Fiscal Year:	FY 2013	**Task Last Updated:**	FY 10/29/2013
PI Name:	Sams, Clarence Ph.D.		
Project Title:	Validation of Procedures for Monitoring Crewmember Immune Function (Integrated Immune - SMO 015/SDBI 1900)		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
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 (2) **Microhost**:Risk of Adverse Health Effects Due to Host-Microorganism Interactions		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Houston	**State:**	TX
Zip Code:	77058-3607	**Congressional District:**	22
Comments:			
Project Type:	FLIGHT	**Solicitation / Funding Source:**	Directed Research
Start Date:	05/03/2005	**End Date:**	09/30/2013
No. of Post Docs:		**No. of PhD Degrees:**	0
No. of PhD Candidates:		**No. of Master' Degrees:**	0
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
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Flight Program:	Shuttle/ISS		
Flight Assignment:	ISS Increment 16 NOTE: changed end date to 9/30/2013 per B. Crucian (Ed., 2/4/2013) NOTE: End date is 3/29/2013 per HRP Master Task List dtd 7/12/2011 (Ed., 8/9/2011) NOTE: End date now 9/30/2013 per JSC (09/2010) NOTE: End date changed to 9/30/2011 per B. Corbin/JSC (3/2009) NOTE: End date changed to 5/31/2011 per PI ; original end date was 4/2010 (2/09)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Pierson, Duane (NASA JSC) Stowe, Raymond (Microgen Laboratories) Crucian, Brian (Wyle Laboratories) Mehta, Satish (EASI, NASA, JSC)		
Grant/Contract No.:	Internal Project		

Performance Goal No.:	
Performance Goal Text:	
Task Description:	SMO 015. Background: Post-flight data suggests immunity is dysregulated immediately following spaceflight. It is currently unknown if immune function is altered during long duration spaceflight. Persistent immune dysregulation during exploration class deep-space missions could result in specific clinical health risks for crewmembers. This study assessed various immune parameters at multiple points during 6-month spaceflight onboard the International Space Station (ISS). Methods: Blood was collected pre-flight, in-flight, and post-flight from up to 22 astronauts participating in 6-month ISS expeditions. Samples were returned to Earth within 48 hours of collection for immediate analysis. Assays included peripheral leukocyte distribution, plasma cytokine levels, T cell function, T cell/monocyte cytokine production profiles following mitogenic stimulation, and viral specific immunity. Results: Some shifts in leukocyte distribution occurred during flight, including alterations within subsets of CD8+ T cells which indicated an increased maturation state. General T cell function (both CD4 and CD8+ subsets) was consistently reduced early in-flight. The percentage of CD4+ T cells capable of producing IL-2 was depressed early in-flight and after landing. Significant and persistent mitogen-specific reductions in culture-stimulated T cell production of IFNg, IL-10, IL-5, TNFa and IL-6 were observed during spaceflight. Monocyte production of IL-10 was reduced, whereas IL-8 production was increased. Plasma cortisol was increased at landing but not in-flight. No significant changes occurred in anti-viral antibodies, but EBV T-cell function was decreased in-flight and was accompanied by an increase in EBV-infected cells in peripheral blood. Conclusions. The data indicate that some alterations in immunity persist during spaceflight and are not merely related to the transitional stress of launch or landing. Ongoing immune dysregulation, reduced immune cell function and/or Th1/Th2 shifts, in conjunction with elevated radiation exposure and limited clinical care may increase specific clinical risks for crewmembers during exploration-class space missions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This investigation provided new insights into the relationship between immunity, stress, and latent viral reactivation during spaceflight. This information may benefit terrestrial medicine. Spaceflight associated immune dysregulation is likely to be an immunodeficiency that could be very analogous to certain immunodeficiencies that occur on Earth. These terrestrial phenomenon may occur as a result of disease, or in humans subjected to unusual factors similar to spaceflight (confinement, physiological stress, etc.). In such cases, the mechanisms and monitoring strategies (and possibly countermeasure information) derived from this flight study could benefit terrestrial medicine.
