# HRP Supplemental Decadal Survey Response

## Executive Summary

## October 2012

The NASA response to the Decadal Survey focused on providing a snap shot of current investments. This documents supplements that report by providing additional information about the past, present and future plan for high priority recommendations (Table 13.1 on pages 13-9 through 13-15 of the Decadal Survey) within the domain of HRP.

The Recommendation Table lists Decadal Recommendations*, EB/E*, expected 5-year investment by risk**, and a brief statement of HRP work status. The color coding of HRPs responsibility for each recommendation is as follows:

- Green=HRP is heavily invested, past or present, in risk definition and development of countermeasures, standards or requirements.
- Yellow=HRP has future work OR other partners are doing the work
- Red=HRP has no present or future work in this area
- No Color - HRP has secondary responsibility for this area.

Additional description of the HRP position past, present or future is also provided by hyperlink within this document.

Many of the Decadal Survey Recommendations do not map directly to the Risk based management architecture of the Human Research Program. The Evidence for the 32 HRP risks and Integrated Research Plan that outlines the approach and research activities to address them can be found at http://humanresearchroadmap.nasa.gov/.

* From Table 13.1 of Decadal Survey

** Historically HRP has funded approximately 200-270 research tasks per year of which 40-70 tasks are new additions to the research portfolio. The allocation of tasks and budget to gaps varies from year to year based on priority. HRP also maintains research in areas not covered by the Decadal Survey Recommendations.

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# Recommendation Table

Recommendation Table (from Table 13.1 DS)

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment (as of 8/12) | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | Relevant HRR Risk/ Gap # |
|---|---|---|---|---|---|---|
| | | | | | | |
| ***Plant and Microbial Biology (Chapter 4)*** | | | | | | |
| P1 | Establish a "microbial observatory" program on the ISS to conduct a long term multi-generational studies of microbial population dynamics. | EB | | $3.4M | Human Research Program has characterized the spacecraft microbial environment. Current efforts are tracking Human Microbiome. Future studies are designed to more fully understand phenotypic and genotypic changes in microorganisms and microbial consortia. | Microhost/ AEH7,8,9,10 |
| P2 | Establish a robust spaceflight program of research analyzing plant and microbial growth and physiological responses to the multiple stimuli encountered in spaceflight environments. | EB | | | Human Research Program has characterized the spacecraft microbial environment. Current efforts are tracking Human Microbiome. Future studies are designed to more fully understand phenotypic and genotypic changes in microorganisms and microbial consortia. | |
| P3 | Develop a research program aimed at demonstrating the roles of microbial-plant systems in long-term life support systems. | EB / E | | | Human Research Program would have a future research role to test microbial safety, nutritional content, and palatability of plant systems. | |

Total Number of Tasks: 10

Investment: $ 3.4 M

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | (Funding as of 8/12) | HRP has primary responsibility G, Y, R<br>HRP has secondary responsibility (no color) | HRR Risk/ Gap # |
|---|---|---|---|---|---|---|
| ***Behavior and Mental Health (Chapter 5)*** | | | | | | |
| B1 | Develop sensitive, meaningful, and valid measures of mission-relevant performance for both astronauts and ground crew. | E | | $.959M (7 tasks) | Several studies targeting these specific aims. Several studies targeting sensitive, meaningful, and valid measures of mission-relevant performance for astronauts. | BMed/BMed 2,3,4,5 |
| B2 | Conduct integrated translational research in which long duration missions are simulated specifically for the purpose of studying the interrelationship between individual functioning, cognitive performance, sleep and group dynamics. | E | | | Involvement in Russian Chamber studies (3 in 105 day study 1 in 520 day, ISS and one multi-disciplinary Antarctica study. Future capabilities for chamber studies in discussion. | |
| B3 | Determine the genetic, physiological and psychological underpinnings of individual differences in resilience to stressors likely encountered during extended space missions, with emphasis to develop a personalized approach to sustaining astronauts during such missions. | E | | Team: $7.46M (22 tasks)<br>Sleep: $1.63 M 7 Tasks)<br>Bmed: $1.16 9 tasks) | No genetic studies due to agency policy. Currently several studies targeting individual behavioral differences. Other investigations may further inform individual differences and resiliencies. NASA has a limitation on facilities that are analogous to extended space missions; so while current studies address individual differences, they are few in the context of long duration, remote missions. | Team/Team Gap 1-9<br>Sleep/ Sleep 1-10<br>Bmed/BMed 1,6,7,8 |
| B4 | Conduct research to enhance cohesiveness, team performance, and effectiveness of multinational crews, especially under conditions of extreme isolation and autonomy. | EB / E | | | Well invested in studies aimed at team effectiveness and performance. Few are in extreme conditions (isolation and autonomy). Those that involve multinational crew, lack a sufficient amount of teams through which to do meaningful analysis. | |

Total Number of Tasks: 45

Investment: $ 11.2 M

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment (as of 8/12) | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| ***Animal and Human Biology (Chapter 6)*** | | | | | | |
| AH1 | The efficacy of bisphosphonates should be tested in an adequate population of astronauts on the ISS during a 6-month mission | EB / E | | | Bisphosphonates flight study nearing completion. | |
| AH2 | The preservation/reversibility of bone structure/strength should be evaluated when assessing countermeasures. | EB / E | | $6.3 m 15 tasks) | Well invested in bone structure changes, with emphasis on bone strength. | Osteo/ Osteo 1-7 |
| AH3 | Bone loss studies of genetically altered mice exposed to weightlessness are strongly recommended. | EB | | | Current ground study with mice on myostatin. No flight studies | |
| AH4 | New osteoporosis drugs under clinical development should be tested in animal models of weightlessness. | EB | | | New ground and flight studies planned when drugs are available. One study of Sclerostin using mice on STS135. Future flight studies are limited. | |
| AH5 | Conduct studies to identify underlying mechanisms regulating net skeletal muscle protein balance and protein turnover during states of unloading and recovery. | EB / E | | $.314M (1 task) | Well invested in protein balance and turnover in states of unloading and recovery. Well invested in effects on muscle composition, volume and strength. Future plans for protein turnover during analog studies. | Muscle/ M 14,23,24 |
| AH6 | Studies should be done to develop and test new prototype exercise devises, and to optimize physical activity paradigms/prescriptions targeting multi-system countermeasures. | EB / E | | $10.4M (17 task) | Well invested in optimizing exercise protocols in flight. New exercise devices under investigation. | Muscle, Aerobic/ M 7,8,9 |
| AH7 | Determine the daily levels and pattern of recruitment of flexor and extensor muscles of the neck, trunk, arms and legs at 1 *g* and after being in a novel gravitational environment for up to 6 months. | EB | | $.152M (1 task) | Flight study of recruitment in leg flexors and extensors selected. Many aspects of this recommendation not in current plan. | Muscle/ M 2 |

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment (as of 8/12) | HRP has primary responsibility G, Y, R<br>HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| AH8 | Determine the basic mechanisms, adaptations, and clinical significance of changes in regional vascular/interstitial pressures (Starling forces) during long duration space missions. | EB / E | | $4M<br>(3 tasks) | Studies of tissue hydration under way to aid countermeasure development. Other aspects are in research plan.<br>Studies of tissue (muscle) fluid content currently done during bed rest and in space. Starling forces cannot today be determined with currently available equipment in-flight. | Arrhythmia, VIIP/<br><br>CV7 |
| AH9 | Investigate the effect of prolonged periods of microgravity and partial (3/8 or 1/6 G) gravity on the determinants of task specific, enabling levels of work capacity. | EB / E | | $3.9M<br>(6 tasks) | Well invested in determinants of work capacity in 0g and return; partial g discontinued | Sensorimotor/ SM 2,26 |
| AH10 | Determine the integrative mechanisms of orthostatic intolerance after restoration of gravitational gradients (both 1 *g* and 3/8 *g*); | EB / E | | $1.1M<br>(2 tasks) | Studies include determinants and integrative modeling of mechanism.<br>Studies on countermeasure development when returning to 1 g. | OI/CV3 |
| AH11 | Collaborative studies among flight medicine and cardiovascular epidemiologists are recommended to determine the best screening strategies to avoid flying astronauts with subclinical coronary heart disease that could become manifest during a long duration exploration class mission (3 years). | EB / E | | $.83M<br>(1 task) | Current medical screening strategies for subclinical heart disease are considered adequate without additional research.<br><br>HRP has research in the area of predictive modeling and biomarker development. | Arrhythmia ExMC/<br><br>CV8<br>ExMC 1.01 |
| AH12 | Determine the amount and site of the deposition of aerosols of different sizes in the lungs of humans and animals in microgravity. | EB/E | | $1.15M<br>(4 tasks) | Active studies in mice and humans to determine aerosol deposition. Human inhalation limits of lunar dust are being developed. | Dust/<br><br>AEH1,2,5, watch item |

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|---|---|---|---|---|---|---|
| AH13 | Multiple parameters of T cell activation in cells should be obtained from astronauts before and after re-entry to establish which parameters are altered during flight. | EB | | $5.595M (11 tasks) | Three studies to determine T-cell activation factors. | Immune/ IM 1,2,3,5,6,7 |
| AH14 | To both address the mechanism(s) of the changes in the immune system and to develop measures to limit the changes, data from multiple "organ/system-based" studies need to be integrated. | EB / E | | | Several studies (flight and international) to address mechanisms of immune changes and potential countermeasures. | |
| AH15 | Perform mouse studies, including immunization and challenge, with immune samples acquired both prior to and immediately upon re-entry on the ISS to establish the biological relevance of the changes observed in the immune system. Parameters examined need to be aligned with those influenced by flight in humans. | EB | | | Guiding human studies focused on identifying human molecular biomarkers and cellular changes. | |
| AH16 | Studies should be conducted on transmission across generations of structural and functional changes induced by exposure to space during development. Ground-based studies should be conducted to develop specialized habitats to support reproducing and developing rodents in space. | EB | | | Not HRP | |

