UPDATE: ANTARCTIC WINTEROVER AS AN ANALOG FOR SPACEFLIGHT IMMUNE DYSREGULATION (CHOICE II study at Concordia Station; CHOICE-Coastal study at Neumayer III Station)

National Aeronautics and Space Administration

George Makedonas[1], Satish Mehta[1], Stephanie Krieger[2], Alexander Chouker[3], Mathias Basner[4], Alexander Stahn[5], Duane Pierson[6], Brian Crucian[6]

[1]JES Tech, [2]KBRwyle, [3]University of Munich, [4]University of Pennsylvania, [5]Charité University Medicine, [6]NASA Johnson Space Center

Orbital spaceflight perturbs the human immune system significantly; Natural Killer (NK) and T-lymphocyte (T) cell functions are most susceptible to spaceflight-induced impairment. This loss of function may manifest in persistent latent virus reactivation (CMV, EBV, VZV), which does occur at a higher frequency in astronauts compared to earthlings.

The definition of a countermeasure strategy to immune depression is a prerequisite for deep-space exploration. To this end, an Earth analog for the space exposome would facilitate the process greatly. Winter-over (WO) missions on Antarctica reproduce profound stressors associated with space: extreme temperatures, circadian misalignment, and isolation. Here, we update the progress of two research projects -- at Concordia Station (interior) and Neumayer-III Station (coastal) -- that assessed the effect of Antarctica WO stay on immunity and latent herpesvirus reactivation.

Previously, the ESA-NASA CHOICE I study evaluated immune dysregulation during WO at the interior Concordia Station. The data revealed significant dysregulation persisted in crewmembers, but many aspects were dissimilar from those defined during spaceflight. The differences may be due to the confounding influence of hypobaric hypoxia; Concordia sits at an elevation of over 14,000 feet. Nonetheless, a follow-up study (CHOICE II) study at Concordia Station was implemented to define a mechanistic understanding of the relationship between stress, isolation, and hypobaric hypoxia on immunity.

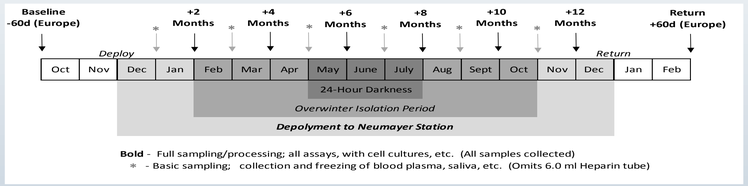
In parallel, NASA selected an immune evaluation to be performed at Neumayer Station -- Choice-Coastal – to determine if the coastal, and relatively normoxic, base recapitulates the space exposome more precisely than the interior base. In association with the Behavioral Hybrid Training investigation (M. Basner, PI), this study incorporated immune assays from the NASA Integrated Immune and ESA Immuno investigations aboard ISS. Therefore we will be able to compare directly previous data from flight-to-ground missions with those from Antarctica interior and coastal (hypoxic versus normoxic, respectively) WO missions.

Our goals are:

1. To define the mechanism of stress-induced immune cell impairment.
2. To identify a ground (Antarctica?) space analog for immune countermeasure development and validation studies.

METHODOLOGY

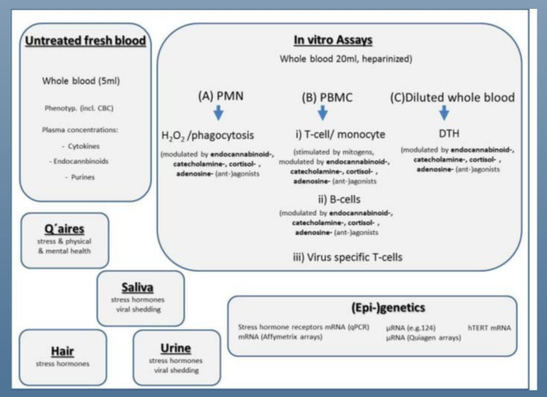
Eight subjects were deployed for winter-over isolation during the first 11 months or each study year, 2016 and 2017 (n =16 total). Blood specimens were collected monthly at the base, and then processed for plasma and flow cytometric analysis.



