HAZARDS OF LUNAR SURFACE EXPLORATION: DETERMINING THE IMMUNOGENICITY/ALLERGENICITY OF LUNAR DUST

Audrie A. Colorado[1], Stephanie Krieger[1], Mayra Nelman-Gonzalez[1], Gailen Marshall[2], Torin Mccoy[3] and Brian Crucian[3]

[1] KBR, Houston, Texas; [2] University of Mississippi Medical Center, Jackson, Mississippi; [3] NASA Johnson Space Center, Houston, Texas

BACKGROUND

Lunar dust is a unique health hazard for lunar surface operations. Due to eons of meteorite bombardment with a complete lack of wind/water-based erosion, the dust is comprised of micron sized extremely sharp particles. The bulk chemical composition of lunar dust varies across the lunar surface, but is about 50% SiO2, 15% Al2O3, 10% CaO, 10% MgO, 5% TiO2 and 5-15% iron, with lesser amounts of sodium, potassium, chromium, zirconium. Trace amounts of virtually all elements ranging from the ppb level to the ppm level, can be found in lunar dust [1]. During the Apollo missions, dust was on the crewmembers and pervasively in the lunar lander vehicle. It is a difficult hazard to 'engineer out' human exposure. There are multiple Apollo program reports of lunar dust (LD) exposure leading to significant upper respiratory symptoms in select crewmembers. Possible mechanisms for upper respiratory symptoms include (1) particulate irritation, (2) oxidization and release of noxious gas, or (3) legitimate adaptive immune-mediated response. Although sterile non-protein matter would not be expected to be an allergen, it is noteworthy that one Apollo flight surgeon reported increasing symptoms upon repeated post-mission exposure over several days. Symptoms increased, mirroring an allergic reaction. The WBC indicated eosinophilia, a hallmark of an allergic reaction [2].

Many ISS crews display a pattern of persistent immune system dysregulation and latent virus reactivation [3,4]. Some ISS crews manifest atypical respiratory and/or dermatitis symptoms which could have an allergic pathogenesis [5]. It is logical to anticipate crew immune dysregulation would worsen during prolonged deep space missions. Planetary surface hazards will only complicate crew health risks.

It is therefore of interest to NASA, as international agencies prepare to support prolonged lunar missions, to determine if lunar dust may cause a substantial and legitimate allergic reaction, or if allergy may be 'ruled out' and symptomology reports ascribed to simple irritation. We propose simple in-vitro experiments to determine if actual lunar dust may cause an immediate or induced-sensitization allergic response. Our laboratory has previous experience assessing lunar dust interactions with immune cells (Figure 1) as part of a previous rodent inhalation study [6,7], although the cultures proposed for this study are novel.

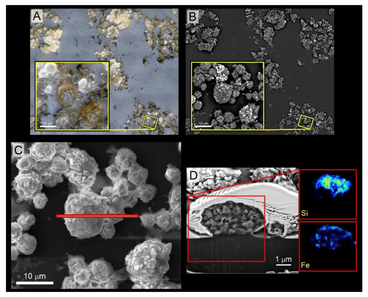


Figure 1. Light, electron, and confocal microscopy of lunar dust interactions with lung cells derived from Lam, C., *et al.* 2013.

AIMS

This study will investigate if LD exposure will elicit an IgE mediated allergic response either to the LD itself or concomitant antigen exposure during spaceflight. Allergic reactivity could adversely increase clinical and operational impacts for long-duration lunar astronauts and affect countermeasure requirements for surface vehicles. We hypothesize that *in vitro* co-culture of primary human blood cells with lunar dust particles will elicit a basophil/histamine-based allergic response. Will test this hypothesis with the following aims:

Aim #1 (Immediate reaction): Does *in vitro* LD exposure result in increased histamine from human peripheral blood basophils?

