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.
<table>
<thead>
<tr>
<th>JSC Immunology Laboratory</th>
<th>Mercer University</th>
<th>Microgen Laboratories</th>
<th>JSC Microbiology Laboratory</th>
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<tbody>
<tr>
<td>• Leukocyte subsets</td>
<td>• Plasma cytokine balance</td>
<td>• Virus specific T cell number</td>
<td>• Latent herpesvirus reactivation (saliva/urine)</td>
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<td>• T cell function</td>
<td>• Leukocyte cytokine RNA</td>
<td>• Virus specific T cell function</td>
<td>• Saliva/urine stress hormones</td>
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<td>• Intracellular/secreted cytokine profiles</td>
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<td>• Plasma stress hormones</td>
<td>• Circadian rhythm analysis</td>
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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 – Intracellular IFNg

Secreted Cytokine Profiles (CD3/CD28 48hr)

INTRACELLULAR CD8+/IFNg+

CBA 3/28 48hr

Secreted Cytokine Profiles (CD3/CD28 48hr)

SHUTTLE

ISS

L-180 L-45 EAR MID LATE R+0 R+30

CBA 3/28 48hr

- IFNg
- TNFa
- IL-10
- IL-5
- IL-4
- IL-2

L-180 L-10 FLT R+0 R+14
B. Leukocyte cytokine mRNA
Gene Expression of Markers of Innate (A) and Adaptive (B) Immune Responses (short-duration flights).

A. Intervals of sample collection

B. 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)**

Intervals of sample collection

Relative Quantification (Folds of Changes)
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

18
16
14
12
10
8
6
4
2

Cortisol on ISS

Collection Time
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
Saliva VZV Assessment

SHUTTLE

VZV copies/ml

0 200 400 600 800 1000 1200

Pre flight  During flight  Post flight

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

-200 -180 -160 -10 0 10 16 24
Saliva VZV Assessment

VZV copies/ml

Pre flight During flight Post flight

ISS

Sub 3
Sub 5
Sub 2
Sub 11
Sub 13
Questions?