Total Number of Tasks: 55
Investment: $ 29.8 M

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|---|---|---|---|---|---|---|
| ***Cross-Cutting Issues for Humans in the Space Environment (Chapter 7)*** | | | | | | |
| CC1 | To ensure the safety of future commercial orbital and exploration crews, post-landing vertigo and orthostatic intolerance should be quantified in a sufficiently large sample of returning ISS crews, as part of the immediate post-flight medical exam. | EB / E | | $.058M (1 task) | Twenty two long duration crew studied with tilt after flight. Stand test medically required (not highly quantitative). | OI/CV3 |
| CC2 | Determine whether artificial gravity is needed as a multi system countermeasure, and whether continuous large radius AG is needed, or intermittent short radius AG is sufficient. Human studies in ground labs are essential to establish dose response relationships, and adequate gravity level, gradient, RPM, duration and frequency. | E | | | Long radius AG complex, not in budget or plan.<br>Short radius pilot study complete. No longer in U.S. plan. Active U.S. collaboration with Japan Aerospace Exploration Agency flight study.<br>Short radius study done to test for mitigation of orthostatic intolerance. | |
| CC3 | Studies on humans are needed to determine whether there is an effect of gravity on micronucleation and/or intrapulmonary shunting, or whether the unexpectedly low DCS prevalence on Shuttle/ISS is due to underreporting and to determine operationally acceptable low suit pressure and hypobaric hypoxia limits. | E | 1 | $1.509 (3 tasks) | One study modeling mechanisms of micronucleation<br>Research plan includes DCS studies to determine acceptable cabin & suit pressures. | DCS /DCS2 |

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| CC4 | Optimizing dietary strategies for crews and food preservation strategies that will maintain bioavailability for 12 or more months. | E | | $ 7.095M (22 tasks) | Several focused on nutrient content over shelf life of foods. Studies on bioavailability of nutrients for exploration. | |
| CC5 | Initiate a robust food science program focused on preserving nutrient stability for three or more years. | E | | | Studies to deliver 3yr food system high in nutrition, palatability through processing, packaging, formulation, and storage environment; and their relationship to behavioral health and performance | AFT/ AFT1,2,3,4 |
| CC6 | Include food and energy intake as an outcome variable in intervention in studies in humans | EB / E | | | Energy balance studied food intake managed. Several studies focused on how acceptability, variety, etc affect food intake | |
| CC7 | Studies of astronauts for cataract incidence, quality, and pathology related to radiation exposures to understand risk from cataracts and to understand radiation-induced late tissue toxicities in humans. | E | | $ 128M (total SRPE gaps) | Clinical and subclinical cataract incidence and exposure measured to determine risk. | |
| CC8 | Conduct animal studies to assess radiation risks from cancer, cataracts, cardiovascular disease, neurologic dysfunction, degenerative diseases, and acute toxicities such as fever, nausea, bone marrow suppression, and others. | E | | 120 tasks<br>7 NSCORs | Well invested in radiation risks, using animals at NASA Space Radiation Laboratory & other venues to create predictive model of risk. | Cancer<br>Degen<br>CNS<br>ARS |
| CC9 | Cellular ground-based studies to develop endpoints and markers that can be used to define acute and late radiation toxicities using radiation facilities that are able to mimic space radiation exposures | E | | | Radiation endpoints and markers studied at cellular, tissue and animal level to understand risks. | |

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| CC10 | Expand our understanding of gender differences in adaptation to the spaceflight environment through flight and ground based research, including potential differences in bone, muscle and cardiovascular function and long-term radiation risks | EB / E | | $ .239K<br>( 9 tasks) | Several studies have specifically studied gender factors. Gender is considered in study design of spaceflight adaptation studies. Research related to gender selection for team composition is also needed. | Cancer 6 |
| CC11 | Investigate the biophysical principles of thermal balance to determine whether microgravity reduces the threshold for thermal intolerance. | EB / E | | | One study of thermoregulation and balance. International cooperation in flight study of thermal regulation and exercise. | No tasks |

Total Number of Tasks: 162
Investment: $ 136.9 M

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment (as of 8/12) | HRP has primary responsibility G, Y, R<br>HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| ***Fundamental Physical Sciences in Space (Chapter 8)*** | | | | | | |
| FP1 | Research on Complex Fluids and Soft Matter. | EB / E | | | | |
| FP2 | Understanding of the fundamental forces and symmetries of Nature. | EB | | Two collaborative investigations with ESA planned | | |
| FP3 | Research related to the physics and applications of quantum gases. | EB / E | | | | |
| FP4 | Investigations of matter near a critical phase transition. | EB | | | | |
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| | ***Applied Physical Sciences in Space (Chapter 9)*** | | | | | |
| AP1 | Reduced-gravity multiphase flows, cryogenics and heat transfer database and modeling, including phase separation and distribution (i.e., flow regimes), phase change heat transfer, pressure drop, and multiphase system stability | EB / E | | | | |
| AP2 | Interfacial flows and phenomena (including induced and spontaneous multiphase flows with or without phase change) relevant to storage and handling systems for cryogens and other liquids, life support systems, power generation, thermal control systems, and other important multiphase systems. | EB / E | | | | |
| AP3 | Dynamic granular material behavior and subsurface geotechnics to enable advanced human and robotic planetary surface exploration and habitation. | E | | | | |
| AP4 | Development of fundamentals-based strategies and methods for dust mitigation to enable advanced human and robotic exploration of planetary bodies. | E | | | | |
| AP5 | Experiments to understand complex fluid physics in a zero-gravity environment enabled by the ISS platform. | EB | | | | |
| AP6 | Fire safety research to improve methods for screening materials in terms of flammability and fire suppression in space environments. | E | | | | |
| AP7 | Combustion processes research, including reduced-gravity experiments with longer durations, larger scales, new fuels, and practical aerospace materials relevant to future missions. | EB / E | | | | |
| AP8 | Numerical simulation of combustion research to develop and validate detailed single and multiphase numerical combustion models. | | | | | |

| ID | Recommendation | Enabled by (EB)and/or Enabling (E) | | Investment (as of 8/12) | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| AP9 | Materials synthesis and processing and control of: microstructure and properties to improve the properties of existing and new materials on the ground | EB/E | | | | |
| AP10 | Design and develop advanced materials that meet new property requirements to enable human exploration at reduced cost using both current and novel materials synthesis and processing techniques and computational methods. | E | | | | |
| AP11 | Fundamental and applied research is required in developing technologies for extraction, synthesis, and processing of minerals, metals, and other materials available on extraterrestrial surfaces | EB / E | | | | |
| | | | | | | |

* The investment for the tasks under APS 1 and APS 2 is till the completion of the research efforts which entail technology demonstration in gas-liquid separation technologies and zero boil-off technologies. Moreover the budget includes life-cycle costs of these developments.

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| ***Translation to Space Exploration Systems (Chapter 10)*** | | | | | | |
| TSES1 | Research should be conducted to address active two-phase flow questions relevant to thermal management. (T1) | E | | | | |
| TSES2 | Research should be conducted in support of zero-boiloff propellant storage and cryogenic fluid management. Physical sciences research includes advanced insulation materials research, active cooling, multi-phase flows, and capillary effectiveness (T2), as well as active and passive storage, fluid transfer, gauging, pressurization, pressure control, leak detection, and mixing destratification (T3). | E | | | | |
| TSES3 | NASA should enhance surface mobility; relevant research includes suited astronaut computational modeling, biomechanics analysis for partial gravity, robotic-human testing of advanced spacesuit joints and full body suits, and musculoskeletal modeling and suited range-of-motion studies (T4), and studies of the human-robot interaction (including teleoperations) for the construction and operation of planetary surface habitats (T26). | E | | | Research on issues related to function allocation and trust between machine and human; and. habitability requirements for exploration. | HARI, HAB |

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| TSES4 | NASA should develop and demonstrate technologies to mitigate the effects of dust on EVA systems and suits, life support systems, and surface construction systems. Supporting research includes impact mechanics of particulates, design of outer layer dust garments, advanced material and design concepts, magnetic repulsive technologies, and the quantification of plasma electrodynamic interactions with EVA systems (T5); electrostatic coupling (T23); and regolith mechanics and gravity-dependent soil models (T27). | E | | | | |
| TSES5 | NASA should define requirements for thermal control, micrometeoroid and orbital debris impact and protection, and radiation protection for EVA systems, rovers, and habitats and develop a plan for radiation shelters. (T19) | E | | | | |
| TSES6 | NASA should conduct research for the development and demonstration of closed-loop life support systems and supporting technologies. Fundamental research includes heat and mass transfer in porous media under microgravity conditions (T6) and understanding the effect of variable gravity on multi-phase flow systems. (T21, T22) | E | | | | |
| TSES7 | NASA should develop and demonstrate technologies to support thermoregulation of habitats, rovers, and spacesuits on the lunar surface. (T20) | E | | | | |

| ID | Recommendation | Enabled by (EB) and/or Enabling (E) | | Investment | HRP has primary responsibility G, Y, R HRP has secondary responsibility (no color) | HRR Risk/Gap |
|---|---|---|---|---|---|---|
| TSES8 | NASA should perform critical fire safety research to develop new standards to qualify materials for flight and to improve fire and particle detectors. Supporting research is necessary in materials qualification for ignition, flame spread, and generation of toxic and/or corrosive gases (T7) and in the characterization of particle size from smoldering and flaming fires in microgravity (T8). | E | | | | |
| TSES9 | NASA should characterize the effectiveness of fire suppression and post-fire recovery strategies. Specific research is needed to develop and implement a standard methodology for qualifying fire suppression systems (T9) and to assess and restore a post-fire environment (T10). | E | | | | |
| TSES10 | Research should be conducted to allow regenerative fuel cell technologies to be demonstrated in reduced gravity environments. (T11) | E | | | | |
| TSES11 | Research is needed to support the development of new energy conversion technologies (T12). In particular, research is required for more efficient primary base-power and to enable the arrays for Solar Electric Propulsion to transfer large masses of propellant and cargo to distant locations. (T18) | E | | | | |
| TSES12 | Research is needed in high-temperature, low-weight materials for power conversion and radiators to enable fission surface power systems. (T13) | E | | | | |

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|---|---|---|---|---|---|---|
| TSES13 | Development and demonstration of ascent and descent system technologies are needed, including ascent/descent propulsion technologies, inflatable aerodynamic decelerators, and supersonic retro propulsion system technologies. Research is needed in propellant ignition, flame stability, and active thermal control (T14); lightweight flexible materials (T15); and dynamics and control (T16). | E | | | | |
| TSES14 | Research is required to support the development and demonstration of space nuclear propulsion systems, including liquid-metal cooling under reduced gravity, thawing under reduced gravity, and system dynamics. (T17) | E | | | | |
| TSES15 | Research is needed to identify and adapt excavation, extraction, preparation, handling, and processing techniques for a lunar water/oxygen extraction system. (T24) | E | | | | |
| TSES16 | NASA should establish plans for surface operations, particularly ISRU capability development and surface habitats. Research is needed to characterize resources available at lunar and martian surface destinations (T25) and to define surface habitability systems design requirements (T28). | E | | | | |

Supplementary Information on

# Major Recommendations from Decadal Survey

### Areas of highest Priority recommended by NRC (Table 13.1, Decadal Survey)

## *Research Area:* PLANT AND MICROBIAL BIOLOGY

### P1. Establish a "microbial observatory" program on the ISS to conduct a long term multi-generational studies of microbial population dynamics.

