Fiscal Year:	FY 2022	**Task Last Updated:**	FY 05/24/2022
PI Name:	Weil, Michael Ph.D.		
Project Title:	NSCOR: NASA Specialized Center of Research on Carcinogenesis		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
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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City:	Fort Collins	**State:**	CO
Zip Code:	80521-2807	**Congressional District:**	4
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2013-14 HERO NNJ13ZSA002N-NSCOR Radiation
Start Date:	06/01/2015	**End Date:**	11/01/2023
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	4	**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 11/1/2023 per NSSC information (Ed., 1/23/23) NOTE: End date changed to 5/31/2023 per JSC Grants Office and NSSC information (Ed., 6/2/22) NOTE: End date changed to 5/31/2022 per NSSC information (Ed., 3/3/2020)		
Key Personnel Changes/Previous PI:	Ed. Note: Per the PI, Dr. Thamm has moved off the grant since completing his role on NSCOR. Dr. Story and Dr. Ullrich have been removed from the CoI list as they now have different roles in the grant (8/10/22). April 2020 report: Dr. Thamm has completed his role on the NSCOR. April 2019 report: Dr. Robert L Ullrich has transitioned from NSCOR Co-Director to Consultant; Dr. Michael D. Story now serves as the Co-Director. Dr. Thomas Borak passed away in 2021 and Dr Alexander Brandl joined the NSCOR as a Physicist in 2021.		
COI Name (Institution):	Borak, Thomas Ph.D. (Colorado State University) Emmett, Mark Ph.D. (University Of Texas, Galveston) Hwang, Tae Hyun Ph.D. (University of Texas Southwestern Medical Center at Dallas) Ray, F. Andrew Ph.D. (Colorado State University) Bacher, Jeff Ph.D. (Promega Corporation) Halberg, Richard Ph.D. (University of Wisconsin, Madison) Raber, Jacob Ph.D. (Oregon Health & Science University) Brandl, Alexander Ph.D. (Colorado State University)		

Grant/Contract No.:	NNX15AK13G
Performance Goal No.:	
Performance Goal Text:	
Task Description:	The proposed Carcinogenesis NASA Specialized Center of Research (NSCOR) addresses several key questions for the assessment of radiation risk. The NSCOR consists of four interrelated projects. Project 1 is a biomarker discovery study using integrative “omics” approaches over multiple levels of biological organization and involving multiple species. Biomarkers predictive of the outcomes of HZE (high energy) ion exposures can be used to extrapolate findings in mice to other species, including humans, that are most relevant to NASA’s exploratory missions. The biomarkers are also critical for understanding underlying carcinogenic mechanisms, early disease detection, and subsequent countermeasure development. Project 2 investigates qualitative differences in tumor progression and metastasis between HZE ion- and gamma ray-induced tumors. Project 3 examines the critical question of risk from protracted exposures to high LET (linear energy transfer) radiation at low doses and dose rates. To estimate the carcinogenic effects of these scenarios, we will use chronic exposures to high LET associated neutron radiation as a surrogate for conditions of space-relevant fluence rates and total doses. Project 4 utilizes the resources (irradiated mice and “omics” results) generated in the first three projects to study the neurobehavioral consequences of HZE ion and neutron exposures and whether they are related to tumorigenesis-related outcome measures and predicted by the same or distinct biomarkers. Two addenda were added to the NSCOR in the April 2017 – March 2018 reporting period. The first was designed to determine if a low dose aspirin regimen could be an effective countermeasure to high LET radiation-induced hepatocellular carcinoma. Two exposure conditions are included, and acute exposure to 0.2 Gy 300 MeV 28Si ions and a chronic exposure to 0.4 Gy of 252Cf neutrons. The second was designed to compare fractioned exposures to a simulated GCR (galactic cosmic radiation) beam to an acute exposure for the induction of hepatocellular carcinoma.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Accurately determining the cancer risk from high energy, charged particle radiation exposure is of great importance for designing human spaceflight missions, but it is becoming increasingly important for cancer radiotherapy as well. Radiation oncology appears poised to transition to charged particle radiotherapy in the form of proton therapy and carbon ion therapy. However, one of the risks of treating cancer with charged particle radiation is that the treatment itself can result in a new cancers, known as a second malignant neoplasms (SMN) (commonly used photon radiotherapy also increases SMN risk). The radiotherapy equipment and the patient treatment plans are designed to minimize SMN, but the models to predict risks from various exposures rest on some of the same assumptions about how charged particle radiation causes cancer that are being tested in this NSCOR grant. The results obtained in this program can be used to improve the design of treatment protocols and thus reduce the risks of SMN in radiotherapy patients.
Task Progress:	In the 2021-2022 funding period, the Carcinogenesis NSCOR entered into a partially funded extension. [Ed. Note: "Carcinogenesis NSCOR" is a shortened name for this NASA Specialized Center of Research (NSCOR) project on the assessment of radiation risk and carcinogenesis.] The main goals were to (1) replace the 252Cf source on the neutron irradiator/vivarium, (2) sequence several radiation-induced murine tumors, and (3) fill in acute neutron exposure data originally proposed for Project 3. Sequencing of Radiation-Induced Tumors: During the funding period covered by this report, we selected 55 hepatocellular carcinomas (HCCs) and 15 thymic lymphomas for genomic sequencing. These tumor samples were archived in the course of previous NASA-funded research. The rationales for selecting HCC and thymic lymphomas are that both tumor types are strongly radiation-induced but have sufficient spontaneous incidences to provide tumors from unexposed mice for controls. Tumors of both types grow large enough in mice to provide material for DNA collection without having to resort to extraction from paraffin blocks. We already know a considerable amount about these tumor types. In addition to genomic sequencing, for the thymic lymphomas we could also perform RNAseq on thymus tissue from unirradiated mice that could be integrated into the data analysis. A total of 70 tumor samples were selected for sequencing: 15 HCCs from unirradiated male mice 15 HCCs from gamma ray irradiated male mice 25 HCCs from HZE ion irradiated male mice 5 thymic lymphomas from unirradiated mice (both males and females) 5 thymic lymphomas from gamma ray irradiated mice (both males and females) 5 thymic lymphomas from HZE ion irradiated mice (both males and females) DNA was extracted from the tumor samples by using DNeasy Blood and Tissue Kit from Qiagen following the manufacturer’s protocol. The DNA quality was good as assessed by the 260/280 and 260/230 ratios calculated from the absorbance values measured by using a Nanodrop spectrophotometer. The DNAs from the samples were submitted to the sequencing core in DNAlink Inc., Los Angeles, CA. For RNAseq we harvested thymuses from unirradiated 6-week old male mice from the 8 founder strains of the HS/Npt stock that was used as a source of tumors for the genomic sequencing. We collected 3 thymuses from each strain. High quality RNA was prepared using a DNase I on-column digestion protocol. Paired end next generation Illumina sequencing was done on a library prepared from poly-A selected RNA by the Genomics and Microarray Core at the University of Colorado Anschutz Medical Campus. The sequencing data have been submitted to the Sequence Read Archive, archived, alignments done, and analysis is now underway. Acute neutron exposures: Project 3 originally included carcinogenesis studies of male and female mice irradiated acutely with neutrons at doses of 0.1, 0.2, and 0.4 Gy. These groups were removed from the study at the direction of the NASA Space Radiation (SR) Element and then added back in the previous funding period. Acute exposures were done at the Radiological Research Accelerator Facility (RARAF) at Columbia University. The female mice were irradiated at the end of 2020. Because of routine maintenance and accelerator downtime at RARAF, we were unable to irradiate the male mice until now. A group of 108 male C3H mice was irradiated with a dose of 0.1 Gy in November 2021 and a further group of 106 mice was irradiated with a dose of 0.2 Gy in December 2021. These mice are currently being monitored for tumor development.

Bibliography Type:	Description: (Last Updated: 09/27/2023)
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