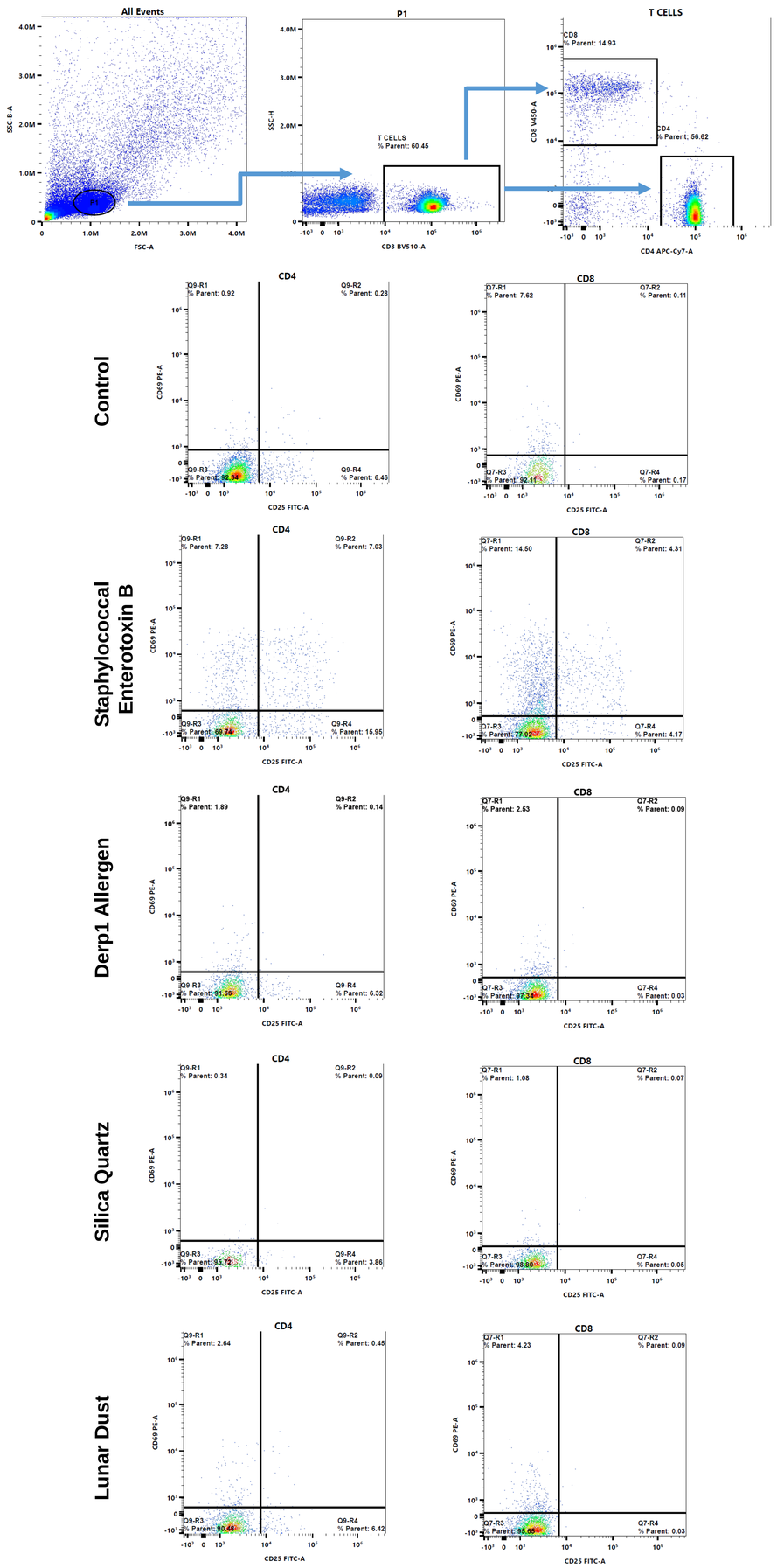
- Mitogen (positive control) and common recall antigens such as Der P1 (antigenic control) will be used in parallel cultures to lunar dust. Outputs include cellular activation antigens, cytokines, histamine, leukotrienes, and IgE. Confocal microscopy will be performed to assess the identity of responding cells and the nature of the response (ie phagocytosis, receptor mediated activation, etc.). Electron microscopy will be performed to, in mixed particle samples such as lunar dust, the elemental nature of the particles that generate a cellular response. Twenty subjects will be recruited for this aim.

Aim #2 (Allergic sensitization): Can LD impact the capacity of CD4+ helper and/or CD19+ B cell-mediated IgE production?

- Both PBMC and whole blood from healthy test subjects will be cultured in the presence of LD. Culture in the presence of mitogens and common recall antigens will serve as control stimuli. A re-stimulation will be performed after 14 days and will last for either 6 hours (intracellular cytokines, B cell activation), 24 hours (T cell intracellular cytokines, T cell activation cytometry), or 48 hours (secreted cytokine profiles). Twenty subjects will be recruited for this aim.

