Fiscal Year:	FY 2020	**Task Last Updated:**	FY 12/12/2019
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Project Title:	Countermeasures Against Adverse Effects of Space Radiation		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
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:	11794-8691	**Congressional District:**	1
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2017-2018 HERO 80JSC017N0001-BPBA Topics in Biological, Physiological, and Behavioral Adaptations to Spaceflight. Appendix C
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No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
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Contact Monitor:		**Contact Phone:**	
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Task Description:	The space environment consists of various types of radiation that are different from those found in the Earth's atmosphere. These include particles with high mass and high energy (heavy particles) such as silicon. Hence, exposure to radiation in space is the greatest hazard to astronauts venturing beyond Earth. It is therefore important to protect astronauts in space environments. To date, the use of shielding materials to prevent radiation exposure in space is inadequate. Consequently, the search for efficient medical countermeasures (protectors, those given prior to exposure; mitigators, those given after exposure) is at high priority in radiation protection in space, as well as on Earth. This is the first task book for Phase 1 study of our project entitled “Countermeasures against adverse effects of space radiation.” The primary goal of our Phase 1 study is to test the efficacy of apigenin (AP) for the prevention and mitigation of cancer in male mice due to exposure to space radiation as measured by incidence, aggressiveness, burden, and latency. Our main hypothesis is that AP exhibits its beneficial effects by suppression of radiation-induced inflammation and oxidative stress during the initiation/promotion steps of carcinogenesis. Although the emphasis will be on the mitigation of lung cancer and lymphoma/leukemia, other types of cancer will be recorded. In this project, we will give food containing AP to male mice before and after exposure to heavy silicon (28Si) ions. There are four groups of mice. These are sham controls (Group 1, no AP diet, no radiation), mice receiving 0.5 Gy of 260 MeV/n 28Si ions radiation only and without AP diet (Group 2), mice receiving AP only with no radiation exposure (Group 3), and mice receiving both AP and radiation (Group 4). Groups of mice from each treatment will be used for a serial sacrifice schedule at 1 week and 6 months post-irradiation. This will test the ability of AP to counteract heavy-ion-induced early- and late-occurring inflammation and oxidative damage in various tissues linked to cancer that are the focus of our study (i.e., bone marrow, lung, thymus, spleen). All remaining mice will be observed for morbidity and mortality until they reach about 700 days of age. Our data enable the evaluation of countermeasure efficacy of AP across tissues at risk for cancer induction, i.e., bone marrow and the lung. This multi-tissue of the same exposed individual approach has not been used in space research. We will also determine the hematological parameters [i.e., white blood cells (WBCs), red blood cells (RBCs), and platelets] collected from the same individual mouse included in the serial sacrifice schedule. It is important to evaluate the hematological parameters after exposure to radiation since it has been well characterized that radiation [either low or high LET (linear energy transfer) radiation found on Earth or in the space environment] induces hematological changes that can further induce the impairment of the immune system enabling susceptibility to infection and inflammation. Ultimately, such detrimental effects from exposure to radiation can lead to cancer and other chronic diseases. Further, we will evaluate the efficacy of AP in protection/mitigation against 28Si-ion-induced damage in the hematopoietic stem cell (HSC) compartment in mice included in the serial sacrifice schedule. Our approach is important since the hallmark properties of the hematopoietic stem cells (HSCs) are the capability of self-renewal and proliferation with pluripotent potentials to give rise to various types of differentiated and functional progenitor cells. Hence, any induced damage in the HSC compartment, if not repair, will be carried onto the next generation an adversely impacted self-renewal and proliferation. Further, it has been well recognized that the HSC compartment is the site of the target cells for radiation-induced leukemia.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	To date, intense efforts have been made to identify agents that can attenuate radiation injuries when given before and after exposure to radiation found on Earth and those found in the space environment. However, novel radiation-countermeasures remain an unmet need for counteracting radiation-induced injuries in exposed individuals. Hence, the search for agents that are safe, easily administered, and effective in diminishing adverse health effects to exposed individuals are urgently needed. In this project, our primary goal is to test the efficacy of AP for the prevention and mitigation of cancer due to space radiation exposure. Our results will fill such a gap of knowledge in radiation countermeasures during the space mission or on Earth. It has been well characterized that radiation-induced hematopoietic failure is the major detrimental biological effects. This is mostly due to the substantial suppression of lymphocytes, platelets, including damage to stem and progenitor cells. Such shortages increase the risk of infection, inflammation, hemorrhage, and death. Further, any induced damage in the HSC compartment, if not repaired, will be carried onto the next generation and adversely impacted self-renewal, proliferation, as well as untoward health outcomes later in life. Our first set of data strongly demonstrate that AP (given before and after irradiation) prevents a loss of white blood cells (leukopenia), inhibits the depletion of platelets (thrombocytopenia), enhances the production of red blood cells (erythropoiesis), and increases the proliferation capacity of hematopoietic stem/progenitor cells (HSPCs). Hence, our findings are of paramount significance not only in radiation protection during the space mission but also in the improvement of radiation therapy on Earth. Further, our data on the efficacy of AP in protection/prevention and/or mitigation of radiation-induced cancer will have a significant impact on the future development of a novel therapeutic strategy to prevent or mitigate the acute or long-term effects of radiation in the event of radiobiological events on Earth, (e.g. a nuclear accident, or terrorisms) or from combats in the battlefield.
Task Progress:	We completed the exposure of male C57BL/6 mice to 0 (sham controls) or 0.5 Gy of 260 MeV/n 28Si ions (delivered at 0.5 Gy/min) on November 21, 2019. We also completed the collection of several tissues for further molecular analyses from the same individual mice included in the sacrifice schedule at d 7 post-irradiation. These samples are blood, BM, lung, spleen, and thymus. A fraction of blood was used to evaluate the hematological parameters, e.g., white blood cells (WBCs), red blood cells (RBCs), and platelets (PLTs). The resulting data are used to determine the efficacy of AP in the protection and mitigation of 28Si-ion-induced damage to the hematopoietic tissue. The remaining of each blood sample was used for plasma preparation and stored in a -80oC freezer for future molecular analyses. To date, we have completed the analyses of hematological parameters and the countermeasure effectiveness of AP against 28Si ion-induced damage in the hematopoietic stem cell compartment in samples collected at 1 wk post-irradiation. The highlights of our findings are: (1) AP prevents a loss of white blood cells (leukopenia), (2) AP enhances the production of red blood cells (erythropoiesis), (3) AP prevents depletion of platelets (thrombocytopenia),

	(4) AP protects and enhances the proliferation capacity of hematopoietic stem/progenitor cells (HSPCs), and (5) AP maintains homeostasis of the hematopoietic system. This set of data is the first and significant indicator of protective and mitigative effectiveness of AP against hematopoietic failure. The data strongly supports our hypothesis in using AP as a countermeasure against space-radiation-induced harmful effects during spaceflights. We will present this set of data at the 2020 NASA Human Research Program, to be held in January 2020, Galveston TX. Plan for the next fiscal year: (1) Monitoring of mice for morbidity and mortality and histological evaluation, (2) Measurements of the levels of multiple cytokines with various biological functions in various tissues collected at d 7 post-irradiation from the same individual mouse, (3) Measurements of the levels of NF-kB, and p38 MAPK activation. In the same tissues that will be used for measuring cytokines, (4) Measurements the levels of enzymes involved in oxidative damage, and (5) Serial sacrifice at 6 mos post-irradiation for further molecular analyses.
Bibliography Type:	Description: (Last Updated: 03/27/2025)
Abstracts for Journals and Proceedings	Rithidech K, Peanlikhit T, Whorton EB. "Countermeasures against adverse effects of space radiation." Space Radiation session. To be presented at 2020 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 27-30, 2020. Abstracts. 2020 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 27-30, 2020. , Jan-2020