The microbial ecology associated with spacecraft has been the subject of multiple studies and published articles (Taylor, Graves et al. 1977; Viktorov, Novikova et al. 1992; Pierson 2001; Castro, Thrasher et al. 2004; Ott, Bruce et al. 2004; Bruce, Ott et al. 2005; Novikova, De Boever et al. 2006). The majority of this research and operational monitoring has focused on microbial concentration and diversity that could impact crew health or the integrity of the vehicle and its systems. The preponderance of the data suggests the microbiota in spacecraft generally contain low levels of common environmental flora, occasionally including opportunistic pathogens, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. New information is expected, as several recent and ongoing spaceflight experiments on International Space Station (ISS) are evaluating the microbial flora of ISS and its crew (HRP: SWAB, PI-Pierson; European Space Agency: SAMPLE, PI -Harmsen; Japan Aerospace Exploration Agency: MICROBE I & II, PI-Makimura). In addition, both NASA and Institute for Biomedical Problems (IBMP) perform periodic monitoring of the ISS environment and the environment of vehicles destined to dock with ISS . The use of ISS as a "microbial observatory" has the potential to provide additional insight by tracking microbial isolates over multiple generations; however, HRP is confident that adequate monitoring techniques have been and are currently being used to evaluate trends in the environmental microorganisms associated with crew health and vehicle integrity. Still, a substantial amount of uncertainty remains concerning the changes which may be occurring in the microbial flora directly associated with the mucosa and other areas of the crew, often referred to as the crew microbiome. Early studies of astronaut flora were thorough, however they were limited by the technology available (Taylor 1974; Lentser, Lentser et al. 1980; Goncharova, Liz'ko et al. 1981; Smirnov and Lizko 1987) and only a few recent studies using more advanced molecular monitoring techniques are available (Pierson, Chidambaram et al. 1996). To address this gap in knowledge, this crew microbiome is currently being investigated by the Human Research Program (PI: Lorenzi). This study is designed to provide solid foundation of information regarding spaceflight-associated changes in the microbial diversity in and on the crewmembers. If this evidence demonstrates substantial changes, further study will be recommended.

References

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Taylor, G. R. (1974). "Recovery of medically important microorganisms from Apollo astronauts." Aerosp Med **45**(8): 824-828.

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Viktorov, A. N., N. D. Novikova, et al. (1992). "[The cabin microflora of manned space vehicles and the problem of the biological destruction of the construction materials used in them]." Aviakosm Ekolog Med **26**(3): 41-48.

Investigations

Harmsen, H. Study of Microbial Communities Exposed to Weightlessness (Sample).
http://www.nasa.gov/mission_pages/station/research/experiments/Sample.html

Lorenzi, H. Study of the impact of long-term space travel on the astronaut's microbiome (Crew Microbiome)

Makimura, K. Microbial Dynamics in International Space Station (Microbe-I&II).
http://www.nasa.gov/mission_pages/station/research/experiments/Microbe-I.html

Pierson, D. A Comprehensive Characterization of Microorganisms and Allergens in Spacecraft Environment (SWAB)
https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=7656

## P2. Establish a robust spaceflight program of research analyzing plant and microbial growth and physiological responses to the multiple stimuli encountered in spaceflight environments.

The overall number of microorganisms that have been investigated during spaceflight is extensive, with over 100 different experimental cultures being evaluated before 1990 (Dickson 1991) and multiple reviews being written to document the findings (Taylor 1974; Volz 1990; Klaus 2002; Nickerson, Ott et al. 2004; Klaus and Howard 2006; Rosenzweig,

Abogunde et al. 2009; Horneck, Klaus et al. 2010). Studies have suggested multiple phenotypic changes in a variety of microorganisms, such as increases in cell density in spaceflight cultures of *Salmonella enterica* serovar Typhimurium aboard Biosatillite 2 compared to ground cultures (Taylor 1974), increased conjugal transfer rate in *Escherichia coli* (Ciferri, Tiboni et al. 1986), and greater cell size and enhanced swarming of *Proteus vulgaris* on Salyut-7(Manko, Kordyum et al. 1986) . The growth of *E. coli* has been evaluated in multiple spaceflight experiments displaying cell density increases similar to those observed with *Salmonella* (Ciferri, Tiboni et al. 1986; Volkmann 1988; Klaus, Simske et al. 1997). A detailed study of the growth kinetics indicated that the lag phase was shortened, the exponential growth phase was extended, and the bacterial cell populations were 88% greater than those of ground controls (Klaus, Simske et al. 1997).

Phenotypic changes in response to spaceflight culture have been observed in fungi as well as bacteria. For example, *Saccharomyces cerevisiae* cultures grown on Apollo 16 also showed an increased phosphate uptake(Berry and Volz 1979). In addition, *S. cerevisiae* cells grown during spaceflight were better able to survive in intradermal lesions in artificially infected mice compared to cells grown on Earth(Hiebel and Volz 1977). Also noted from Apollo 16 experiments were morphological changes in hyphal structure, colony development, and cell shape in *Trychophyton terrestre* and *Chaetomium globosum* (Volz 1990).

The results of the Cytos 2 experiment performed aboard Salyut 7 in 1982 were of particular interest in relation to crew health care. In this experiment, the minimum inhibitory concentration of oxacillin, chloramphenicol, and erythromycin for *Staphylococcus aureus* and of colistin and kanamycin for *E. coli* were compared to those of ground controls (Tixador, Richoilley et al. 1985). These results indicated an increased resistance of both *S. aureus* and *E. coli* to all antibiotics used in this experiment (Tixador, Richoilley et al. 1985). However, the observed alterations in microbial antibiotic resistance during spaceflight may be transient, as attempts to reproduce these changes after return to Earth were unsuccessful(Lapchine, Moatti et al. 1986). Spaceflight experiments culturing *E. coli* during STS-69 and STS-73 suggested gentamicin on agar slants that were flown was as effective as and possibly more effective than the antibiotic on ground-based control cultures(Kacena and Todd 1999). In 1999, Juegensmeyer, *et. al.* observed both increased sensitivity and resistance by cultures of *S. aureus*, *P. aeruginosa*, *Bacillus subtilis*, and *E. coli* that had been re-grown after having been on the MIR space station for 4 months (Juergensmeyer, Juergensmeyer et al. 1999).

Recent studies into the response of microorganisms to the spaceflight environment have improved our knowledge of the spaceflight response dramatically. Spaceflight experiments aboard STS-115 investigated both the changes in virulence, morphology, and gene expression of spaceflight cultured *S. enterica* serovar Typhimurium compared to identical organisms cultured on Earth (Wilson, Ott et al. 2007). *Salmonella* cultures grown during flight displayed a 2.7 fold lower $LD_{50}$ in a murine model when compared to inoculation with ground control cultures. In addition, spaceflight cultured *Salmonella* also displayed an extracellular matrix not observed in the ground-based culture. Global microarray and

proteomic analyses revealed that 167 transcripts and 73 proteins changed expression compared to ground cultured organisms. Importantly, the conserved RNA-binding protein Hfq was identified as a likely global regulator involved in the response to this environment. This experiment was the first to advance the potential of a defined molecular mechanism behind the responses observed in microorganisms during spaceflight culture. The finding of increased virulence in spaceflight cultured *Salmonella* was reproduced in a subsequent experiment aboard STS-123 (Wilson, Ott et al. 2008). This experiment further elucidated the mechanism behind these changes by demonstrating that the enhanced virulence could be modulated by the ion concentration in the media.

Based upon this evidence, the Human Research Program established and addresses the *Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions* to further study changes that are occurring to microorganisms, the infected host, and the specific interaction between host and microorganism. Through this process, the Human Research Program is currently addressing spaceflight associated microbial responses by focusing on alterations in virulence, virulence factors, and the cellular and molecular mechanisms behind these changes.

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## P3. Develop a research program aimed at demonstrating the roles of microbial-plant systems in long-term life support systems.

To further address limitations in vehicle resources to accommodate prepackaged foods, it is also envisioned that once on the lunar or Mars surface, crops would be grown. Fresh fruits and vegetables, such as spinach, lettuce, tomatoes, carrots, bell peppers, onions, potatoes, and strawberries could be grown hydroponically in environmentally-controlled chambers. The use of fresh fruits and vegetables on the lunar and Mars surface can provide the crew with a variety of fresh foods and associated nutrients. These fresh foods should provide at least some of the vitamins that may be lost over time in the processed foods, enhancing the nutritional intake of the crew and associated health and wellbeing, and reducing the risk. However, there is a potential risk that the space radiation may reduce the nutritional content of the food.

The addition of the freshly grown fruits and vegetables may increase the acceptability of the lunar and Mars missions' food system. These fresh foods would increase the acceptability of the food system by introducing bright colors, crunchy textures, and fresh aromas, encouraging more caloric intake and boosting crew morale by creating a more familiar food system in a hostile and unfamiliar environment. Many studies have evaluated food production scenarios that rely on Martian candidate crops (Levine et al., 2008, Veillard et al., 2007, Moraru et al., 2004), and have stressed the importance of final food quality as a selection criterion in selecting appropriate crops.

