Fiscal Year:	FY 2019	**Task Last Updated:**	FY 05/06/2020
PI Name:	Grabham, Peter Ph.D.		
Project Title:	A Determination of Bioactive Proteins Secreted by the Human Vasculature in Response to Low Dose 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) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	10032-3702	**Congressional District:**	13
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2017 HERO 80JSC017N0001-Crew Health and Performance (FLAGSHIP1, OMNIBUS). Appendix A-Flagship1, Appendix B-Omnibus
Start Date:	08/01/2018	**End Date:**	07/31/2020
No. of Post Docs:	1	**No. of PhD Degrees:**	1
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
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 7/31/2020 per NSSC information (Ed., 1/29/2020)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Brown, Lewis Ph.D. (Columbia University)		
Grant/Contract No.:	80NSSC18K1492		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The specific purpose of the research proposed here is to determine the proteins that are potentially released into the blood stream by the lining of the human vasculature in response to exposure to space radiation. This would create a useful database for radiobiology studies and comparisons with the proteins secreted in astronaut blood. Such proteins have the potential to cause pathological processes such as inflammation, they are also spread around the body in the blood, and are important factors in many pathologies. The microvasculature permeates all tissues at the microscopic level so the whole body is a target for charged particles. A single heavy ion particle would be expected to traverse many microvessels as it passes through the body causing a more widespread response. Studies on the effect of different charged particles on human 3D microvessel models shows that both developing and mature microvessels lose structure and function after exposure to very low doses of various charged particles. Mature microvessels lose structure detectible as low as 1.25 cGy. Angiogenesis, the growth of new vessels, is inhibited by light ions and heavy ions detectible at 1.25 cGy. Even more striking, the combined effect of each ion has a synergistic effect detectible as low as 0.6 cGy. The low fluence of these doses indicates a bystander effect where the response is transmitted to other cells and such a mechanism would involve the secretion of molecules by the target cell. We propose to use proteomics and other techniques to determine the proteins secreted by the human microvessel models. A database of these proteins secreted by human tissue models would not only be of great use to a number of researchers investigating a diverse number of pathologies related to space radiation but also provide insights into the mechanisms of the vascular response to charged particles. The specific purpose of the research proposed here is to determine the proteins that are potentially released into the blood stream by the lining of the human vasculature in response to exposure to space radiation. This would create a useful database for radiobiology studies and comparisons with the proteins secreted in astronaut blood. Such proteins have the potential to cause pathological processes such as inflammation, they are also spread around the body in the blood, and are important factors in many pathologies. The microvasculature permeates all tissues at the microscopic level so the whole body is a target for charged particles. A single heavy ion particle would be expected to traverse many microvessels as it passes through the body causing a more widespread response. Studies on the effect of different charged particles on human 3D microvessel models shows that both developing and mature microvessels lose structure and function after exposure to very low doses of various charged particles. Mature microvessels lose structure detectible as low as 1.25 cGy. Angiogenesis, the growth of new vessels, is inhibited by light ions and heavy ions detectible at 1.25 cGy. Even more striking, the combined effect of each ion has a synergistic effect detectible as low as 0.6 cGy. The low fluence of these doses indicates a bystander effect where the response is transmitted to other cells and such a mechanism would involve the secretion of molecules by the target cell. We propose to use proteomics and other techniques to determine the proteins secreted by the human microvessel models. A database of these proteins secreted by human tissue models would not only be of great use to a number of researchers investigating a diverse number of pathologies related to space radiation but also provide insights into the mechanisms of the vascular response to charged particles. Amended Aims—November 2019 Additional aims were included for the determination of relative biological effectiveness (RBEs) for the 5 ion galactic cosmic radiation (GCR) simulations. Aim 1. Create RBEs for the vascular damage endpoints. Aim 1a Carry out Gamma radiation studies at Brookhaven National Laboratory (BNL) for the determination of reference RBEs. Aim 1b Carry out charged particle studies at BNL for the determination of RBEs. Aim 2. Identify the proteins secreted by the endothelial cells during angiogenesis and in mature human 3 D micro-vessel tissue models in response to radiation. Aim 2a Development of the proteomics assay. Aim 2b Identify the proteins secreted by the endothelial cells during angiogenesis and in mature human 3 D micro-vessel tissue models in response to gamma radiation. Aim 2c Identify the proteins secreted by the endothelial cells during angiogenesis and in mature human 3 D micro-vessel tissue models in response to the Simplified GCR sim.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	Note information below is from report submitted to Human Research Program November 2019. 1) By the summer of 2019 Aims 1a and b had been partially carried out for Mature vessels. 2) Aim 1a and 1b for developing microvessels (angiogenesis) were not yet completed. The new protocol requested by NASA that entails remaining at Brookhaven for an extra day does not appear to be compatible with microvessel growth. The reasons for this are unknown but we continued to trouble shoot the assay through the summer. 3) By the Fall run (19C – the last possible run for the current time limit) culture problems had been resolved. In the 2 visits for this run we have completed one dose response for angiogenesis in addition to proteomics samples and the samples are now being processed. 4) Work on the sample preparation for proteomics studies has been carried out and, as expected, a scale up of the cultures was necessary. A larger gel matrix proved to be less stable and detached from the flasks. 5) A goal of 5 samples for each condition (20 total) was set by the Proteomics expert CoInvestigator Dr. Brown. These goals were reached by the end of the Fall (19C) run. Samples will be processed and delivered to Dr. Brown.
Bibliography Type:	Description: (Last Updated: 03/04/2024)