Fiscal Year:	FY 2023	**Task Last Updated:**	FY 09/28/2023
PI Name:	Simpson, Richard Ph.D.		
Project Title:	The Impact of an ISS Mission on the Anti-Viral and Functional Properties of NK-cells, T-cells, B-cells and Dendritic Cells		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Immune**:Risk of Adverse Health Event Due to Altered Immune Response		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	rjsimpson@email.arizona.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	713-397-0121
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City:	Tucson	**State:**	AZ
Zip Code:	85721-0001	**Congressional District:**	3
Comments:	NOTE: Formerly at University of Houston until September 2017 move to University of Arizona.		
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-MIXEDTOPICS. Appendix E: Behavioral Health & Human Health Countermeasures Topics
Start Date:	06/01/2016	**End Date:**	05/31/2024
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**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:	Stenger, Michael	**Contact Phone:**	281-483-1311
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Flight Program:	ISS		
Flight Assignment:	NOTE: End date changed to 5/31/2024 (original end date was 5/31/2019) per T. Sirmons/JSC (Ed., 5/16/23) NOTE: End date changed to 12/31/2022 (original end date was 5/31/2019) per NSSC information (Ed., 1/17/22) NOTE: End date changed to 12/31/2021 (original end date was 5/31/2019) per NSSC information (Ed., 2/22/21) NOTE: End date changed to 12/31/2020 (original end date was 5/31/2019) per NSSC information (Ed., 7/2/19)		
Key Personnel Changes/Previous PI:	Per the PI, Dr. Guillaume Spielmann is no longer involved in the study (Ed., 9/28/23)		
COI Name (Institution):	Bigley, Austin Ph.D. (University of Houston) Laughlin, Mitzi Ph.D. (University of Houston) LaVoy, Emily Ph.D. (University of Houston) Rezvani, Katayoun M.D., Ph.D. (University of Texas M D Anderson Cancer Center)		
Grant/Contract No.:	NNX16AG02G		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	NOTE: This is an integrated project consisting of Dr. Brian Crucian's "Functional Immune Alterations, Latent Herpesvirus Reactivation, Physiological Stress, and Clinical Incidence Onboard the International Space Station" directed research; and Dr. Richard Simpson's "The Impact of an ISS Mission on the Anti-Viral and Functional Properties of NK-cells, T-cells, B-cells and Dendritic Cells," Dr. Kanokporn Rithidech's "Effects of Space Flights on the Proteome of Astronauts' Plasma," and Dr. Honglu Wu's "DNA Damage in the ISS Astronaut's Lymphocytes and Their Association with Stress-Induced Immune Dysfunction" solicited research. Immune system dysregulation is known to occur after both short and long-duration spaceflight, which may leave astronauts at risk of an adverse health event during exploration-class missions. The consistent and profound observation that spaceflight induces latent viral reactivation is a strong indication that immunity is compromised in flight. Moreover, the viruses themselves pose a very real risk to the crew and may compromise their safety and jeopardize mission success. It is pertinent therefore to comprehensively determine how spaceflight impacts the anti-viral properties of the immune system so that effective countermeasures can be developed to mitigate these risks. The parent 'Functional Immune' study will markedly advance our understanding in this area and the present proposal aims to contribute by determining the impact of an International Space Station (ISS) mission of the anti-viral properties of NK-cells and T-cells, and the function of B-cells and dendritic cells (DCs). In our ongoing ISS flight study ('Salivary Markers'), we have found that NK-cell function is drastically impaired during flight and that latent viral reactivation still occurs despite a robust expansion of viral-specific T-cells. It is possible, therefore, that it is the anti-viral capabilities of T-cells and NK-cells that are compromised in flight and we propose to address this question here using both standard and cutting-edge analytical techniques (CyTOF). We will also address the paucity of spaceflight