

<b>Fiscal Year:</b>	FY 2012	<b>Task Last Updated:</b>	FY 04/10/2012
<b>PI Name:</b>	Sams, Clarence Ph.D.		
<b>Project Title:</b>	Validation of Procedures for Monitoring Crewmember Immune Function (Integrated Immune - SMO 015/SDBI 1900)		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>	HUMAN RESEARCH		
<b>Program/Discipline--Element/Subdiscipline:</b>	HUMAN RESEARCH--Biomedical countermeasures		
<b>Joint Agency Name:</b>	<b>TechPort:</b>	No	
<b>Human Research Program Elements:</b>	(1) <b>HHC</b> :Human Health Countermeasures		
<b>Human Research Program Risks:</b>	(1) <b>Immune</b> :Risk of Adverse Health Event Due to Altered Immune Response (2) <b>Microhost</b> :Risk of Adverse Health Effects Due to Host-Microorganism Interactions		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Organization Name:</b>	NASA Johnson Space Center		
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<b>City:</b>	Houston	<b>State:</b>	TX
<b>Zip Code:</b>	77058-3607	<b>Congressional District:</b>	22
<b>Comments:</b>			
<b>Project Type:</b>	FLIGHT	<b>Solicitation / Funding Source:</b>	Directed Research
<b>Start Date:</b>	05/03/2005	<b>End Date:</b>	09/30/2013
<b>No. of Post Docs:</b>		<b>No. of PhD Degrees:</b>	0
<b>No. of PhD Candidates:</b>		<b>No. of Master' Degrees:</b>	0
<b>No. of Master's Candidates:</b>		<b>No. of Bachelor's Degrees:</b>	0
<b>No. of Bachelor's Candidates:</b>		<b>Monitoring Center:</b>	NASA JSC
<b>Contact Monitor:</b>	Baumann, David	<b>Contact Phone:</b>	
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<b>Flight Program:</b>	Shuttle/ISS		
<b>Flight Assignment:</b>	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)		
<b>Key Personnel Changes/Previous PI:</b>			

<b>COI Name (Institution):</b>	Pierson, Duane ( NASA JSC ) Stowe, Raymond ( Microgen Laboratories ) Crucian, Brian ( Wyle Laboratories ) Mehta, Satish ( EASI, NASA, JSC )
<b>Grant/Contract No.:</b>	Not Available
<b>Performance Goal No.:</b>	
<b>Performance Goal Text:</b>	
<b>Task Description:</b>	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.
<b>Rationale for HRP Directed Research:</b>	
<b>Research Impact/Earth Benefits:</b>	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 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 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.
<b>Task Progress:</b>	<p>As of April, 2012, Integrated Immune has been manifested on 9 Space Shuttle missions. In this time period, 18 short-duration crewmembers, and 16 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. The short duration component is now completed, it is anticipated that the long duration component should be completed on Soyuz 29S in mid-2012. 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:</p> <p>JSC Immunology Laboratory</p> <p>Leukocyte subsets</p> <p>T cell function</p> <p>Intracellular/secreted cytokine profiles</p> <p>Mercer University</p> <p>Plasma cytokine balance</p> <p>Leukocyte cytokine RNA</p> <p>Microgen Laboratories</p> <p>Virus specific T cell number</p> <p>Virus specific T cell function</p> <p>Plasma stress hormones</p> <p>Antiviral antibody titers</p> <p>JSC Microbiology Laboratory</p> <p>Latent herpesvirus reactivation (saliva/urine)</p> <p>Saliva/urine stress hormones</p> <p>Circadian rhythm analysis</p> <p>As this study has progressed, 2 formerly long duration subjects with mission durations of ~45 days were reclassified as short duration. This allowed the short duration component to be completed on schedule, thus saving program resources, and also provided additional subject slots for full 6-month duration crewmembers. In all cases, no adverse clinical events except some bruising related to venipuncture have been reported. Most all urine and saliva samples were collected as planned.</p> <p>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.</p> <p>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</p>

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.

The final completed short duration data was recently presented at the 2010 NASA HRP Investigators Workshop. The abstract for that presentation may be found here: <http://www.dsls.usra.edu/meetings/hrp2010/pdf/Immunology/1151CrucianMehta-IntImm.pdf> In general, the data show that alterations in the distribution and function of the peripheral leukocytes, as well as alterations in viral specific immunity, physiological stress, and latent viral reactivation occur during short-duration spaceflight.

Mid-point long-duration data was presented at the April 2011 Humans in Space meeting, Houston, Texas. This presentation is completed and the long duration data are intriguing. The abstract for the ISS presentation may be found here: <http://www.dsls.usra.edu/meetings/IAA/pdf/2104.pdf>.

Also, via collaboration with the NASA-JSC Nutrition Laboratory and the in-flight Nutrition flight study (SMO-016E), the assessment of plasma cytokines, an original component of the Immunology flight study, has been expanded to include additional in-flight timepoints. The additional samples were provided by the Nutrition Laboratory, and augment the timepoints originally baselined by the Immunology flight study. This is fortuitous, because Immunology samples are collected during high-stress docked-operations timeperiods, near to undocking. Nutrition samples are collected away from docked-operations, and frozen for later transport to Earth. The joint-analysis allows a more complete sampling for both studies, including both high-stress and lower-stress in-flight periods. The initial joint-study plasma cytokine data was recently presented at the February 2012 NASA Human Research Program Investigators' Meeting. The abstract may be found here: <http://www.dsls.usra.edu/meetings/hrp2012/pdf/4165.pdf>

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 do indeed persist for the duration of a 6-month ISS mission. This may represent a clinical risk to crewmember during exploration-class missions. Risks could include hypersensitivities, autoimmunity, infection, and malignancies. The ISS 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.

<b>Bibliography Type:</b>	Description: (Last Updated: 06/29/2023)
<b>Abstracts for Journals and Proceedings</b>	Crucian BE, Zwart SR, Quiarte HA, Smith SM, Sams CF. "Plasma cytokine levels during long-duration spaceflight." 2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. 18th IAA Humans in Space Symposium, Houston, TX, April 11-15, 2011.  2012 NASA Human Research Program Investigators' Workshop, Houston, TX, February 14-16, 2012. , Feb-2012
<b>Articles in Peer-reviewed Journals</b>	Crucian B, Stowe R, Quiarte H, Pierson D, Sams C. "Monocyte phenotype and cytokine production profiles are dysregulated by short-duration spaceflight." Aviat Space Environ Med. 2011 Sep;82(9):857-62. PubMed <a href="https://pubmed.ncbi.nlm.nih.gov/21888268/">PMID: 21888268</a> , Sep-2011