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| **Fiscal Year:** | FY 2018 | **Task Last Updated:** | FY 03/13/2018 |
| **PI Name:** | Bowles, Dawn Ph.D. | | |
| **Project Title:** | Proteomic Signatures of Space Radiation Induced Cardiovascular Degeneration | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | | | |
| **Program/Discipline--Element/Subdiscipline:** | HUMAN RESEARCH--Radiation health | | |
| **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 | | |
| **PI Email:** | dawn.bowles@duke.edu | **Fax:** | FY |
| **PI Organization Type:** | UNIVERSITY | **Phone:** | 919-668-1947 |
| **Organization Name:** | Duke University | | |
| **PI Address 1:** | Department of Surgery | | |
| **PI Address 2:** | Msrb1 Room 401B, DUMC 2642 | | |
| **PI Web Page:** | | | |
| **City:** | Durham | **State:** | NC |
| **Zip Code:** | 27710-0001 | **Congressional District:** | 4 |
| **Comments:** | | | |
| **Project Type:** | GROUND | **Solicitation / Funding Source:** | 2014-15 HERO NNJ14ZSA001N-RADIATION. Appendix D: Ground-Based Studies in Space Radiobiology |
| **Start Date:** | 05/12/2016 | **End Date:** | 05/11/2020 |
| **No. of Post Docs:** | | **No. of PhD Degrees:** | |
| **No. of PhD Candidates:** | 1 | **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:** | | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | Abraham, Dennis M.D. ( Duke University )<br>Kidane, Yared Ph.D. ( Wyle Laboratories, Inc. )<br>Mao, Lan M.D. ( Duke University )<br>Dewhirst, Mark D.V.M., Ph.D. ( Duke University )<br>Moseley, Martin Ph.D. ( Duke University ) | | |
| **Grant/Contract No.:** | NNX16AK20G | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

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| **Task Description:** | Radiation damage and the cell's attempt to repair it triggers a myriad of signal transduction pathways which alter gene, and ultimately, protein expression. Space radiation may affect biomolecules, cellular processes, and ultimately the cellular protein content (the proteome) differently than radiation present on Earth. Epidemiological analysis of terrestrial radiation exposure indicates that single high- or multiple low-dose radiation exposure can culminate in a wide array of cardiac injury and malfunction over time. Based on terrestrial data, it is believed that cardiovascular disorders may develop in astronauts from exposure to the space radiation environment. Indeed, a recent study by Yan et al. (2014), found that a single full body exposure to a low dose of proton or iron particle radiation, which somewhat mimics the space radiation environment, was sufficient to induce a significant, long term, negative effect on murine cardiovascular function. In this proposal, we take advantage of our expertise with bioinformatics analysis of cardiovascular proteomic data sets and murine cardiovascular physiology to evaluate the consequences of low dose, chronic space radiation, or mixed field space radiation on the dynamics of the cardiac proteome and to understand how the radiation induced changes relate to cardiovascular function. In doing so, we will extend Yan et al.'s work by identifying a proteomic signature that predicts the development of permanent cardiovascular degeneration from a single low dose space radiation exposure. Further, we seek to evaluate whether the proteomic signatures differ when mice experience repeated exposures of space-like radiation or mixed field space radiation. This information will lead to a mechanistic understanding of the altered cellular and molecular processes contributing to the development of cardiovascular dysfunction at the organ and organismal level in scenarios better mimicking the space radiation environment. This information is needed to predict, monitor, and prevent cardiac damage during long term space flight.<br>Yan, X., et al., Cardiovascular risks associated with low dose ionizing particle radiation. PLoS One, 2014. 9(10): p. e110269. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | Limited information is known regarding the impact of chronic low level radiation on cardiovascular molecular biology and function both terrestrially and during extended space exploration. Our research is expected to provide information in regards to terrestrial and astronaut heath. Innovative technologies that may arise from our studies may include novel biomarkers predictive of cardiovascular susceptibility to chronic low level radiation as well as countermeasures that may be employed both on Earth as well as during space exploration. |
| **Task Progress:** | Five trips to Brookhaven National Laboratory (BNL) for mice experimentation have been planned for this grant (Fall 2016, Spring 2017, Fall 2017, Summer 2018, and Fall 2018). Thus far three trips have occurred (Fall 2016, Spring 2017, and Fall 2017).<br>Male C57B6 mice are purchased from Jackson Laboratories. Mice are shipped to Duke University Medical Center where at 5 months of age they undergo transthoracic echocardiograms to establish baseline cardiac function (pre IR echo). Parameters evaluated included (a) M-mode (done in both long and short axis), (b) Septal and posterior wall width in diastole, (c) End diastolic dimension and end systolic dimension, (d) aortic valve velocity, and (e) aortic ejection time (all measured and averaged over 3 consecutive beats). Echocardiogram images acquired are also evaluated for measurement of diastolic dysfunction and strain.<br><br>Mice are then shipped to the NASA Space Radiation Laboratory (NSRL) at BNL where they are subjected to single full body irradiation at 6 months of age under the following conditions: a) gamma (50cGy, 100cGy, 200cGy), b) 16O (15cGy, 25cGy, 50cGy/ 600 MeV/n), c) 56Fe (15cGy, 25cGy, 50cGy 1 GeV/n). Control (sham irradiated) animals also travel back and forth from Duke to NRSL and back to Duke in order to experience identical stressors as the irradiated mice. Evaluations include: a) serial transthoracic echocardiograms capturing all above parameters. These are done at 1, 2, 3, 7, and 9 months post irradiation; b) terminal pressure volume loop hemodynamic assessments; and c) mass spectrometry based proteomics assessments (quantitative, dynamic, and post-translational modification proteomics) of the cardiac proteome.<br><br>All studies are ongoing. Therefore, the data set is still preliminary and conclusions presented in this report should be considered preliminary.<br><br>To date, we have not observed a significant difference in any parameter evaluated that allows us to make a statement that cardiovascular function is affected at any time point, radiation type, or dose post irradiation compared to control sham irradiated control mice. |
| **Bibliography Type:** | Description: (Last Updated: 07/11/2023) |
| **Abstracts for Journals and Proceedings** | Bishawi M, Brown Z, Roan J, Bishawi M, Lee F, Abraham D, Isaac D, Mao L, Slaba T, Kidane Y, Thompson JW, Moseley MA, Truskey G, Dewhirst MW, Bowles DE. "Proteomic Signatures of Space Radiation Induced Cardiovascular Degeneration." 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.<br>2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. , Jan-2018 |
| **Abstracts for Journals and Proceedings** | Brown ZD, Bishawi M, Feger BJ, Carnell LS, Blattnig S, Bowles DE. "A Systematic Literature Review of Radiation-Induced Cardiovascular Disease." 2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018.<br>2018 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2018. , Jan-2018 |