data on B-cells and dendritic cells by assessing B-cell responses to viral peptide stimulation and the differentiation of monocytes to dendritic cells, their antigen uptake capabilities, and ability to activate and expand autologous viral-specific T-cells. All assays will be performed in crewmembers and healthy controls before, during, and after spaceflight using blood volumes that are conducive to the restrictions associated with flight experiments. The studies described in this proposal will make a significant contribution to the parent 'Functional Immune' study and will allow us to determine if spaceflight affects the anti-viral properties of cellular and humoral-mediated immunity. On conclusion of this study, it is expected that all 'immune risks' will be identified and the focus can shift to the development of countermeasures to preserve crew 'immune health' during future exploration-class spaceflight mission.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	The study was initiated in August 2016. As of July 2023, we have completed sample collection for 11 astronauts and 11 controls. A total of 5 participants (3 astronauts and 2 controls) were dropped from the study after the L-45/L-180 sample collection for logistical reasons. Dr. LaVoy at the University of Houston has completed sample analysis of the monocyte-dendritic cell differentiation function. Data are currently being analyzed. Dr. Rezvani's group at MD Anderson Cancer Center were responsible for detailed immunophenotyping and NK-cell functional assays. They have completed all of the immunophenotyping work and have sent the raw data to the PI (Dr. Simpson) for analysis. While the immunophenotyping work was successful, they did, however, report problems with cell viability for many samples, most likely due to the samples being 'aged' for 48h prior to cryopreservation. This has, unfortunately, limited the number of samples we have been able to get usable NK-cell functional data from. Cryopreserved samples were shipped to the PI's laboratory at the University of Arizona for the analysis of effector lymphocyte function against a range of tumor target cells. While we had similar problems with cell viability, we were able to expand effector lymphocyte populations in vitro (using zoledronic acid and IL-2) and test their function against multiple tumor target cells in a subset of samples. These data are currently being analyzed.
Bibliography Type:	Description: (Last Updated: 09/27/2023)
Articles in Peer-reviewed Journals	Mylabathula PL, Li L, Bigley AB, Markofski MM, Crucian BE, Mehta SK, Pierson DL, Laughlin MS, Rezvani K, Simpson RJ. "Simulated microgravity disarms human NK-cells and inhibits anti-tumor cytotoxicity in vitro. " Acta Astronaut. 2020 Sep;174:32-40. http://www.sciencedirect.com/science/article/pii/S009457652030151X , Sep-2020
Articles in Peer-reviewed Journals	Kunz HE, Agha NH, Hussain M, LaVoy EC, Smith KA, Mylabathula P, Diak D, Baker FL, O'Connor DP, Bond RA, Katsanis E, Bollard CM, Simpson RJ. "The effects of ß1 and ß1+2 adrenergic receptor blockade on the exercise-induced mobilization and ex vivo expansion of virus-specific T cells: Implications for cellular therapy and the anti-viral immune effects of exercise. " Cell Stress Chaperones. 2020 Aug 10;25:993-1012. https://doi.org/10.1007/s12192-020-01136-7 ; PMID: 32779001; PMCID: PMC7591642 , Aug-2020
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Articles in Peer-reviewed Journals	Agha NH, Mehta SK, Rooney BV, Laughlin MS, Markofski MM, Pierson DL, Katsanis E, Crucian BE, Simpson RJ. "Exercise as a countermeasure for latent viral reactivation during long duration space flight." FASEB J. First published: 03 January 2020. https://doi.org/10.1096/fj.201902327R ; PubMed PMID: 31908052 , Jan-2020
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Articles in Peer-reviewed Journals	Kunz HE, Spielmann G, Agha NH, O'Connor DP, Bollard CM, Simpson RJ. "A single exercise bout augments adenovirus-specific T-cell mobilization and function." Physiol Behav. 2018 Oct 1;194:56-65. Epub 2018 Apr 30. https://doi.org/10.1016/j.physbeh.2018.04.035 ; PubMed PMID: 29723594 , Oct-2018