Fiscal Year:	FY 2023	**Task Last Updated:**	FY 03/15/2023
PI Name:	Rithidech, Kanokporn Ph.D.		
Project Title:	Effects of Space Flights on the Proteome of Astronauts' Plasma		
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:	Kanokporn.Rithidech@sbumed.org	**Fax:**	FY (631) 444-3424
PI Organization Type:	UNIVERSITY	**Phone:**	(631) 444-3446
Organization Name:	State University New York at Stony Brook		
PI Address 1:	Department of Pathology		
PI Address 2:	BHS T9 Health Sciences Center		
PI Web Page:			
City:	Stony Brook	**State:**	NY
Zip Code:	11794-8691	**Congressional District:**	1
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-MIXEDTOPICS. Appendix E: Behavioral Health & Human Health Countermeasures Topics
Start Date:	04/01/2016	**End Date:**	05/31/2024
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:	Stenger, Michael	**Contact Phone:**	281-483-1311
Contact Email:	michael.b.stenger@nasa.gov		
Flight Program:			
Flight Assignment:	Flight definition NOTE: End date changed to 05/31/2024 per T. Sirmons/JSC (Ed., 5/16/23). NOTE: End date changed to 12/31/2023 per PI and NSSC information (Ed., 3/21/23). NOTE: End date changed to 04/26/2023 per T. Sirmons/JSC (Ed., 3/3/23). NOTE: End date changed to 12/31/2022 per NSSC information (Ed., 1/4/22) NOTE: End date changed to 12/31/2021 per NSSC information (Ed., 12/31/20) NOTE: End date changed to 12/31/2020 per NSSC information (Ed., 6/12/20) NOTE: End date changed to 3/31/2020 per NSSC information (Ed., 3/25/19)		

Key Personnel Changes/Previous PI:	
COI Name (Institution):	Martin, Dwight Ph.D. (State University of New York, Stony Brook)
Grant/Contract No.:	NNX16AH80G
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. Space flight results in exposure of astronauts to several stressors, such as space radiation, microgravity, and physiological stress, that could exacerbate the risks of adverse health effects. To protect astronauts, we must improve our understanding of molecular changes that influence immunological conditions associated with increased astronaut health risks. The in vivo response to the space environment is complex, involving multiple proteins associated with various signal transduction cascades, resulting in different outcomes. Molecular mechanisms responsible for such diverse consequences are poorly understood. It is, therefore, essential to characterize the protein signatures of responses to the space environment in blood plasma samples from astronauts, collected at pre-, in-, and post-flights. Such analyses should help to reveal a particular set of proteins causing adverse immunological changes and to develop methods that help to prevent, or at least to counteract, these effects. In this flight definition project, we will use cutting age proteomic technology to determine protein alterations, qualitatively and quantitatively, in plasma samples collected from astronauts before, during, and after space flights. Our findings will help to provide an understanding of the time course and etiology of immune changes induced by the space environment. Furthermore, since pre- and post-flight samples, in addition to the in-flight samples, will be evaluated in the same astronaut, the direct effects of the space environment can be determined. Hence, our findings will provide high-priority and highly relevant information to NASA. We will further correlate protein expression profiles to the available data on immune dysfunction detected in each astronaut. This approach makes it possible to determine potential predictive biomarkers for space-flight-induced immune dysregulation. Consequently, effective countermeasures against such harmful effects of the space environment can be identified.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our findings will deliver important information that should advance our understanding of the time course and etiology of immune changes induced by the space environment. Hence, our findings will provide high-priority and highly relevant information to NASA. Importantly, we will correlate protein expression profiles to the available data on immune dysfunction detected in each astronaut. This approach makes it possible to determine potential predictive biomarkers for space-flight-induced immune dysregulation. Such knowledge is important for the assessment of health risks and will facilitate the development of countermeasures that can help astronauts, space travelers, and people on Earth with the impairment of the immune system.
