Fiscal Year:	FY 2021	**Task Last Updated:**	FY 12/02/2020
PI Name:	Gerecht, Sharon Ph.D.		
Project Title:	Using Human Stem-Cell Derived Vascular, Neural, and Cardiac 3D Tissues to Determine Countermeasures for Radiation		
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		
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Zip Code:	21218	**Congressional District:**	7
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2020 TRISH Space Radiation Solicitation TSRAD-2020. Translational Research Institute for Space Health (TRISH) Human-Based Models to Study Effects of Space Radiation and Countermeasures
Start Date:	10/01/2020	**End Date:**	09/30/2023
No. of Post Docs:		**No. of PhD Degrees:**	
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:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Boehler, Kenneth Ph.D. (Johns Hopkins University) Chancellor, Jeffrey Ph.D. (Louisiana State University) Hienz, Robert Ph.D. (Johns Hopkins University) Kim, Deok-Ho Ph.D. (Johns Hopkins University) Lee, Gabsang Ph.D. (Johns Hopkins University) Shelhamer, Mark Sc.D. (Johns Hopkins Medical School) Xu, Jinchong Ph.D. (Johns Hopkins University) Tung, Leslie Ph.D. (Johns Hopkins University) Spangler, Jamie Ph.D. (Johns Hopkins University) Mallick, Parag Ph.D. (Stanford University)		
Grant/Contract No.:	NNX16AO69A-RAD0102		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	In this study a skilled team with diverse expertise will examine 3D human tissue models for their response to radiation, with an eye to the development of countermeasures. Cardiovascular and neuronal degeneration are established risks of exposure to deep-space radiation (galactic cosmic rays, GCR). Inflammation and oxidative damage are dominant mechanisms, which are being addressed with appropriate pharmaceuticals or supplements. There are, however, various forms of protein modification including oxidation, reduction, and changes in expression. These have been demonstrated at relatively high dosages with terrestrial radiation sources, providing an impetus for further investigation into damage mechanisms that impact protein structure and function. Thus, we propose here a broad assay for altered protein expression and changes in protein function, which may lead to genetic and proteomic interventions that target the most-affected sites. This is complemented with an investigation of the signaling pathways that might propagate these effects. We analyze responses of three human tissue models to low-dose protracted GCR simulations, and identify and develop countermeasures using optogenetics and molecular antagonists. Human tissue models include vascular, cerebrovascular, and cardiac. These are 3D constructs generated from human pluripotent stem cells (hPSCs) and are well characterized. Radiation exposures are in alignment with NASA guidelines. In a slight departure, we make use of a newly developed method to modify the standard GCR beam at NASA Space Radiation Laboratory (NSRL) in order to provide a GCR spectrum that better emulates one inside a spacecraft. This alleviates some of the concerns with the existing radiation sources, and provides a more direct transfer of our results to the actual spaceflight situation. The project is organized into three specific aims. First, we determine the effect of radiation exposure on cell viability and cell cycle, tissue integrity and functionality, and the activation of oxidative stress and high mobility group box 1 (HMGB1) pathways. This will validate the usefulness of our biological models, and radiation exposures, for the subsequent investigation of countermeasures. Second, we use an integrative systems approach to identify therapeutic (countermeasure) targets to mitigate radiation damage. This is accomplished with large- scale quantitative proteomics, multi-data fusion and network analysis, and conformational inhibition tests. Ultimately, in aim three, we develop and test countermeasures based on optogenetics and protein antagonists, to activate or inhibit pathways impacted by radiation. The results of this project will help to determine if complex human models can serve as an effective test bed for the effects of space radiation on intact humans, and will identify and assess possible countermeasures to these effects.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2021.
Bibliography Type:	Description: (Last Updated: 03/19/2024)