

<b>Fiscal Year:</b>	FY 2023	<b>Task Last Updated:</b>	FY 11/07/2023
<b>PI Name:</b>	Story, Michael D Ph.D.		
<b>Project Title:</b>	Determining Gender Differences in the Incidence of Lung Adenocarcinoma After Space Radiation Exposure		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>			
<b>Program/Discipline-- Element/Subdiscipline:</b>			
<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.story@utsouthwestern.edu">michael.story@utsouthwestern.edu</a>	<b>Fax:</b>	FY 214 648 5995
<b>PI Organization Type:</b>	UNIVERSITY	<b>Phone:</b>	214 648 5557
<b>Organization Name:</b>	University of Texas, Southwestern Medical Center		
<b>PI Address 1:</b>	Division of Molecular Radiation Biology		
<b>PI Address 2:</b>	2201 Inwood Rd., Room NC7.206		
<b>PI Web Page:</b>			
<b>City:</b>	Dallas	<b>State:</b>	TX
<b>Zip Code:</b>	75235-7320	<b>Congressional District:</b>	30
<b>Comments:</b>			
<b>Project Type:</b>	GROUND	<b>Solicitation / Funding Source:</b>	2016-2017 HERO NNJ16ZSA001N-SRHHC. Appendix E: Space Radiobiology and Human Health Countermeasures Topics
<b>Start Date:</b>	09/01/2018	<b>End Date:</b>	08/31/2024
<b>No. of Post Docs:</b>	0	<b>No. of PhD Degrees:</b>	
<b>No. of PhD Candidates:</b>	2	<b>No. of Master' Degrees:</b>	
<b>No. of Master's Candidates:</b>		<b>No. of Bachelor's Degrees:</b>	
<b>No. of Bachelor's Candidates:</b>		<b>Monitoring Center:</b>	NASA JSC
<b>Contact Monitor:</b>	Elgart, Robin	<b>Contact Phone:</b>	281-244-0596 (o)/832-221-4576 (m)
<b>Contact Email:</b>	<a href="mailto:shona.elgart@nasa.gov">shona.elgart@nasa.gov</a>		
<b>Flight Program:</b>			
<b>Flight Assignment:</b>	NOTE: End date changed to 08/31/2024 per JSC Grants Office and NSSC information (Ed., 4/11/23)		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Lianghao, Ding Ph.D. ( University of Texas Southwestern Medical Center, Dallas )		
<b>Grant/Contract No.:</b>	80NSSC18K1676		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

<b>Task Description:</b>	<p>Uncertainties in radiation induced lung cancer risk estimation and its associated mortality rates are among the primary factors limiting the number of safe days an astronaut can spend in space. Initial lung cancer risks are based off epidemiological-based modeling and include cohorts such as the atomic bomb survivor life span study (LSS) whose estimates contain large confidence intervals and whose populations may not reflect astronauts on deep space missions. In order to calculate the permissible exposure limit (PEL) for astronauts it is necessary to collect further information on the risk of lung carcinogenesis due to radiation quality differences (relative biological effectiveness--RBE), sex disparities, and how effective biological countermeasures may reduce or mitigate these risks.</p> <p>The goal of this project is to provide sufficient data to bolster risk estimates and RBE values for lung carcinogenesis from the individual small, intermediate, and heavy charged particles that comprise galactic cosmic rays (GCRs) with doses comparable to what an astronaut may receive on a Mars mission. Additionally we will delineate any sex differences in radiogenic lung cancer risk resulting from space radiation exposure, provide sufficient evidence to validate GC4419, a Food &amp; Drug Administration (FDA) investigational new drug (IND), as an effective pharmaceutical countermeasure, and mechanistically define the biological processes associated with space radiation induced lung carcinogenesis.</p>
<b>Rationale for HRP Directed Research:</b>	
