Fiscal Year:	FY 2017	**Task Last Updated:**	FY 06/13/2017
PI Name:	Simpson, Richard Ph.D.		
Project Title:	Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:			
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:	rjcimpson@email.arizona.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	713-397-0121
Organization Name:	University of Arizona		
PI Address 1:	College of Agriculture and Life Sciences; College of Medicine		
PI Address 2:	1177 E. Fourth Street, Room 308, Shantz Building		
PI Web Page:			
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:**	2010 Crew Health NNJ10ZSA003N
Start Date:	11/03/2011	**End Date:**	05/02/2018
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	5	**No. of Master' Degrees:**	2
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Vos, Jessica	**Contact Phone:**	
Contact Email:	jessica.r.vos@nasa.gov		
Flight Program:	ISS		
Flight Assignment:	ISS Flight Definition phase NOTE: End date changed to 5/2/2018 per NSSC information (Ed., 11/22/17) NOTE: End date changed to 11/2/2017 per NSSC information (Ed., 1/23/17) NOTE: End date changed to 11/2/2016 per NSSC information (Ed., 7/17/15) NOTE: Gap Immune05 deleted per IRP Rev E (Ed., 3/24/14)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Clarke, Mark Ph.D. (University of Houston) Crucian, Brian Ph.D. (Wyle Laboratories, Inc.) O'Connor, Dan Ph.D. (University of Houston) Pierson, Duane Ph.D. (NASA Johnson Space Center) Spielmann, Guillaume Ph.D. (University of Houston)		
Grant/Contract No.:	NNX12AB48G		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	Immune system dysregulation has been documented during and after spaceflight, but it is not known if these changes increase infection susceptibility or pose a significant health risk to crewmembers. Inherent problems with current in-flight research are small sample sizes and the difficulty to control for the many confounding factors that impact on the immune system. As such, it is not known if changes in immunity are due to the microgravity environment per se, or to the stressors associated with landing and re-adaptation to the 1G environment. The present project proposes a Flight Definition investigation, utilizing a longitudinal repeated measures design to determine the effects of long-term exposure to microgravity on a host of salivary antimicrobial proteins (AMPs) associated with innate host immune defense, whilst also considering the impact of other acute stressors such as launch, Soyuz landing, and extravehicular activity (EVA). Saliva samples will be collected from crewmembers selected for International Space Station (ISS) mission and ground-based controls at bi-weekly intervals for 6 months prior to flight, during the 6-month period on the ISS, and for 1 month on return to Earth. Saliva sampling was selected because it is an excellent biological fluid with which to detect broad-spectrum biomarkers of front-line host immune defense and is suitable for the spaceflight environment. Attempts will also be made to establish relationships between AMPs and other stressors associated with spaceflight (i.e., mood state disturbances, circadian desynchronization, sleep loss/disruption, stress biomarkers) using serial data. Finally, blood samples will be collected before and after the mission to determine the impact of spaceflight on cellular aspects of innate immunity. Given the potential of salivary AMPs to serve as an indicator of weakened immunity during spaceflight, this project will serve as a foundation for future countermeasure developments and technological advances to detect real time changes during subsequent lunar or Mars missions.		
Rationale for HRP Directed Research:			
Research Impact/Earth Benefits:	This project will improve our understanding on how acute and long-term stress impacts on multiple aspects of the immune system. These research findings will be useful to determine if any immune related health problems might exist in individuals exposed to stressful environments (i.e., soldiers, caregivers).		