During surface preparation of fresh food, safety is no longer ensured as it is through ground operations. If the fresh fruits and vegetables are consumed without a heat (cooking) step, there is a potential for food contamination and hence foodborne illness. Hence, there may be a need to wash or sanitize. As part of HRP directed research, Perchonok & French (2004) examined cleaning protocols through which fresh produce shelf life might be extended. Hydrogen peroxide was used as an antimicrobial agent at varying levels to clean an assortment of produce items. The effectiveness of the hydrogen peroxide treatments was compared against the cleanliness of control samples of each produce item that were washed in distilled water. Most produce had an initial reduction in microbial count on day 0, followed by a rapid increased that essentially rendered counts across treatments indistinguishable. Additionally, degradation in color and texture occurred at hydrogen peroxide concentrations greater than or equal to 5% for some vegetables. The study did note some microbial reduction for carrots and radishes, which suggests that an item-specific washing procedure may be

appropriate for use in space. Fine-tuning of the produce handling processes would be required to ensure safety and maximize shelf life of the foods for use in a bioregenerative system.

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## *Research Area:* BEHAVIOR AND MENTAL HEALTH

### B1 Develop sensitive, meaningful, and valid measures of mission-relevant performance for both astronauts and ground crew.

Sensitive, meaningful and valid measures of mission-relevant performance are needed for both astronauts and ground crews (HRP Evidence, 2008, HRP-47060). Mission-relevant performance is a multi-faceted variable related to individual behavioral health as well as individual and team outcomes. In regards to cognitive performance, HRP invested in highly applied research to develop and validate a brief performance measure that is sensitive to the effects of fatigue caused by sleep loss, circadian desynchrony and workload (PI: Dinges). The 3-minute Psychomotor Vigilance Task (PVT-B), developed with NASA, National Space Biomedical Research Institute (NSBRI) and Department of Homeland Security (DHS) support, has been validated in laboratory studies and in spaceflight analog environments, and is currently on International Space Station (ISS) (as the Reaction Self Test) to evaluate the effects of fatigue and time in mission on the stability of attention during performance and psychomotor responses. The PVT-B provides performance feedback to the individual thus enabling the astronaut to gauge functional capability for performing critical mission tasks and/or countermeasure implementation. A performance algorithm based on astronauts' PVT performances while in NASA Extreme Environment Mission Operations (NEEMO) missions provided the normative database for the PVT-B on ISS. The PVT is also serving as a primary outcome measure for other investigations supported by HRP, including a study evaluating neurobehavioral effects of light (PI: Brainard); an investigation assessing behavioral and performance effects with sleep medications, upon abrupt awakening (PI: Smith); and in long duration analog investigations (PI: Dinges, Lockley). Two studies evaluating fatigue countermeasures with NASA ground controllers have utilized the longer version of the PVT (PI: Barger). In addition, to enhance the meaningfulness of the results generated by the PVT, a current

investigation is assessing its predictive validity by measuring performance on the robotic arm in conjunction with PVT performance, under varying conditions of sleep duration (PI: Oman).

Future missions to distant planetary surfaces will be of longer duration and unprecedented distances, and crews will become increasingly autonomous. HRP is developing additional tools that can be used during autonomous operations to assess a broader range of cognitive processes while providing a more 'game like' engaging experience for crewmembers. CogGauge is a cognitive measure based on the Automated Neuropsychological Assessment Metrics (ANAM) battery of tests (PI: Ahmad), with the intent to provide a 'video game' experience. The tool is currently being validated through NASA support and that of the Department of Homeland Security. Likewise, the Cognitive Assessment Tool (PI: O'Donnell) provides a promising theoretical model for mapping cognitive state to specific spaceflight tasks and yielding a more diagnostic tool to assess cognitive function.

Upcoming spaceflight investigations will include additional rapid objective measures of mission-relevant performance through a neurocognitive assessment toolkit for spaceflight (NeuroCATS) that contains brief, real-time measures of brain functions across a range of key neurocognitive domains critical for effective performance and fatigue management in space (PI: Basner). NeuroCATS is brief by virtue of utilizing state-of-the-art adaptive testing, and it permits assessment of specific brain regions (due to published neuroimaging norms for the tasks). An additional newly funded investigation seeks to characterize neurostructural changes (if any) before and following spaceflight (PI: Siedler). Future plans include the "BHP Dashboard" (PI: Mollicone), which will integrate data from various measures as available on the ISS, equipping the end user with more meaningful information to make informed decisions regarding a crewmember's neurobehavioral health and performance status. Hence, results from relevant measures will be provided in the context of spaceflight stressors (e.g., mission timeline, radiation exposure, $CO_2$ levels, and other environmental factors.

Countermeasure and monitoring technologies to characterize and assess team performance are essential to support the behavioral health and individual well being of the crew, as evidence indicates that a cohesive team can serve as a "buffer," mitigating stressors are likely to be found in future exploration spaceflight environments. Hence, in the Team risk area, HRP is developing measures that evaluate various aspects of performance, i.e. coordination and psychosocial adaptation. A current investigation has developed a potential assay of cooperation among team members, and will be testing this measure in teams in Antarctica (PI: Roma). Other team performance studies are developing methods through which individual behaviors are related to team outcomes and team performance itself, and can be unobtrusively evaluated (PIs: Huber, Thompson, Kozlowski). A final study (PI: Keeton) is assessing individual and team performance related to different intervals of comm. delay that will be characteristic of future, more autonomous exploration missions. The latter study will inform countermeasure development, including comm. quality, psychosocial support, and training.

Further efforts to ensure meaningfulness of results will be enhanced by collaborations with the Space Human Factors Engineering (SHFE) discipline, as SHFE currently supports the development of embedded measures of performance to

provide an additional assessment of performance capability during long duration exploration missions. Validated measures of workload tend to be time consuming and very intrusive, and focus on relatively short periods of time. HRP is reviewing all available workload measures and extending the concepts to longer durations (PI: Gore) and beginning development of a tool to predict and evaluate workload effects (PI: Sebok).

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## B2 Conduct integrated translational research in which long duration missions are simulated specifically for the purpose of studying the interrelationship between individual functioning, cognitive performance, sleep and group dynamics.

BHP is tasked with conducting and supporting research to characterize the likelihood and consequence of adverse outcomes related to individual well being, cognitive performance, sleep and team dynamics (HRP Evidence, 2008, HRP-47060). These factors are highly interrelated; HRP has invested in several research tasks with a multidisciplinary approach. The Objective Monitoring of Crew Neurobehavioral Functions in Mars 520-day Simulation (PI: Dinges), for instance, seeks to evaluate changes in crew members neurobehavioral functions throughout the 520-day mission (>17 months). Constructs being assessed include sleep quantity and quality, activity levels, workload, fatigue, mood, stress, depression, conflicts among crew and with mission controllers, and cognitive performance. The strengths of the Mars 520-day simulated mission are that it includes a multi-national crew similar to astronauts, a space mission simulation involving nearly a year and a half of confinement, and simulated flight activities, work schedules, mission control, time delays, etc. The limitations are that the study is based on only a single 6-person crew, and multiple concurrent investigations through other space agencies participating in the Institute for Biomedical Problems (IMBP) study, which need to be evaluated as potentially confounding factors. HRP is also conducting a spaceflight study on International Space Station (ISS) missions (PI: Dinges), using some similar neurobehavioral measures (i.e., PVT-B, visual analog scales to assess stress and sleep quality). When considering future spaceflight missions however, this study is limited in its duration to the current 6-month ISS missions (relative to an anticipated 12-36 month exploration mission), and the current ISS missions provide astronauts with behavioral countermeasures (e.g., crew care packages and real time communications with family and ground support), that will not be possible (in the same form or frequency) for future exploration missions beyond low Earth orbit. Hence, findings will not be fully generalizable to long duration exploration missions.

BHP also supports multidisciplinary studies utilizing Antarctic stations. One study completing data collection evaluates the relationship between affect, team cohesion, sleep, circadian rhythms and performance in several winter over stations (PI: Lockley), thus yielding a multi-national study that will inform team research gaps related to cultural differences. A second study, scheduled for the winter over at the Concordia station, is jointly funded by the National Space Biomedical Research Institute (NSBRI) and HRP, and will provide an assessment of the dynamic interactions between fatigue, stress,

physiology, sensorimotor adaptation, performance, and crew cohesion in the same subjects over a long duration, winter-over stay (PI: Roma). This European Space Agency (ESA)-sponsored multidisciplinary study involves six multinational co-investigators. An additional investigation at Concordia Station (Antartica) is looking at stress-associated immune changes, that result from confinement living under moderate hypobaric hypoxia comparable to those possible living situations in future lunar habitats (PI: Sams).

Antarctica research simulates some aspects of an exploration mission (e.g., long duration, remoteness, danger, isolation). However, there are also limitations affecting the generalizability of the findings to long-duration space flight (e.g., dissimilarity of the participants to astronauts, the number of participants at some of the Antarctic stations are much larger than the 4-6 member team currently being planned for exploration missions, and the Antarctic involves potential confounding factors not present in an exploration mission, such as alcohol use, and multiple, competing investigations). Future studies related to the interrelationship between relevant factors in high fidelity simulated long duration space analog environments are needed. HRP however faces a highly constrained budget, and lack of access to high fidelity analog environments. While future spaceflight missions are currently undefined, such assessments should be implemented in the near term as they will inform countermeasure development and integration of monitoring and countermeasures needed to support the human (individual and crews) for future exploration missions.

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**B3 Determine the genetic, physiological and psychological underpinnings of individual differences in resilience to stressors likely encountered during extended space missions, with emphasis to develop a personalized approach to sustaining astronauts during such missions.**

HRP agrees that determining the physiological and psychological underpinnings of individual differences in resilience to stressors likely encountered during extended spaceflight missions is essential to develop a personalized approach to sustaining astronauts during such a mission. While HRP currently supports research that will inform an individualized approach to mitigating deleterious behavioral and performance outcomes (PIs: Dinges, Lockley, Mollicone, Brainard, Johnston, Keeton, Siedler, Phillips, Rose, Klerman, Czeisler and Strangman, Johnston)including the work of the HHC Element looking at the relationship between sleep loss and circadian misalignment, and adverse cardiac events (PI: Shea)- very few of these studies are conducted in the context of a long duration isolated and confined environment. HRP has completed evidence reviews related to individual differences, including a review on biomarkers for vulnerabilities to sleep disruption and circadian desynchronization (PI: Lockley); such reviews will help to define the future research strategy in this area. Current studies in long duration isolation and confined analogs (PIs: Dinges, Lockley) are limited by sample size and/or fidelity to future exploration missions. Findings from investigations in the current ISS environment (i.e., 6-month missions where crew care packages and real time communication are readily available) are informative, but they will not be fully generalizable to future extended duration space missions in far more remote spaceflight environments beyond low Earth orbit.

