Fiscal Year:	FY 2009	**Task Last Updated:**	FY 02/05/2009
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 In Mission Impacts, Adverse Health Events or Long-Term Health Impacts 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:**	09/30/2011
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: 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)		
Grant/Contract No.:	Not Available		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	SMO 015. The objective of this experiment is to understand the effects of space flight on the human immune system, and determine any clinical risk for exploration related to immune dysregulation. Numerous investigations have demonstrated a decrease in specific immune cell functions following space flights of varied duration. Should it persist for extended durations, this decrease in host defense may increase the potential for illness in crewmembers. To assess this, crewmember white blood cells collected during flight will be tested for changes in function or response to stimulation. The concentrations of factors that regulate immune function will also be determined. These data will be correlated with reactivation and shedding of latent herpes viruses and measurements of stress hormones. This information is needed to determine the crewmembers' risk of adverse clinical events related to immunology that may occur during space flight, and in particular for exploration-class missions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This investigation will provide new insights into the relationship between immunity, stress and latent viral reactivation that may benefit terrestrial medicine. Spaceflight associated immune dysregulation is likely to be an immunodeficiency that could be very analagous 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 space flight (confinement, physiological stress, etc.). In such cases, the mechanisms and monitoring strategies (and possibly countermeasure information) derived during this flight study could benefit terrestrial medicine.
Task Progress:	As of January 28, 2009 Integrated Immune has been manifested on 5 Space Shuttle missions. In this time period, 9 short-duration crewmembers, and 4 long-duration crewmembers have successfully completed the study requirements. The total 'n' for Integrated Immune will be 17 long-duration crewmembers and 17 short-duration crewmembers. Samples for Integrated Immune per crew time point are 18.5 ml blood, 1 ml liquid saliva a dry saliva sample (pre-, in- and post-flight) and 4.0 ml of a 24hr urine pool (pre- and post-flight only). In-flight urine will be obtained via sample sharing if any other in-flight study is making the collection. The assays included in the study and the responsible laboratory are as follows: JSC Immunology Laboratory: Leukocyte subsets ; T cell function ; Intracellular/secreted cytokine profiles Mercer University: Plasma cytokine balance ; Leukocyte cytokine RNA Microgen Laboratories: Virus specific T cell number ; Virus specific T cell function ; Plasma stress hormones ; Antiviral antibody titers JSC Microbiology Laboratory: Latent herpesvirus reactivation (saliva/urine) ; Saliva/urine stress hormones Circadian rhythm analysis Of 12 planned in-flight blood collections for long-duration crewmembers to date, 11 were successful. Of 11 planned in-flight blood collections for short-duration crewmembers, 9 were successful and 1 was completed partially. The combined success rate for in-flight blood collections is 20 out of 23. In all cases, no adverse clinical events except some bruising related to venipuncture have been reported. All urine and saliva samples were collected as planned. From a technical perspective, the Integrated Immune science continues according to plan. All in-flight samples have been collected within 24-48 hours of landing/undocking, and for all in-flight samples the cellular viability upon sample processing has been acceptable. To date, live cells are being returned to Earth within the required timeframe to allow an in-flight determination of immune cell functional capabilities. The investigator team is grateful to the mission planners, schedulers and crewmembers for enabling this to occur. The science team is satisfied with the data obtained thus far. The distribution of the peripheral leukocyte populations, T cell functional characteristics, viral-specific immune parameters, the status of latent herpesvirus reactivation and physiological stress has been determined for all completed subjects. For ISS subjects, 2-3 data collections have occurred per mission, allowing a determination of the kinetics related to observed changes. In most cases, this is completely novel data and represents our first comprehensive observation of the in-flight status of the immune system. Although the 'n' completed to date is too low to allow statistical calculations, a summation of the data through the indicated 'n' follows: Immunophenotype: • No in-flight changes in bulk leukocyte subsets • Postflight granulocytosis • Late in-flight/postflight elevated B cells, reduced NK cells • In-flight, postflight trend toward elevated CD4:CD8 ratio, elevated memory T cell subsets • In-flight elevated effector memory, central memory T cells • No change in peripheral constitutively activated T cells T cell function: • Reduced T cell function consistently observed early in-flight (shuttle + ISS early), with at some indication of partial recovery (note: number of long-duration subjects at later in-flight points is reduced). • Dysregulated cytokine production profiles observed in-flight. The most consistently observed alteration is an in-flight reduction in IFNg production following activation, at levels similar to post-flight observations. Viral specific immunity: • Reduced function of EBV specific T cells in-flight and post-flight. Latent herpesvirus reactivation: • CMV reactivation via urine DNA analysis elevated post-flight. In-flight determination in-progress. • VZV reactivation via salivary DNA analysis elevated in-flight and post-flight. In-flight data indicate no resolution as long-duration missions progress. Conclusion

	This flight study is progressing well from a technical perspective, with robust crew participation and consistent positive feedback from the crewmembers. To date, the data indicate that some of the parameters that define spaceflight-associated immune dysregulation from prior post-flight studies seem to be in-flight phenomenon as well. Although this does not indicate immediate illness, if these alterations were to persist for the duration of exploration-class missions there could be clinical risk. Risks could include hypersensitivities, autoimmunity, infection and malignancies. The data will become better defined from a statistical perspective as the study progresses and the 'n' increases. Following completion of this study, it is expected that a monitoring strategy may be defined, that focuses on the most relevant parameters that are altered in-flight.
Bibliography Type:	Description: (Last Updated: 06/29/2023)
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." Presented at the NASA-HRP Investigators' Workshop, Southshore Harbor, Texas, February 2-4, 2009. NASA-HRP Investigators' Workshop, Southshore Harbor, Texas, February 2-4, 2009. p 29. , Feb-2009