CARDIOPULMONARY INFLAMMATORY RESPONSES TO SUBACUTE METEORITE DUST EXPOSURES – IMPLICATIONS FOR HUMAN SPACE EXPLORATION A.D. Harrington[1,2,3], F.M. McCubbin[1], J. Kaur[3], K.E. Vander Kaaden[4], A. Smirnov[3,5], K. Galdanes[2], M.A.A. Schoonen[3,6], L.C. Chen[2], and T. Gordon[2] [1]NASA Johnson Space Center. [2]Dept. of Environmental Medicine, New York University School of Medicine. [3]Dept. of Geosciences, Stony Brook University, [4]Jacobs Technology, NASA JSC [5]Geology Dept., Lone Star College. [6]Environmental Sciences Dept., Brookhaven National Laboratory. Andrea.D.Harrington@nasa.gov

Introduction: The previous manned missions to the Moon represent milestones of human ingenuity, perseverance, and intellectual curiosity. However, one of the major ongoing concerns is the array of hazards associated with lunar surface dust. Not only did the dust cause mechanical and structural integrity issues with the suits, the dust 'storm' generated upon reentrance into the crew cabin caused "lunar hay fever" and "almost blindness [1-3]" (Figure 1). It was further reported that the allergic response to the dust worsened with each exposure [4]. The lack of gravity exacerbated the exposure, requiring the astronauts to wear their helmet within the module in order to avoid breathing the irritating particles [1]. Due to the prevalence of these high exposures, the Human Research Roadmap developed by NASA identifies the *Risk of Adverse Health and Performance Effects of Celestial Dust Exposure* as an area of concern [5]. Extended human exploration will further increase the probability of inadvertent and repeated exposures to celestial dusts. Going forward, hazard assessments of celestial dusts will be determined through sample return efforts prior to astronaut deployment.

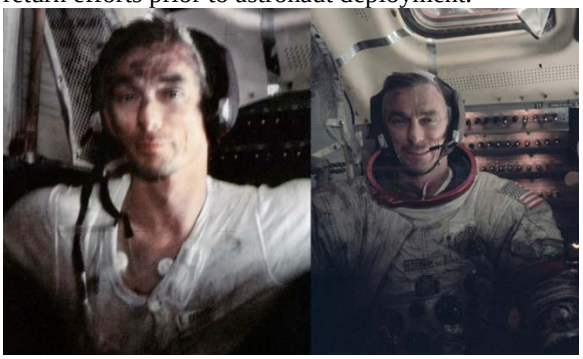

Figure 1. Eugene Cernan after a spacewalk (Apollo 17)

Studies on the lunar highland regolith indicate that the dust is not only respirable but also reactive [2, 6-9], and previous studies concluded that it is moderately toxic; generating a greater response than titanium oxide but a lower response than quartz [6]. The presence of reactive oxygen species (ROS) on the surface of the dust has been implicated. However, there is actually little data related to physicochemical characteristics of particulates and pulmonary toxicity, especially as it relates to celestial dust exposure.

As a direct response to this deficit, the authors initiated an extensive study evaluating the role of a particulate's innate geochemical features (e.g., bulk chemistry, internal composition, morphology, size, and reactivity) in generating adverse toxicological responses *in vitro* and *in vivo*. This highly interdisciplinary study evaluates the relative toxicity of six meteorite samples representing either basalt or regolith breccia on the surfaces of the Moon, Mars, and Asteroid 4Vesta; three potential candidates for future human exploration or colonization. Terrestrial mid-ocean ridge basalt (MORB) is also used for comparison as a control sample.

Preliminary research demonstrated that there are significant differences in the pulmonary inflammation generated upon acute exposure to the six celestial materials utilized, as well as the mid-ocean ridge basalt. More specifically, the acute exposure studies reveal relationships between toxicity and a meteorite sample's origin, its pre-ejected state (unweathered versus processed), and geochemical features (Table 1) [10].

Table 1. Sample Data Comparison to MORB

Sample	Iron[a]	H_2O_2[b]	ISR[c]	PMNs[d]
	% of MORB			
Tissint	83	208	618	163
NWA 7034	20	4	318	132
NWA 4734	30	83	246	172
NWA 7611	2	28	145	128
Berthoud	20	11	180	106
NWA 2060	19	53	174	120

[a] Iron leached from dust in simulated lung fluid after 8 days
[b] H_2O_2 formed in water after 25 minutes
[c] Cellular ISR at 24 hours post exposure only
[d] Polymorphonuclear leukocytes (PMNs) infiltration in BALF

