CONCORDIA STATION, DOME C, ANTARCTICA AS A GROUND-BASED ANALOG FOR SPACEFLIGHT/PLANETARY EXPLORATION

Consequences of Longterm-Confinement and Hypobaric Hypoxia on Immunity in the Antarctic Concordia Environment (ESA - CHOICE Study)

Brian Crucian, Alexander Chouker, Duane Pierson, Satish Mehta, Raymond Stowe, Alex Salam and Clarence Sams
Spaceflight-associated immune dysregulation

- Microbes increase virulence
- Stress
- Microgravity
- Disrupted circadian rhythms
- Radiation
- Isolation
- Reduced immune cell function
- Altered cytokine balance
- Latent viral reactivation
- Altered wound healing

Questions:
- Infection?
- Hypersensitivity?
- Autoimmunity?
- Cancer?
Risk: Crew Adverse Health Event Due To Altered Immune Response

Human immune function is altered in- and post-flight, but it is unclear if this change leads to an increased susceptibility to disease. Reactivation of latent viruses has been documented in crewmembers, though this reactivation has not been directly correlated with the immune changes nor with observed disease. Further research may elucidate whether microgravity exposure impairs the immune system, and whether this change represents a health risk to crews.
SAT Report, Immune-related Knowledge Gaps

IM1  Lack of in-flight immune data. In-flight data required to determine risk.

IM2  Formulation of an improved immunology standard for exploration spaceflight.

IM2  This is not a research gap, but will be derived from the filling of gap: Lack of in-flight immune data. In-flight data required to determine risk.

IM3  Lack of ground analog studies. Suitable ground analogs for immune dysregulation have been identified. Forward work may be expedited using these opportunities.**

IM4  Lack of in-flight hardware to evaluate hematology /infection/immunity. Capability must be developed prior to exploration missions.

IM5  Investigation of individual records of in-flight illness for clarification of time course/etiology.

**Specific directive from program review: evaluate Antarctica winter-over as potential analog for SAID.
(Human) Ground-based Space Flight Analogs

Extended head-down bed rest

MARS-500 (IBMP – Moscow)

Closed Chamber Confinement

NEEMO Aquarius Station

Haughton-Mars Project

Antarctica winter over

Best Analogs for SAID

An analog which simulates (or actual) mission-deployment, associated risk, adverse environment, isolation, psychological/physiological stress, disrupted circadian rhythms, etc.
ANNOUNCEMENT OF OPPORTUNITY
FOR MEDICAL, PHYSIOLOGICAL AND PSYCHOLOGICAL RESEARCH
USING THE CONCORDIA ANTARCTIC STATION

Consequences of long-term confinement and Hypobaric Hypoxia on Immunity in the Antarctic Concordia Environment (CHOICE – Study)

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• PMN number, function, bactericidal
• In-vitro DTH
• Apoptosis/necrosis
• Cellular mRNA expression
• Plasma purine markers of inflammation/hypoxia
• Erythropoietin activity
• Stress test
• Stress hormones
• Components of exhaled air
Effects of Space Flight

Immune System Changes (Status and Function)

Adverse clinical outcomes (Latent Viral Reactivation)
NASA Integrated Immune Assays

**JSC Immunology Laboratory**
- Leukocyte subsets
- T cell function
- Intracellular/secerted 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
### INTEGRATED IMMUNE

**PRE-FLIGHT**
- B Single blood collection
- L Single liquid saliva collection in A.M.
- D Single day of dry saliva collections (5 throughout day)
- U Single 24 hour urine collection (void by void).

**IN-FLIGHT**
- B Single blood collection
- L Single liquid saliva collection in A.M.
- D Single day of dry saliva collections (5 throughout day)
- U Single 24 hour urine collection (void by void).

**POST-FLIGHT**
- B Single blood collection
- L Single liquid saliva collection in A.M.
- D Single day of dry saliva collections (5 throughout day)
- U Single 24 hour urine collection (void by void).

**KEY:**
- **B** Single blood collection
- **L** Single liquid saliva collection in A.M.
- **D** Single day of dry saliva collections (5 throughout day)
- **U** Single 24 hour urine collection (void by void).

*Early/mid ISS samples to be collected only if sample return possible by other returning/visiting Shuttle/Soyuz vehicle. All ground blood collections coincide with AME or Med-Ops draws when possible.

**CHOICE**

- **WB, urine, saliva**
- **Frozen plasma, urine, saliva**
- **WB, urine, saliva**

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Shuttle or Soyuz undocking occurs. ISS crew (staying on station) to be sampled during last full day of docked operations. Samples to be returned on Shuttle/Soyuz.

~1 month
ALL ANTARCTIC STATIONS ARE NOT THE SAME...
Antarctica
Area covered: 5580x4900km
Altitude range: 0 (black) to 5022m (white)
Vertical exaggeration: x2000
Difficult travel in/out
Extreme isolation, even greater than ISS
Altitude 3200m (10,500 ft)
Air pressure 645hPa (mbar)
12-13 Vol% of O₂
Lack of CO₂ in air
Higher ionization in air (increases oxidative metabolism)

THE CONCORDIA ENVIRONMENT
chronic hypobaric hypoxia

• Relative humidity 3-5%
• Snowfall ~1cm/yr
• High winds
• Elevated UV exposure (summer), UV deficiency (winter)
• Mean winter temperature -60 C (-72 F)
• Mean summer temperature -30 C (-22 F)
• Disrupted circadian rhythms.
HUMAN FACTORS

• Isolation, confinement for prolonged duration
• Limited communication capability
• International crew, multiple languages
• Sleep/wake cycles disrupted
• Actual deployment w/ associated risks
• Winter over crew: 12
• Summer crew: ~50
Summer Transition period – Incidence Rates
(mid-November to mid-January)

• Approx. 50% of summer participants contacted infectious disease

• Historically, extremely high incidence rate

• Three periods of epidemic viral infections:
  
  Period 1: Flu-like (mid-Nov. to mid-Dec.)
  
