Fiscal Year:	FY 2013	**Task Last Updated:**	FY 01/23/2014
PI Name:	Lam, Chiu-wing Ph.D.		
Project Title:	Pulmonary Toxicity Studies of Lunar Dust in Mice and Rats		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Environmental health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SHFH**:Space Human Factors & Habitability (archival in 2017)		
Human Research Program Risks:	(1) **Dust**:Risk of Adverse In-Mission Health and Performance Effects and Long-Term Health Effects Due to Celestial Dust Exposure		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	chiu-wing.lam-1@nasa.gov	**Fax:**	FY
PI Organization Type:	NASA CENTER	**Phone:**	281-483-7223
Organization Name:	Wyle Laboratories/NASA Johnson Space Center		
PI Address 1:	1290 Hercules Drive		
PI Address 2:	Mail Code Wyle/HEF/37A		
PI Web Page:			
City:	Houston	**State:**	TX
Zip Code:	77058	**Congressional District:**	22
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	10/02/2006	**End Date:**	09/30/2013
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No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:	1	**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmore, Mihriban	**Contact Phone:**	281-244-1004
Contact Email:	mihriban.whitmore-1@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2013 per John James (Ed., 8/24/2012) NOTE: Project extended to 9/30/2011 (from 12/31/2010), per B. Woolford/JSC (1/2011) NOTE: Start/end dates changed to 10/2/2006-12/31/2010 (previously 4/30/2006-1/31/2011) per B. Woolford/JSC via S. Steinberg-Wright/JSC (9/2009)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):			
Grant/Contract No.:	Directed Research		
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Performance Goal Text:			

Task Description:	NASA will build an outpost on the lunar surface for long-duration human habitation and research. The surface of the Moon is covered by a layer of fine, reactive dust, and the living quarters in the lunar outpost are expected to be contaminated by lunar dust. NASA established the Lunar Airborne Dust Toxicity Advisory Group (LADTAG) to evaluate the risk of exposure to the dust and to establish safe exposure limits for astronauts working in the lunar habitat. Because the toxicity of lunar dust is not known, LADTAG has recommended investigating its toxicity in the lungs of laboratory animals. After receiving this recommendation, NASA directed the JSC Toxicology Laboratory to determine the pulmonary toxicity of lunar dust in exposed rodents. The rodent pulmonary toxicity studies proposed here are the same as those proposed by the LADTAG. Studies of the pulmonary toxicity of a dust are generally done first in rodents by intratracheal instillation (ITI). This toxicity screening test is then followed by an inhalation study, which requires much more of the test dust and is labor intensive. We succeeded in completing an ITI study on JSC-1 lunar dust simulant in mice (Lam et al., Inhalation Toxicology 14:901-916, 2002, and Inhalation Toxicology 14: 917-92, 2002), and are now proposing to do a study with Apollo lunar dust samples. This study will be similar to our study with the lunar dust simulant. Groups of mice and rats will be intratracheally instilled with a suspension of lunar dust. Lung lavage fluid will be assayed for biomarkers of toxicity, and lung tissues will be examined microscopically for pathological lesions. In the study, reference dusts that have known toxicities and industrial exposure limits will be studied in parallel so the relative toxicity of lunar dust can be determined. The ITI results will also be useful for choosing an exposure concentration for the animal inhalation study on the lunar dust, which is included as a part of this proposal. The animal inhalation exposure will be conducted with lunar dust simulant will prior the inhalations exposure study with the lunar dust. The simulant exposure will ensure that the study techniques used with actual lunar dust will be successful. The results of ITI and inhalation studies with real lunar dust are essential for setting limits for human exposure to lunar dust.
Rationale for HRP Directed Research:	This research is directed because it contains highly constrained research, which requires focused and constrained data gathering and analysis that is more appropriately obtained through a non-competitive proposal.
Research Impact/Earth Benefits:	