Long duration simulations with *exploration* astronaut -like individuals living in an extreme isolated and confined high fidelity environment would yield additional insight into individual differences in resilience to stressors as well as a personalized approach to mitigating risk during future spaceflight operations. Such studies while deemed critical in HRP's risk to mitigation strategy may not be practical; resources are not available to support long duration studies of teams and individuals in high-fidelity environments. HRP lacks a facility and the budget to support the development of such a facility and related investigations.

A more feasible approach in the interim may be to leverage large, well-characterized databases on subjects exposed to a stressor in order to identify markers of resiliency. HRP has recently begun discussions with the Department of Defense to understand their approach to resiliency, for potential leveraging of this work. An HRP study is planned but unfunded in the future for studying individual differences related to mechanisms of adaptation in extreme isolated and confined environments.

Ideally, investigations are needed sooner rather later since studies would include individuals as well as team observations over long durations. The next step would include evaluating and enhancing individualized countermeasure approaches to mitigate deleterious outcomes under such conditions. Given HRP's current and anticipated budget in this area, these studies, while deemed essential, are not feasible.

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https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8495

Seidler, R. Spaceflight Effects on Neurocognitive Performance: Extent, Longevity, and Neural Bases.
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8526

Shea, S. Identification of cardiometabolic vulnerabilities caused by effects of synergistic stressors that are commonly encountered during space missions https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8460

Strangman. G. Objective Detection, Evaluation and Countermeasures for In-flight Depression.
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8073

## B4 Conduct research to enhance cohesiveness, team performance, and effectiveness of multinational crews, especially under conditions of extreme isolation and autonomy.

Enhancing team cohesiveness and maintaining effective team performance is critical when considering the multiple complexities that long duration missions will entail, including crew-specific (multi-national crewmembers, technical roles, social composition, etc.) and mission-specific (extreme isolation, communication delays, increase in crew autonomy, etc.) factors. Within HRP, the gaps comprising the Team Risk (http://humanresearchroadmap.nasa.gov/Risks/?i=101) are designed specifically to address areas of risk relevant to team outcomes including team performance and teamwork (e.g., cohesion, an important component of the team). These gaps include the identification of important team-related issues and the development and implementation of the appropriate countermeasures to adequately address the risk these issues pose. While HRP currently supports research that addresses many of these gaps, especially when considering countermeasure development (PIs: Cartreine, Kozlowski, Huber, Miller, Salas, Thompson, Tannenbaum), much work is still needed to adequately address these gaps and effectively mitigate the risk associated with these team-related issues.

Specifically, current studies seek to develop unobtrusive monitoring technologies (PIs: Huber, Kozlowski and Miller) to observe and monitor teamwork behavior as well as other technologies to aid the crew during their mission (PIs: Cartreine, Thompson), augment current standards and requirements for selection and composition of long duration crews (to address both technical and non-technical aspects of crew membership) (PIs: Tannenbaum), and identify the training that will be needed to maintain effective teamwork and team performance (PIs: Salas). However, it should be noted that many of these current studies are limited in terms of the sample size and/or fidelity to future exploration missions. In addition to these studies, HRP has completed evidence reviews that will help guide the future research strategy in this area. These reviews also cover the gap topics at a high level: identification of other unobtrusive monitoring technologies that may be necessary within the long duration mission context (PI: Stanton), virtual technologies that can be utilized as countermeasures (PI: Morie), selection and composition strategies based on previous astronaut data (PI: Musson), and training topics that must be addressed for this context (PI: Noe).

Even though much of the current research is addressing many aspects of risk related to the team context, additional research will be needed to adequately address the crew-specific and mission-specific issues that are expected for future long duration missions. In particular, it is necessary to understand the scope of impact that conditions such as increases in autonomy, the environmental constraints of communication delays, the group dynamic that will entail a multi-national crew, and the increase physical and social distance that is expected between mission control and the crew will ultimately have on the crew and their performance and well-being. It will be prudent for HRP to continue to seek alternative ways to try and answer these questions and fund future research within a constrained budget and limited resources. As such, HRP has multiple planned but unfunded studies in the future for examining these issues; though necessary, these studies are not feasible to continue within the current budget.

References
Risk of Performance Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team. http://humanresearchroadmap.nasa.gov/Risks/?i=101

Investigations
Cartreine, J. Countermeasure for Managing Interpersonal Conflicts in Space: A Continuation Study. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8074

Huber, M. Automated Behavior and Cohesion Assessment Tools. https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=7703

Kozlowski, S. Developing, Maintaining, and Restoring Team Cohesion.https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8399

Miller, C. Examination of Cultural Interactions Using Archival Data Footage on ISS.

Morie, J. Literature Review and Operational Assessment of Countermeasures Related to BHP

Musson, D. Investigating the Influence of Personality on Performance within the Astronaut Population

Noe, R. Literature Review and Operational Assessment of Training Strategies related to BHP

Salas, E. Optimizing Crew Performance in Long Duration Space Exploration: Best Practices for Team Training and Cohesion Measurement https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8398

Stanton, J. Literature Review and Operational Assessment of Monitoring Tools and Technologies related to BHP.

Tannenbaum, S. Composing and Developing Resilient, Adaptive, and Self-Sustaining Teams for Long Duration Space Exploration. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8534

Thompson, J. Behavior Tracking Software Enhancement and Integration of a Feedback Module https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8172

## *Research Area:* ANIMAL AND HUMAN BIOLOGY$_1$ *MUSCLO-SKELETAL and SENSORI-MOTOR*

### AH1 The efficacy of bisphosphonates should be tested in an adequate population of astronauts on the ISS during a 6- month mission.

An in flight bisphosphonate study is in progress with expected completion in 2016. Loss in bone density and strength occurs during spaceflight even though aerobic and resistive exercise is performed (HRP Evidence, 2008, HRP-47060).Therefore, NASA is currently performing an in-flight study in collaboration with the Japan Aerospace Exploration Agency (PI: LeBlanc) to investigate the effects of bisphosphonates (Alendronate) in combination with exercise on bone mineral density and strength determined by DXA scans and QCT. The study was commenced in 2006, and five subjects have been completed to date with an N=8. Preliminary data show that administration of an oral dose of 70 mg of Alendronate once a week in-flight maintains bone mineral density and strength in most anatomical areas. The study, however, was done in combination with improved exercise equipment, so it is unknown whether the drug alone maintains bone mineral density and strength. Therefore, the study has been expanded to include determination of bone mineral

density and strength in a control group of 10 exercising astronauts using approximately the same exercise regimen as when bisphosphonates were administered. Based on the preliminary results to date, NASA is fairly confident that improved exercise equipment and protocols in combination with a bone pharmaceutical countermeasure should buy down the risk of early onset osteoporosis and bone fracture. Bisphosphonates have been linked to increased risk of several types of cancer in humans (ex. Esophagus) 10 years after use which may limit usage of this medication in the future. This issue, however, is heavily debated, so it may not be an issue at all.

References

HRP Evidence. 2008. Risk of Accelerated Osteoporosis. Human Research Program HRP #47060. http://humanresearchroadmap.nasa.gov/evidence/

Investigations

LeBlanc, A. Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss: SMO-021. https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8480&CFID=395055&CFTOKEN=42169503

## AH2 The preservation/reversibility of bone structure/strength should be evaluated when assessing countermeasures.

HRP is well invested in investigations of bone structure changes caused by spaceflight and the effects of countermeasures to mitigate it with at present several ongoing studies. Loss in bone density and strength occurs during spaceflight even though aerobic and resistive exercise is performed (HRP Evidence, 2008). Therefore, HRP has completed animal hind limb suspension as well as human bed rest studies evaluating the efficiency of different countermeasures on bone strength (Allen et al., 2006; Swift et al., 2010). Based on this a bed rest and an ISS study have been started (SPRINT , Ploutz-Snyder et al.), which utilizes an increase in the intensity and a reduction in the volume of resistance exercises, inclusion of very short, but high intensity interval-type aerobic exercises as early as possible into the flight (1st week). Pre-, in- and post-flight testing and data sharing with selected on-going medical assessment tests are used to assess the effectiveness of this candidate prescription including assessing bone strength from QCT. In addition, a study is about to be initiated (Sibonga et al., in preparation), whereby the bone strength of each astronaut up to 12 months after flight will be related to the type of exercise countermeasure used on ISS. Completion of these studies is expected in 2015 - 17.

References

HRP Evidence. 2008. Risk of Early Onset Osteoporosis & Risk of Impaired Performance Due to Reduced Muscle Mass, Strength andEndurance Human Research Program HRP #47060. http://humanresearchroadmap.nasa.gov/evidence/

Allen, M.R. Hogan, H.A, Bloomfield, S.A. 2006. Differential bone and muscle recovery following hindlimb unloading in skeletally mature male rats. J. Musculoskelet. Neuronal. Interact. 6:217-25

Swift, J. M., Nilsson, M. I., Hogan, H. A., Sumner, L. R., Bloomfield, S. A. 2010. Simulated resistance training during hindlimb unloading abolishes disuse bone loss and maintains muscle strength. JBMR. 25:564-74.

Investigations

Ploutz-Snyder, L. Integrated Resistance and Aerobic Training Study (Sprint).
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8000

Sibonga, J. Occupational Risk Surveillience for Bone. Pilot Study: In-flight Countermeasure Effects on Sub-regional Bone Loss and On Biomechanics of Proximal Femur

**AH3 Bone loss studies of genetically altered mice exposed to weightlessness are strongly recommended.**

To investigate how genetics modulate bone quantity and micro-architecture and, more specifically, to identify the specific chromosomal regions that predispose individuals to the loss of musculo-skeletal tissue in space, mice were subjected to hind-limb suspension to simulate the unloading effects of weightlessness (Judex et al.). The studies was completed in 2007, and the data indicate strong influence of genetic variations on the changes in bone morphology and strength induced by rapid changes in its mechanical milieu and emphasize that is critical to preserve bone's micro-architecture before individual trabecular connections are lost, and suggest that the genes modulating changes in morphology during disuse are, at least in part, distinct from those regulating tissue recovery. These results might aid NASA in the future to predict which individuals are more susceptible to bone loss than others.