Experimental Details: The meteorite and terrestrial samples were first crushed using an agate mortar and pestle and then ground using an agate ball mill to a respirable size fraction (<10µm). The bulk chemistry was determined by electron probe microanalyses of the shocked glass generated by heating a representative aliquot of powdered sample to greater than 1600°C for 25 minutes and then quenching the samples [11]. The mineralogy was determined via x-ray diffraction. The geochemical reactivity of the dust was evaluated by quantifying

iron solubility (FerroZine UV-Vis method) and *in situ* reactive oxygen species (ROS) generation (ISO-HPO-100 Microsensor for hydrogen peroxide). Both *in vitro* and *in vivo* toxicological techniques were used to determine the pulmonary inflammation caused by acute exposure. The *in vitro* method utilized a technique first published in [10], where the inflammatory stress response (ISR) of the cells to the presence of the dust is quantified systematically over 24 hours. *In vivo* dust exposure was administered via oropharyngeal aspiration of dust slurries in acute (single dose) exposures and two different subacute exposures; specifically a 3-consecutive day and a three week exposure. The experimental endpoints were evaluated 24 hours after final dose. Cytokine dysregulation and neutrophil infiltration into the bronchoalveolar lung fluid (BALF) were quantified to evaluate the body's inflammatory pulmonary response to the presence of the particles. Wire myography was utilized to determine the difference in vasoconstriction and vasorelaxation of the aorta after exposure in order to understand cardiovascular health risks.

Discussion: One of the main results of the subacute exposure study is that geochemical and toxicological correlations made during acute studies do not hold, however other correlations developed. For example, there is no correlation with bulk iron content and neutrophil (or PMN) infiltration into the lungs in subacute studies as there was for acute exposure but there is a correlation with particle derived reactive oxygen species (ROS) formation and PMN infiltration (Figure 1). Given the role that ROS have in the body's inflammatory response, it is not unexpected that this correlation would develop over time. In fact, one of the possible explanations for why there was no acute correlation with particle derived ROS is that there was not enough time for the particulate generated ROS to overwhelm the initial biological inflammatory response to the particles.

Although no longer correlated with PMN infiltration, there is a correlation between bulk chemical composition and cardiopulmonary

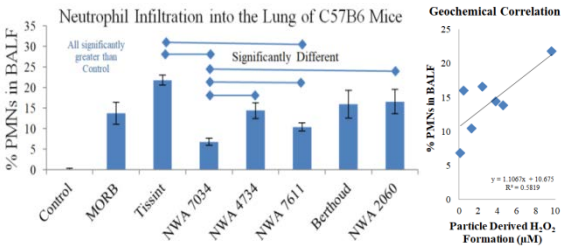

Figure 1. Neutrophil Infiltration into BALF after 3 Consecutive Day Dust Exposure and Geochemical Correlation

endpoints. Specifically, there are strong correlations

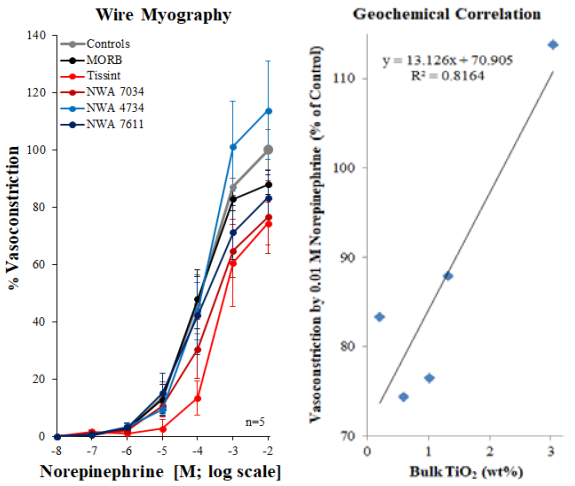

Figure 2. Aortic Vasoconstriction after 3 Consecutive Day Dust Exposure and Geochemical Correlations

between: 1) IL-1β dysregulation and chromium and manganese content after a three day exposure (both positive), 2) IL-1β dysregulation and chromium and titanium content after a three week exposure (positive and negative, respectively), and 3) TNF-α dysregulation and titanium content (negative). There is also a very strong correlation indicating that increasing titanium concentrations enhance vasoconstriction (Figure 2).

Summary: This comprehensive dataset allows for not only the toxicological evaluation of celestial materials but also clarifies important correlations between geochemistry and health. Furthermore, the utilization of an array of celestial samples from Moon, Mars, and asteroid 4Vesta enabled the development of a geochemical based toxicological hazard model that can be used for: 1) mission planning, 2) rapid risk assessment in cases of unexpected exposures, and 3) evaluation of the efficacy of various *in situ* techniques in gauging surface dust toxicity.

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