Task Progress:	This task is completed. This study investigated the status of the immune system during short duration spaceflight by collecting blood samples from US crewmembers during spaceflight. Flight blood samples were returned for terrestrial laboratory analysis. To our knowledge, this was the first study that returned live, ambient storage blood samples for functional assays. This approach allows an in-flight data point to be achieved without flying complicated laboratory instruments. The L-180 data were considered baseline for comparison of in-flight and landing day data. An additional sample was collected from ISS subjects at L-45, and for the Shuttle subjects at L-10; however, the L-10 sample was dictated by operational constraints. Astronauts are under considerable stress by L-10, so data at this timepoint may possibly be influenced by pre-launch stress and is not considered the best baseline measurement. The second baseline for ISS subjects was at L-45. Summary data findings are as follows: There were alterations in the peripheral leukocyte distribution during short duration missions that were largely absent during long-duration ISS missions. However, there was an elevated WBC count and a maturation shift in CD8+ T cells during ISS missions. T cell function was depressed during Shuttle missions in a mitogen specific fashion, with the more physiological relevant stimulus showing a consistent defect in T cell function. During ISS missions this reduction in T cell function was more apparently early, and trending to resolve as 6-month missions progressed. A more downstream measure of T cell function, cytokine secretion, was profoundly dysregulated in ISS subjects for the duration of a 6-month mission. Plasma cytokine levels in ISS astronauts were dysregulated for the duration of a 6-month mission. A significant increase in constitutively activated CD8+ T cells was observed during ISS missions. Latent viral reactivation for three herpes viruses, EBV, VZV, and CMV was observed significantly in crewmembers during both short and long duration spaceflight. Their viral load increased during flight than both before and after flight as well as the healthy controls on the ground. This effect was more pronounced in long duration space flight as compared to short duration spaceflight. Also shedding of VZV in saliva and CMV in urine of the ISS crewmembers continued up to 30 days or more after the spaceflight as compared to 5-7 days in space shuttle crewmembers. Although not significant due to subject number and inter-subject variability, antiviral antibodies were generally elevated consistent with the increased viral load. EBV- and CMV-specific CD8+ T-cell number did not significantly change in either the Shuttle or ISS crewmembers. However, there was a pronounced decrease in function in EBV- and CMV-specific T-cells in the Shuttle crewmembers during and after flight. For ISS crewmembers, there was a decrease in EBV-specific T-cell function during and after flight. However this effect, except for landing, was not observed for CMV in long-duration flight. Even though some changes in salivary cortisol levels as well as their circadian rhythm were observed in both ISS and Space Shuttle crewmembers, the differences were not significantly different. Likewise, plasma cortisol was not significantly changed during short- or long-duration flights although elevated levels were found at landing for both Shuttle and ISS missions. These data indicate that immune system dysregulation, a previously established post-flight phenomenon, actually occurs during spaceflight prior to any physiological stress associated with landing and readaptation. This means that

	flight-associated variables such as microgravity, radiation, or the unique stresses that occur during missions, do influence human immunity. These may include microgravity exposure, confinement, disrupted circadian rhythms, or the physiological stress associated with spaceflight itself. The extremely busy work schedules associated with a short duration Space Shuttle mission also have the potential to impact immunity. In fact, stress effects on crewmember immunity, ahead of any in-flight variables, have been documented during L-10 to L-3 pre-flight studies. During ISS missions, it is far more likely that the observations do reflect 'space normal' for immunity during prolonged spaceflight. No matter which variable, or combination of variables, caused the observed in-flight changes, we now consider it established that immunity is dysregulated during spaceflight. The clinical consequences of immune system dysregulation during short-duration space flight are likely to be low for short duration space missions. If immune dysregulation were found to persist for the duration of an exploration class deep space mission, consisting of elevated radiation exposure, limited clinical care, and other exploration-specific variables, clinical risk for adverse health events would likely be substantially elevated.
Bibliography Type:	Description: (Last Updated: 06/29/2023)
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