Fiscal Year:	FY 2016	**Task Last Updated:**	FY 02/01/2017
PI Name:	Patel, Zarana Ph.D.		
Project Title:	Development of a Flow-Perfused and Immunocompetent 3-D Vascular Model for Radiation Risk Assessment of Cardiovascular Disease and Countermeasure Screening		
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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PI Organization Type:	NASA CENTER	**Phone:**	281-483-3723
Organization Name:	KBRwyle/NASA Johnson Space Center		
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PI Address 2:	2400 NASA Parkway		
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77058	**Congressional District:**	22
Comments:	NOTE: PI moved to Wyle in 2014; previously at Universities Space Research Association.		
Project Type:	GROUND	**Solicitation / Funding Source:**	2013 HERO NNJ13ZSA002N-Crew Health OMNIBUS
Start Date:	03/01/2015	**End Date:**	09/01/2016
No. of Post Docs:	1	**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:**	NASA JSC
Contact Monitor:	Simonsen, Lisa	**Contact Phone:**	
Contact Email:	lisa.c.simonsen@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: Extended to 9/1/2016 per S. Monk/SR HRP (Ed., 3/14/16) NOTE: change in period of performance per PI (originally 10/1/2014-9/30/2015)--Ed., 7/11/15		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Grande-Allen, K. Jane Ph.D. (Rice University)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Radiation exposure is known to result in degenerative effects on the cardiovascular system, resulting in ischemic heart disease and strokes and includes the development of atherosclerosis. Data from low-LET (linear energy transfer) exposures, including from radiotherapy, occupational, and environmental exposures, show a dose-dependent effect. However, only a few studies have examined the effects of heavy ion radiation on atherosclerosis, and at lower, space-relevant doses, the association between exposure and cardiovascular pathology is more varied and unclear. To date, there has been very limited use of in vitro coculture systems that include multiple cell types for space radiation risk assessment of degenerative cardiovascular diseases. The objective of this work was to utilize an innovative, tissue engineering approach to address the Human Research Program (HRP) Space Radiation Degen-1 knowledge gap with the development of cocultures of human endothelial cells and smooth muscle cells using hydrogel scaffolds. These 3D models can be used to profile the effects of radiation on markers of endothelial dysfunction, an important and early indicator of heart disease.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Development and validation of this model will allow for the quantitative assessment of the degenerative risk of radiation exposure on heart disease and allow for countermeasure screening without the use of animals. This has direct relevance to radiation-related cardiotoxicities that are being observed in the clinic, either due to radiotherapy for cancer treatments, occupational exposures to cardiologists, or by environmental exposures from nuclear accidents.
Task Progress:	We have developed a pilot vascular co-culture model that incorporates human coronary artery smooth muscle cells (hCASMCs) into the body of a PEG hydrogel and human coronary artery endothelial cells (hCAECs) on to the surface of the hydrogel. The hydrogel is functionalized with two different peptides to facilitate degradation by the SMCs and adhesion of the ECs (endothelial cells). Optimized seeding densities for the two cell types was established. We tested the feasibility of using the co-culture hydrogels as a model to study radiation-induced atherosclerosis by irradiating the hydrogels with gamma irradiation and costaining with alpha-smooth muscle actin and markers of DNA damage (53BP1). Further experimentation revealed that staining for an endothelial marker such as CD31 allowed for easier differentiation between the cell types. The co-culture gels were stained to visualize cell nuceli, alpha-SMA, and 53BP1. Foci formation has been quantified over a time course of 24 hours. Markers of endothelial dysfunction will also be quantified.
Bibliography Type:	Description: (Last Updated: 08/25/2020)
Abstracts for Journals and Proceedings	Patel ZS, Hada M, Kang MK, Grande-Allen KJ. "Irradiation Effects on Vascular Dysfunction in a 3D Human Cell Vascular Model." Presented at the 62nd Annual Meeting of the Radiation Research Society, Big Island, Hawaii, October 16-19, 2016. 62nd Annual Meeting of the Radiation Research Society, Big Island, Hawaii, October 16-19, 2016. , Oct-2016
Abstracts for Journals and Proceedings	Kang MK, Patel ZS, Hada M, Grande-Allen KJ. "Irradiation Effects on Vascular Dysfunction in a 3D Human Cell Vascular Model." Presented at the Gulf Coast Vascular Research Consortium, Shreveport, LA, August 26-27, 2016. Gulf Coast Vascular Research Consortium, Shreveport, LA, August 26-27, 2016. , Aug-2016
Abstracts for Journals and Proceedings	Patel ZS, Hada M, Kang MK, Grande-Allen KJ. "Project Summary of 3D Vascular Model Development." Presented at the 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016. 2016 NASA Human Research Program Investigators' Workshop, Galveston, TX, February 8-11, 2016. , Feb-2016
Abstracts for Journals and Proceedings	Patel ZS, Hada M, Kang MK, Grande-Allen KJ. "Radiation Quality Effects on Markers of Endothelial Dysfunction in a Human Vascular Model." Presented at the 61st Annual Meeting of the Radiation Research Society, Weston, FL, September 19-22, 2015. 61st Annual Meeting of the Radiation Research Society, Weston, FL, September 19-22, 2015. , Sep-2015
Abstracts for Journals and Proceedings	Patel ZS, Hada M, Grande-Allen KJ. "Effects of Low- and High-LET Radiation on Markers of Endothelial Dysfunction in a Human Vascular Model." Presented at the 15th International Congress of Radiation Research (ICRR), Kyoto, Japan, May 25-29, 2015. 15th International Congress of Radiation Research (ICRR), Kyoto, Japan, May 25-29, 2015. , May-2015
Articles in Peer-reviewed Journals	Sylvester CB, Abe JI, Patel ZS, Grande-Allen KJ. "Radiation-induced cardiovascular disease: Mechanisms and importance of linear energy transfer." Front Cardiovasc Med. 2018 Jan 31;5:5. https://doi.org/10.3389/fcvm.2018.00005 ; PMID: 29445728; PMCID: PMC5797745 , Jan-2018
Articles in Peer-reviewed Journals	Ko KA, Wang Y, Kotla S, Fujii Y, Vu HT, Venkatesulu BP, Thomas TN, Medina JL, Gi YJ, Hada M, Grande-Allen J, Patel ZS, Milgrom SA, Krishnan S, Fujiwara K, Abe JI. "Developing a reliable mouse model for cancer therapy-induced cardiovascular toxicity in cancer patients and survivors." Front Cardiovasc Med. 2018 Apr 5;5:26. https://doi.org/10.3389/fcvm.2018.00026 ; PMID: 29675417; PMCID: PMC5896304 , Apr-2018