

<b>Fiscal Year:</b>	FY 2016	<b>Task Last Updated:</b>	FY 04/02/2016
<b>PI Name:</b>	Weil, Michael Ph.D.		
<b>Project Title:</b>	NSCOR: NASA Specialized Center of Research on Carcinogenesis		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>			
<b>Program/Discipline--Element/Subdiscipline:</b>	HUMAN RESEARCH--Radiation health		
<b>Joint Agency Name:</b>	<b>TechPort:</b>	No	
<b>Human Research Program Elements:</b>	(1) <b>SR</b> :Space Radiation		
<b>Human Research Program Risks:</b>	(1) <b>Cancer</b> :Risk of Radiation Carcinogenesis		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
<b>PI Email:</b>	<a href="mailto:michael.weil@colostate.edu">michael.weil@colostate.edu</a>	<b>Fax:</b>	FY
<b>PI Organization Type:</b>	UNIVERSITY	<b>Phone:</b>	970-491-5902
<b>Organization Name:</b>	Colorado State University		
<b>PI Address 1:</b>	Department of Environmental & Radiological Health Sciences		
<b>PI Address 2:</b>	1618 Campus Delivery		
<b>PI Web Page:</b>			
<b>City:</b>	Fort Collins	<b>State:</b>	CO
<b>Zip Code:</b>	80521-2807	<b>Congressional District:</b>	4
<b>Comments:</b>			
<b>Project Type:</b>	GROUND	<b>Solicitation / Funding Source:</b>	2013-14 HERO NNJ13ZSA002N-NSCOR Radiation
<b>Start Date:</b>	06/01/2015	<b>End Date:</b>	05/30/2020
<b>No. of Post Docs:</b>	1	<b>No. of PhD Degrees:</b>	0
<b>No. of PhD Candidates:</b>		<b>No. of Master' Degrees:</b>	0
<b>No. of Master's Candidates:</b>	1	<b>No. of Bachelor's Degrees:</b>	0
<b>No. of Bachelor's Candidates:</b>	1	<b>Monitoring Center:</b>	NASA JSC
<b>Contact Monitor:</b>	Simonsen, Lisa	<b>Contact Phone:</b>	
<b>Contact Email:</b>	<a href="mailto:lisa.c.simonsen@nasa.gov">lisa.c.simonsen@nasa.gov</a>		
<b>Flight Program:</b>			
<b>Flight Assignment:</b>			
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	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 ) Liber, Howard Ph.D. ( Colorado State University ) Ray, F. Andrew Ph.D. ( Colorado State University ) Thamm, Douglas V.M.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 ) Story, Michael Ph.D. ( University of Texas Southwestern Medical Center at Dallas ) Ullrich, Robert Ph.D. ( University of Texas, Galveston )		
<b>Grant/Contract No.:</b>	NNX15AK13G		
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<b>Performance Goal Text:</b>			

Task Description:	<p>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.</p>
Rationale for HRP Directed Research:	<p>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.</p>
Research Impact/Earth Benefits:	<p>This is the first year of funding, so much of the work to date has been logistical to prepare for mouse irradiations. We have arranged for beam time at NASA Space Radiation Laboratory (NSRL) in Fall 2016 and secured approval from 4 different institutions for the use of mice in the experiments. Because some of the strains of mice needed are not commercially available in sufficient numbers, we have established breeding colonies for them at Colorado State University and the University of Wisconsin.</p> <p>In Project 1 we have optimized a lipidomic screen for use with mouse samples. In Project 2 we have reviewed the pathology on 210 cases of mouse hepatocellular carcinomas (HCC) and characterized them for histological features that may be relevant to their propensity to metastasize to the lung, including fibrosis, local invasion, vascular invasion, cellular and nuclear pleomorphism, tumor subtype, and mitotic index. One feature, high microvessel density, appears to be more common in metastatic HCC. 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.</p> <p>Project 3 requires us to install a neutron irradiator in a heavily shielded building that also meets the animal care requirements for long term mouse housing. We have secured a suitable building and begun the process of renovating it. We are also drawing up the specifications for the radioactive source in the neutron irradiator.</p> <p>For Project 4 we have identified the neurobehavioral assays that will be most sensitive to radiation effects.</p>
Task Progress:	Bibliography Type: Description: (Last Updated: 09/27/2023)
Abstracts for Journals and Proceedings	<p>Weil MM, Ullrich RL, Story MC, Bacher JS, Ray FA, Borak TB, Liber HL, Thamm HL, Raber J, Emmett MR, Hallberg R, Hwang TH. "Carcinogenesis NSCOR." Presented at 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016.</p> <p>2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016. , Feb-2016</p>
Articles in Peer-reviewed Journals	<p>Locke PA, Weil MM. "Personalized cancer risk assessments for space radiation exposures." Front Oncol. 2016 Feb 22;6:38. eCollection 2016. Review. <a href="http://dx.doi.org/10.3389/fonc.2016.00038">http://dx.doi.org/10.3389/fonc.2016.00038</a> ; PubMed <a href="https://pubmed.ncbi.nlm.nih.gov/26942127/">PMID: 26942127</a>; PubMed Central <a href="https://pubmed.ncbi.nlm.nih.gov/PMC4762001/">PMCID: PMC4762001</a> ; Feb-2016</p>