Acronym: Integrated Immune

Title: Validation of Procedures for Monitoring Crewmember Immune Function

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Sponsoring Agency: National Aeronautics and Space Administration (NASA)

Increment(s) Assigned: 16, 17, 18, 19, 20

Brief Research Summary (PAO): Validation of Procedures for Monitoring Crew Member Immune Function (Integrated Immune) will assess the clinical risks resulting from the adverse effects of space flight on the human immune system and will validate a flight-compatible immune monitoring strategy. Researchers will collect and analyze blood, urine and saliva samples from crewmembers before, during and after space flight to monitor changes in the immune system. Changes in the immune system will be monitored by collecting and analyzing blood and saliva samples from crewmembers during flight and blood, urine, and saliva samples before and after space flight.

Research Summary:

- There is ample postflight evidence to suggest that space flight has a negative effect on the immune system however, little inflight data has been collected. The inflight data that exists suggests immune dysregulation occurs during flight. There are several possible causes ranging from microgravity to stress to radiation. Complications arising from an immune system dysregulation have the potential to pose a clinical risk for exploration class space missions.

- In order to develop countermeasures to reduce inflight immune dysfunction, a monitoring strategy must be developed.

- The objective of this study is to validate a monitoring strategy that will allow future countermeasures to be developed.

Detailed Research Description: The Validation of Procedures for Monitoring Crewmember Immune Function - Short Duration Biological Investigation (Integrated Immune) is to develop and validate an immune monitoring strategy consistent with operational flight requirements and constraints. There are no procedures currently in place to monitor immune function or its influence on crew health. Immune dysregulation has been demonstrated to occur during space flight, yet precious little inflight immune data has been generated to assess this clinical problem. Integrated Immune assesses the clinical risks resulting from the adverse effects of space flight on the human immune system and will validate a flight-compatible immune monitoring strategy. Characterization of the clinical risk and the development of a monitoring strategy are necessary prerequisite activities prior to validating countermeasures.

Preflight, inflight and postflight assessments will be performed. The inflight samples will allow a distinction between legitimate inflight alterations and the physiological stresses of landing which are believed to alter landing day assessments. The overall status of the immune system during flight (activation, deficiency, dysregulation) and the response of the immune system to specific latent virus reactivation (known to occur during space flight) will be thoroughly assessed.

Following completion of the investigation, the data will be evaluated to determine the optimal set of assays for routine monitoring of crewmember immune system function. It is intended that the determined set of relevant assays will be incorporated into the Clinical Status Evaluation (CSE) and utilized to monitor the effectiveness of human medical countermeasures related to immune function (exercise, medication, diet regulation-supplementation, immune modulators, etc.). In addition, the assays validated here will have significant benefit for the routine monitoring of crewmember's immune system status with regard to diagnosis and prognosis of immune-related disease states.

Project Type: Payload

Images and Captions:


The image above is the kit that contains all the items the crew will need for taking blood samples. Image courtesy of NASA, Johnson Space Center.


Pictured here is the kit that will be used to collect the saliva samples. In the upper left of the image the rolled gaze is seen; this will be place into the mouth to absorb saliva. Image courtesy of NASA, Johnson Space Center.

Operations Location: ISS Inflight

Brief Research Operations:

- Preflight and postflight activities include collecting blood, urine and saliva samples at certain timepoints depending on whether the crewmembers are participating on short- or long-duration missions.

- Shuttle crewmembers will collect a saliva sample every other day for the duration of their mission with a blood draw occurring on the day before they land.

- ISS crewmembers will perform three sessions (early, mid and late mission) in which they will collect blood and saliva samples.

- For both Shuttle and ISS subjects, all inflight samples are returned to the ground for analysis.

Operational Requirements: Preflight, each subject performs two sessions: one at L-180 (launch minus 180) days and another at L-45 days. Each session consists of four liquid saliva collections (performed every other day), with the blood draw, 24-hour urine and dry book saliva sample collection occurring on the day between the 2nd and 3rd liquid saliva collection.

Postflight, each subject performs two sessions: one at R+0 collecting four liquid saliva samples collected every other day starting on R+0 in conjunction with a blood draw and 24-hour urine collection. The second session two occurs at R+ 30 days collecting four liquid saliva samples (performed every other day) with a blood draw and 24-hour urine collection occurring on the day between the second and third liquid saliva collections. Dry book saliva samples are collected on R+1 and R+ 30 days.