<b>Research Impact/Earth Benefits:</b>	<p>There are two areas where this research may benefit life on Earth.</p> <p>1) Differences in both the incidence of and mortality arising from lung cancer between men and women have long been appreciated, with women generally having higher incidences and mortality rates than men. Epidemiological studies comparing pre- and post-menopausal women treated with hormone replacement therapy (HRT) have demonstrated that female sex hormones both elevated the incidence and aggressiveness at the time of presentation. These effects likely enhance the efficacy of other carcinogens such as radiation or tobacco smoke.</p> <p>2) GC4419 is a radioprotector for radiation-induced mucositis and lung fibrosis from radiation exposure. What is not known, although the preliminary evidence suggests it could, is whether GC4419 has anti-carcinogenic effects. If it does, the potential to reduce the risk for cancer in humans after environmental or diagnostic radiation exposures is compelling.</p>
<b>Task Progress:</b>	<p>For all Aims, 4,565 animals have been irradiated or served as controls. 3,975 animals have completed the study. There are still 2 cohorts of animals under study those being the avasopasem treated unirradiated animals and the cohort irradiated with 1.5 Gy 137Cs and treated with avasopasem for a total of 483 mice remaining. 556 suspected lung tumors have been collected and roughly 240 have been sent to pathology for processing. 160 are ready for pathologic analysis to confirm and describe lung tumors in a blinded fashion. Interestingly, other non-cancer pathologies have been identified including hematologic ovarian cysts and tumors, and hepatosplenomegaly. Interestingly, survival of the 1.5 Gy 137Cs-irradiated cohort treated with avasopasem is higher than the cohort not treated with avasopasem although the p-value at this point is ~0.06. This avasopasem-treated cohort will continue until the termination point. The avasopasem-treated unirradiated cohort will continue for another approximately 6 months.</p> <p>Constraints: While lung tissue, lung masses and tumor.</p> <p>Oral Presentations: 2023 NASA Human Research Program Investigators' Workshop (IWS), Galveston, Texas, February 7-9, 2023. Oral presentation by Sorour Hosseini. Is lung cancer risk after space radiation exposure higher in females than in males, and can SOD mimetic GC4419 act as a radiation countermeasure? S. Hosseini, Division of Molecular Radiation Biology, Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, Texas.</p> <p>Hosseini S, Sishe BJ, Ramnarain D, Polsdofer EM, Story MD. 2023 American Association of Physicists in Medicine (AAPM) 65th Annual Meeting Houston, Texas. July 23-27, 2023. Oral presentation by Sorour Hosseini. Avasopasem manganese protects and mitigates radiation-induced lung fibrosis, reduces radiogenic lung cancers and extends survival in mice irradiated with either low LET or high LET radiations simulating the space environment.</p> <p>Poster Presentations: Hosseini S, Polsdofer EM, Felix D, Nicholson J, Ding L-H, Wight-Carter M, Story MD. 2023 International Congress on Radiation Research (ICRR), Montreal, Canada, August 26-30, 2023. Poster presentation, Michael Story. Evaluating the potential of the SOD mimetic Avasopasem Manganese as a radiation countermeasure for space radiation-induced lung cancer.</p>
<b>Bibliography Type:</b>	Description: (Last Updated: 12/14/2023)
<b>Abstracts for Journals and Proceedings</b>	<p>Hosseini S, Sishe BJ, Ramnarain D, Polsdofer EM, Story MD. "Avasopasem manganese protects and mitigates radiation-induced lung fibrosis, reduces radiogenic lung cancers and extends survival in mice irradiated with either low LET or high LET radiations simulating the space environment." AAPM 2023. 65th Annual Meeting and Exhibition of the American Association of Physicists in Medicine, Houston, Texas, July 23-27, 2023.</p> <p>Abstracts. AAPM 2023. 65th Annual Meeting and Exhibition of the American Association of Physicists in Medicine, Houston, Texas, July 23-27, 2023. , Jul-2023</p>