Investigations

Judex, S. Recovery of Musculoskeletal Quantity and Quality upon Multiple Microgravity Exposure.
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8446

**AH4 New osteoporosis drugs under clinical development should be tested in animal models of weightlessness.**

Future studies are expected to include testing of new bone protecting drugs when approved by the FDA. At this time it is too early to test for bone drug stability in-flight, but an in-flight study conducted by the Human Research Program has been completed and published (Du et al., 2011) on drug stability in general on the ISS showing that there is drug degradation during storage on ISS. The mechanisms for this, however, are not clear yet. A new ground-based study is being planned in this regard (Dr. Wotring).

References

Du B, Daniels VR, Vaksman Z, Boyd JL, Crady C, Putcha L. Evaluation of physical and chemical changes in pharmaceuticals flown on space missions. AAPS J. 2011 Jun;13(2):299-308. Epub 2011 Apr 9

**AH5 Conduct studies to identify underlying mechanisms regulating net skeletal muscle protein balance protein turnover during states of unloading and recovery.**

A study was conducted in hindlimb unloaded mice and completed in 2009, where selected compounds, nutritional supplements and pharmacologic agents, that may oppose oxidative stress in muscle and protect against weakness and fatigue, were tested (Reid et al.). An additional study in humans were completed (Reid et al., 2009), which evaluated N-acetylcysteine (NAC) as a countermeasure for handgrip fatigue in humans. It had previously been shown that NAC inhibits human muscle fatigue, and in a final series of experiments in healthy volunteers, the preparation and dosage of oral NAC administration for use in future countermeasure testing was developed. A related study has identified the antioxidant L-2-Oxothiazolidine-4-carboxylate (OTC) as a promising anti-fatigue agent and an alternative to NAC. Whether these compounds can be used as countermeasures against muscle protein degradation during spaceflight remains to be determined. More detailed studies on protein turnover are planned to be conducted for the future during bed rest and on the International Space Station (2017-20).

Investigations
Reid, M. Redox Modulation of Skeletal Muscle Function in Microgravity.
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=7926

**AH6 Studies should be done to develop and test new prototype exercise devises, and to optimize physical activity paradigms/prescriptions targeting multi-system countermeasures.**

For humans living in a microgravity environment, the optimal exercise regimen, including the mode(s), intensity, and volume needed to minimize or fully mitigate risk is not known (HRP Evidence, 2008, HRP-47072). An appropriate exercise prescription must, therefore, be developed and validated during spaceflight. HRP has multiple ongoing efforts in this regard scheduled for completion around 2020: a) Exercise countermeasures development (PI: Ploutz-Snyder) in the project entitled SPRINT (International Space Station (ISS) investigation), iRATS (bed rest experiment), and Testosterone (PI: Urban, bed rest experiment, an add-on countermeasure to optimize effectiveness of SPRINT). SPRINT constitutes a high-intensity, integrated aerobic and resistance exercise protocol to optimize maintenance of muscle strength, volume, endurance, aerobic capacity and bone strength. b) Treadmill Kinematics (in-flight) and ARED Kinematics (planned in-flight – PI: DeWitt) to help determine the loading on the bone of current exercise protocols. c) Harness investigation (PI: Perusek - recently completed) aimed at improving comfort and determinations of the mechanical loads for crewmembers exercising on the ISS treadmill. d) Hardware development such as a Flywheel concept (PI: Adams, collaboration with National Space Biomedical Research Institute (NSBRI)), which has demonstrated that a very modest amount of time invested in exercise using the multi-mode exercise device (M-MED) can produce substantial increases in muscle function and cardiovascular fitness. This equipment and associated protocols have been developed specifically for space flight related application and may provide a basis for a broader use in situations, where space and time constraints may limit access to effective exercise. Thus, our portfolio in this area is well funded and international collaboration has been done

within this area with the European Space Agency (ESA: PI: P. Tesch, Swedish Space Corporation) and NSBRI. The next step for HRP is to develop the next generation exercise devices for long duration exploration missions t. NASA is in the process of planning for development of new exercise devices, which are smaller, less voluminous and with less mass than the current ones on ISS. A workshop has been held in the fall of 2011 with the purpose of defining the scientific requirements for such devices and which had scientists and engineers interact. Also a solicitation for development of exercise devices for long term space exploration missions has been issued in 2011.

References

HRP Evidence. 2008. Risk if Reduced Physical Performance Capability due to Reduce Aerobic Capacity & Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance Human Research Program HRP #47060. http://humanresearchroadmap.nasa.gov/evidence/

Investigations

Adams, G. Integrated Endurance and Resistance Exercise Countermeasures Using a Gravity Independent Training Device. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8387

DeWitt, J. Biomechanical Analysis of Treadmill Locomotion on the International Space Station. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8477

Perusek, G. A New Harness For Use with Exercise Countermeasures-Validation of Improved Comfort and Loading with the Center for Space Medicine (CSM) Harness https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8196

Ploutz-Snyder, L. Integrated Resistance and Aerobic Training Study (Sprint). https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8000

Urban, R. Testosterone Supplementation as a Countermeasure against Musculoskeletal Losses during Space Exploration. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8362

## AH7 Determine the daily levels and pattern of recruitment of flexor and extensor muscles of the neck, trunk, arms and legs at 1 g and after being in a novel gravitational environment for up to 6 months.

NASA has since the nineties been well invested in conducting studies on recruitment of flexor and extensor muscles before and after spaceflight (Layne et al., 1998; Layne et al., 1997), where it was observed that the sensory-motor system can generate neuromuscular-activation strategies that permit treadmill walking, but subtle changes in lower-limb neuromuscular activation are present that may contribute to increased lower limb kinematic variability and oscillopsia also present during post flight walking. In more recent investigations (Miller et al., 2010), an increased risk of tripping was observed which may pose a hazard during locomotion immediately upon return to Earth, especially in an emergency scenario. However, tripping risk on subsequent days was not different than preflight. The joint angle analysis suggested that the crewmembers tried to reestablish their normal walking pattern post flight, instead of developing a new motor

control strategy. Based on outcome of these investigations and additional ones, new research has not been initiated within this area.

References

Layne, C. S., McDonald, P. V., Bloomberg, J. J. 1997. Neuromuscular activation patterns during treadmill walking after space flight Exp. Brain Res. 113:104-16.

Layne, C. S., Lange, G. W., Pruett, C. J., McDonald, P. V., Merkle, L. A., Mulavara, A. P., Smith, S. L., Kozlovskaya, I. B., Bloomberg, J. J. 1998Adaptation of neuromuscular activation patterns during treadmill walking after long-duration space flight. Acta Astronautica 43:107-19

Miller, C. A., Peters, B. T., Brady, R. R., Richards, J. R., Ploutz-Snyder, R., Mulavara, A. P., Bloomberg, J. J. 2010. Changes in Toe Clearance During Treadmill Walking After Long-Duration Spaceflight 10:919-28

## *Research Area:* ANIMAL AND HUMAN BIOLOGY$_2$ *CARDIO-PULMONARY*

### AH8 Determine the basic mechanisms, adaptations, and clinical significance of changes in regional vascular/interstitial pressures (Starling forces) during long duration space missions.

HRP has just solicited for investigations into the how fluid shifts during spaceflight affect intracranial and intraocular pressures, because of observed vision problems in astronauts during spaceflight. It is hypothesized that intracranial and thus intraocular pressures are increased by weightlessness. In addition, HRP is in the process of initiating a study to look into the temporal profile of changes in cardiac pre-load as a result of the currently used inflight ISS fluid and salt loading procedure during simulation of weightlessness by head-down tilt. It is anticipated that this will deliver further insight into the compartmental fluid volume shifts in space. Direct measurements of starling forces such as hydrostatic capillary and colloid osmotic pressures will not be possible to conduct during spaceflight because of lack of available equipment for in flight use but indirect measures such as venous pressures and plasma concentration of proteins are planned to be done on ISS (2015-20) to characterize the vision impairment and intracranial pressure problems in flight.

### AH9 Investigate the effect of prolonged periods of microgravity and partial (3/8 or 1/6 G) gravity on the determinants of task specific, enabling levels of work capacity.

Partial gravity:

Lack of physiologic data collected during previous (Apollo) true lunar activities or their accurate simulation has limited the ability to predict, if an astronaut is physically capable of completing multiple partial gravity (e. g. lunar) activities that may be required during long-duration missions. Therefore, HRP has done a study (Barstow et al.), which developed a

mobile test bed to accurately simulate partial-G (lunar) activities, and determine subject performance and the concomitant physiological responses to these activities. This allowed the creation of a series of standardized tests that can be performed in a pre-flight setting to determine the readiness of an astronaut to perform physically demanding activities during partial (1/6) gravity. Preliminary simple regression analysis of the results for 10 subjects has shown that there was a modest correlation ($r = 0.583$, $p<0.05$) between 10 km walk-back time and maximal aerobic work capacity, and there were highly significant relationships between both 10 km time ($r = 0.894$, $p<0.0005$) and average pace ($r = 0.872$, $p<0.001$) with critical velocity. The total time to perform the material transport test was inversely and significantly correlated with upper body work capacity and critical power, and with static hand grip endurance.

Microgravity:

HRP is currently performing measurements of aerobic work capacity in µ g on the ISS (Moore et al.), which have shown that it can be maintained during missions up to 6 months duration with the current exercise regimes.

Investigations

Barstow, T. Standardized 'Pre-flight' Exercise Tests to Predict Performance during Extravehicular Activities in a Lunar Environment. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8345

Moore, A. Maximal Oxygen Uptake (VO2max) and Submaximal Estimates of VO2max Before, During and After Long Duration International Space Station Missions. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8085

## AH10 Determine the integrative mechanisms of orthostatic intolerance after restoration of gravitational gradients (both 1 g and 3/8 g).

HRP is well invested in exploring countermeasures against orthostatic intolerance after simulation of weightlessness and/or short- and long term spaceflight. Studies on the effects of an antigravity garment and fluid loading will be completed in 2012 and looks very promising for mitigating orthostatic intolerance (Platts et al.). Also a cardiovascular study is being conducted in flight on ISS (Bungo & Levine et al.) to obtain a comprehensive picture on how the cardiovascular system in humans adapt to spaceflight and whether cardiac dysfunction plays a role for post flight orthostatic intolerance. In addition, NASA has set up a project (Digital Astronaut project), whereby tools for understanding the integrative mechanisms of orthostatic tolerance can be developed. It is expected that the full countermeasure complement for mitigating orthostatic intolerance after spaceflight can be implemented in 2012.