  Period 2: Rhinoparyngitis (mid-Dec. to early Jan.)
  
  Period 3: Gastro-enteritis (late-Dec. to early Jan.)

-Data from Concordia Base, Chief Medical Officer
## NASA CHOICE Assays

<table>
<thead>
<tr>
<th>BLOOD ASSAYS</th>
<th>Pre, post sampling</th>
<th>In-sampling</th>
<th>Details</th>
<th>NASA Lab</th>
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</thead>
<tbody>
<tr>
<td>Comprehensive immunophenotype</td>
<td>WB</td>
<td>(see panel)</td>
<td></td>
<td>Immune</td>
</tr>
<tr>
<td>Intracellular cytokine profiles (T cell)</td>
<td>WB</td>
<td>PMA+ION, LPS</td>
<td></td>
<td>Immune</td>
</tr>
<tr>
<td>T cell function</td>
<td>WB</td>
<td>CD3/CD28, A+B</td>
<td></td>
<td>Immune</td>
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<tr>
<td>Secreted cytokine profiles</td>
<td>WB</td>
<td>Th1/Th2, Inflam.</td>
<td></td>
<td>Immune</td>
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<tr>
<td>Viral DNA - PBMC</td>
<td>WB</td>
<td>EBV</td>
<td></td>
<td>Mcggn</td>
</tr>
<tr>
<td>Circulating viral-specific T cells</td>
<td>WB</td>
<td>EBV, CMV</td>
<td></td>
<td>Mcggn</td>
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<td>Viral-specific T cell function</td>
<td>WB</td>
<td>EBV, CMV</td>
<td></td>
<td>Mcggn</td>
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<tr>
<td>Viral antibodies titers</td>
<td>Plasma</td>
<td>Plasma</td>
<td>EBV, CMV</td>
<td>Mcggn</td>
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<tr>
<td>Viral antibodies titers</td>
<td>Plasma</td>
<td>Plasma</td>
<td>VZV</td>
<td>Micro</td>
</tr>
<tr>
<td>Plasma stress hormones</td>
<td>Plasma</td>
<td>Plasma</td>
<td>cortisol</td>
<td>Mcggn</td>
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</tbody>
</table>

### SALIVA ASSAYS

<table>
<thead>
<tr>
<th></th>
<th>Dry Saliva</th>
<th>Dry Saliva</th>
<th>cortisol, DHEA</th>
<th>Micro</th>
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</thead>
<tbody>
<tr>
<td>Saliva stress hormones, Diurnal</td>
<td>Dry Saliva</td>
<td>Dry Saliva</td>
<td>cortisol, DHEA</td>
<td>Micro</td>
</tr>
<tr>
<td>Viral DNA by PCR</td>
<td>Liquid Saliva</td>
<td>Liquid Saliva</td>
<td>CMV*, EBV, VZV</td>
<td>Micro</td>
</tr>
</tbody>
</table>

### URINE ASSAYS

<table>
<thead>
<tr>
<th></th>
<th>24hr. URINE</th>
<th>24hr. URINE</th>
<th>CMV</th>
<th>Micro</th>
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</thead>
<tbody>
<tr>
<td>Viral DNA by PCR</td>
<td>24hr. URINE</td>
<td>24hr. URINE</td>
<td>CMV</td>
<td>Micro</td>
</tr>
<tr>
<td>Urine stress hormones</td>
<td>24hr. URINE</td>
<td>24hr. URINE</td>
<td>cortisol*, cat.*</td>
<td>Micro</td>
</tr>
</tbody>
</table>
LYMPHOCYTE SUBSETS

Percent

L-60  EARLY  LATE  R+60

GRAN  LYM  MONO  T  B  NK  CD4  CD8
Increase in memory CD4, memory CD8 during deployment. Similar to flight crew, reflects immune activation.

Shift among CD8 subsets, increases in late activation, senescent subsets, reflective of chronic activation.
Increase in terminally differentiated memory CD8, also reflective of chronic activation, corresponding decrease in the effector memory subsets.
Increases in constitutively activated CD4+ and CD8+ T cells
CD8+/IFNγ+

NORMAL

EARLY
CBA Assay: secreted cytokine profiles

- L-60
- Early
- WO #1
- WO #2
- WO #3
- WO #4
- WO #5
- WO #6
- WO #7
- WO #8
- Late
- R+30

- WB, urine, saliva

- Frozen plasma, urine, saliva

- WB, urine, saliva

- JAN
- FEB
- MAR
- APR
- MAY
- JUNE
- JULY
- AUG
- SEPT
- OCT

~1 month

Pre
CONCORDIA
Post
Secreted cytokine culture supernatants: 10 day RT stability

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

- FROZEN
- 10 DAYS COLD
- 10 DAYS R.T.
Secreted cytokine culture supernatants: multiple freeze-thaw
CBA Assay: secreted cytokine profiles

3 TCR 'responder CHOICE subjects; 4 control subjects
Unplanned ‘bonus’ mid-winter testing

• Partec cytometer plan: bring in/out for support of each early/late timepoint.
• Revised to leave during winter over, with Dr. Salam to process samples.
• Reagents issues
• Consumable supply issues
• Data/training issues
• Additional assays as training/reagents/consumables allowed, phenotype, cell cultures.
• First run: deployment month #2. Samples collected at DC, data acquired at DC, data emailed to JSC, analysis performed at JSC.