ABSTRACT
The United States has been contemplating returning to the moon to conduct further research and long-duration exploration, and to use the moon as a stepping-stone to Mars; other spacefaring nations are planning to send humans to the moon for the first time. The moon is covered by a layer of fine dust, composed of particles having a surface that is potentially reactive due to space weathering. No toxicity information exists about this surface-reactive dust. We ground two lunar dusts derived from an Apollo 14 soil to increase their surface reactivity and compared the toxicity of ground and unground lunar respirable dusts with those of quartz and titanium dioxide (TiO2), two reference dusts with well-known toxicities. Rats were intratracheally instilled with these dusts, and toxicity in the lungs was assessed. All dusts caused dose-dependent increases in toxicity; lunar dust was moderately toxic (TiO2 < lunar dust < quartz). All three lunar dust preparations were equally toxic, despite the zirconia ball-milled lunar dust being 14-fold more surface-reactive than the native dust. We then exposed groups of rats to four concentrations of a jet-milled lunar dust by inhalation for 1 month. All these data are useful for setting permissible exposure limits, and designing appropriate dust decontamination systems for a lunar habitat or landing vehicle. Detailed results can be found in peer-reviewed journals.

Background and Objective

The moon is our nearest celestial neighbor, but its geology, environment, and atmosphere remained undisturbed for more than a billion years. NASA's six short Apollo visits left the majority of the lunar surface unexplored, but lunar research is the foundation for planetary science. In situ research on the moon, utilizing advanced technologies, would generate new and useful data that could help us understand formation of our Earth and the rest of the solar system. NASA has been contemplating a human mission to Mars, which prompted President Bush, in 2004, to call upon NASA to return Americans to the moon for long-duration exploration and research and to use the moon as a stepping stone to Mars. NASA's Constellation program was subsequently created, and construction of a lunar outpost was planned. The projected tour of duty in the lunar habitat could be as long as 180 days. The moon is covered by a thick layer of fine, reactive dust. Exposure to fine, reactive mineral terrestrial dusts is known to pose a risk of lung toxicity. No toxicity information is available to assess the health risk of humans exposed to lunar dust for up to 180 days. Toxicity information would be needed by NASA to support future human lunar missions.

Even though a long-duration human exploration of the moon is not a current primary objective of the American space program, returning to the moon is still a future NASA option. Other spacefaring nations, including European countries, Russia, China, Japan, and India, are planning to send humans to the moon for the first time. In light of humans' instinct for exploration, advancing technology, and a recent discovery of ice on the moon, extraterrestrial colonization starting with the moon would be an achievable and worthwhile goal. Lunar mining to extract helium-3 as fuel for thermonuclear fusion to generate safe and clean energy on Earth has long been advocated.

The thick footprints of Apollo astronauts on the moon were the subject of vivid images revealing that the moon is covered by a thick layer of regolith (soil). A substantial fraction of the regolith consists of fine dust. Alan Bean of Apollo 12 noted, "The entire lunar surface was covered with this mantle of broken-up material, fine dust of varying depth. As a result, everything looked pretty much the same…" Lunar regolith has been formed by volcanism and by impact of asteroids, meteoroids, and micrometeoroids on surface rocks and other native materials. Volcanic activity can spread ash into surrounding areas, and such activity occurred during the early lunar history.

Formation of fine dust over the whole lunar surface is caused mainly by 4 billion years of constant micrometeoroid bombardment of surface materials. These micrometeoroids or cosmic dusts, typically 50 µm (0.002 inch) in diameter or less, strike the moon at high speeds. When they hit rocks, they chip off fine particles; when they strike surface regolith, the impacts, which generate temperatures reaching 2000°C or higher, crush, melt, and/or partially vaporize surface particles. The lofted molten particles drop back to the surface and weld surrounding grains together into jagged-edged glassy agglutinates, which are pulverized to fine dust particles upon subsequent impacts. Solar radiation imparts electrical charges to lunar surface material. By lunar nightfall, the charges have built up to levels high enough that submicron particles are repelled as high as 100 km (62 miles or ~330,000 feet) and can remain aloft on the low-gravity lunar surface for long periods. The constant micrometeoroid bombardment and daily dust electrostatic levitation during the 4-billion-year geological history of the moon have caused the lunar surface to be covered with a relatively uniform blanket of fine dust.

