Fiscal Year:	FY 2018	**Task Last Updated:**	FY 02/22/2018
PI Name:	Porada, Christopher Ph.D.		
Project Title:	Novel Microfluidic Biomarker Detection Platforms to Monitor In Vivo Effects of Solar Particle Events and Galactic Cosmic Rays Radiation, Using Mice with Human Hematopoietic Systems		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	cporada@wakehealth.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	336-713-1655
Organization Name:	Wake Forest Institute for Regenerative Medicine		
PI Address 1:	391 Technology Way		
PI Address 2:			
PI Web Page:			
City:	Winston Salem	**State:**	NC
Zip Code:	27157	**Congressional District:**	5
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2017 HERO NNJ16ZSA001N-TRIRT. Appendix C: Translational Research Institute for Space Health (TRISH) Research Topics
Start Date:	11/01/2017	**End Date:**	10/31/2021
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No. of PhD Candidates:		**No. of Master' Degrees:**	
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No. of Bachelor's Candidates:		**Monitoring Center:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Almeida-Porada, Graca M.D. (Wake Forest University) Langefeld, Carl Ph.D. (Wake Forest University) Walker, Stephen Ph.D. (Wake Forest University) Wilson, Paul Ph.D. (University Of California, Davis) Coleman, Matthew Ph.D. (Wake Forest University) Zenhausern, Frederic Ph.D. (University of Arizona)		
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Task Description:	We propose the following Specific Aims: Aim 1: We will utilize mice with “humanized” hematopoietic systems to define changes in human and mouse radiation/stress blood biomarkers in response to mission-relevant doses of simulated space radiation employing a microfluidic-based transcriptomic/proteomic biomarker detection platform; Aim 2: Validate the ability of nanoparticles (nanolipoproteins; NLPs) loaded with curcumin as effective countermeasures against the effects of simulated space radiation in both the human hematopoietic and mouse GI systems; Aim 3: Assess the suitability of curcumin-NLPs for use as radiation countermeasures in the space environment by: a) assessing their long-term stability for storage/use aboard the International Space Station (ISS) and long duration deep-space missions; b) evaluating their suitability for lyophilization/resuspension for oral delivery; and c) supplementing the diet of a small cohort of “humanized” mice with an optimized formulation to further evaluate their potential for both radioprotection (pre-irradiation supplementation) and radiation mitigation (post-irradiation supplementation). Aim 4: Use the innovative Human-Microbial Cross-Talk human “gut-on-a-chip” model (HuMiX) to perform the first studies defining critical biomarker responses of mission-relevant doses of simulated space radiation on the human GI tract. Approach: We will use “humanized” immunodeficient (NSG) mice (huMice) whose hematopoietic system has been repopulated with human hematopoietic stem cells (HSC) from astronaut-age M/F donors. Using these huMice (3–4 months post-repopulation) as our experimental model, we will measure space radiation-induced human and mouse blood transcriptomic and proteomic changes using our low LET (linear energy transfer) photon-validated radiation biomarker detection panel and microfluidic-based detection platform. We will also test a promising curcumin-based nanolipoprotein (NLP)-based countermeasure that we have recently shown significantly improves human HSC proliferation and differentiation in vitro following low doses of high-energy proton and iron ions delivered at NASA Space Radiation Laboratory (NSRL). The huMice will serve as “avatars” allowing us to study in vivo responses and leukemogenic potential of human hematopoietic systems exposed to modeled space radiation. HuMice will be developed and matured at Wake Forest Institute for Regenerative Medicine (WFIRM) and transported to Brookhaven National Laboratory (BNL), as will HuMiX “gut-on-a-chip” populated with intestinal cells from healthy human donors (both sexes) of typical astronaut age. At NSRL, the huMice “avatars” and HuMiX chips will be exposed to mission-relevant doses of high-energy protons, intermediate and high LET ions, and the GCR (galactic cosmic radiation) simulator. HuMiX chips will be monitored for short-term human GI cell biomarker responses, and the animals will be monitored for both short and long-term human and mouse biomarker responses, using our established low LET cesium-137 gamma radiation-specific protein biomarkers coupled to an ELISA-based microfluidic device that we will further optimize for ISS/in-flight use. Biomarker responses measured in these devices will be validated using qPCR, RNASeq, Western blotting, and several traditional and molecular radiobiological techniques. We will serially monitor animals for short- and long-term blood-based biomarker responses and physiological radiation effects (specifically leukemogenesis). We will submit tissue/organ samples of huMice to the NASA Human Research Program (HRP) Shared Tissue Repository, and our biomarker datasets will be deposited into the NASA GeneLab database.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2018.
Bibliography Type:	Description: (Last Updated: 01/30/2023)