An on-location flow cytometer was installed at Concordia Station for real-time acquisition. Pre- and post- mission samples (baseline) were collected in Europe. The flow cytometry data was sent to the Immunology lab at JSC for analysis in 2018. A shipment containing all the frozen plasma and whole blood specimens from both the WO 2016 and 2017 seasons was received at JSC in November 2018; analyses of these samples will be completed in FY2019.

A variety of ESA-led assays to define “omics” and epigenetic alterations during prolonged confinement in hypobaric hypoxic conditions. NASA will contribute a suite of previously validated assays that defined immune dysregulation in astronauts.

ESA assays



NASA-JSC assays

T cell intracellular cytokine production
Plasma and salivary cytokine concentration
Stress Hormones
Clinical questionnaire
Viral Reactivation by PCR detection: EBV, VZV

A. PERIPHERAL LEUKOCYTE DISTRIBUTION

	Ex:	488			633
	Em:	530	575	695	660
	(fresh blood staining)	FITC **FL1**	PE **FL2**	PC5.5 **FL3**	APC **FL6**
A	Leukocytes subsets, B, NK	CD14	CD16+56	CD19	CD45
B	T cells, subsets	CD8	HLA-DR	CD3	CD45
C	Central Memory	CD62L	CD45RA	CD3	CD8
D	B Cell subsets	IgD	CD27	CD19	CD45
E	Viral-Specific	CD8	EBV-BMLF	CD3	CMV-PP65
F	Treg	CD25	CD127	CD3	CD4

B. CELL CULTURE ASSAYS

(24h culture)				
SEA+SEB culture	CD25	CD69	CD8	CD4
anti3/28 soluble	CD25	CD69	CD8	CD4

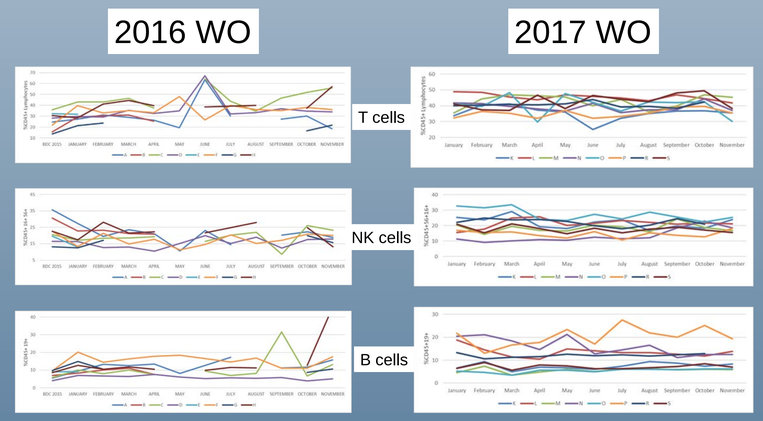
(48h culture)
media control
anti-3/28 soluble
anti-3/28 bead
PMA-I
LPS
— Freeze supernatants

PROGRAM RELEVANCE

- HHC risk: ‘Risk of adverse crew health event due to altered immune response’
- HHC GAP IM-03: ‘Lack of a suitable ground analog for spaceflight-associated immune dysregulation’, as identified in the SAT report and the current HRP IRP rev D.
- The identification of the most appropriate ground based space flight analog for spaceflight-associated immune dysregulation is necessary to enable mechanistic assessments, development of a validation strategy, and the ground-based validation of immune countermeasures. Any likely analog will be validated by comparing its ground data to the in-flight immune data generated during the Integrated and Functional Immune flight studies (SMO-015).

PRELIMINARY RESULTS

- Bulk leukocyte distribution (A protocol), for the CHOICE II subjects



SUMMARY CONCLUSION

- Data collection during the 2017 session versus the 2016 session was much more consistent. While the results from 2016 demonstrate profound fluctuations during the winter months, those from 2017 indicate a relatively constant frequency in all cell types. Without a knowledge of particular activities or events that may have influenced the data, the gaps in sample collection and the overall inferior quality of the flow data from the 2016 session suggest the discrepancy in the data patterns between the two WO sessions is most likely attributable to technical error rather than true immune perturbations.
- Data from the remaining samples in repository will determine the prospect of a coastal base as a site for countermeasure validation.