

<b>Fiscal Year:</b>	FY 2019	<b>Task Last Updated:</b>	FY 07/22/2019
<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		
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<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>	08/31/2022
<b>No. of Post Docs:</b>	1	<b>No. of PhD Degrees:</b>	
<b>No. of PhD Candidates:</b>	1	<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>		<b>Contact Phone:</b>	
<b>Contact Email:</b>			
<b>Flight Program:</b>			
<b>Flight Assignment:</b>			
<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 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. We are following the production of estrogen for 8 weeks post-IR (irradiation) to determine whether space radiation is more effective at reducing estrogen via the radioresponse of the mouse ovary. We will follow lung cancer in mice with lower estrogen to determine the impact on ovarian function and risk for radiation-induced lung cancer. We may also consider estrogen replacement to determine how "hormone replacement" alters lung cancer risk from radiation exposure.</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>As we are nearing completion of Year 1, the only really significant progress is in the numbers of animals irradiated. At the point there has not been an opportunity to collect histologic, enzymatic, or omics data. Indeed, the significance of the representative estrous cycling measurements is not yet clear. Furthermore, many of these endpoints require collection only and are processed at a later time to avoid "batch effects" associated with sample processing.</p> <p>To date we have irradiated 10 of 19 cohorts of animals based upon radiation type, dose, and sex. Ovaries have been harvested for nearly all cohorts and have been sent to the pathology core for processing and tissue mounting. Estrous cycles have been examined in nearly all groups as well.</p> <p>Tissues and serum for omics analysis has not yet been collected as we are not at the first 6 month post-irradiation time point.</p>
<b>Bibliography Type:</b>	Description: (Last Updated: 12/14/2023)