Fiscal Year:	FY 2007	**Task Last Updated:**	FY 04/25/2007
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 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:	rpstowe@microgenlabs.com, brian.crucian-1@nasa.gov	**Fax:**	FY 409-935-6705
PI Organization Type:	INDUSTRY	**Phone:**	409-935-6700
Organization Name:	Microgen		
PI Address 1:	903 Texas Avenue		
PI Address 2:			
PI Web Page:			
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:		**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
Contact Email:	suzanne.g.mccollum@nasa.gov		
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:	Since our last task progress report, we have collected samples from an additional 14 Shuttle crewmembers and 7 ISS crewmembers. Multiple pre- and post-flight samples were collected in this study to better characterize changes in neuroendocrine hormones, immune function, and latent herpesvirus reactivation. We measured plasma and urinary stress hormones, and intracellular cytokine production by antigen-specific T cells. In addition, we performed nested RT-PCR on isolated B-cells to determine the EBV gene expression pattern before and after space flight. Our results demonstrate that mission duration significantly affects neuroimmune responses and latent EBV reactivation. Elevated levels of cortisol were found in blood and urine after landing for Shuttle crewmembers. For ISS crewmembers, cortisol was significantly higher at landing and 3-5 times higher than levels found for Shuttle crewmembers. Production of intracellular tumor necrosis factor-alpha and interferon-gamma by SEB-stimulated 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. EBV gene expression, grouped according to latent, immediate early/early (IE/E), and late replicative transcription (LR), was assessed in blood samples taken from healthy young and elderly subjects to compare with data from the Shuttle and ISS astronaut samples. In samples from younger control subjects (n=24), EBV gene expression was highly restricted (5 samples positive for latent genes, 3 samples positive for IE/E, no samples positive for LR). EBV gene expression in samples from elderly subjects displayed frequent transcription of latent and LR genes that was indicative of chronic EBV reactivation. In Shuttle astronaut samples, EBV gene expression shifted towards the IE/E expression. Notably, for ISS crewmembers there were increases in both latent and IE/E transcripts. Furthermore, LR transcripts (BALF5 and gp220) were present in samples collected immediately after landing but not before flight. The pattern of EBV gene transcription from ISS astronauts was similar to that found in aging samples. Overall, these results indicate that stress and spaceflight-associated changes (e.g., anticipation of launch, acute changes in g-forces, sleep deprivation, etc.) resulted in decreased cell-mediated immunity and reactivation of latent EBV in both Shuttle and ISS crewmembers.
Bibliography Type:	Description: (Last Updated: 03/07/2019)
Books/Book Chapters	Pierson DL, Mehta SK, Stowe RP. "Reactivation of Latent Herpes Viruses in Astronauts." in "Psychoneuroimmunology, Fourth Edition." Ed. R. Ader. Boston : Academic Press , p. 851-868, 2007., Jan-2007