Investigations

Bungo, M. and Levine, B. Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capacity, and Risk of Cardiac Arrhythmias https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8152

Platts, S. Evaluation of Commercial Compression Garments to Prevent Post-Space Flight Orthostatic Intoleranc

**AH11 Collaborative studies among flight medicine and cardiovascular epidemiologists are recommended to determine the best screening strategies to avoid flying astronauts with subclinical coronary heart disease that could become manifest during a long duration exploration class mission (3 years).**

Current medical screening strategies for subclinical heart disease are considered adequate without additional research. Whether, however, spaceflight induces detectable electrophysiological changes in the heart that may later develop into cardiac disease is currently being investigated on International Space Station (ISS) (Bungo & Levine et al.). Completion of this study is expected in 2013.

Investigations

Bungo, M. and Levine, B. Cardiac Atrophy and Diastolic Dysfunction During and After Long Duration Spaceflight: Functional Consequences for Orthostatic Intolerance, Exercise Capacity, and Risk of Cardiac Arrhythmias
https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8152

**AH12 Determine the amount and site of the deposition of aerosols of different sizes in the lungs of humans and animals in microgravity.**

## *Research Area:* ANIMAL AND HUMAN BIOLOGY$_3$ *IMMUNOLOGY, ENDOCRINOLOGY and REPRODUCTION*

**AH13 Multiple parameters of T cell activation in cells should be obtained from astronauts before and after re-entry to establish which parameters are altered during flight.**

A current study is being conducted on International Space Station (ISS) for exploration of effects of long-term spaceflight on the immune function, stress and latent herpes virus reactivation (including multiple parameters of T cell activation). For the short duration component of this study, 17 astronauts on 9 shuttle flights have been completed. The ISS part of this study (also n=17) is expected to be completed in 2012. The objective is to understand the effects of space flight on the human immune system and determine any clinical risk for exploration related to immune down regulation. The findings from the shuttle flights show changes by spaceflight in the peripheral leukocyte distribution, including the maturation state of CD8+ cytotoxic T cells, and various components of T-cell activation. T cell stimulation with Staphylococcal enterotoxin was dramatically reduced in-flight and cytokine profiles were dysregulated. The final Shuttle data summary is available (Crucian et al., 2010), as is the mid-study n=10 ISS data (Crucian et al., 2011). In conjunction with the

spaceflight studies, parallel ground analog studies are being conducted by NASA (Sams et al.) during undersea deployment (NASA Extreme Environment Mission Operations (NEEMO)/Aquarius station, Key Largo, Florida) and during Antarctica winter-over at the French-Italian Concordia Station (Dome C, interior Antarctica).

References

Crucian, B. et al, NASA/HRP Investigators Workshop 2010, Houston, Texas
http://www.dsls.usra.edu/meetings/hrp2010/pdf/Immunology/1151CrucianMehta-IntImm.pdf

Crucian, B. et al, IAA Humans in Space Symposium. 2011, Houston, Texas, http://www.dsls.usra.edu/meetings/iaa2011/pdf/2104.pdf

Investigations

Sams, C. Immune Function Changes During a Spaceflight-analog 12-day Undersea Mission (NEEMO IIH ROI)
https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=7659

Sams, C. Consequences of Long-Term Confinement and Hypobaric Hypoxia on Immunity in the Antarctic Concordia.
https://taskbook.nasaprs.com/publication/index.cfm?action=public_query_taskbook_content&TASKID=8257

**AH14 To both address the mechanism(s) of the changes in the immune system and to develop measures to limit the changes, data from multiple "organ/system-based" studies need to be integrated.**

NASA concurs that data from multiple organ systems must be interpreted jointly to ascertain inter-system interactions and sensitivities. In fact, the 2009 Standing Review Panel specifically called for a more inter-discipline approach for HRP life sciences research. Generally, a move towards such integration is progressing. A joint nutrition-immunology study examining plasma cytokine levels in the context of nutritional status and measures of oxidative damage is being conducted onboard ISS. Also, a recent radiation-nutrition-immunology rat study examined the effect of space-radiation on nutritional and immunological parameters. To further address this concern, it is planned that future spaceflight studies will indeed be inter-discipline and allow for joint-interpretation of flight data. Also, many countermeasures planned for evaluation may have broad spectrum benefits, also requiring inter-discipline evaluation. Currently, NASA is in the planning phase of developing a strategy for future oxidative stress and damage experiments as well as a roadmap for translational studies.

**AH15 Perform mouse studies, including immunization and challenge, with immune samples acquired both prior to and immediately upon re-entry on the ISS to establish the biological relevance of the changes observed in the immune system. Parameters examined need to be aligned with those influenced by flight in humans.**

HRP concurs with the suggestion that mouse studies, and immunization/challenge studies in particular, should be performed to address clinical relevance for immune changes. This need has recently been addressed with the addition of

the 'Host-Pathogen' Risk to the HRP Integrated Research Plan (IRP). Some preliminary work has been performed to define specific adaptive immune changes during spaceflight. Further studies are planned to determined innate immune status during spaceflight, and in this case an innate immune study has been selected for flight (Simpson et al. 2011). Recently, studies (Nickerson et al.) have demonstrated that certain pathogens increase their virulence characteristics during spaceflight. As the Host-Pathogen risk is incorporated into the IRP, future studies will be defined to address this risk. Those will include studies as suggested, murine immunization/challenge experiments. It is anticipated that the variables of immune dysregulation and virulence will first be examined separately and then jointly in animal subjects, to finally determine clinical risk related to host-pathogen interactions during spaceflight. As suggested, immune functional measures should be similar to those which define immune dysregulation in crewmembers.

References

Nickerson, C. et al. 2004. Microgravity as a Novel Environmental Signal Affecting Salmonella enterica Serovar Typhimurium Virulence. Infection and Immunity, June 2000, p. 3147-3152, Vol. 68, No. 6

Wilson JW, Ott CM, Quick L, Davis R, Bentrup K. H., Nickerson, C. et al. (2008) Media Ion Composition Controls Regulatory and Virulence Response of *Salmonella* in Spaceflight. PLoS ONE 3(12): e3923. doi:10.1371/journal.pone.0003923

**AH16 Studies should be conducted on transmission across generations of structural and functional changes induced by exposure to space during development. Ground-based studies should be conducted to develop specialized habitats to support reproducing and developing rodents in space.**

## *Research Area:* CROSS-CUTTING ISSUES FOR HUMANS IN THE SPACE ENVIRONMENT$_1$

**CC1 To ensure the safety of future commercial orbital and exploration crews, post-landing vertigo and orthostatic intolerance should be quantified in a sufficiently large sample of returning ISS crews, as part of the immediate post-flight medical exam.**

NASA has completed numerous post flight testing of orthostatic tolerance in astronauts returning from short- (weeks) and long-term (months) missions (Meck et al. & Platts et al.) so that a data base has been created which makes it possible to quantify this syndrome in a sufficiently large number of subjects. In particular an antigravity garment has been developed to mitigate orthostatic intolerance after flight and preliminary results indicate that in flight and post flight fluid and salt loading in combination with the garment can efficiently mitigate orthostatic intolerance in virtually all returning crew members returning from long term missions to the ISS.

Investigations

Meck, J. or Platts, S. Numerous completed investigations located at: https://taskbook.nasaprs.com/Publication/index.cfm

**CC2 Determine whether artificial gravity is needed as a multi-system countermeasure, and whether continuous large radius AG is needed, or intermittent short radius AG is sufficient. Human studies in ground labs are essential to establish dose response relationships, and adequate gravity level, gradient, RPM, duration and frequency.**

NASA is not currently involved in artificial gravity studies except that NASA equipment is used by an EPSCOR study (Evans et al.) at Ames Research center to investigate the effects of centrifugation on orthostatic tolerance and that NASA collaborates with international partners (Japan), who plans to incorporate a human powered centrifuge on the ISS.

Investigations
Evans et al. Artificial Gravity Exposure Effects on Cardiovascularly Deconditioned Women's and Men's Orthostatic Tolerance Limit

**CC3 Studies on humans are needed to determine whether there is an effect of gravity on micronucleation and/or intrapulmonary shunting, or whether the unexpectedly low DCS prevalence on Shuttle/ISS is due to underreporting and to determine operationally acceptable low suit pressure and hypobaric hypoxia limits.**

HRP is in the process of establishing the Risk of Decompression Sickness (DCS); the research plan has just been developed. This study will in a very systematic and comprehensive form study all sorts of aspects of mitigating DCS with different prebreathing maneuvers and determination of acceptable cabin and suit pressures. In one study, modeling mechanisms of micronucleation and bubble formation is being performed.

**CC4 Optimizing dietary strategies for crews and food preservation strategies that will maintain bioavailability for 12 or more months.**

Nutrients degrade in food due to the processing method, storage time and environment (HRP Evidence, 2008, HRP-47052). Therefore HRP performed accelerated shelf life tests (JFS paper in publication), Shelf Stability tests (Smith et al) and currently is studying the effects of processing and storage (PI: Cooper). Preliminary data show that four nutrients, vitamins A and C, folic acid, and thiamin show significant losses due to processing and after storage at room temperature for up to 3 years. The expected completion date of this study is 2016. Based on the results, HRP expects that further study will need to be conducted to identify technologies to retain or protect nutrients. The next step in the research plan is a study to understand the kinetics of degradation in foods. Future studies may include the use of nanomaterials or

encapsulation to protect the nutrients, fortification of the nutrients, or using new technologies, such as high pressure processing or microwave sterilization that preserve food with less loss to nutrients. HRP is partnering with Department of Defense Combat Feeding Program to investigate the new preservation technologies.

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Investigations

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## *Research Area:* CROSS-CUTTING ISSUES FOR HUMANS IN THE SPACE ENVIRONMENT$_2$

### CC5 Initiate a robust food science program focused on preserving nutrient stability for three or more years.

In the past few years HRP has initiated a food science program to address nutrient stability. The HRP food science program is modest in size but growing. The quality of the food, nutrient content, acceptability, and safety, is dependent on four major factors; environment, packaging, preservation method, and formulation (HRP Evidence, 2008, HRP-47052). Available data on the vitamin content of certain processed foods at various temperatures over 2 years of storage demonstrate the potential for significant nutrient loss (Kamman et al., 1981; Kim et al., 2000; Kramer, 1974; Lund, 1975; Pachapurkar and Bell, 2005). Therefore, nutritional loss at 3 to 5 years, which has not been studied, could likely result in inadequate nutrition in the food system. While lower temperatures during storage could help alleviate the storage issues, International Space Station (ISS) and space shuttle missions do not have the mass or power capabilities to provide cold storage (Perchonok and Bourland, 2002). Currently, the commercial food industry does not require foods to have shelf-lives longer than 2 years. In the process of maintaining quality, mission resources such as mass, volume, power, waste, and crew time must be efficiently balanced.