Inflight, only blood and saliva samples are collected. There is no urine sample requirement for inflight operations. Subjects perform three sessions in-flight: early, mid and late increment. Each session consists of four liquid saliva collections (performed every other day), with a blood draw and dry book saliva sample collection occurring on the last day of the liquid saliva collections. For the late increment session, the final liquid saliva sample, the blood draw and dry book saliva sample collections occur on R-1. Blood samples are required to be returned for ground analysis within 48 hours of collection, therefore, the blood draws must occur in conjunction with a Shuttle or Soyuz flight to ISS.

Operational Protocols: Operations for this experiment consist of three types of sample collections: blood, urine and saliva. There are two types of saliva samples collected. Liquid saliva samples require the subject to soak a piece of cotton with saliva and place the cotton in a salivette bag. Dry book saliva samples are collected on filter paper bound in a small, specialized book at certain time intervals throughout the collection day. For preflight and postflight BDC only, 24-hour urine collections require the subject to collect all urine starting with the first void of the day and continuing for a full 24-hour period.

Review Cycle Status: PI Reviewed

Category: Human Research and Countermeasure Development for Exploration

Sub-Category: Immune System

Space Applications: The study will result in the validation of a monitoring strategy that will allow the development of effective countermeasures, which, when implemented, will safeguard the health of the crew during long duration space missions.

Earth Applications: The data collected during this investigation may lead a greater understanding of how the immune system is affected by different factors from stress to the environment. This data could potentially be used to help develop new treatments and preventative measures for immune dysfunctions.

Manifest Status: Continuing

Supporting Organization: Exploration Systems Mission Directorate (ESMD)

Previous Missions: Increment 16 was the first mission for Integrated Immune.

Web Sites:
International Space Station Medical Project (ISSMP)

Related Payload(s): Epstein-Barr, Integrated Immune-SDBI

Last Update: 10/20/2008

SDBI-1900, SMO-015 – *INTEGRATED IMMUNE*

Validation of Procedures for Monitoring Crewmember Immune Function

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Duane Pierson and Clarence Sams

ABSTRACT

There is ample evidence to suggest that space flight leads to immune system dysregulation. This may be a result of microgravity, confinement, physiological stress, radiation, environment or other mission-associated factors. The clinical risk (if any) from prolonged immune dysregulation during exploration-class space flight has not yet determined, but may include increased incidence of infection, allergy, hypersensitivity, hematological malignancy or altered wound healing. Each of the clinical events resulting from immune dysfunction has the potential to impact mission critical objectives during exploration-class missions. To date, precious little in-flight immune data has been generated to assess this phenomenon. The majority of recent flight immune studies have been post-flight assessments, which may not accurately reflect the in-flight status of immunity as it resolves over prolonged flight. There are no procedures currently in place to monitor immune function or its effect on crew health. The objective of this Supplemental Medical Objective (SMO) is to develop and validate an immune monitoring strategy consistent with operational flight requirements and constraints. This SMO will assess immunity, latent viral reactivation and physiological stress during both short and long duration flight. Upon completion, it is expected that any clinical risks resulting from the adverse effects of space flight on the human immune system will have been determined. In addition, a flight-compatible immune monitoring strategy will have been developed with which countermeasures validation could be performed. This study will determine, to the best level allowed by current technology, the in-flight status of crewmembers immune system. The in-flight samples will allow a distinction between legitimate in-flight alterations and the physiological stresses of landing and readaptation which are believed to alter R+0 assessments. The overall status of the immune system during flight (activation, deficiency, dysregulation) and the response of the immune system to specific latent virus reactivation (known to occur during space flight) will be thoroughly assessed. The first in-flight activity for Integrated Immune very recently occurred during the STS-120 Space Shuttle mission. The protocols functioned well from a technical perspective, and accurate in-flight data was obtained from 1 Shuttle and 2 ISS crewmember. Crew participation rates for the study continue to be robust.

