Fiscal Year:	FY 2005	**Task Last Updated:**	FY 01/22/2007
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 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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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:**	12/31/2008
No. of Post Docs:	1	**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:	McCollum, Suzanne	**Contact Phone:**	281 483-7307
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Flight Program:	Shuttle/ISS		
Flight Assignment:	STS-108, -109, -110, -111, -113, -114; ISS-5, -6 In flight development phase (data collection has begun)		
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)		
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.
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:	Multiple pre- and post-flight samples were collected in this study to better characterize changes in neuroendocrine hormones, immune function, and latent herpesvirus reactivation. To date, we have collected longitudinal samples from six International Space Station crewmembers from Expeditions 5 and 6; the duration was 184 days and 161 days, respectively. We measured plasma and urinary cortisol, plasma cytokines (IL-6, -10), intracellular cytokine production by antigen-specific T cells, and viral load in peripheral blood. Elevated levels of cortisol were found in blood and urine after landing. Altered levels of IL-6 and IL-10 were also observed. Production of intracellular tumor necrosis factor-alpha and interferon-gamma by CD4+ T cells were decreased just before launch as compared to baseline levels indicating a generalized stress-induced decrease in immune function. Cytokine production was also decreased immediately after space flight and returned to baseline levels within a few days after landing. Notably, viral load was higher in peripheral blood collected at landing as compared to preflight levels suggesting an expansion of virally-infected lymphocytes during flight. Collectively, these preliminary data indicate 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 load after space flight. Our next ISS experiment will begin with Expedition 11, and our next Shuttle mission will begin with STS-114.
Bibliography Type:	Description: (Last Updated: 03/07/2019)
Articles in Peer-reviewed Journals	Pierson DL, Stowe RP, Phillips TM, Lugg DJ, Mehta SK. "Epstein-Barr virus shedding by astronauts during space flight." Brain Behav Immun. 2005 May;19(3):235-42. PMID: 15797312 , May-2005