Task Progress:	Our contribution to this Flight Definition is to identify and characterize plasma proteins in the blood plasma of astronauts that can be used as predictive biomarkers of immunological dysfunction due to space flight. The in-flight duration for each astronaut was 6 months. Samples from eight astronauts were available for proteomic analysis. We applied the label-free quantitative mass spectrometry-based proteomics method by using an Orbitrap Fusion Lumos mass spectrometer coupled to a Dionex Ultimate 3000 nanoflow High Performance Liquid Chromatography (HPLC) system. This mass spectrometer system offers very high resolution for determining the mass-to-charge ratio (m/z) of ions, enabling us to achieve more in-depth coverage of the proteome than the use of other mass spectrometry (except the Fourier-transform ion cyclotron resonance mass spectrometry). We grouped the samples based on the sampling times. There was one preflight sampling time (L45, i.e., 45 days before flight), one in-flight sampling time (In-flight, ~2-4 months in the International Space Station/ISS), and three post-flight sampling times, i.e., within 24 hrs of returning to Earth (R+0), 30 days after returning to Earth (R+30), and 90 days after returning to Earth. We identified 694 unique and non-redundant proteins (at > 99% confidence). Numbers of unique and non-redundant proteins in each group are: 315 proteins from the L45 sample group 315 proteins from the In-flt sample group 320 proteins from the R+0 sample group 249 proteins from the R +30 sample group 287 proteins from the R+90 sample group These proteins are involved in inflammatory response, actin cytoskeleton organization, defense responses, phagocytosis, extracellular matrix organization, platelet degradation, and tissue homeostasis. Such changes are pronounced in the in-flight samples. Subsequently, the levels of few proteins return to the preflight levels, e.g., cluster of differentiation 14 (CD14). However, we found that the expression levels of proteins involved in actin cytoskeleton and platelet degradation (e.g., filamin A or FLNA), and platelet releasate cytosolic proteins (PLEK) organization were decreased in samples collected at post-flight, while the expression levels of some proteins are increased in samples collected post-flight, e.g., insulin-like growth factor-binding protein 4 (IGFBP4) and tenascin XB (TNXB). Thus, changes in these proteins (i.e., increased or decreased) may potentially have functional roles in response to space flight or re-adaptation to returning to Earth and may affect cell/tissue integrity and homeostasis, leading to late-occurring health risks. In summary, the highlights of our findings are: • Proteins with positive regulation of cytokine secretion are highly expressed in samples collected in-flight. These include: CD14 (Cluster of differentiation 14), COTL1 (Coactosin-like protein-1, an actin binding protein), ORM1 (Orosomucoid or Alpha-1-acid glycoprotein 1, acute phase protein) SERPINA4 (Serine protease inhibitor A4, one of proteins in the Serpin family), SAA1 (Serum amyloid A1 or SAA1, acute phase protein), and MASP1 (Mannan-binding

	lectin serine protease 1, innate immunity). However, the levels of these proteins return to or near the preflight level at d-90 post-flight. • The expression levels of some proteins involved in anti-inflammation, controlling the homeostasis of cytoskeleton, and normal blood coagulation are reduced at d 90 post-flight. Examples of such proteins are: FLNA (Filamin A), PLEK (Platelet releasate cytosolic proteins), and TLN1 (TLN1). • At 90 days post-flight, expression levels of some proteins are higher than those of the preflight levels: IGFBP4 (Insulin-like growth factor-binding protein4 or IGFBP4), TNXB (Tenascin or TNXB, involved in cytoskeleton), and BASP1 (Brain acid soluble protein 1 or BASP1).
Bibliography Type:	Description: (Last Updated: 05/17/2023)
Abstracts for Journals and Proceedings	Rithidech K, Aryal U, Moallem R, Peanilkhit T, Makedonas G, Makedonas G, Crucian B. "Proteomic analysis of plasma collected from astronauts: preflight, in-flight, and post-flight." 2022 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-10, 2022. Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-10, 2022. , Feb-2022