It is noteworthy that mineral samples collected from Itokawa Asteroid by Japan's Hayabusa spacecraft in 2005 were composed of tiny dust grains and presumably had been formed by similar micrometeoroid “long-term thermal annealing and subsequent impact shock…,” as the Japanese investigators reported. The mechanism of formation of fine dusts on airless and waterless celestial rocky bodies appears to be “universal.”

The average diameter of the lunar regolith particles is 70 µm. The finer fraction, with average dust particle diameter less than 20 µm, accounts for 10% to 20% of lunar surface regolith; the fine dust fraction with particle sizes of ? 3 ?m accounts for 1% to 2%. Silica-rich glassy mineral grains, which are formed by impact shock on and fracture of agglutinates, account for about 80% of the fine dust portion. Analysis of lunar regolith samples collected from different Apollo mission landing sites has revealed that the major chemical components in lunar regolith are common minerals such amorphous silica, alumina, calcium oxide, iron oxide, magnesium oxide, and ilmenite ($FeTiO_3$). Apollo 14 regolith has been considered to be a good representative of the lunar surface material mare low-Ti basalt, and sample #14163 has served as a yardstick that lunar simulants (low Ti) have been compared against. Ash of San Francisco Volcano (near Flagstaff, AZ), which has physical and mineral properties similar to this Apollo 14 sample, was mined and designated as NASA’s lunar simulant JSC-1 or JSC-1A. These simulants have been used by NASA and European Space Agency (ESA) engineers and scientists for various lunar-related tests including our previous toxicity studies. ESA is using JSC-1A as a surrogate to study the possibility of using lunar soil for shielding astronauts from cosmic radiation during deep-space exploration. Lunar simulants CAS-1 of China and FJS-1 of Japan both also emulate the Apollo sample #14163.

Looking back at Apollo crews’ brief encounters with lunar dust can help us visualize how dust contamination in the habitable volumes of future lunar landers and habitat would be a great health concern. Astronaut John Young of the Apollo 16 mission noted, after returning from outside into the Lunar Module, “… our feet and hands and our arms were all full of dust ….” Apollo 17 astronaut Gene Cernan commented, “… after rendezvous and docking when I took off my helmet in zero-g and we had the lunar module cabin [fan with filter] running the whole time. I did all the transfer with my helmet and gloves off, and I’m sorry I did because the dust really began to bother me. It bothered my eyes, it bothered my throat, and I was tasting it and eating it and I really could feel it working back and forth between the tunnel and the LM [lunar module]….” Dr. Harrison Schmitt, Geologist and Cernan’s crewmate, commented, “… there was considerable dust in the cabin. It would be stirred up by movements of the suit and the gear that we had. Almost immediately upon removing my helmet, I started to pick up the symptoms that you might associate with hay fever symptoms…” On the ground, a flight surgeon who inhaled some moon dust during unpacking of the spacesuits from stowage experienced respiratory immunological symptoms, which progressively worsened after exposure following the two subsequent missions.

As mentioned above, the projected duration of future human habitation on the moon is longer than the brief visits of the Apollo astronauts, and the living quarters could be contaminated with dust brought inside on spacesuits or hardware during each outside activity; exposure of humans to lunar dust will be inevitable. Therefore, information about the toxicity of lunar dust is essential for assessing the health risks of longer exposures, setting permissible exposure limits, and designing appropriate dust decontamination systems for a lunar habitat or landing vehicle. The present project was carried out to acquire toxicity information about airborne lunar dust for these purposes.

Task Progress:

Shortly after President Bush called for returning humans to the moon, the Lunar Airborne Dust Toxicity Assessment Group (LADTAG) was formed. It consisted of lunar geologists, toxicologists, medical doctors, and one Apollo astronaut/geologist. LADTAG was bestowed the important NASA lunar dust toxicity project by the Chief Health and Medical Officer (CHMO) of NASA. In 2005, the members of this group of national experts inside and outside NASA held their first meeting at NASA Headquarters. The geology team was given the responsibility of acquiring lunar regolith samples for the toxicity study; they also prepared and characterized the fine lunar dust samples for toxicity studies. A biomedical group at NASA Ames Research Center took on studies of lunar dust irritancy in skin and toxicity of lunar dust in cell culture. The Toxicology Laboratory residing at the NASA Johnson Space Center (JSC) was responsible for evaluating the toxicity of lunar dust in rodents. LADTAG met roughly once a year. During annual review meetings, the leads of the investigating teams presented their study proposals, experiment progress, and experiment results to CHMO; they also received input and comments from fellow LADTAG members. For the pulmonary toxicity studies in rodents, the central and the most important part of the NASA lunar dust toxicity project, we invited the collaboration of the National Institute for Occupational Safety and Health, and the University of Texas Medical Center in Houston. The studies were completed while we mourned the great loss of our geology team leader, Dr. David S. McKay, who was the most knowledgeable scientist on lunar dust mineral properties. Dr. McKay was NASA Chief Scientist in lunar geology and the instructor for the Apollo 11 crew on-ground geology field training. His contributions to preparation and characterization of the lunar fine dust for our toxicity studies was essential and is gratefully acknowledged.

Toxicological Assessment of Lunar Dust

To evaluate toxicity of dust particles in human lungs, studies are generally carried out in rodents. In a toxicity study conducted by the DuPont toxicology laboratory to assess five mineral dusts in in vitro lung cell cultures (epithelial cells and macrophages) and in rats, the investigators concluded that the effects of dusts in cell cultures do not correlate with the pulmonary toxicity observed in rats. Generally, pulmonary toxicity investigation is first done in rats or mice by an intratracheal or intrapharyngeal instillation (ITI / IPI). In an ITI / IPI study, a test dust is suspended in saline solution or another nontoxic medium, and is instilled into the upper respiratory tract of a rodent, where the instillant is aspirated directly into the lungs. Such a study allows comparative toxicity testing of the dust of unknown toxicity with reference dusts of known toxicities at several doses and several time points. Relatively small amounts of test dusts will be needed. However, dust administration by ITI / IPI is an unnatural exposure route, and an ITI/IPI study is normally followed by an inhalation study.

In our ITI study in rats, a native (unground) and two ground lunar dust samples of respirable sizes, prepared by the geology team from the parent Apollo 14 regolith sample (14003,93), were tested simultaneously with two common reference dusts, TiO_2 and crystalline silica (quartz). The pulmonary toxicities of these two reference dusts are well characterized: TiO_2 is low in toxicity, whereas quartz is a fibrogenic dust that can produce a spectrum of lung lesions. The Occupational Safety and Health Administration (OSHA) and the American Conference of Governmental Industrial Hygienists have set occupational exposure limits on both dusts.

