Objectives

• Address significant lack of data regarding immune status *during* flight.
• Replace several recent immune studies with one comprehensive study that will include in-flight sampling.
• Determine the in-flight status of immunity, physiological stress, viral immunity/reactivation.
• Determine the clinical risk related to immune dysregulation for exploration class spaceflight.
• Determine the appropriate monitoring strategy for spaceflight-associated immune dysfunction, that could be used for the evaluation of countermeasures.
**ASSAYS FOR INTEGRATED IMMUNE**

**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

**JSC Microbiology Laboratory**
- Latent herpesvirus reactivation (saliva/urine)
- Saliva/urine stress hormones
- Circadian rhythm analysis
SUBJECTS

Completed to date:
- 10 Short duration
- 5 Long duration

Total ‘n’:
- 17 Short duration
- 17 Long duration
A. Immunophenotype, T cell function, intracellular/secreted cytokine profiles.
• No in-flight changes in bulk leukocyte subsets
• Post-flight granulocytosis
• Late in-flight/postflight elevated B cells, reduced NK cells
• In-flight, post-flight trend towards elevated CD4:CD8 ratio, elevated memory T cell subsets
• Elevated effector memory, central memory in-flight
• No change in peripheral constitutively activated T cells
CD8+ T CELL FUNCTION: A+B 24 hours

ISS

SEA+SEB 24hr

- CD4/CD69
- CD8/CD69
- CD4/CD69/CD25
- CD8/CD69/CD25

CD8+ T CELL FUNCTION: A+B 24 hours

CD69+ CD25+
CD8+ T cell – Intracellular IFNg

SECRETED CYTOKINE PROFILES (CD3/CD28 48hr)

**INTRACELLULAR CD8+/IFNg+**

- SHUTTLE
- ISS

**CBA 3/28 48hr**
- IFNg
- TNFa
- IL-10
- IL-5
- IL-4
- IL-2
B. Leukocyte cytokine mRNA
Gene Expression of Markers of Innate (A) and Adaptive (B) Immune Responses (short-duration flights).

A.

TNF-α

IL-1

IL-6

IFN-γ (Th1 clones)

IL-4 (Th2 clones)

IL-10 (Treg clones)

Intervals of sample collection
Gene Expression of Markers of Innate (A) and Adaptive (B) Immune Responses (long-duration flights).

A.

- TNF-α
- IL-1
- IL-6

B.

- IFN-γ (Th1 clones)
- IL-4 (Th2 clones)
- IL-10 (Treg clones)
C. Virus specific T cell number, function, plasma stress hormone levels.
Plasma cortisol levels - ISS

Collection Time
L-180  L-45  14d  2-4m  6m  R+0  R+30
ug/dL

 ug/dL

Cortisol on ISS

Collection Time
L-180  L-45  14d  2-4m  6m  R+0  R+30
EBV T cell function - ISS

% CD8 T-cells

Collection Time

L-180  L-45  14d  2-4m  6m  R+0  R+30
D. Latent herpesvirus reactivation (saliva/urine), saliva/urine stress hormones, circadian rhythm analysis.
Urine CMV Assessment
Urine CMV Assessment

ISS

CMV copies/ml

L-180 L-10 R+0 R+14
Saliva VZV Assessment

SHUTTLE

VZV copies/ml

Pre flight

During flight

Post flight

-200 -180 -160 -10 0 10 4 14 24

Sub 7
Sub 15
Sub 12
Sub 9
Sub 8
Sub 14
Sub H
Questions?