Fiscal Year:	FY 2020	**Task Last Updated:**	FY 06/24/2020
PI Name:	Porada, Christopher Ph.D.		
Project Title:	Effects of Microgravity on the Risks of Space Radiation-induced Leukemogenesis		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology (2) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Immunology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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City:	Winston Salem	**State:**	NC
Zip Code:	27157	**Congressional District:**	5
Comments:			
Project Type:	Ground,NASA GeneLab	**Solicitation / Funding Source:**	2016 Space Biology (ROSBio) NNH16ZTT001N-GeneLab. Appendix A: Translational Systems Biology and Informatics Research Using the GeneLab Data System
Start Date:	02/01/2017	**End Date:**	01/31/2020
No. of Post Docs:	1	**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	1
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	2	**Monitoring Center:**	NASA ARC
Contact Monitor:	Griko, Yuri	**Contact Phone:**	650-604-0519
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Flight Program:			
Flight Assignment:	NOTE: Extended to 1/31/2020 per F. Hernandez/ARC (Ed., 7/23/19) NOTE: Extended to 7/31/2019 per F. Hernandez/ARC (Ed., 2/14/19)		
Key Personnel Changes/Previous PI:	June 2020 report: Jonathan Diaz, a Master's Biomedical Engineering student joined the project during this past year.		
COI Name (Institution):	Almeida-Porada, Maria Graca M.D., Ph.D. (Wake Forest University) Walker, Steve Ph.D. (Wake Forest University) Wilson, Paul Ph.D. (University of California, Davis)		
Grant/Contract No.:	NNX17AE49G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	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 (μG) 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 aforementioned GeneLab studies support this hypothesis, as these data have shown that μG: 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 μG 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 μG 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.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our research has thus far revealed that conditions of microgravity lead to marked alterations in the ability of human hematopoietic stem/progenitor cells (HSC) to repair DNA double strand breaks (DSBs) that are characteristic of the damage that occurs following exposure to ionizing radiation. Moreover, microgravity also appears to impair the ability of human HSC to generate functional dendritic cells, which act as critical sentinels within the immune system, detecting infectious invaders and cells that have undergone malignant transformation, and alerting/priming immune effectors to eliminate these threats. Further adding to these deleterious effects, we have also found that microgravity negatively affects the ability of human natural killer (NK) cells to recognize and lyse human leukemic cells. Taken together, our results to date have shown that conditions of microgravity present during spaceflight could add to the risks of leukemogenesis as a result of exposure to space radiation, both by impairing the ability of human HSC to repair the induced damage and by crippling the generation and function of the immune cells needed to recognize and eliminate cells damaged by the radiation. An understanding of the mechanism(s) by which microgravity affects and impairs these different processes could lead to the development of novel methods to target and augment these pathways, and thereby enhance the processes of DNA repair and anti-tumor immunity. Such developments could have a profound impact on the treatment of cancer and on the lives of patients suffering from this disease.
Task Progress:	We have now finished writing the manuscript detailing the effects microgravity exerts on the plasticity/differentitative potential of human mesenchymal stromal cells, unveiling their latent ability to give rise to novel tissues and cell types upon transplantation in vivo. We have also finished gathering all necessary data to prepare a manuscript detailing all of our findings regarding the impact microgravity exerts on human NK cell activity and the ability of these critical immune cells to recognize and lyse human leukemic cells. These findings support our initial hypothesis that conditions of microgravity may add to the risk of leukemogenesis due to exposure to space radiation by knocking down the ability of the immune system to recognize and eliminate malignant hematopoietic clones that arise.
Bibliography Type:	Description: (Last Updated: 01/30/2023)
Abstracts for Journals and Proceedings	Kuhlman BM, Almeida-Porada G, Porada C. "Effects on Anti-Leukemic Activity of Human Natural Killer Cells in a Continuous Microgravity Environment." Presentation at 35th Annual Meeting of the American Society for Gravitational and Space Research, Denver, CO, November 20-23, 2019. 35th Annual Meeting of the American Society for Gravitational and Space Research, Denver, CO, November 20-23, 2019. , Nov-2019
Abstracts for Journals and Proceedings	Kuhlman BM, Almeida-Porada G, Porada CD. "Microgravity Impairs Anti-Leukemic Activity of Human NK Cells." Presentation at 2019 International Space Station Research and Development Conference (ISSRDC), Atlanta, GA, July 29-August 1, 2019. 2019 International Space Station Research and Development Conference (ISSRDC), Atlanta, GA, July 29-August 1, 2019. , Jul-2019