Fiscal Year:	FY 2022	**Task Last Updated:**	FY 03/21/2023
PI Name:	Fornace, Albert M.D.		
Project Title:	Radiation Carcinogenesis by GCRsim in Animal Models for High Priority Cancer Types (NSCOR)		
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:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	http://www9.georgetown.edu/		
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	05/25/2022	**End Date:**	05/24/2023
No. of Post Docs:	1	**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:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Shubhankar, Suman Ph.D. (Georgetown University) Shay, Jerry (University of Texas Southwestern Medical Center at Dallas) Brenner, David (Columbia University)		
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	Considering the high spontaneous incidence of gastrointestinal (GI) and lung cancer, an even modest increase by space radiation exposure could have a significant effect on astronauts' health risk estimates during and after long-duration manned space flights. However, there is substantial uncertainty for GI and lung cancer risk estimation from space radiation due to the lack of in vivo human data. The overarching goal of the current proposal is to specifically investigate cellular and molecular hypothesis-driven mechanisms in relevant mouse models that will contribute to carcinogenic risk estimates of GI and lung cancer after exposure to space radiation beams prioritized by NASA's Human Research Program (HRP). Specifically, this proposal builds on the data generated from previous NSCOR studies and seeks to determine incidence, tumor frequency, and grade as well as identify molecular perturbations in the target cells associated with GI and lung tumorigenesis through monitoring of changes in the tumor number, histology, gene/protein		

Task Description:	expression, and metabolome of the proposed model system after exposure to space radiation type beams. Having found modest effects in earlier studies with protons and considering the importance of assessing the effects of mixed beams, we have chosen high priority Galactic Cosmic Radiation (GCR) type beams for comparison with low-LET (gamma-rays) radiation in our proposed studies. The full-spectrum (33-ion) acute (single dose) and protracted (up to 6 weeks) GCRsim beams closely mimic the mixed particle radiation environment in deep space. Our overall hypothesis is that GCRsim exposure is more carcinogenic due to important qualitative differences from low-LET gamma rays. The overall objective of this proposal is to acquire quantitative and qualitative cancer data after full-spectrum GCRsim exposure to model the relative risk of GI and lung tumorigenesis and compare it to gamma radiation where human epidemiologic data are available. Our proposed Aims are: Aim 1. Quantitatively assess GI tumorigenesis in mouse models of GI cancer and collect samples for qualitative analysis. Aim 2. Understanding molecular signaling associated with space radiation-induced GI-tumorigenesis and functional alterations. Aim 3. Quantitatively and qualitatively compare effects of GCR-type irradiations on lung cancer initiation and progression in normal as well as lung cancer susceptible mice. Aim 4. Development of mathematical modeling for GI and lung cancer risk assessment.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research.
Research Impact/Earth Benefits:	According to estimations from the American Cancer Society (ACS), the lifetime risk of developing colorectal (1 in 23 for men and 1 in 25 for women) and lung (1 in 16 for men and 1 in 17 for women) cancer is significantly high in the US population. Considering the high prevalence of GI and lung cancer, an even slight increase in the incidence of GI and lung cancer in astronauts due to space radiation exposure is a critical health concern and has a significant impact on the planning of upcoming manned deep space exploration missions. In addition to cancer risk estimation studies after space radiation exposure, investigations on the persistence of oxidative and inflammatory stress after space radiation and its role in GI and lung cancer development may provide insight into mutagenic processes affecting genome integrity and carcinogenesis. The significance and deliverable of this project are to improve the estimates of GI and lung cancer risk after simulated galactic cosmic radiation (GCR) exposure and to identify plausible targets for the development of medical countermeasures (MCM).
Task Progress:	New project for FY22.
Bibliography Type:	Description: (Last Updated: 05/15/2025)