INTEGRATED IMMUNE

February 2, 2009
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

ISS

SEA+SEB 24hr

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

CD8+ T CELL FUNCTION: A+B 24 hours
CD8+ T cell – Intracellular IFNg

Secreted Cytokine Profiles (CD3/CD28 48hr)
B. Leukocyte cytokine mRNA
Gene Expression of Markers of Innate (A) and Adaptive (B) Immune Responses (short-duration flights).

A.

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

A.

TNF-α

Intervals of sample collection

B.

RelaQuant (Folds of Changes)

TNF-α

IL-1

IL-6

IFN-γ (Th1 clones)

IL-4 (Th2 clones)

IL-10 (Treg clones)

Subj 6
Subj 7
Subj 8
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

Cortisol on ISS

ug/dL

L-180  L-45  14d  2-4m  6m  R+0  R+30

Collection Time
EBV T cell function - ISS

% CD8 T-cells

Collection Time
D. Latent herpesvirus reactivation (saliva/urine), saliva/urine stress hormones, circadian rhythm analysis.
Urine CMV Assessment

SHUTTLE

CMV copies/ml vs Time (hours)

- Sub 3
- Sub 5
- Sub 2
- sub 11
- sub 13

L-180 to R+30
Urine CMV Assessment
Saliva VZV Assessment

SHUTTLE

![Graph showing VZV copies/ml during pre-flight, during flight, and post-flight stages for different subjects.](Image)
Questions?