

|   |   |                                       |   |
|---|---|---------------------------------------|---|
| <b>Fiscal Year:</b>                               | FY 2020   | <b>Task Last Updated:</b>             | FY 09/17/2020   |
| <b>PI Name:</b>                                   | Suzuki, Carolyn Ph.D.   |                                       |   |
| <b>Project Title:</b>                             | Tissue Sharing Project- Effects of Space Radiation on the Cardiac Mitochondrial Stress Response                               |                                       |   |
| <b>Division Name:</b>                             | Human Research  |                                       |   |
| <b>Program/Discipline:</b>                        |   |                                       |   |
| <b>Program/Discipline--Element/Subdiscipline:</b> | HUMAN RESEARCH--Radiation health  |                                       |   |
| <b>Joint Agency Name:</b>                         | <b>TechPort:</b>  | No                                    |   |
| <b>Human Research Program Elements:</b>           | (1) <b>SR:</b> Space Radiation  |                                       |   |
| <b>Human Research Program Risks:</b>              | (1) <b>Cardiovascular:</b> Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes |                                       |   |
| <b>Space Biology Element:</b>                     | None  |                                       |   |
| <b>Space Biology Cross-Element Discipline:</b>    | None  |                                       |   |
| <b>Space Biology Special Category:</b>            | None  |                                       |   |
| <b>PI Email:</b>                                  | <a href="mailto:suzukick@njms.rutgers.edu">suzukick@njms.rutgers.edu</a>  | <b>Fax:</b>                           | FY  |
| <b>PI Organization Type:</b>                      | UNIVERSITY  | <b>Phone:</b>                         | 973-972-1555  |
| <b>Organization Name:</b>                         | New Jersey Medical School- The State University of New Jersey Rutgers   |                                       |   |
| <b>PI Address 1:</b>                              | Department of Microbiology, Biochemistry and Molecular Genetics   |                                       |   |
| <b>PI Address 2:</b>                              | 225 Warren St E450S   |                                       |   |
| <b>PI Web Page:</b>                               |   |                                       |   |
| <b>City:</b>                                      | Neward  | <b>State:</b>                         | NJ  |
| <b>Zip Code:</b>                                  | 07103-3535  | <b>Congressional District:</b>        | 10  |
| <b>Comments:</b>                                  |   |                                       |   |
| <b>Project Type:</b>                              | Ground  | <b>Solicitation / Funding Source:</b> | 2016-2017 HERO<br>NNJ16ZSA001N-Crew Health<br>(FLAGSHIP, OMNIBUS). Appendix<br>A-Omnibus, Appendix B-Flagship |
| <b>Start Date:</b>                                | 07/01/2017  | <b>End Date:</b>                      | 06/30/2020  |
| <b>No. of Post Docs:</b>                          | 1   | <b>No. of PhD Degrees:</b>            | 1   |
| <b>No. of PhD Candidates:</b>                     |   | <b>No. of Master' Degrees:</b>        |   |
| <b>No. of Master's Candidates:</b>                |   | <b>No. of Bachelor's Degrees:</b>     |   |
| <b>No. of Bachelor's Candidates:</b>              |   | <b>Monitoring Center:</b>             | NASA JSC  |
| <b>Contact Monitor:</b>                           | Zawaski, Janice   | <b>Contact Phone:</b>                 |   |
| <b>Contact Email:</b>                             | <a href="mailto:janice.zawaski@nasa.gov">janice.zawaski@nasa.gov</a>  |                                       |   |
| <b>Flight Program:</b>                            |   |                                       |   |
| <b>Flight Assignment:</b>                         | NOTE: End date changed to 6/30/2020 per NSSC information (Ed., 12/4/19)   |                                       |   |
| <b>Key Personnel Changes/Previous PI:</b>         | May 2018 report: There are no personnel changes.  |                                       |   |
| <b>COI Name (Institution):</b>                    | Azzam, Edouard Ph.D. ( RUTGERS Biomedical and Health Sciences - New Jersey Medical School )                                   |                                       |   |
| <b>Grant/Contract No.:</b>                        | 80NSSC17K0113   |                                       |   |
| <b>Performance Goal No.:</b>                      |   |                                       |   |
| <b>Performance Goal Text:</b>                     |   |                                       |   |

|   |  |
|---|--|
| <b>Task Description:</b>                    | <p>Mitochondria are the powerhouses of the cell, which make up ~30% of the volume of cardiac myocytes. They provide the crucial energy supply needed for the heart to beat and to provide blood and oxygen throughout the body. The goal of this ground-based Tissue Sharing project is to determine the effects of low dose/low fluence space ionizing radiation on the mitochondrial stress response in the heart. We will examine heart tissue collected by our collaborator Dr. Edouard Azzam, whose current NASA-funded project is investigating "Oxidative Stress and the Cancer Risk of Space Radiation." His study employs 10 month-old male mice, which is an age that is equivalent to active astronauts who are between 35-55 years old. These mice are exposed to low mean absorbed doses of isovelocity (1 GeV/n) protons or high atomic number, high energy (HZE) particles, which are a component of galactic cosmic rays. Another group of mice are exposed to <math>^{137}\text{Cs}</math> gamma rays as reference radiation. Using these heart samples, we will employ histological techniques, as well as biochemical and molecular biological approaches to measure biomarkers of the mitochondrial stress response in heart in response to HZE particles and reference radiation. Cardiac inflammation and fibrosis will be examined histologically. Radiation-induced changes in mitochondrial DNA copy number and damage and mitochondrial RNA and protein expression will be measured. Space radiation has been shown to induce reactive oxygen species, which oxidatively damage nucleic acids, proteins, and lipids. We will also determine the relative protein levels and activity of crucial mitochondrial stress response proteins, which are expected to mitigate cardiac injury that may be caused by radiation-induced oxidative damage. The results of these experiments will fill knowledge gaps about radiation-induced degeneration or injury to cardiac mitochondria, and the adaptive stress response mechanisms, which potentially promote or mitigate potential risks to the heart.</p> |
| <b>Rationale for HRP Directed Research:</b> |  |
| <b>Research Impact/Earth Benefits:</b>      | <p>The mechanisms underlying radiation-associated cardiovascular and degenerative diseases are currently unknown. However, studies suggest that radiation-induced oxidative stressors promote cardiac dysfunction and injury. The identification and validation of biomarkers of cardiac oxidative stress and dysfunction are needed as they may provide surrogate markers of disease outcomes. Identifying the stressors as well as the stress response mediators will contribute to developing countermeasures to mitigate cardiac damage as a result of space radiation exposure.</p>   |
| <b>Task Progress:</b>                       | <p>We have made progress during the last year of this project. We have determined using cardiac tissue of mice exposed to space radiation, that after 2 weeks of exposure there is marked cellular stress response occurring in mitochondria and the endoplasmic reticulum (ER). We studied biomarkers of mitochondrial and ER stress response and observed increased gene and protein expression. This stress response was not observed after 15 months, in general. The importance of these findings is that mitochondrial and ER stress will induce a variety of signaling pathways regulating cellular defense systems and energy metabolism, which function to mitigate the potentially damaging effects of space radiation. Identifying the key players that mediate these cell stress defense mechanisms and signaling pathways will allow investigators to identify and optimize approaches for preventing and/or ameliorating physiological injury during space flight.</p>   |
| <b>Bibliography Type:</b>                   | Description: (Last Updated: )  |