Fiscal Year:	FY 2019	**Task Last Updated:**	FY 02/12/2020
PI Name:	Goukassian, David A M.D., Ph.D.		
Project Title:	Space Relevant Radiation-Induced Cardiovascular Disease Risk Thresholds: Effect of Gender on the Outcome--80NSSC19K1079		
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) **Arrhythmia**:Risk of Cardiac Rhythm Problems (2) **Degen-IRP Rev J**:Risk of Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation Exposure and Secondary Spaceflight Stressors (IRP Rev J)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Comments:	NOTE: PI moved to Icahn School of Medicine at Mount Sinai from Temple University in October 2018.		
Project Type:	GROUND	**Solicitation:**	2016-2017 HERO NNJ16ZSA001N-SRHHC. Appendix E: Space Radiobiology and Human Health Countermeasures Topics
Start Date:	04/10/2019	**End Date:**	04/09/2023
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:**	NASA JSC
Contact Monitor:	Simonsen, Lisa	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: Continuation of "Space Relevant Radiation-Induced Cardiovascular Disease Risk Thresholds: Effect of Gender on the Outcome," grant 80NSSC18K0921, due to PI move to Icahn School of Medicine at Mount Sinai from Temple University. (Ed., 2/10/2020)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	80NSSC19K1079		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Ed. note 2/10/2020: Continuation of "Space Relevant Radiation-Induced Cardiovascular Disease Risk Thresholds: Effect of Gender on the Outcome," grant 80NSSC18K0921 with the same Principal Investigator Dr. David Goukassian, due to PI move to Icahn School of Medicine at Mount Sinai from Temple University. During the future Moon, near Earth asteroids, and Mars missions, astronauts will be exposed to higher total doses of space irradiation (IR) (~0.4-0.5 Gy) from galactic cosmic rays (GCR). Most of what we know about harmful effects of IR on cardiovascular (CV) system is from epidemiological studies of long-term survivors of cancer radiotherapy (RT). A recent study of 2,168 women who underwent RT for breast cancer has shown that the rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per Gy, with no apparent lower or upper threshold. In this study, it was determined that average of the mean doses to the whole heart was 4.9 Gy with the range of 0.03 - 27.72 Gy. Furthermore, metabolomics studies, in patients undergoing hematopoietic stem cell (HSC) transplantation as part of cancer treatment (1.25 Gy total-body irradiated), identified seven urine-based biomarkers with distinct differences between pre- and post-exposure samples. The levels of these markers were found to be gender-dependent suggesting that separate biomarker signatures may exist for males and females. Hypotheses: Our central hypothesis is that low-dose proton and HZE (high energy) particle IR-induced biological responses are long-lasting, IR type- and dose-dependent and may augment excess relative risk (ERR) estimates for the development of CV diseases during and after long-duration space missions. In addition, we hypothesize that gender differences could further modify radio-biologically effective (RBE) IR thresholds for CV risk estimates. Gene expression and epigenetic modifications in protein and microRNA (miRNA) in exosomes from the blood (e.g., plasma/serum) may be altered before the onset of the cardiac symptoms, which could be used as potential biomarkers to predict the CV disease risks. We will test our hypotheses with the following specific aims: AIM 1. Determine the longitudinal effect of IR type, dose, and gender on cardiovascular physiology in wild type mice and ApoE null mice after full-body 5-ion simplified mixed field and gamma radiation. AIM 2. Determine space-type IR mediated modulations in exosomal cargo in the blood, and determine whether these changes are associated with alterations in the heart function, structure, and vasculature before manifestation of clinical symptoms. AIM 3. Utilize known and newly identified bio-markers in the blood to develop human-relevant point-of-care tests (POCT) for predicting and monitoring possible CV alterations before and during the space flights. We anticipate that the results of our proposed work may be beneficial for human space exploration and could (1) Determine single, low-dose 1H, 56Fe, and mixed field dose-responses, radio-biologically effective IR thresholds in the heart and cardiac vasculature, and whether gender differences could modify radio-biologically effective IR thresholds for CV risk estimates; 2) Determine whether space radiation leads to modifications in the circulating exosomal cargo contents and whether IR-induced exosomal cargo modulations are reflective of subclinical changes in the cells and organs of origin; 3) Ascertain if modulations of exosomal cargo may be representative of chronic oxidative stress and inflammation and could serve as early bio-markers of IR-induced CV disease initiation and progression; 4) Integrate physiological CV endpoint data sets with gene expression and epigenetic data to identify bio-markers in bio-fluids that could be used for prediction of asymptomatic CV disease in the setting of space IR, which will include known early and intermediate bio-markers of cardiac damage, inflammation, and oxidative stress, as well as currently unknown novel radiation-associated cardiac bio-markers.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	We anticipate that the results of our work could be beneficial for human space exploration as well as for the Earth-based applications on several levels -- (1) determine whether low dose space-type and terrestrial IR may present an increased risks for CV disease development during and after prolonged space missions, as well as after conventional and particle cancer radiotherapy; (2) determine the underlying molecular signaling of CV alterations; (3) identify bio-markers in the blood that could be used for prediction of asymptomatic CV disease, which will include known early and intermediate bio-markers of cardiac damage, as well as currently unknown novel cardiac biomarkers; (4) the identification of sub-clinical CV disease biomarkers that could be used for monitoring the effectiveness of mitigating factors for prevention and treatment of IR-induced CV diseases in space and in Earth-bound civilian population, in general.
Task Progress:	New project for FY2019. NOTE: Continuation of "Space Relevant Radiation-Induced Cardiovascular Disease Risk Thresholds: Effect of Gender on the Outcome," grant 80NSSC18K0921 with the same Principal Investigator Dr. David Goukassian, due to PI move to Icahn School of Medicine at Mount Sinai from Temple University. See that project for previous reporting. (Added in February 2020 to Task Book when received information on new grant.)
Bibliography Type:	Description: (Last Updated: 02/18/2020)