

Fiscal Year:	FY 2021	Task Last Updated:	FY 12/31/2020
PI Name:	Rithidech, Kanokporn Ph.D.		
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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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:	
No. of Bachelor's Candidates:		Monitoring Center:	NASA JSC
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 5/30/2022 per NSSC information (Ed., 3/29/21)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
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Task Description:	<p>This is the task book for the Phase 1 study of our project entitled “Countermeasures against adverse effects of space radiation” in which only male mice are included. 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. We gave food containing AP to male mice before and after exposure to 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 were used for a serial sacrifice schedule at 1-week and 1-year post-irradiation. This will test the ability of AP to counteract heavy-ion-induced early- and late-occurring inflammation in various tissues linked to cancer that are the focus of our study, i.e. bone marrow (BM) and lung. All remaining mice will be observed for morbidity and mortality until they reach about 600-700 days of age. Our data enable the evaluation of countermeasure efficacy of AP across tissues at risk for cancer induction, i.e. BM and the lung. This multi-tissue of the same exposed individual approach has not been used in space research. At 1-week (wk) post-irradiation, a total of six mice from each treatment group were randomly selected for sample collection. We collected blood, BM, lung, spleen, and thymus from the same individual mouse for further analyses. A fraction of blood was used to evaluate the hematological parameters, e.g. white blood cells, red blood cells, and platelets. The remainder of each blood sample was used for plasma preparation, to be used for future molecular analyses (i.e. inflammation and oxidative damage). We also investigated the countermeasure effectiveness of AP against 28Si-ion-induced damage to the hematopoietic stem cell (HSC) compartment of exposed mice. We used the well-established colony-forming unit assay (CFU-A) as a tool for this purpose. This is important because the HSCs are believed to be cells most at risk for leukemia induction. The BM cells from each mouse were used to determine the levels of activated nuclear factor-kappa B (NF-kappa B), and NF-kappa B-regulated pro-inflammatory cytokines (i.e. TNF-alpha, IL-1alpha, IL-1 beta, and IL-6). Further, we investigated the effectiveness of AP in reducing the frequencies of chromosome aberrations (determined by the in vivo blood erythrocytes micronucleus assay) since a high frequency of chromosome aberrations (CAs) is linked to the induction of genomic instability. It is known that a high level of genomic instability is associated with a high risk of cancer induction.</p>
Rationale for HRP Directed Research:	<p>Despite significant efforts, advances in developing radiation countermeasures, both those given before (protectors) and after (mitigators) radiation exposure are still an unmet need. Hence, the search for efficient countermeasures is at high priority to protect the victims in the event of nuclear terrorism or accident, as well as in the battlefield (in the event of radiological explosive devices are used), as well as astronauts and space travelers. 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. It has been well characterized that radiation-induced hematopoietic failure is the major detrimental biological effects. This is mostly due to the extensive 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 resulting data obtained from the analyses of samples collected from groups of mice at 1-wk post-irradiation are the first set of data demonstrating the countermeasure efficacy of AP given as a diet supplement to irradiated mice. Our results indicate that AP 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). Moreover, we also found that AP consumption reduces the frequencies of radiation-induced chromosome aberrations (CAs) in the BM cells of exposed mice. It is known that the occurrence of CAs is closely linked to the induction of genomic instability (a critical event in cancer induction). Therefore, our findings are of paramount significance in radiation protection during the space mission and 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 during a space mission, in the event of radiobiological events on earth, (e.g. a nuclear accident or terrorisms) or in the battlefield.</p>
Research Impact/Earth Benefits:	<p>Our data from samples collected at 1-wk post-irradiation from groups of mice show the efficacy of AP in protection and mitigation against radiation-induced injuries in hematopoietic cells of exposed mice. The first set of our data demonstrate for the first time the effectiveness of AP given to mice via food consumption (AP 20 mg/kg/bw) in counteracting injuries to the hematopoietic tissues induced by space radiation (28Si ions). The highlights of our data are: AP prevents a loss of white blood cells (leukopenia), AP prevents the depletion of platelets (thrombocytopenia), AP enhances the production of red blood cells (erythropoiesis), and AP enhances the proliferation capacity of hematopoietic stem/progenitor cells. Further, we found that AP is very effective in the suppression of inflammation. Our results suggest that AP given as a diet supplement protects 28Si-ion-induced damage in the hematopoietic tissues of irradiated male C57BL/6 mice via its anti-inflammation activity. In summary, our data clearly show the efficacy of AP in counteracting radiation-induced harmful effects on the hematopoietic system. Further, consumption of AP at 20 mg/kg body weight does not induce damage to the hematopoietic system of exposed mice. In contrast, AP consumption significantly enhances HSPC proliferation. These findings strongly suggested that daily consumption of AP is safe.</p>
Task Progress:	<p>Our data from samples collected at 1-wk post-irradiation from groups of mice show the efficacy of AP in protection and mitigation against radiation-induced injuries in hematopoietic cells of exposed mice. The first set of our data demonstrate for the first time the effectiveness of AP given to mice via food consumption (AP 20 mg/kg/bw) in counteracting injuries to the hematopoietic tissues induced by space radiation (28Si ions). The highlights of our data are: AP prevents a loss of white blood cells (leukopenia), AP prevents the depletion of platelets (thrombocytopenia), AP enhances the production of red blood cells (erythropoiesis), and AP enhances the proliferation capacity of hematopoietic stem/progenitor cells. Further, we found that AP is very effective in the suppression of inflammation. Our results suggest that AP given as a diet supplement protects 28Si-ion-induced damage in the hematopoietic tissues of irradiated male C57BL/6 mice via its anti-inflammation activity. In summary, our data clearly show the efficacy of AP in counteracting radiation-induced harmful effects on the hematopoietic system. Further, consumption of AP at 20 mg/kg body weight does not induce damage to the hematopoietic system of exposed mice. In contrast, AP consumption significantly enhances HSPC proliferation. These findings strongly suggested that daily consumption of AP is safe.</p>
Bibliography Type:	Description: (Last Updated: 05/17/2023)
Abstracts for Journals and Proceedings	<p>Rithidech K, Peanlikhit T, Honikel L, Zimmerman T. "Countermeasure efficacy of apigenin given as a diet supplement before and after exposure of mice to silicon ions on hematopoietic tissues." To be presented at the virtual 2021 NASA Human Research Program Investigators' Workshop, February 1st 2021. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021</p>
Abstracts for Journals and Proceedings	<p>Peanlikhit T, Honikel L, Rithidech K. "Apigenin as a countermeasure for chromosome aberrations induced by whole-body exposure to silicon (28Si) ion." To be presented at the virtual 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021</p>

Abstracts for Journals and Proceedings	Rithidech K, Peanlikhit T, Zimmerman T, Honikel L, Whorton E. "Apigenin counteracts adverse effects of space radiation to the hematopoietic system." Presented at the 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
Articles in Peer-reviewed Journals	Rithidech KN, Mortazavi SMJ, Brooks AL. "Letter to Editor Re: Fang et al. entitled 'Assessment of genomic instability in medical workers exposed to chronic low-dose X-Rays in Northern China.' " Dose Response. 2020 Apr-Jun;18(2):1559325820922101. https://doi.org/10.1177/1559325820922101 ; PMID: 32577116; PMCID: PMC7288825 [The authors comment on the article by Fang et al. in Dose Response. 2019 Nov 28;17(4):1559325819891378. PMID: 31819742] , Apr-2020