Fiscal Year:	FY 2022	**Task Last Updated:**	FY 05/07/2022
PI Name:	Gonzalez-Juarbe, Norberto		
Project Title:	Understanding the Impact of Hypobaric Hypoxia and Confinement Stress on Intestinal Immunity and Host-Microbiome Interactions		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (2) **Hypoxia**:Risk of Reduced Crew Health and Performance Due to Hypoxia [inactive]		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Rockville	**State:**	MD
Zip Code:	20850-6380	**Congressional District:**	6
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2019 HERO 80JSC018N0001-HHCHFBP: Human Health Countermeasures, Human Factors, Behavioral Performance. Appendix D
Start Date:	05/10/2021	**End Date:**	05/10/2023
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:	Whitmire, Alexandra	**Contact Phone:**	
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 05/10/2023 per NSSC information (Ed., 6/6/22).		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Lorenzo, Hernan Ph.D. (National Institute of Health)		
Grant/Contract No.:	80NSSC21K1116		
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Task Description:	Background: It is expected that future crewed space missions involving extravehicular activities (EVA) will require novel EVA architectures including a slightly hypobaric hypoxic cabin atmosphere (8.2 psia, 34% O2). Humans are well-adapted to live at Earth altitudes with similar O2 partial pressures. However, it is not clear if the combined effect of hypobaric hypoxia (HH) with other space-associated stressors such as microgravity, altered circadian rhythm or confinement, will have a synergistic detrimental effect on crew health. Several studies suggest that some hypoxic conditions may affect the host immune response and gut microbiota (1-4). Also, healthy individuals exposed for ~1-year to the HH environment of the Antarctic Concordia station show immune sensitization (5, and Life Sciences Data Archive (LSDA) experiment: Confinement and Hypobaric Hypoxia on Immunity in the Antarctic Concordia Environment (CHOICE)). The Antarctic Neumayer and Concordia stations represent a high-fidelity spaceflight ground analog, reflecting some conditions of long-duration space missions, such as extreme isolation and altered circadian rhythm. Neumayer is a coastal base located at the sea level. Concordia resides 1,000 km inland at an altitude of 3,232 m and therefore, has a HH environment. Herein, we propose to investigate the combined impact of long-term HH and isolation on the human microbiome and immune system homeostasis in the intestinal tract by using an existing collection of stool specimens derived from 34 healthy individuals that spent ~1-year at either the Concordia or Neumayer stations. Hypothesis: We hypothesize that the combined effect of HH and confined environment stressors will induce changes to the human intestinal immune response and gut microbiota in the context of microbial diversity, activity, composition, and protein post-translational modifications (PTMs, such as acetylation and oxidation), which tend to be associated with impaired host metabolism, immune response and aggravated cellular damage (1, 2). Aims: Aim 1. Characterization of gut microbiota and immune profiles of Concordia and Neumayer crewmembers. 16S rRNA sequencing and mass spectrometry based meta-proteomic approaches will be employed to investigate both the microbial composition and host immune responsive proteins. Aim 2. Global profiling of gut protein PTMs. Enrichment (e.g., antibody-based) and quantitative (e.g., chemical labeling) strategies will be utilized to examine protein acetylation and oxidation, which will be correlated to host metabolism and oxidative damage. Methods: Stool specimens were collected from healthy individuals before, during, and after a ~1-year stay at the Neumayer or Concordia stations and kept frozen for further analysis at the J. Craig Venter Institute. We will apply the well-established protocols in our laboratories to extract genomic DNA and proteins from stool samples for taxonomic profiling and proteomic analyses. Deliverables: A detailed qualitative and quantitative analysis of the impact of Neumayer and Concordia extreme conditions and HH on human gut microbiome and host immunity, interpretation of identified microbial PTMs, and assessment of potential risks to human health. Significance: The crosstalk between the intestinal microbiome and immune system is essential to human health. Understanding the response of intestinal microbiota and immunity to extreme stress conditions at the taxonomic, metaproteome and PTM levels will offer novel insights into the immune system-microbiome interactions during HH and isolation conditions, and may set the bases for potential therapeutic targets for spaceflight-induced immune and microbial dysregulation. References: 1. Zhang X, Ning Z, Mayne J, Deeke SA, Walker K, Farnsworth CL, Stokes MP, Mack D, Stintzi A, Figeys D. Deep characterization of the protein lysine acetylation in human gut microbiome and its alterations in patients with Crohn's disease. Systems Biology. bioRxiv; 2019. p. 337 2. Berlett BS, Stadtman ER. Protein oxidation in aging, disease, and oxidative stress. J Biol Chem. 1997 Aug 15;272(33):20313–20316. PMID: 9252331
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2021.
Bibliography Type:	Description: (Last Updated:)