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

CD69+

CD25+
CD8+ T cell – Intracellular IFNγ

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

**Gene Expression of Markers of Innate (A) and Adaptive (B) Immune Responses:**

**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.
EBV T cell function - ISS

% CD8 T-cells vs 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

ISS

CMV copies/ml

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

**VZV copies/ml**

- Pre flight
- During flight
- Post flight

**Time (days)**

0 10 16

**VZV Assessment**

- Sub 7
- Sub 15
- Sub 12
- Sub 9
- Sub 8
- Sub 14
- Sub H

**SHUTTLE**

- Saliva VZV Assessment

**Graph Details**

- X-axis: Time (days)
- Y-axis: VZV copies/ml

- Pre flight: Low VZV copies/ml
- During flight: Increase in VZV copies/ml
- Post flight: Stabilization or decrease in VZV copies/ml
Saliva VZV Assessment

VZV copies/ml

Pre flight

During flight

Post flight
Questions?