Task Progress:	Study Progress: The study was initiated in September 2012 and data collection started in March 2013. As of November 2016, we have enrolled the required number of subjects giving us a sample size of eight crewmembers and seven ground-based controls including a crewmember who completed a 1-year ISS mission. Baseline blood, urine, and saliva samples have been collected from all crewmembers and ground-based control subjects. All crewmembers and ground-based controls have completed all experimental procedures. We have obtained in flight samples and ambient blood returns from all enrolled crewmembers. All baseline and in flight ambient blood samples were processed and analyzed successfully. Saliva, urine, and blood plasma samples have been stored at -80°C until analysis. Frozen samples are currently being analyzed for all subjects. The IRB (Institutional Review Board) protocol was renewed in July 2014. Publications and Presentations: Our validation work for this project allowed us to assess NK-cell function in the context of latent cytomegalovirus infection, age, and exercise. This led to publications by Bigley et al. (2016) in the journals Cellular Immunology and Clinical and Experimental Immunology, and Bigley et al. (2015) in Oxidative Medicine and Cellular Longevity and Brain, Behavior, and Immunity. We also published a manuscript in European Journal of Applied Physiology, which stemmed from the validation work of our saliva assays for this project (Kunz et al., 2015). In addition, Spielmann et al. (2016) used the validation work from the viral T-cell quantification component of the 'Salivary Markers' study for a publication in the Nature affiliated journal Scientific Reports. NASA funding was acknowledged in all of these publications. The work supported by this research grant was presented at the National Space Biomedical Research Institute (NSBRI) Summer Bioastronautics Institute and American College of Sports Medicine annual meeting in July 2016 and the Human Research Program Investigator's Workshop in February 2016. Current and Future Work: The study protocol is ongoing. By the end of year 5, we expect to have all data processed and analyzed for all crewmembers and ground-based controls. The remainder of FY17 will be spent analyzing frozen biological samples, interpreting data, and producing scientific papers. Applications and Acquisition of Funding: Work on the 'Salivary Markers' project has allowed us to apply for further research funding. We have received additional research funding for space life science specific research projects but also from the National Institutes of Health (NIH). The latter project requires us to assess the impact of latent CMV infection on NK-cell phenotype and cytotoxicity in multiple myeloma patients following autologous stem cell transplantation. Our ideas for this project and preliminary data stemmed from the 'Salivary Markers' project. We also received a student research grant from the American College of Sports Medicine to analyze archived data related to astronaut fitness levels and latent viral reactivation. Bibliography The following are some of the published papers supported by this work (see also Task Book Bibliography below): Bigley AB, Rezvani K, Shah N, Sekine T, Spielmann G, Pistillo M, Agha N, Kunz H, LaVoy ECP, Bollard CM & R.J. Simpson (2016). Latent CMV infection enhances anti-tumor cytotoxicity through accumulation of NKG2C+ NK-cells in healthy humans. Clinical and Experimental Immunology, 185, 239-251. Bigley AB, Spielmann G, Agha N, O'Connor, D.P. & R.J. Simpson (2016). 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Simpson (2015) Fitness level impacts salivary antimicrobial responses to a single bout of cycling exercise. European Journal of Applied Physiology, 115, 1015-27. Spielmann, G., Bollard, C.M., Kunz, H., Hanley, P.J. & R.J. Simpson (2016). A single exercise bout enhances the ex vivo manufacture of viral-specific T-cells from healthy donors: implications for allogeneic adoptive transfer immunotherapy. Scientific Reports, 16; 6:25852. The following presentations were delivered and supported by this work: Simpson, R.J., Bigley, A.B., Spielmann, G., Kunz, H.E., Agha, N., Baker, F., Rooney, B., Mylabathula, P.L., Graff, R.M., Crucian, B.E., Laughlin, M., Mehta, S.K., & D.L. Pierson. Long duration spaceflight impairs NK-cell function in astronauts. ACSM Annual Meeting, Boston, MA, USA, May 31st – June 4th, 2016. Bigley, A.B. The role of microgravity and stress-related humoral factors in dysregulated NK-cell function during spaceflight. NSBRI Summer Bioastronautics Institute, Houston, TX, USA, May 31st – June 3rd, 2016. Bigley, A.B. The effects of exercise and spaceflight on NK-cells. Invited Presentation at University of Calgary, Human Performance Laboratory Seminar, Sports Medicine Centre, Calgary, AB, Canada, March 30th – March 31st, 2016. Mylabathula, P.L., Bigley, A.B., & R.J. Simpson. Simulated microgravity 'disarms' human NK-cells and inhibits cytotoxicity. HRP Investigators' Workshop, Galveston, TX, USA, February 8th – February 11th, 2016.		

	Simpson, R.J. Immune responses to prolonged spaceflight: the 'Salivary Markers' study. NASA Human Research Program Investigator's Workshop, Galveston, TX, USA, Feb 8th – Feb 11th 2016. Interviews/Press Releases: Simpson, R.J. interviewed for: Want a stronger immune system? Try hitting the gym. NBC Nightly News with Lester Holt: http://www.nbcnews.com/ Simpson, R.J. interviewed for: After record 340 days in space, Scott Kelly is coming down to Earth by Kim McGuire. Houston Chronicle, February 27, 2016: http://www.houstonchronicle.com/ Simpson, R.J. Article in the Houston Chronicle regarding Dr Simpson's NASA-funded research: <a target="_blank" href="http://www.houstonchronicle.com/local/history/city-of-possibilities/article/Trying-to-make-space-exploration-a-healthier-10415337.php?t=cd985e8469438d9cbb&cmpid=email-premium#photo-11641970">http://www.houstonchronicle.com/<
Bibliography Type:	Description: (Last Updated: 09/27/2023)
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