Toxicity of Lunar Dust Assessed in Rats Exposed by Intratracheal Instillation

If an irritative or toxic dust lands deep in the lung on the alveolar surface, it can irritate or injure the alveolar epithelial cells that line the alveolar surface. This will trigger the cells to produce cytokines or chemokines. Some of these cellular mediators (literally, SOS signals) reach the blood to recruit white blood cells (WBCs), while others induce dilation of capillary walls, making them porous and thus allowing the WBCs and serum proteins to enter the alveolar space. These events are similar to those observed in pulmonary infection. In an infection, the recruited WBCs, particularly the neutrophils, possess destructive oxidants that can kill the invading microorganisms. However, in the case of dust exposure, oxidants have no defensive roles. These harmful molecules could be released from the short-lived recruited WBCs, especially the neutrophils, when they die; the released oxidants can kill the lung cells and cause tissue injury. Injured or dead alveolar epithelial cells would release their cellular contents, including enzymes. The alveolar fluid can be obtained by lung lavage to assess these biomarkers (or indices) of toxicity. Persistent inflammation, characterized by continuous influx of neutrophils, can result in a spectrum of lesions, which can be revealed by microscopic examination of lung tissues. We showed that all five of the respirable dusts we tested caused dose-dependent increases in levels of the biomarkers of toxicity that were assessed in bronchoalveolar lavage fluids and lesions in the lungs. The toxicity of lunar dust was moderate, greater than that of TiO_2 but less than that of quartz. As pointed out above, the surface of lunar dust particles on the moon could be reactive. However, grinding lunar dust by zirconia ball mill, which increased surface reactivity of the dust as much as 14-fold, had no impact on its toxicity. Three lunar dusts, ground or not ground, were equally toxic. The comparative toxicity obtained in our ITI study in rats allows us to propose an exposure limit of airborne lunar dust for humans.

Toxicity of Lunar Dust Assessed in Rats Exposed by Inhalation

As pointed out above, an ITI study is generally followed by an inhalation study. The latter requires a greater amount of test dust and is technologically more difficult to perform. The results of our ITI study showed that the respirable lunar dusts isolated from ground (either by jet mill or ball mill) and unground lunar soil samples produced comparable pulmonary toxicity. Thus we concluded that the jet-milled lunar dust is a good surrogate for the unground parent sample. In the inhalation exposure study, we exposed rats to air only or to four different lunar dust (jet-milled) concentrations (roughly 2, 7, 20, and 60 mg/m3) for 4 weeks or 1 month (6 hours/day, 5 days/week). The rat lungs were assessed 1 day, 1 week, 4 weeks, and 13 weeks after the last inhalation exposure. Pulmonary toxicity was evaluated in a manner similar to that described above. The findings, that a dose of 7 mg/m3 produced no observable toxicity, allows us to propose exposure limits for different exposure durations.

Summary of the NASA Lunar Dust Toxicity Study

Humans will set foot on the moon again and be exposed to lunar dust, and information about the toxicity of lunar dust is essential for assessing the health risks of human exposure, setting permissible exposure limits, and designing appropriate dust decontamination systems for a lunar habitat or landing vehicle. The present studies were carried out to acquire toxicity information on airborne lunar dust for these purposes. The overall results from the rat studies showed that the toxicity of lunar dust was moderate, greater than that of TiO_2 but less than that of quartz. The data have been presented to the NASA Chief Health and Medical Officer and reviewed by a nonadvocate committee. Details of the pulmonary studies have been published or are to be published in eight peer-reviewed journals (see titles below).

Manuscripts Generated from this NASA-funded Lunar Dust Toxicity Project

Pulmonary Studies

Lam C-W, Scully RR, Zhang Y, Renne RA, Hunter RL, McCluskey RA, Chen BT, Castranova V, Driscoll KE, Gardner DE, McClellan RO, Cooper BL, McKay DS, Marshall L, James JT. Toxicity of lunar dust assessed in inhalation-exposed rats. Inhalation Toxicology 25(12):661-78, 2013.

James JT, Lam C-W, Santana P, Scully RR. 2013. Estimate of safe human exposure levels for lunar dust based on comparative benchmark dose modeling. Inhalation Toxicology 25:243-256. 2013.

Scully RR, Lam C-W, James JT. Estimating safe human exposure levels for lunar dust using benchmark dose modeling of data from inhalation studies in rats. Inhalation Toxicology. 25(14):785-93. 2013.

