Fiscal Year:	FY 2021	**Task Last Updated:**	FY 12/01/2020
PI Name:	Boerma, Marjan Ph.D.		
Project Title:	Gamma-Tocotrienol as a Countermeasure against High-Energy Charged Particle-Induced Carcinogenesis, Cardiovascular Disease, and Central Nervous System Effects		
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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City:	Little Rock	**State:**	AR
Zip Code:	72205-7101	**Congressional District:**	2
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:	01/31/2019	**End Date:**	10/31/2022
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:	Elgart, Robin	**Contact Phone:**	281-244-0596 (o)/832-221-4576 (m)
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 10/31/2022 per NSSC information (Ed., 5/17/21) NOTE: End date changed to 3/31/2022 per NSSC information (Ed., 11/4/20)		
Key Personnel Changes/Previous PI:	December 2020 report: No changes in PI or other key personnel.		
COI Name (Institution):	Landes, Reid Ph.D. (University of Arkansas, Little Rock) Weil, Michael Ph.D. (Colorado State University) Pathak, Rupak Ph.D. (University of Arkansas, Little Rock)		
Grant/Contract No.:	80NSSC19K0437		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Recent evidence shows that radiation encountered during deep space travel is associated with increased risks of cancer. Administration of a dietary radiation countermeasure before and/or during the mission is an attractive option to reduce the carcinogenesis risk. Gamma-tocotrienol is one of the strongest radiation protectors of all natural compounds tested so far. It is safe, non-toxic and well tolerated, exhibits no interactions with other medications and requires no special storage conditions. It has anti-oxidant and anti-inflammatory properties and protects against endothelial dysfunction. Moreover, studies with tocotrienol administration in human subjects and animal models have shown cancer prevention. In our preliminary studies, gamma-tocotrienol reduced radiation-induced genomic instability, as detected by studying chromosomal aberrations, in human endothelial cells and in bone marrow cells of gamma-ray exposed mice. Altogether, based on its safety profile, biological properties, and our preliminary results, gamma-tocotrienol has high potential as radiation countermeasure during space travel. Here, we use a mouse model to test whether gamma-tocotrienol protects against radiation-induced carcinogenesis. For this purpose, genetically modified mice will be used that show a low spontaneous cancer rate, but increased tumor incidence in response to low-dose radiation. Male and female adult mice will be exposed to mixed charged particle beams to mimic galactic cosmic rays at the NASA Space Radiation Laboratory. Twenty-four hours before each radiation exposure, mice will be administered gamma-tocotrienol. Mice will be followed for 18 months after irradiation and inspected daily for tumor formation. In addition, bone marrow cells will be collected to assess the effects of gamma-tocotrienol on genomic instability by cytogenetic analysis. These studies will advance the countermeasure readiness level of gamma-tocotrienol against carcinogenesis risks of space radiation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	There is concern about increased carcinogenesis risk after chronic exposures to low-dose ionizing radiation, such as from medical treatments, occupational low-dose exposures, and radiological accidents. The current project will provide evidence for gamma-tocotrienol as a safe countermeasure against radiation-induced carcinogenesis. This information will not only contribute to reducing the risk of radiation exposure during deep-space travel, but also the risks of carcinogenesis from exposure to low-dose rate radiation exposures on Earth.
Task Progress:	A total of 387 male and female P53deltaP mice (on an FVB/Jax genetic background) of the age of ~6 months were transported from a breeding colony at the University of Arkansas for Medical Sciences to Brookhaven National Laboratory. A total of 129 mice were assigned to the control group, 129 mice were exposed to a single dose of 0.75 Gy full-spectrum simulated galactic cosmic rays at the NASA Space Radiation Laboratory, and 129 mice were exposed to a single dose of 3 Gy gamma-rays. After irradiation, all mice were transported to Colorado State University where they are being followed for 18 months after irradiation to determine tumor formation. The mice are currently at the age of ~1 year. In all groups, about 50% of all males and 70-80% of all females have developed cancer. It is yet to soon after radiation exposure to draw conclusions on the effects of gamma or galactic cosmic rays on tumorigenesis.
Bibliography Type:	Description: (Last Updated: 09/01/2023)
Articles in Peer-reviewed Journals	Upadhyay M, Rajagopal M, Gill K, Li Y, Bansal S, Sridharan V, Tyburski JB, Boerma M, Cheema AK. "Identification of plasma lipidome changes associated with low dose space-type radiation exposure in a murine model." Metabolites. 2020 Jun 17;10(6):E252. https://doi.org/10.3390/metabo10060252 ; PMID: 32560360; PMCID: PMC7345467 , Jun-2020
Articles in Peer-reviewed Journals	Sridharan V, Seawright JW, Landes RD, Cao M, Singh P, Davis CM, Mao XW, Singh SP, Zhang X, Nelson GA, Boerma M. "Effects of single-dose protons or oxygen ions on function and structure of the cardiovascular system in male Long Evans rats." Life Sci Space Res (Amst). 2020 Aug;26:62-8. https://doi.org/10.1016/j.lssr.2020.04.002 ; PMID: 32718688; PMCID: PMC7387753 , Aug-2020