Figure 1:

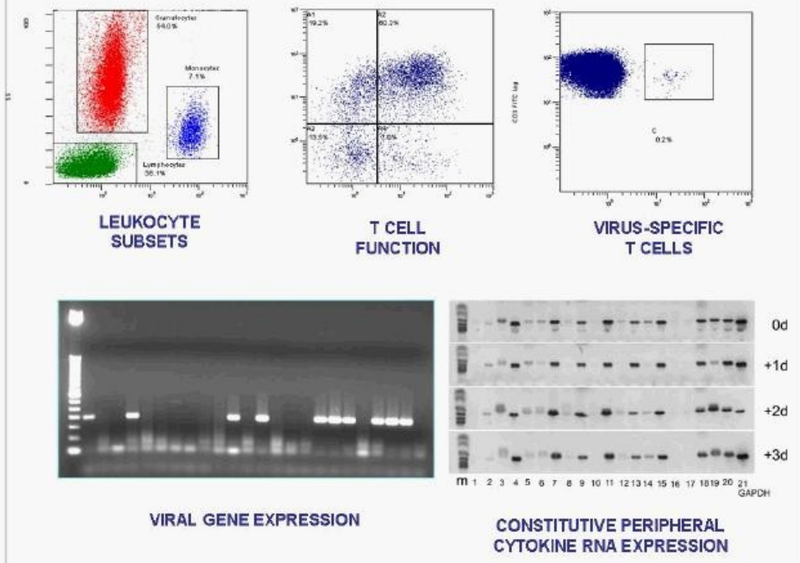
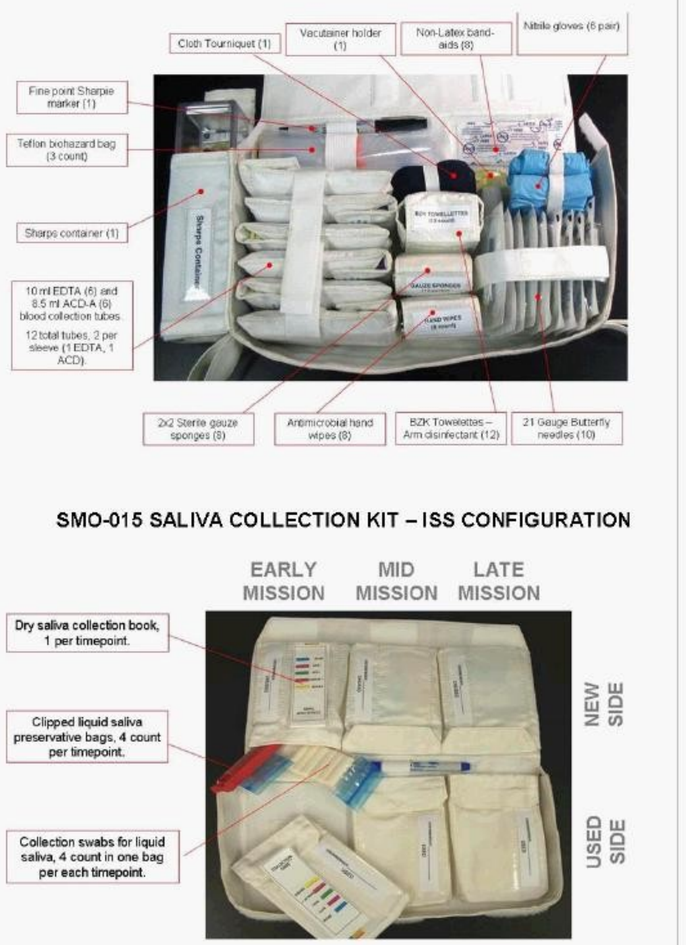


Figure 1: Representative data demonstrating some selected analysis techniques that will be employed during the Integrated Immune on-orbit assessment of immune status and function.

Figure 2:



- In-flight activity for *Integrated Immune* first occurred during Space Shuttle mission STS-120 and ISS Expedition-16 are participating.
- This study is designed to be a comprehensive, multi-laboratory effort that will assess immunity, latent viral reactivation and physiological stress in-flight. In-flight measurements are important since post-flight assessments are potentially skewed by the high-G entry and readaptation to gravity.
- Specific assays to be performed include peripheral phenotype, T cell function, cytokine production profiles, reactivation of herpesviruses, and the levels of stress hormones. Representative data are presented in Figure 1.
- Study samples will be whole blood and saliva (pre-, in-, and post-flight) and 24 hour urine (pre- and post-flight only). The in-flight sample collection kits are presented in Figure 2.

The *Integrated Immune* sample timepoints are presented in Figure 3.

Figure 3: