DEEP-SPACE ENVIRONMENTAL EFFECTS ON IMMUNE, OXIDATIVE STRESS AND DAMAGE, AND HEALTH AND BEHAVIORAL BIOMARKERS IN HUMANS. B. Crucian[1], S. Zwart[2], S. M. Smith[1], L. C. Simonsen[3], T. Williams[1], E. Antonsen[1], [1]NASA Johnson Space Center (2101 NASA Pkwy, Houston, TX 77058, brian.crucian-1@nasa.gov, scott.m.smith@nasa.gov, erik.l.antonsen@nasa.gov, thomas.j.williams-1@nasa.gov), [2]UTMB (301 University Blvd, Galveston, TX 77555, sara.zwart-1@nasa.gov), [3]NASA Langley Research Center (1 NASA Drive, Hampton, VA 23666, lisa.c.simonsen@nasa.gov).

Introduction:
Cell-mediated immunity has been demonstrated to be reduced in human subjects during long-duration spaceflight [1], and a relationship between the observed immune changes and reactivation of latent viruses has been confirmed. Postflight human testing has revealed severely depressed T-cell function after 6 months of flight but unaltered function after short-duration flight. Altered cytokine production patterns and potentially a shift to the Th2 pattern have been observed after spaceflight. Natural killer cell, monocyte, and neutrophil functions have all been found to be reduced after spaceflight. Latent herpes viruses reactivate to a high level during short-duration spaceflight, and new preliminary data indicate that this phenomenon also persists during long-duration flight. Long-duration flight has also recently been shown to result in elevations in an array of plasma cytokines, indicating that in vivo immune alterations associated with various physiological adaptations persist during flight. In addition, stress hormone levels have been found to be elevated during and after flight and to be heavily dependent on mission duration as well as biomarkers for oxidative stress and damage [2].

The question is, therefore, whether the immune system, oxidative stress and damage, and changes in antioxidant status may affect behavioral stress and other systems to a larger extent in deep space than in low Earth orbit because of synergistic or additive effects of deep space radiation with the other spaceflight environmental factors (e.g., 0*g* and isolation). Such synergistic effects on physiology may increase specific health risks for exploration crewmembers. Since the deep space radiation effects cannot be simulated on the ground in humans, Gateway research in astronauts is needed to answer this question.

Methods: The methods will be based on biomarker detection in biological samples (stabilized or dry saliva, blood, urine, and feces) that will be returned to Earth at various intervals, mirroring (where feasible) collection timepoints such as those currently used when collecting such samples from crewmembers on the International Space Station (ISS). For these purposes, collection devices will be needed in the Gateway habitat. Current assays on the returned samples include (1) stress hormones, (2) cytokine concentration, and (3) latent viral DNA. This affords an assessment of stress, immune status, inflammation, and latent viral reactivation (an adverse clinical outcome that can be measured).

Alternatively, to minimize sample return, an option could be to conduct some onboard analysis of blood cell distribution, leukocyte subsets, various soluble proteins, cytokines, and stress hormones.

Collection of longitudinal physiological and behavioral metrics (such as cognition, fine motor skills, task monitoring, and others) and monitoring of in-mission clinical events will enable an assessment of whether in-flight changes in the proposed biomarkers can be used as early predictive measures.

Resources Required: In order for blood to be collected (for serum or whole-blood assays), a blood collection kit containing items such as skin-disinfecting wipes, gauze, band-aids, butterfly needles, blood tubes, and gloves (total mass 0.266 kg, total volume 3071 cm^3), and a sharps container (0.125 kg, 1742 cm^3) of some sort would also be needed. Serum separator tubes (SST) would be required (minimum tube size available is 3.5 mL, 13 x 75 mm plastic with clot activator/polymer gel), as well as a centrifuge. Portable centrifuge models currently available are in the range of 27.94 cm x 27.94 cm x 25.4 cm (19828 cm^3) and weigh about 10 lb. A freezer capable of cooling to at least -20ºC would be required. Whole ambient blood samples collected in a preservative may be returned to enable leukocyte distribution assays to be done. The preserved samples could be stored for 7 to 14 days.

For urine collection, a urine collection kit containing single-void urine collection devices, wipes, adapters, tubes, and a urine containment bag would need to be flown to collect single-void urine samples (mass ~ 1.5 kg, volume 17749 cm^3).

Fluid saliva collection requires salivette bags and salivette tubes (0.019 kg, 258 cm^3) and would be done using passive salivation into a salivette, centrifuging the sample, and then freezing at -20ºC.

Alternatively, dry saliva collection hardware is already flight certified for ISS, and used as part of the "Functional Immune" study. Dry saliva books measure 4″ x 1.25″ and are paper thin. Assay development would be required to expand this technology for additional analytes.

Fecal collection for microbiome analyses requires a fecal collection kit containing fecal swab tubes, swabs, outer fecal container bags (total mass 0.826 kg and volume 1524 cm^3).

For in-flight analysis of fluid-based biomarkers, in-vehicle imaging cytometry and immunoassay techniques will be required.

References:

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