Fiscal Year:	FY 2017	**Task Last Updated:**	FY 04/03/2017
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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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:**	05/30/2020
No. of Post Docs:		**No. of PhD Degrees:**	1
No. of PhD Candidates:	5	**No. of Master' Degrees:**	0
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA JSC
Contact Monitor:	Simonsen, Lisa	**Contact Phone:**	
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
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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.
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 Project 1, we have irradiated all of the mice for the first two aims with 28Si ions at NASA Space Radiation Laboratory (NSRL). We have collected serum, plasma, tissue samples, and feces for the one month time point, and we have established fibroblast cultures from 300 of the irradiated F2 mice. We have designed, produced, and validated directional genomic hybridization probes for mouse chromosomes 1 to 4 and begun to use the probes to screen fibroblasts from mice previously irradiated with 28Si ions. We have optimized a lipidomic screen for use with mouse samples. In Project 2 we have reviewed the pathology on 208 cases of mouse hepatocellular carcinomas (HCC) from the previous Carcinogenesis NSCOR to allow correct classification of cases as metastatic and nonmetastatic. Each case has been assigned a histologic subtype and mitotic index, and semi-quantitatively scored for local invasion, vascular invasion, cellular pleomorphism, nuclear pleomorphism, degree of differentiation, and presence of fibrosis. We have also begun to look for mutations in the tumors by sequencing DNA from five of them (whole exome sequencing). We have detected mutations in these tumors that are also common in human HCC. We have begun experimental metastasis studies with MMTV-PyMT and Afp-mCherry transgenic mice. MMTV-PyMT mice are a model for mammary tumor metastasis to the lungs. We have irradiated forty-four of these mice on two different strain backgrounds and followed them for mammary tumor development. We are now quantifying the extent of metastases in the mice. Viable tumors have been cryopreserved and serially transplanted for further work. Ninety Afp-mCherry mice were irradiated or sham irradiated at NSRL. These mice are used to study HCC metastasis to the lung. The mice are being monitored for circulating tumor cells, and some have been sacrificed 3 months post-irradiation to detect the earliest stages of tumorigenesis using newly developed tissue clearing and optical approaches. Project 3 involves the commissioning of a neutron irradiator in a shielded vivarium that meets the animal care requirements for long term mouse housing. Over the past year we renovated the building, calculated the activity of radioactive material required, and acquired the source and the irradiator. For Project 4, we completed neurobehavioral testing for the one month time point and collected tissues from the mice that were tested.
Bibliography Type:	Description: (Last Updated: 09/27/2023)
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