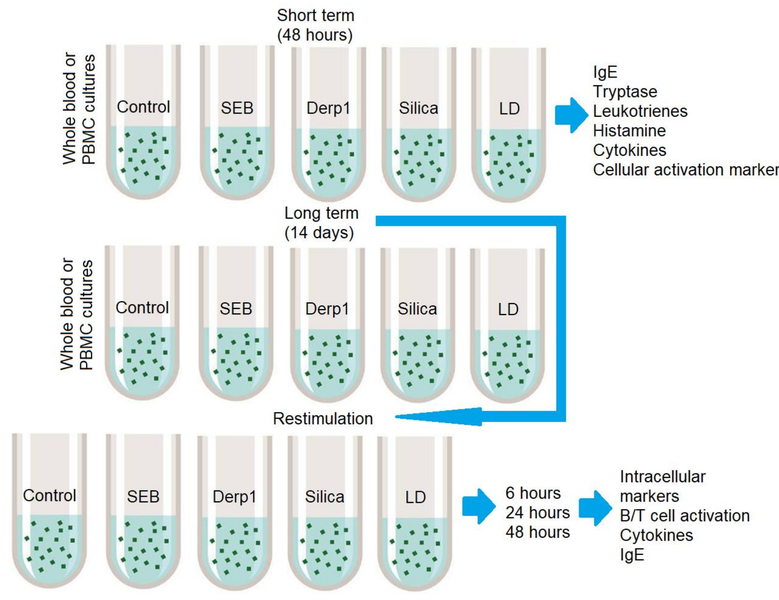
PRELIMINARY RESULTS

Preliminary *in vitro* cultures assessing the activation of T cells have been performed. Compared to the control, no stimulation, culture and the Staphylococcal Enterotoxin B stimulated culture, LD exposure does not activate T cells. This is also seen in the LD simulant, silica quartz, and in the recall antigen, common house dust mite allergen, Derp1. Cultures assessing the basophil and eosinophil cell population activation, and histamine, tryptase, IgE, and cytokine responses still need to be performed to fully determine if LD will elicit an IgE allergic response. These experiments are currently ongoing.



METHODS

We propose a set of *in vitro* cell culture experiments (short and long term) using human peripheral blood mononuclear cells (PBMC) and basophils from both atopic and non-atopic individuals. Cells will be co-cultured with cellular mitogens, common recall antigens (Der p1), silica quartz (as a possible allergenic component of LD), or LD, to study whether LD exposure for varying time intervals will alter the generation of selective immune responses associated with clinical allergic reactions. Measured outputs include supernatant-derived IgE, tryptase, histamine and selected cytokine levels. Cellular activation will be monitored by assessing activation markers via flow cytometry. Light microscopy and electron microscopy/x-ray analysis will be used to determine cellular interactions with dust particles (and the elemental nature of the particles).



EXPECTED OUTCOMES

We anticipate that all subjects will demonstrate viable immune cells with appropriate functional responses to all positive control stimuli. We anticipate that a subset of subjects with a history of allergy will demonstrate responsiveness to some of the recall antigens. The lunar dust data will indicate, for some or all subjects, presence/absence of existing sensitivity to lunar dust (Aim 1), or the ability to have a sensitivity to lunar dust induced by long term co-culture (Aim 2). These data will have utility for determining vehicle requirements and the likelihood of surface hazard regarding lunar dust and allergy.

REFERENCES

1. Loftus DJ, Tranfield EM, Rask JC, McCrosssin C. The Chemical Reactivity of Lunar Dust Relevant to Human Exploration of the Moon. : 8.
2. Scheuring RA, Jones JA, Novak JD, Polk JD, Gillis DB, Schmid J, et al. The Apollo Medical Operations Project: Recommendations to improve crew health and performance for future exploration missions and lunar surface operations. Acta Astronautica. 2008;63: 980–987. doi:10.1016/j.actaastro.2007.12.065
3. Crucian B, Stowe RP, Mehta S, Quiriarte H, Pierson D, Sams C. Alterations in adaptive immunity persist during long-duration spaceflight. npj Microgravity. 2015;1: 15013. doi:10.1038/npjmgrav.2015.13
4. Mehta SK, Laudenslager ML, Stowe RP, Crucian BE, Feiveson AH, Sams CF, et al. Latent virus reactivation in astronauts on the international space station. NPJ Microgravity. 2017;3. doi:10.1038/s41526-017-0015-y
5. Crucian B, Johnston S, Mehta S, Stowe R, Uchakin P, Quiriarte H, et al. A case of persistent skin rash and rhinitis with immune system dysregulation onboard the International Space Station. J Allergy Clin Immunol Pract. 2016;4: 759-762.e8. doi:10.1016/j.jaip.2015.12.021
6. Crucian B. Immune Alterations in Rats Exposed to Airborne Lunar Dust. 2014 Oct 10. Available: https://ntrs.nasa.gov/search.jsp?R=20140012423
7. Lam C, Scully RR, Zhang Y, Renne RA, Hunter RL, McCluskey RA, et al. Toxicity of lunar dust assessed in inhalation-exposed rats. Inhal Toxicol. 2013;25: 661–678. doi:10.3109/08958378.2013.833660

ACKNOWLEDGEMENTS

This project is funded by the Human Research Program (HRP) at NASA under 2019 HERO 80JSC019N0001-FLAGSHIP & OMNIBUS: Human Research Program Crew Health. Appendix A&B.