancer risk prediction as well as risk management approach due to paucity of in vivo data. The purpose of the proposed studies is to reduce the margins of uncertainty for breast cancer risk prediction and to initiate experiments to understand quantitatively and qualitatively the effects of space radiation dose rates on breast cancer risk including establishing the initial shape of the response curve at low fluence (less than one ion per cell). The proposed project is based on our initial discovery that showed exposing wild type female C57BL/6J mice to a whole-body non-lethal dose of gamma radiation (2 Gy) led to persistent estrogenic response (PER) at the systemic in serum and urine as well as at the tissue level in mammary glands. Our preliminary data in female APCMin/+ mice in C57BL/6J background show increased mammary tumor frequency and grade along with systemic and local PER after exposure to proton radiation relative to gamma-rays. Since estrogen is a key promoter of breast cancer, we will test the hypothesis that space radiation-induced PER will be higher with increased mammary gland tumorigenesis irrespective of dose rates relative to gamma radiation and that blocking radiation-induced PER will lower the risk of mammary gland tumorigenesis. The overall goal of this project is to understand space radiation-induced PER, its mechanisms and relation to mammary gland tumorigenesis, and whether a Food and Drug Administration (FDA) approved selective estrogen receptor modulator (SERM) could be used to block radiation-induced PER to reduce tumorigenic risk. The current proposal will compare the results of priority beams in the current solicitation at different dose rates using ? radiation data as the baseline in female APCMin/+ mice to 1) develop breast cancer risk prediction models, 2) identify early markers of breast cancer risk, and 3) test tamoxifen, an FDA approved breast cancer chemoprevention agent, for space radiation-induced breast cancer risk mitigation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2020. (Note: project added to Task Book when received information in December 2020.)
Bibliography Type:	Description: (Last Updated: 04/18/2024)