Fiscal Year:	FY 2021	**Task Last Updated:**	FY 04/09/2021
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 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		
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:**	12/31/2021
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:	Brocato, Becky	**Contact Phone:**	
Contact Email:	becky.brocato@nasa.gov		
Flight Program:			
Flight Assignment:	Flight definition 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:	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. 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. Specifically, we characterize the proteome of blood plasma collected from the same astronauts at different times, i.e. pre-, in-, and post-flight. Previously, we analyzed the data by comparing pre-vs-in-flight and in-vs-post-flight separately. During the past few months, we analyzed the data by studying the temporal changes of each protein in samples collected at pre, in-, and post-flight from the same astronauts. The results from this approach not only help us to understand the temporal changes of proteins during space flights but also are highly relevant to the effects of space flight on protein expression. Using this approach, we detected new low abundance proteins with altered expression levels that have never been reported. Our data demonstrate that there are 19 proteins with significant changes, i.e., increased or decreased, in expression levels due to space flight. Among the 19 proteins with significant changes in expression levels, there were seven proteins with significantly decreased levels. These include lumican (LUM), extracellular matrix protein 1 (ECM1), vitronectin (VTN), filaggrin-2 (FLG2), ceruloplasmin (CP), Desmoplakin (DSP), CD5 antigen-like (CD5L). These proteins are involved in cell defense responses, inflammatory responses, and cell/tissue repair. Hence, a reduction in the expression levels of these proteins may be associated with the impairment of the immune system and the repair of damaged tissues. The deficiency of filaggrin-2 (FLG2) is involved in skin inflammation. Although further studies are needed, a reduction in the expression level of FLG2 may play a role in the occurrence of skin rashes in some astronauts. It is known that lumican (LUM) is a major keratan sulfate proteoglycan of the cornea responsible for circumferential growth, corneal transparency, epithelial cell migration, and tissue repair. Hence, LUM is critical in maintaining corneal clarity. Further, a loss of LUM expression is associated with corneal inflammation. Hence, persistent decreases in the level of LUM after space flight would impair the homeostasis of the eyes. Taken together, it is plausible to hypothesize that a reduction in LUM level may be associated with vision impairment that has been observed in many astronauts after space flight. Our findings warrant further investigation of the potential role of LUM in vision impairment detected in astronauts. The levels of the remaining 12 proteins were significantly increased. These are antithrombin-II (SERPINC1), fibronectin (FN1), protein disulfide-isomerase A (PDIA 3), titin (TTN), tropomodulin (TMOD3), zyxin (ZYN), bridging integrator 2 (BIN2), apolipoprotein A-II (APOA2), platelet factor 4 variant (PF4V1), beta-Ala-His dipeptidase (CNDP1), alpha-2-HS-glycoprotein (AHSG), pigment epithelium-derived factor (SERPINF1). The majority of these proteins are involved in inflammatory responses, cytoskeleton organization, and aging. Increased expression levels of CNDP1 may be indicative of increased oxidative stress in the brain and the muscle since CNDP1 degrades carnosine and

	homocarnosine (proteins with anti-oxidative activity mostly concentrated in the brain and the muscle). The protein in the SERPIN (serine protease inhibitor) family, i.e., SERPINC1, and SERPINF1, is the majority of those with increased expression levels. The SERPIN protease inhibitors comprise a large family of molecules involved in inflammation, immune response, blood clotting, hormone transport, and complement activation, dementia, and tumorigenesis. Hence, our findings suggest that dysregulation of these proteins may affect cell/tissue integrity and homeostasis, leading to late occurring health risks. Based on these findings, we are preparing a manuscript to be submitted for possible publication in Acta Astronautica. In addition to the preparation of a manuscript, we are currently using Orbitrap Fusion Lumos Tribrid MS coupled with Thermo Ultimate 3000 HPLC system to investigate the pattern of protein expression profiles of astronauts' plasma. This strategy helps us to achieve more in-depth coverage of the proteome than the MudPIT. However, it was not available in our laboratory in the past. We are currently analyzing the data generated by this highly sensitive and accurate mass spectrometer system. We anticipate another publication from this analysis.
Bibliography Type:	Description: (Last Updated: 03/27/2025)