Lam C-W, Zeidler-Erdely PC, Castranova V, Zhang Y, Scully RR, Hunter RL, et al. (2014) Toxicity of lunar dusts and a proposed mechanism for the pathogenesis of particle-induced lung diseases (submitted to Toxicological Sciences).

Lam C-W, Zhang Y, Scully RR, Driscoll KE, and James JT. Toxicity of mineral dusts and a proposed mechanism for the pathogenesis of particle-induced lung diseases. (submitted to Toxicological Sciences).

Zhang Y, Lam C-W, Scully RR., Williams K, Zalesak S., Theriot C1, Yeshitla, Wu HL, John T. James JT. Persistent expression changes of fibrosis related genes in the lung tissues of rats exposed to lunar dust (To be submitted for publication).

Lam C-W, James JT, et al. Lunar dust toxicity, mineral properties, and recommended exposure limits (in preparation, to be submitted to Planetary and Space Science)

Crucian B, Lam C-W. et al. Pulmonary and Systemic Immune Responses to Airborne Lunar Dust in exposed rats (in preparation, to be submitted journal for publication).

Ocular Study

Meyers VE, Garcia HD, Monds K, Cooper KM, James JT. Ocular toxicity of authentic lunar dust. BMC Ophthalmology 2012, 12:26

Bibliography Type:	Description: (Last Updated: 07/16/2023)
Articles in Peer-reviewed Journals	Scully RR, Lam CW, James JT. "Estimating safe human exposure levels for lunar dust using benchmark dose modeling of data from inhalation studies in rats." Inhalation Toxicology. 2013 Dec;25(14):785-93. http://dx.doi.org/10.3109/08958378.2013.849315 ; PubMed PMID: 24304305 , Dec-2013

Articles in Peer-reviewed Journals	Lam CW, Scully RR, Zhang Y, Renne RA, Hunter RL, McCluskey RA, Chen BT, Castranova V, Driscoll KE, Gardner DE, McClellan RO, Cooper BL, McKay DS, Marshall L, James JT. "Toxicity of lunar dust assessed in inhalation-exposed rats." Inhalation Toxicology. 2013 Oct;25(12):661-78. http://dx.doi.org/10.3109/08958378.2013.833660 ; PubMed PMID: 24102467 , Oct-2013
Articles in Peer-reviewed Journals	James JT, Lam CW, Santana PA, Scully RR. "Estimate of safe human exposure levels for lunar dust based on comparative benchmark dose modeling." Inhalation Toxicology. 2013 Apr;25(5):243-56. http://dx.doi.org/10.3109/08958378.2013.777821 ; PubMed PMID: 23614726 , Apr-2013
Articles in Peer-reviewed Journals	Meyers VE, Garcìa HD, Monds K, Cooper BL, James JT. "Ocular toxicity of authentic lunar dust." BMC Ophthalmol. 2012 Jul 20;12:26. http://dx.doi.org/10.1186/1471-2415-12-26 ; PubMed PMID: 22817808 , Jul-2012
Articles in Peer-reviewed Journals	Khan-Mayberry N, James JT, Tyl R, Lam CW. "Space toxicology: protecting human health during space operations." International Journal of Toxicology. 2011 Feb;30(1):3-18. http://dx.doi.org/10.1177/1091581810386389 ; PubMed PMID: 21266660 , Feb-2011
Articles in Peer-reviewed Journals	Lam CW, Castranova V, Zeidler-Erdely PC, Renne R, Hunter R, McCluskey R, Scully RR, Wallace WT, Zhang Y, Ryder VE, Cooper B, McKay D, McClellan RO, Driscoll KE, Gardner DE, Barger M, Meighan T, James JT. "Comparative pulmonary toxicities of lunar dusts and terrestrial dusts (TiO_2 & SiO_2) in rats and an assessment of the impact of particle-generated oxidants on the dusts' toxicities." Inhal Toxicol. 2022. 34(3-4):51-67. https://doi.org/10.1080/08958378.2022.2038736 ; PMID: 35294311 , Mar-2022