Several studies have been conducted to identify packaging requirements, materials, and configurations (Cooper et al. 2011). Additionally, three Phase II SBIR studies have concentrated on packaging materials (PI: Sadler, PI: Belcher, PI: Cogan). NASA is partnering with Department of Defense Combat Feeding Program to investigate the new preservation technologies and packaging materials. Some studies are concentrating on surface missions, which could include food processing and preparation using freshly grown fruits and vegetables (PI: Cooper, PI: Wijeratne). A current study, is

studying the Integration of Product, Package, Process, and Environment: A Food System Optimization (PI: Cooper) and will be completed 2014. To date, the majority of the current ISS food items only have a shelf life of 18 -24 months. Research plans include investigation of processing and packaging to develop the technologies to reach a 3 year shelf life, as well as the integration of product, process, packaging and environment. In addition, the HRP is monitoring progress in the areas of Bioregenerative Life Support to understand implications to the entire food system, microbial load, appropriate vegetable selection, etc.

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## Investigations

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**CC6 Include food and energy intake as an outcome variable in intervention in studies in humans.**

The acceptability of the food system has been linked to caloric intake and associated nutritional benefits (HRP Evidence, 2008, HRP-47052). Vickers (1999) reports that studies that were conducted by the U.S. armed forces in the 1950s showed that most foods decreased in acceptability when they were repeatedly consumed. The degree of loss of acceptability depended on the specific food. If food is not acceptable to a crew, the crew will not eat an adequate amount of it and will be compromised nutritionally. Large improvements and advances in space food systems have been made up to the present ISS era. However significant challenges remain, including changes in crew preferences in space and limited variety of food. A current study, Effects of Retronasal Smelling, Variety, and Choice on Appetite and Satiety (PI: Hunter) will be using a bed rest study and an analog to study food acceptability. The expected completion date of this study is 2013. Another study, Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions (PI: Vickers) will be validating some ground studies on the International Space Station (ISS) testing food consumption and acceptability effect to mitigate stress. The expected completion date of this study is 2014. Additional studies are planned to address acceptability factors, effect of microgravity on taste and based on the results of the two current on-going studies could drive additional investigations.

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Investigations

Hunter, J. Effects of Retronasal Smelling, Variety and Choice on Appetite and Satiety. https://taskbook.nasaprs.com/Publication/index.cfm?action=public_query_taskbook_content&TASKID=8479

Vickers, Z. Factors Contributing to Food Acceptability and Consumption, Mood, and Stress on Long-term Space Missions

**CC7 Studies of astronauts for cataract incidence, quality, and pathology related to radiation exposures to understand risk from cataracts and to understand radiation-induced late tissue toxicities in humans.**

The NASA Study of Cataracts in Astronauts (NASCA) study using clinically validated objective lens imaging methods documented an association between low doses of space radiation and cortical and posterior subcapsular (PSC) cataracts in 224 astronauts and ground controls (Chylack et al., 2010) confirming earlier results using non-validated

methods (Cucinotta et al., 2001). The second goal of NASCA was to measure the progression rates in astronauts with the NASCA protocols requiring 5 lens exams per subject; however the NASCA study was discontinued in 2009 after 3.8 lens exams per subject. It may be possible to continue the measurements and compare to the existing NASCA data in the future. Measurements of space radiation effects are challenging due to the low doses of past crew and the strong effect of age, and may require long time lines post exposure.

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Investigations

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## CC8 Conduct animal studies to assess radiation risks from cancer, cataracts, cardiovascular disease, neurologic dysfunction, degenerative diseases, and acute toxicities such as fever, nausea, bone marrow suppression, and others.

The NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory opened for research in October of 2003. Since that time we have supported a large number of animal studies in these areas of research (see below for a snapshot of recent publications; full publication database is available at http://spaceradiation.usra.edu/resDatabase). These studies are expected to continue at current or increased levels in the future to meet NASA safety requirements for exploration missions. A larger number of studies on Central Nervous System (CNS) risks and genetic sensitivity and biological countermeasure approaches for solid cancer risks will need to be supported than is possible with current funding levels. A new galactic cosmic radiation (GCR) simulation capability at NSRL is being planned to stream-line biological countermeasure (BCM) and possibly other studies, however will require new infrastructure at NSRL for magnets and power supplies.

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## CC9 Cellular ground-based studies to develop endpoints and markers that can be used to define acute and late radiation toxicities using radiation facilities that are able to mimic space radiation

The NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory opened for research in October of 2003. Since that time we have supported a large number of cell and molecular studies in these areas of research (see below for a snapshot of recent publications; full publication database is available at http://spaceradiation.usra.edu/resDatabase). These studies are expected to continue at current or increased levels in the future to meet NASA safety requirements for exploration missions. A larger number of studies on Central Nervous System (CNS) risks and genetic sensitivity and biological countermeasure approaches for solid cancer risks will need to be supported than is possible with current funding levels. A new galactic cosmic radiation (GCR) simulation capability at NSRL is being planned to stream-line biological countermeasure (BCM) and possibly other studies however will require new infrastructure at NSRL for magnets and power supplies.

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## *Research Area:* CROSS-CUTTING ISSUES FOR HUMANS IN THE SPACE ENVIRONMENT$_3$

### CC10 Expand our understanding of gender differences in adaptation to the spaceflight environment through flight and ground based research, including potential differences in bone, muscle and cardiovascular function and long-term radiation risks.

In all studies supported by HRP attempts are made to obtain gender equality in the composition of subjects. Thus, knowledge regarding most of the physiological systems related to gender can be extracted from almost all studies. Spaceflight studies, however, exhibit dominance of males because of the lack of female astronauts, but this is expected to change in the future. Completed studies on post flight orthostatic intolerance after spaceflight have include specific focus on gender differences with the conclusion that females exhibited lower orthostatic tolerance than males (Waters, 2002; Harm, 2001; Summers, 2010)

Gender differences occur in cancer and degenerative risk from radiation exposure due to differences in organ sensitivity, natural lifespan, and genetic factors, and in the potential interactions of radiation with other gender specific non occupational factors associated with these risks. NASA projects astronaut risks from space radiation using a gender and age independent risk limit of 3% risk of exposure induced death (REID). The REID limit is considered at a 95% confidence level (CL) to protect against uncertainties in risk projection models. However, age and gender specific dose limits occur due to differences in radiation sensitivity. Recently, HRP has considered differences in risk projections that

occur between a population of never smokers relative to a U.S. average population. Important age and gender difference occur for the reasons cited above.

Age and gender are included in HRP projection models of circulatory diseases. Studies of Acute and Late Central Nervous System (CNS) effects from space radiation are being supported by HRP at the NASA Space Radiation Laboratory (NSRL), but face obstacles related to limited resources, knowledgeable investigators' able to pass peer review, and constraints in available biological models. Acute CNS risks include possible changes in cognition and performance during or soon after a space missions. Late CNS risks include increased risk or earlier time of appearance of Alzheimer's disease of other neuronal diseases that occur in the aged. Currently one NSCOR and about 12 individual investigations are supported. HRP is carrying out computational investigations of CNS risks. Gender differences could arise because of the longer lifespan of females and genetic factors including the expression of the ApoE gene, which has been shown to increase CNS risks from radiation in mice. The translation of results in small rodent models to humans is a major challenge. A large number of other genetic factors may play a role in individual sensitivity to degenerative and cancer risks from space radiation and their study is a long term goal of the HRP.

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## CC11 Investigate the biophysical principles of thermal balance to determine whether microgravity reduces the threshold for thermal intolerance.

## *Research Area:* TRANSLATION TO SPACE EXPLORATION SYSTEMS

### TSES 3 NASA should enhance surface mobility; relevant research includes suited astronaut computational modeling, biomechanics analysis for partial gravity, robotic-human testing of advanced spacesuit joints and full-body suits, and musculoskeletal modeling and suited range-of-motion studies (T4), and studies of the human-robot interaction (including teleoperations) or the construction and operation of planetary surface habitats.

Since the human is a key piece of human-robot interactions (HRI), the Human Research Program's Space Human Factors Engineering project is conducting studies of several aspects of HRI. One research thrust addresses levels of machine autonomy and transitions among levels of human oversight and human manual control. Two of these studies are being carried out at Massachusetts Institute of Technology (MIT) (Robotic systems – PI:Oman; Lunar Lander – PI: Duda); another (MIDAS-FAST – PI: Sebok) is being conducted at University of Michigan with support from Christopher Wickens, a seminal researcher in the field. Another research thrust focuses on the close coupling of the human and robots. Teleops with Delays (PI: Adelstein) at NASA/Ames Research Center (ARC) looks at the control issues induced by time delays between operator and robot, as would be the case in controlling robots on the lunar surface from Earth, or on a distant body from an approaching, orbiting, or departing spacecraft. Additionally, we are identifying tools that will enable mission planners and engineers to systematically allocate tasks and functions between humans and robots or automated systems (Needs Assessment – PI: Feary, ARC). Plans for future research address issues of trust and complacency with respect to autonomous systems, and tools to support design of distributed control teams. A current data mining project will lead to detailed studies of methodologies, tools and metrics for planning multi-agent (human and robotic) teaming.

Planetary surface habitats must accommodate human physical and psychological needs. In April 2011, the HRP sponsored an interdisciplinary workshop on Habitability Requirements to address a question from the Human Exploration Focus Team. Participants included psychologists, architects, mission planners, crewmembers, and participants with experience in Antarctic winter-over and other isolated and confined environments. The report, to be published this fall, will outline research questions that should be addressed to inform decisions on habitat design and operations. A pilot study (PI: Thaxton, JSC) to develop a questionnaire for consistent systematic evaluation of habitats is in process, and will yield a tool for collecting data that will drive habitability requirements.

Investigations

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