Fiscal Year:	FY 2020	**Task Last Updated:**	FY 03/15/2021
PI Name:	Goukassian, David A M.D., Ph.D.		
Project Title:	Degenerative Cardiovascular Disease Risks Due to Single HZE or Mixed Ion 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:	10029	**Congressional District:**	12
Comments:	NOTE: PI moved to Icahn School of Medicine at Mount Sinai from Temple University in October 2018.		
Project Type:	GROUND	**Solicitation / Funding Source:**	2016-2017 HERO NNJ16ZSA001N-Crew Health (FLAGSHIP, OMNIBUS). Appendix A-Omnibus, Appendix B-Flagship
Start Date:	06/28/2017	**End Date:**	04/09/2020
No. of Post Docs:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:	2	**No. of Master' Degrees:**	1
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Elgart, Robin	**Contact Phone:**	281-244-0596 (o)/832-221-4576 (m)
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Flight Program:			
Flight Assignment:	NOTE: PI moved to Icahn School of Medicine at Mount Sinai from Temple University in October 2018. Grant continues at Icahn School of Medicine at Mount Sinai through 4/9/2020 with new grant number 80NSSC19K1078 (Ed., 3/30/2020)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	80NSSC19K1078 ; 80NSSC17K0112		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	During the future Moon and deep space missions to Mars, astronauts will be exposed to higher total doses of ionizing space radiation (IR, ~0.4-0.5 Gy) from galactic cosmic rays (GCR), especially during Mars missions that are currently estimated to be 30 to 36 months. Due to GCR, each cell in an astronaut's body will be traversed by a proton (1H) every week, helium (2He) nuclei every few weeks, and high charge and energy (HZE) nuclei (e.g., 6C, 8O, 14Si, 22Ti, 56Fe) every few months. These frequencies and qualities of IR exposures could have significant effects on cardiovascular (CV) health of astronauts during and after exploration-type space missions. In spite of healthy worker factor (unsurpassed training and fitness of astronauts) such factors are of extreme importance as majority of experienced astronauts are middle-aged and at higher risk for developing serious CV complications. We hypothesize that low-dose proton and HZE particle IR-induced biological responses are long-lasting, IR type-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 different sequence of proton vs. HZE and mix beam radiation regimens could further modify radio-biologically effective (RBE) IR thresholds for CV risk estimates. To determine qualitative differences and quantify RBEs for biological damage induced by proton and HZE particles for various HZE ions and mix beam IR regimens and how this may influence late degenerative CV disease risks, we will use our own archived heart samples from fractionated proton and single iron IR used in various sequences. In addition, we plan to use the archived samples from experiments conducted by Drs. Eleanor Blakely and Polly Chang where they used CB6F1/Hsd female mice of 100-120 days at the time of initial exposure and tissues were harvested 16 months after IR. These samples fit very well with our own low dose proton and iron single and fractionated studies, as ions and energies used in these studies are complementary to our studies. Additionally, these samples provide an experimental synergy and continuity to our archived samples for testing the effect of low dose gamma and various HZE particle IR of different doses, energies, and sequences on IR responses in the heart. We anticipate that the results of our work could be beneficial for human space exploration on several levels: (1) determine whether low dose space-type IR may present an increased risks for late degenerative CV disease development including, but not limited to, fibrosis, atherosclerosis, and vascular changes; (2) determine whether there may be low dose thresholds for radiation-induced changes in the heart tissue; (3) lay a foundation for identification of common bio-markers for different species and energies of space-type IR that could be used for prediction of asymptomatic CV disease in the setting of space IR; (4) provide an insight, on the cardiac tissue level, of molecular targets/pathways for development of mitigating factor and biological countermeasures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The results of these studies could be beneficial for human space exploration on several levels: Research Impact: (1) determine whether low dose space IR may present an increased risk for CV disease development; (2) elucidate whether manifestation of sub-clinical or environmentally induced CV diseases due to space radiation could be predicted; (3) elucidate underlying molecular mechanisms of CV alterations; (4) lay foundation for identification of predictive biomarkers to monitor CV risks and sub-clinical CV pathologies due to low dose single and mix ion fractionated HZE particle radiation regimens; Earth and Space benefits: (5) provide mechanistic insights for molecular targets/pathways for development of mitigating factors to prevent CV morbidity in astronauts during and after exploration type space missions and in civilian population after treatment with conventional and particle cancer radiotherapy.
Task Progress:	Compared to low doses of gamma irradiation (gamma-IR), high-charge-and-energy (HZE) particle IR may have different biological response thresholds in cardiac tissue at lower doses, and these effects may be IR type and dose dependent. Three- to four-month-old female CB6F1/Hsd mice were exposed once to one of four different doses of the following types of radiation: gamma-IR 137Cs (40-160 cGy, 0.662 MeV), 14Si-IR (4-32 cGy, 260 MeV/n), or 22Ti-IR (3-26 cGy, 1 GeV/n). At 16 months post-exposure, animals were sacrificed and hearts were harvested and archived as part of the NASA Space Radiation Tissue Sharing Forum. These heart tissue samples were used in our study for RNA isolation and microarray hybridization. Functional annotation of twofold up/down differentially expressed genes (DEGs) and bioinformatics analyses revealed the following: (i) there were no clear lower IR thresholds for HZE- or gamma-IR; (ii) there were 12 common DEGs across all 3 IR types; (iii) these 12 overlapping genes predicted various degrees of cardiovascular, pulmonary, and metabolic diseases, cancer, and aging; and (iv) these 12 genes revealed an exclusive non-linear DEG pattern in 14Si- and 22Ti-IR-exposed hearts, whereas two-thirds of gamma-IR-exposed hearts revealed a linear pattern of DEGs. Thus, our study may provide experimental evidence of excess relative risk (ERR) quantification of low/very low doses of full-body space-type IR-associated degenerative disease development.
Bibliography Type:	Description: (Last Updated: 03/06/2024)
Articles in Peer-reviewed Journals	Garikipati VNS, Arakelyan A, Blakely EA, Chang PY, Truongcao MM, Cimini M, Malaredy V, Bajpai A, Addya S, Bisserier M, Brojakowska A, Eskandari A, Khlgatian MK, Hadri L, Fish K, Kishore R, Goukassian DA. "Long-term effects of very low dose particle radiation on gene expression in the heart: Degenerative disease risks." Cells. 2021 Feb 13;10(2):387. https://doi.org/10.3390/cells10020387 ; PMID: 33668521; PMCID: PMC7917872 , Feb-2021