Fiscal Year:	FY 2010	**Task Last Updated:**	FY 10/15/2010
PI Name:	Stowe, Raymond Ph.D.		
Project Title:	Space Flight-Induced Reactivation of Latent Epstein-Barr Virus		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Operational and clinical research		
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		
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Organization Name:	Microgen		
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City:	La Marque	**State:**	TX
Zip Code:	77568-3318	**Congressional District:**	22
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	98-HEDS-02
Start Date:	07/01/2004	**End Date:**	06/30/2010
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:**	1
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Meck, J@n	**Contact Phone:**	281-244-5405
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Flight Program:	Shuttle/ISS		
Flight Assignment:	STS-122, STS-123, STS-124, STS-125, STS-126 STS-108, -109, -110, -111, -113, -114; -116; -118; ISS-5, -6, -11, 12, -13, -14, -15, and -16 In flight development phase (data collection has begun) NOTE: End date is 6/30/2010 per JSC information (2/2010) NOTE: End date changed to 1/22/2010 per J. Dardano/JSC (1/2009)		
Key Personnel Changes/Previous PI:	Raymond Stowe replaced Alan Barrett as PI, effective July 2004 (per info from S. McCollum/M. Anderson, 12/2006). See also Barrett for FY02-04 information/reports.		
COI Name (Institution):	Pierson, Duane L (NASA Johnson Space Center) Sams, Clarence (NASA-Johnson Space Center)		
Grant/Contract No.:	NNJ06HB73A		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	The majority of humans are infected with Epstein-Barr virus (EBV) early in life and thereafter carry the virus in a latent form. Reactivation of latent EBV may be an important threat to crew health during extended space missions. EBV is the causative agent of infectious mononucleosis as well as nasopharyngeal carcinoma, Burkitt's lymphoma, and different kinds of B-lymphocyte lymphomas in immunosuppressed individuals. Control of replication in vivo is mediated primarily by EBV- specific cytotoxic T-lymphocytes, and severe clinical symptoms have been associated with reactivation of latent viruses in patients with defective cellular immunity. Decreased cellular immune function has been reported both during and after space flight. Preliminary studies have demonstrated increased EBV shedding in saliva as well as increased antibody titers to EBV lytic proteins. Based on these observations, we hypothesize that the combined effects of microgravity along with associated physical and psychological stress will decrease EBV-specific T-cell immunity and reactivate latent EBV in infected B- lymphocytes. The specific aims to test this hypothesis are: (1) determine if antibody titers to EBV-specific antigens are increased after space flight; (2) determine T-lymphocyte immunocompetence using a EBV-specific autologous T-cell killing assay; (3) characterize the viral burden and gene expression in peripheral blood cells using PCR/RT-PCR; and (4) measure stress hormones in plasma and urine. To determine the mechanisms underlying altered virus-specific T cell immunity and reactivation of latent EBV in B lymphocytes. See also http://www.nasa.gov/
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This experiment will address fundamental questions on spaceflight and virus-specific immunity. One potential concern is the development of a virally associated disease or lymphoma within an infected individual. In addition, reinfection or transmission to a previously uninfected individual (resulting in primary infection) may be another concern. Thus, spaceflight may result in an increased frequency and/or severity of both primary and reactivated disease. If increased reactivation and clonal expansion of infected B- lymphocytes is detected, then pharmacological measures can be developed and instituted prior to onset of overt clinical disease.
Task Progress:	Eight separate samples of peripheral blood were collected from each of 63 astronauts; 45 flew on fourteen Space Shuttle missions (39 men, 6 women, mean age 46 ± 5) and 18 flew on eight ISS missions (15 men, 3 women, mean age 48 ± 4); the average length of the Shuttle missions was ~11 days while the average length of the ISS missions was ~180 days. Space Shuttle missions included STS-108, -109, -110, -111, -113, 114, -115, -116, -118, -121, -123, -124, -125, and -126. ISS missions included ISS-5, -6, -11, 12, -13, -14, -15, and -16. Peripheral blood was collected 180 days before launch (L-180), L-65-44, L-10, L-2, within 4 h after return/landing (R+0), R+3, R+14-30, and R+180. We analyzed blood and urine samples for: 1) stress hormone levels; 2) general and virus-specific immunity; and 3) latent herpesvirus reactivation. Our data showed that stress- and space flight-associated changes (e.g., anticipation of launch, acute changes in g-forces, sleep deprivation, etc.) resulted in a decline in cellular immunity and an increase in viral reactivation. We propose that the accumulative effects of microgravity (i.e., muscle loss and generalized physiological deconditioning) associated with longer duration missions resulted in increased sympathetic nervous system activation and increased hypothalamic pituitary adrenal axis activation at landing. This would be a possible explanation for the differences observed in results from the ISS crewmembers versus those from Shuttle crewmembers. This data also further supports our hypothesis that a Th1-to-Th2 shift in cytokine production may be partially responsible for many of the immune alterations in astronauts.
Bibliography Type:	Description: (Last Updated: 03/07/2019)
Abstracts for Journals and Proceedings	Crucian B, Stowe R, Mehta S, Uchakin P, Quiriarte H, Pierson D, Sams C. "Validation of Procedures for Monitoring Crewmember Immune Function." NASA Human Research Program Investigators' Workshop, League City, TX, February 2009. Program and abstracts. http://www.dsls.usra.edu/meetings/hrp2010/pdf/Immunology/1151CrucianMehta-IntImm.pdf , Feb-2010 , Feb-2009
Abstracts for Journals and Proceedings	Stowe RP, Komanduri K, St. John LS, Sams CF, Pierson DL. "Spaceflight and aging: Immune system parallels." NASA Human Research Program Investigators' Workshop, League City, TX, February 2009. Program and abstracts: http://www.dsls.usra.edu/meetings/hrp2009/pdf/Immune/1114Stowe.pdf , Feb-2009
Articles in Peer-reviewed Journals	Stowe RP, Kozlova EV, Sams CF, Pierson DL, Walling DM. "Latent and lytic Epstein-Barr virus gene expression in the peripheral blood of astronauts." J Med Virol. 2011 Jun;83(6):1071-7. http://dx.doi.org/10.1002/jmv.22079 ; PubMed PMID: 21503923 , Jun-2011
Articles in Peer-reviewed Journals	Stowe RP, Sams CF, Pierson DL. "Adrenocortical and immune responses following short- and long-duration spaceflight." Aviat Space Environ Med. 2011 Jun;82(6):627-34. PubMed PMID: 21702314 , Jun-2011
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Articles in Peer-reviewed Journals	Benjamin CL, Stowe RP, St John L, Sams CF, Mehta SK, Crucian BE, Pierson DL, Komanduri KV. "Decreases in thymopoiesis of astronauts returning from space flight." JCI Insight. 2016 Aug 4;1(12):e88787. https://doi.org/10.1172/jci.insight.88787 ; PubMed PMID: 27699228 ; PubMed Central PMCID: PMC5033888 , Aug-2016

Books/Book Chapters	Stowe RP, Goodwin JS. "Effects of aging on immune function." in "Principles and Practice of Geriatric Surgery. 2nd edition." Ed. R.A. Rosenthal, M.E. Zenilman, M.R. Katlic. New York : Springer, 2011. p. 46-64., Jul-2011