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| <b>Fiscal Year:</b>                               | FY 2017                                                                                                                                                                        | <b>Task Last Updated:</b>             | FY 02/08/2017                                                                                                                                               |
| <b>PI Name:</b>                                   | Porada, Christopher Ph.D.                                                                                                                                                      |                                       |                                                                                                                                                             |
| <b>Project Title:</b>                             | Effects of Microgravity on the Risks of Space Radiation-induced Leukemogenesis                                                                                                 |                                       |                                                                                                                                                             |
| <b>Division Name:</b>                             | Space Biology                                                                                                                                                                  |                                       |                                                                                                                                                             |
| <b>Program/Discipline:</b>                        |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Program/Discipline--Element/Subdiscipline:</b> |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Joint Agency Name:</b>                         |                                                                                                                                                                                | <b>TechPort:</b>                      | No                                                                                                                                                          |
| <b>Human Research Program Elements:</b>           | None                                                                                                                                                                           |                                       |                                                                                                                                                             |
| <b>Human Research Program Risks:</b>              | None                                                                                                                                                                           |                                       |                                                                                                                                                             |
| <b>Space Biology Element:</b>                     | (1) Cell & Molecular Biology<br>(2) Animal Biology: Vertebrate                                                                                                                 |                                       |                                                                                                                                                             |
| <b>Space Biology Cross-Element Discipline:</b>    | (1) Immunology                                                                                                                                                                 |                                       |                                                                                                                                                             |
| <b>Space Biology Special Category:</b>            | (1) Translational (Countermeasure) Potential                                                                                                                                   |                                       |                                                                                                                                                             |
| <b>PI Email:</b>                                  | <a href="mailto:cporada@wakehealth.edu">cporada@wakehealth.edu</a>                                                                                                             | <b>Fax:</b>                           | FY                                                                                                                                                          |
| <b>PI Organization Type:</b>                      | UNIVERSITY                                                                                                                                                                     | <b>Phone:</b>                         | 336-713-1655                                                                                                                                                |
| <b>Organization Name:</b>                         | Wake Forest Institute for Regenerative Medicine                                                                                                                                |                                       |                                                                                                                                                             |
| <b>PI Address 1:</b>                              | 391 Technology Way                                                                                                                                                             |                                       |                                                                                                                                                             |
| <b>PI Address 2:</b>                              |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>PI Web Page:</b>                               |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>City:</b>                                      | Winston Salem                                                                                                                                                                  | <b>State:</b>                         | NC                                                                                                                                                          |
| <b>Zip Code:</b>                                  | 27157                                                                                                                                                                          | <b>Congressional District:</b>        | 5                                                                                                                                                           |
| <b>Comments:</b>                                  |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Project Type:</b>                              | GeneLab,GROUND                                                                                                                                                                 | <b>Solicitation / Funding Source:</b> | 2016 Space Biology (ROSBio)<br>NNH16ZTT001N-GeneLab. Appendix A:<br>Translational Systems Biology and Informatics<br>Research Using the GeneLab Data System |
| <b>Start Date:</b>                                | 02/01/2017                                                                                                                                                                     | <b>End Date:</b>                      | 01/31/2019                                                                                                                                                  |
| <b>No. of Post Docs:</b>                          |                                                                                                                                                                                | <b>No. of PhD Degrees:</b>            |                                                                                                                                                             |
| <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 ARC                                                                                                                                                    |
| <b>Contact Monitor:</b>                           | Sato, Kevin                                                                                                                                                                    | <b>Contact Phone:</b>                 | 650-604-1104                                                                                                                                                |
| <b>Contact Email:</b>                             | <a href="mailto:kevin.y.sato@nasa.gov">kevin.y.sato@nasa.gov</a>                                                                                                               |                                       |                                                                                                                                                             |
| <b>Flight Program:</b>                            |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Flight Assignment:</b>                         |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Key Personnel Changes/Previous PI:</b>         |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>COI Name (Institution):</b>                    | Almeida-Porada, Maria Graca M.D., Ph.D. ( Wake Forest University )<br>Walker, Steve Ph.D. ( Wake Forest University )<br>Wilson, Paul Ph.D. ( University of California, Davis ) |                                       |                                                                                                                                                             |
| <b>Grant/Contract No.:</b>                        | NNX17AE49G                                                                                                                                                                     |                                       |                                                                                                                                                             |
| <b>Performance Goal No.:</b>                      |                                                                                                                                                                                |                                       |                                                                                                                                                             |
| <b>Performance Goal Text:</b>                     |                                                                                                                                                                                |                                       |                                                                                                                                                             |

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| <b>Task Description:</b>                    | <p>We will specifically be making use of data generated as part of GeneLab experiment sets GLDS-53, GLDS-55, and GLDS-25 as the basis for the novel hypothesis to be tested in the current proposal: microgravity (<math>\mu\text{G}</math>) acts in concert with solar particle event (SPE) and galactic cosmic ray (GCR) radiation to produce deleterious effects on the human hematopoietic system, which may lead to an enhanced risk of leukemogenesis, as a result of both increased genomic damage to cells of the hematopoietic system, and a reduced ability of the immune system to recognize and clear hematopoietic cells that have undergone malignant transformation as a result of exposure to SPE/GCR radiation and conditions of microgravity. Data generated from the afore-mentioned GeneLab studies support this hypothesis, as these data have shown that <math>\mu\text{G}</math>: 1) induces higher levels of spontaneous DNA damage in human hematopoietic cells; 2) markedly alters the ability of mature human immune cells to respond appropriately to stimuli; 3) diminishes the ability of human lymphocytes to efficiently repair DNA damage in response to ionizing radiation; and 4) leads to alterations in the levels of multiple miRNAs that have been implicated in a variety of human hematopoietic malignancies. We have also generated a wealth of data to support the hypothesis that <math>\mu\text{G}</math> and space radiation likely act synergistically to increase astronaut risk of leukemogenesis during a prolonged mission beyond LEO (low Earth orbit). In the present proposal, we will build upon these data by performing studies to directly test the ability of <math>\mu\text{G}</math> to increase the risk of leukemic transformation in human hematopoietic stem/progenitor cells (HSC), while simultaneously reducing the ability of generated immune cells from recognizing and removing any malignant clones that arise.</p> |
| <b>Rationale for HRP Directed Research:</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Research Impact/Earth Benefits:</b>      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <b>Task Progress:</b>                       | New project for FY2017.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>Bibliography Type:</b>                   | Description: (Last Updated: 01/30/2023)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |