

Fiscal Year:	FY 2019	Task Last Updated: FY 08/31/2018	
PI Name:	Spielmann, Guillaume Ph.D.		
Project Title:	The Impact of Long Duration Spaceflight on the Function of B-cells and Biomarkers of Inflammation		
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 In Mission Impacts, Adverse Health Events or Long-Term Health Impacts due to Altered Immune Response		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	70803-0001	Congressional District:	6
Comments:			
Project Type:	Flight	Solicitation / Funding Source:	2015-16 HERO NNJ15ZSA001N-Crew Health (FLAGSHIP, NSBRI, OMNIBUS). Appendix A-Crew Health, Appendix B-NSBRI, Appendix C-Omnibus
Start Date:	11/01/2016	End Date:	10/31/2018
No. of Post Docs:	0	No. of PhD Degrees:	0
No. of PhD Candidates:	0	No. of Master' Degrees:	0
No. of Master's Candidates:	0	No. of Bachelor's Degrees:	0
No. of Bachelor's Candidates:	0	Monitoring Center:	NASA JSC
Contact Monitor:	Norsk, Peter	Contact Phone:	
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Flight Program:	ISS		
Flight Assignment:	Postflight sample analysis NOTE: Extended to 10/31/2018 per NSSC information (Ed., 9/12/18)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Campbell, John Ph.D. (Louisiana State University and A&M College) Crucian, Brian Ph.D. (NASA Johnson Space Center) Laughlin, Mitzi Ph.D. (University of Houston) Simpson, Richard Ph.D. (University of Houston)		
Grant/Contract No.:	NNX17AB16G		
Performance Goal No.:			
Performance Goal Text:			

<p>Task Description:</p>	<p>Long duration spaceflights reportedly induce dysregulation of the immune system, which is considered a risk to astronaut safety and mission success. Recent studies have examined the impact of long-duration spaceflight on specific markers of adaptive and innate immunity, but no study to date has comprehensively evaluated humoral immunity and serological markers of B-cell function. The aim of this study was to characterize changes in B-cell numbers and phenotypes, along with plasma immunoglobulins and polyclonal free light chains (FLC) – near ‘real-time’ biomarkers of immunoglobulin synthesis – in response to a ~6-month mission to the International Space Station (ISS).</p> <p>Methods: Whole blood and plasma samples were collected before flight, during ("Early flight", "Mid-flight" and "Late flight"), immediately upon return, and during a recovery period (R+18, R+30/R+33 and R+60/R+66) from 23 ISS crewmembers and 6 healthy ground-based controls. Total plasma immunoglobulin (Ig) and FLC levels were measured throughout the duration of the mission</p> <p>Results: There was no effect of spaceflight on kappa FLC concentrations ($p>0.05$), and only a marginal reduction was observed in lambda FLC levels upon return to Earth ($p<0.05$). Furthermore, IgG and IgM remained unchanged during and after spaceflight, when compared to pre-flight values ($p>0.05$). Of note, plasma IgA concentrations were elevated in-flight when compared to baseline and recovery values ($p<0.05$).</p> <p>Conclusion: These results indicate that B-cell homeostasis is maintained during long duration spaceflight in astronauts, advocating for potential in-flight vaccination as viable countermeasures against viral reactivation during exploration-class missions.</p>
<p>Rationale for HRP Directed Research:</p>	
<p>Research Impact/Earth Benefits:</p>	<p>This project bolstered our understanding of how physical and psychological stressors impact our immune system. We found that spaceflight-induced physical and psychological stressors led to an increase in serum IgA concentration, and that B-cell and plasma cell homeostasis were not affected by long duration spaceflight. Furthermore, this project highlighted the use of novel biomarkers of immune activation, plasma Free Light Chains, to monitor immune function in special populations (children, first responders, soldiers, elderly, etc.).</p>
<p>Task Progress:</p>	<p>The task is completed.</p> <p>This study investigated the impact of long duration spaceflight on plasma immunoglobulin Free Light Chains (FLC), IgA, IgG, and IgM. Additionally, we correlated changes in plasma FLC with salivary FLC, to identify non-invasive methods aimed at assessing changes in immune function during spaceflight.</p> <p>There was no change in plasma IgG and IgM concentrations in astronauts and ground-based controls throughout the mission ($p>0.05$). Astronauts exhibited an increase in plasma IgA during flight, when compared to baseline values (L-60/L-45). Upon return on Earth, plasma IgA concentrations decreased from in-flight levels, and were back to pre-flight values (L-60/L-45) during recovery (R+30) ($p=0.047$). All changes withstood adjustment for latent viral reactivation status and DNA load, along with estimated Glomerular Filtration Rate, an estimated measure of kidney function.</p> <p>There was no effect of spaceflight on plasma Kappa FLC ($p>0.05$), and only a minor decrease in the concentration of plasma Lambda FLC was observed immediately upon return on Earth (R+0) in crewmembers when compared to in-flight plasma Lambda FLC concentrations (Early: $p=0.03$; Mid: $p=0.005$ and Late/R-1: $p=0.012$). The preferential reduction in plasma Lambda FLC at landing without any change in plasma Kappa FLC concentration led to a minor decrease in Kappa/Lambda ratio at the Mid-flight timepoint when compared to baseline L-60/L-45 and return R+0 and R+30 / ratio ($p_{L-45}=0.029$; $p_{R+0}=0.037$; $p_{R+18}=0.053$; $p_{R+33}=0.037$). As plasma FLC levels can be impacted by altered production from plasma cells and/or impaired clearance from renal metabolism, Cystatin C was measured to calculate estimated glomerular filtration rate (eGFR) and account for variation in renal function during spaceflight. There was no change in kidney function during flight ($p>0.05$), however post-flight eGFR values (R+30) were significantly lower than pre-flight values (L-60/L-45) ($p=0.015$). Subtle changes in plasma FLC withstood adjustment for eGFR.</p> <p>There was no effect of spaceflight on salivary flow rate (mL/min), and salivary Kappa FLC (mg.L) level ($p<0.05$). Interestingly however, reductions in salivary Lambda FLC (mg.L) levels upon return on Earth, mimicked changes observed in plasma FLC levels. As such, real-time measurement of salivary FLC could be used as a less-invasive alternative to assessing changes in immune function than plasma FLC measurements.</p> <p>In conclusion, this is the first study to comprehensively show that long-duration spaceflight in human astronauts has no – or very limited – effect on plasma cell antibody output. These important results suggest that plasma immune competency is maintained in microgravity, and that future in-flight vaccine-based countermeasures are likely to be efficient at further protecting astronauts from immune dysregulation and symptomatic latent viral reactivations during prolonged exploration class missions.</p> <p>A manuscript detailing the work supported by this research grant is currently under review by the Journal of Applied Physiology.</p>
<p>Bibliography Type:</p>	<p>Description: (Last Updated: 02/03/2020)</p>
<p>Abstracts for Journals and Proceedings</p>	<p>Spielmann G, Campbell J, Crucian BE, Laughlin MS, Simpson RJ. "The Impact of Long Duration Spaceflight on the Function of Plasma Cells." American College of Sports Medicine 65th Annual Meeting, Minneapolis, MN, May 29-June 2, 2018.</p> <p>Medicine & Science in Sports & Exercise. 2018 May;50(Suppl 1 5S):336.</p> <p>https://doi.org/10.1249/01.mss.0000536188.85345.86 , May-2018</p>
<p>Articles in Peer-reviewed Journals</p>	<p>Spielmann G, Agha NH, Kunz HE, Simpson RJ, Crucian BE, Mehta SK, Laughlin M, Campbell J. "B-cell homeostasis is maintained during long duration spaceflight." J Appl Physiol (1985). 2019 Feb 1;126(2):469-476. Epub 2018 Nov 29.</p> <p>https://doi.org/10.1152/japplphysiol.00789.2018 ; PubMed PMID: 30496712; PubMed Central PMCID: PMC6397409 , Feb-2019</p>