Fiscal Year:	FY 2023	**Task Last Updated:**	FY 09/14/2022
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:**	10/31/2023
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**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 10/31/2023 per V. Lehman/JSC (Ed., 6/20/23) 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:	Ed. note - PI addition to Nov 2021 report: We are currently in a phase of the grant in which Drs. Pathak and Landes are no longer CoInvestigators. At this point in the project, only Dr. Weil is a CoInvestigator (CoI). No changes in Principal Investigator (PI) or other key personnel.		
COI Name (Institution):	Weil, Michael Ph.D. (Colorado State University)		
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 and it has shown cancer prevention properties in human subjects and animal models. It is safe, non-toxic and well tolerated, exhibits no interactions with other medications, and requires no special storage conditions. Altogether, gamma-tocotrienol has high potential as a radiation countermeasure during space travel. In this project, we develop a mouse model of radiation carcinogenesis that may be used to test the protective properties of gamma-tocotrienol and other countermeasures. For this purpose, we are searching for a genetically modified mouse model that shows a low spontaneous cancer rate, but increased tumor incidence in response to low-dose radiation. P53deltaP mice carry a mutation in the P53 gene that makes them more susceptible to carcinogenesis. We obtained P53deltaP mice and created a breeding colony. However, at around 100 days of age, these mice started developing a range of hematologic and solid tumors, and this unexpectedly high rate of tumor formation in untreated animals made the mice unsuitable for studying long-term carcinogenesis from low doses of ionizing radiation. Therefore, the project is now focused on crossing P53deltaP mice onto a different genetic background that we expect will lower the number of spontaneous tumors.
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. This project aims to develop a mouse model of low-dose radiation-induced carcinogenesis that may be used to test gamma-tocotrienol and other countermeasures. 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 on Earth.
Task Progress:	In prior project years, P53deltaP mice on an FVB/Jax genetic background were obtained and used to create a breeding colony. However, at around 100 days of age, these mice started developing a range of hematologic and solid tumors, including lung tumors, mammary tumors, and subcutaneous tumors. The unexpectedly high rate of tumor formation in untreated animals make P53deltaP mice on an FVB/Jax genetic background unsuitable for studying long-term carcinogenesis from low doses of ionizing radiation. Therefore, we began crossing P53deltaP mice onto a mixed C57BL/6J and 129S4/SvJae background. We expect that this genetic background will lower the number of spontaneous tumors. We are following a breeding strategy, combined with single nucleotide polymorphism (SNP) based assessment of genetic background to select the mice with the most desirable background. This reduces the number of generations required to create P53deltaP mice onto the mixed C57BL/6J and 129S4/SvJae background. The crossing onto the C57BL/6J background is complete, and we are currently following a breeding strategy to introduce the 129S4/SvJae genetic background. Colonies of mice on both the C57BL/6J background and the mixed genetic background will be maintained. Then, mice created from both colonies will be exposed to low-dose radiation or control treatment to observe tumor formation.
Bibliography Type:	Description: (Last Updated: 09/01/2023)
Abstracts for Journals and Proceedings	Boerma M, Sridharan V, Landes RD, Weil MM. "Gamma-tocotrienol as a countermeasure against high-energy charged particle-induced carcinogenesis." 2022 NASA Human Research Program Investigators' Workshop, February 7-10, 2022. Abstract. 2022 NASA Human Research Program Investigators' Workshop, February 7-10, 2022. , Feb-2022
Articles in Peer-reviewed Journals	Nemec-Bakk AS, Sridharan V, Landes RD, Singh P, Cao M, Dominic P, Seawright JW, Chancellor JC, Boerma M. "Effects of low-dose oxygen ions on cardiac function and structure in female C57BL/6J mice." Life Sci Space Res (Amst). 2022 Feb;32:105-112. https://doi.org/10.1016/j.lssr.2021.12.004 ; PubMed PMID: 35065756; PubMed Central PMCID: PMC8803400 , Feb-2022