NASA HRP INVESTIGATORS MEETING

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.
| JSC Immunology Laboratory | • Leukocyte subsets  
|                          | • T cell function  
<table>
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<th>• Intracellular/secreted cytokine profiles</th>
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| 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

CD25+

CD69+

CD25+
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.

#### Intervals of sample collection

- L-180
- L-45
- IN
- R+0
- R+30

#### Gene Expression of Markers

- **TNF-α**
- **IL-1**
- **IL-6**

#### Relative Quantification (Folds of Changes)

- Subj 1
- Subj 2
- Subj 3
- Subj 4

### B.

#### IFN-γ (Th1 clones)

- IL-1
- IL-10 (Treg clones)

#### IL-4 (Th2 clones)

- IL-6

#### Relative Quantification (Folds of Changes)

- Subj 1
- Subj 2
- Subj 3
- Subj 4

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

Cortisol on ISS

ug/dL

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

Collection Time
EBV T cell function - ISS

Collection Time

% CD8 T-cells

EBV T-cell function - ISS

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

SHUTTLE

CMV copies/ml

L-180 L-45 R+0 R+30

Sub 3 Sub 5 Sub 2 sub 11 sub 13

L-180 L-45 R+0 R+30
Urine CMV Assessment

ISS

CMV copies/ml

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

ISS

VZV copies/ml

Pre flight

During flight

Post flight

Sub 3

Sub 5

Sub 2

Sub 11

Sub 13

-200 -180 -160 0 20 40 60 80 100 120 140 160 180

0 200 400 600 800 1000 1200

4 14 24
Questions?