

National Aeronautics and Space Administration



HUMAN RESEARCH PROGRAM

ANNUAL REPORT
FY2016
ADVANCING
HUMAN EXPLORATION



Table of Contents

| | |
|--|----|
| Human Research Program Overview | 01 |
| • <i>Background</i> | |
| • <i>Goal and Objectives</i> | |
| • <i>Program Organization</i> | |
| • <i>Partnerships and Collaborations</i> | |
| Major Program-Wide Accomplishments | 07 |
| International Space Station Medical Projects Element | 17 |
| Space Radiation Element..... | 29 |
| Human Health Countermeasures Element | 37 |
| • <i>Vision and Cardiovascular Portfolio</i> | |
| • <i>Exercise and Performance Portfolio</i> | |
| • <i>Multisystem Portfolio</i> | |
| • <i>Bone and Occupant Protection Portfolio</i> | |
| • <i>Technology and Infrastructure Portfolio</i> | |
| Exploration Medical Capability Element | 49 |
| Human Factors and Behavioral Performance Element | 57 |
| • <i>Behavioral Medicine and Sleep Risk Portfolio</i> | |
| • <i>Team Risk Portfolio</i> | |
| • <i>Space Human Factors Engineering Portfolio</i> | |
| Engagement and Communications..... | 69 |
| Publications..... | 75 |



Overview

Background

Crew health and performance are critical to successful human exploration beyond low Earth orbit. Hazards include physiologic effects from radiation, hypogravity, and planetary environments, as well as unique challenges associated with the distance from Earth. The scientists and engineers of the Human Research Program (HRP) investigate and reduce the greatest risks to human health and performance, and provide essential countermeasures and technologies for human space exploration.

HRP delivers products and strategies to protect the health and safety of spaceflight crews and increase their productivity while living and working in space. Research is performed onboard the International Space Station (ISS), on the ground in analog environments that have features similar to those of spaceflight, and in laboratory environments. Data from these experiments further the understanding of how the space environment affects the human system. These research results contribute to scientific knowledge and technology developments that address the human health and performance risks from exposure to the hazards of exploration missions.

As shown in this report, HRP continues to make significant progress toward developing medical care and countermeasure systems for space exploration missions which will ultimately reduce risks to crew health and performance.

Goal and Objectives

The goal of the Human Research Program is to provide human health and performance countermeasures, knowledge, technologies, and tools to enable safe, reliable, and productive human space exploration. The specific objectives of the HRP are:

- 1) Develop capabilities, necessary countermeasures, and technologies in support of human space exploration, focusing on mitigating the highest risks to crew health and performance. Enable the definition and improvement of human spaceflight medical, environmental and human factors standards.
- 2) Develop technologies that serve to reduce medical and environmental risks, to reduce human systems resource requirements (mass, volume, power, data, etc.) and to ensure effective

Overview

tive human-system integration across exploration mission systems.

3) Ensure maintenance of Agency core competencies necessary to enable risk reduction in the following areas: space medicine, physiological and behavioral effects of long duration space-flight on the human body, space environmental effects, including radiation, on human health and performance and space human factors.

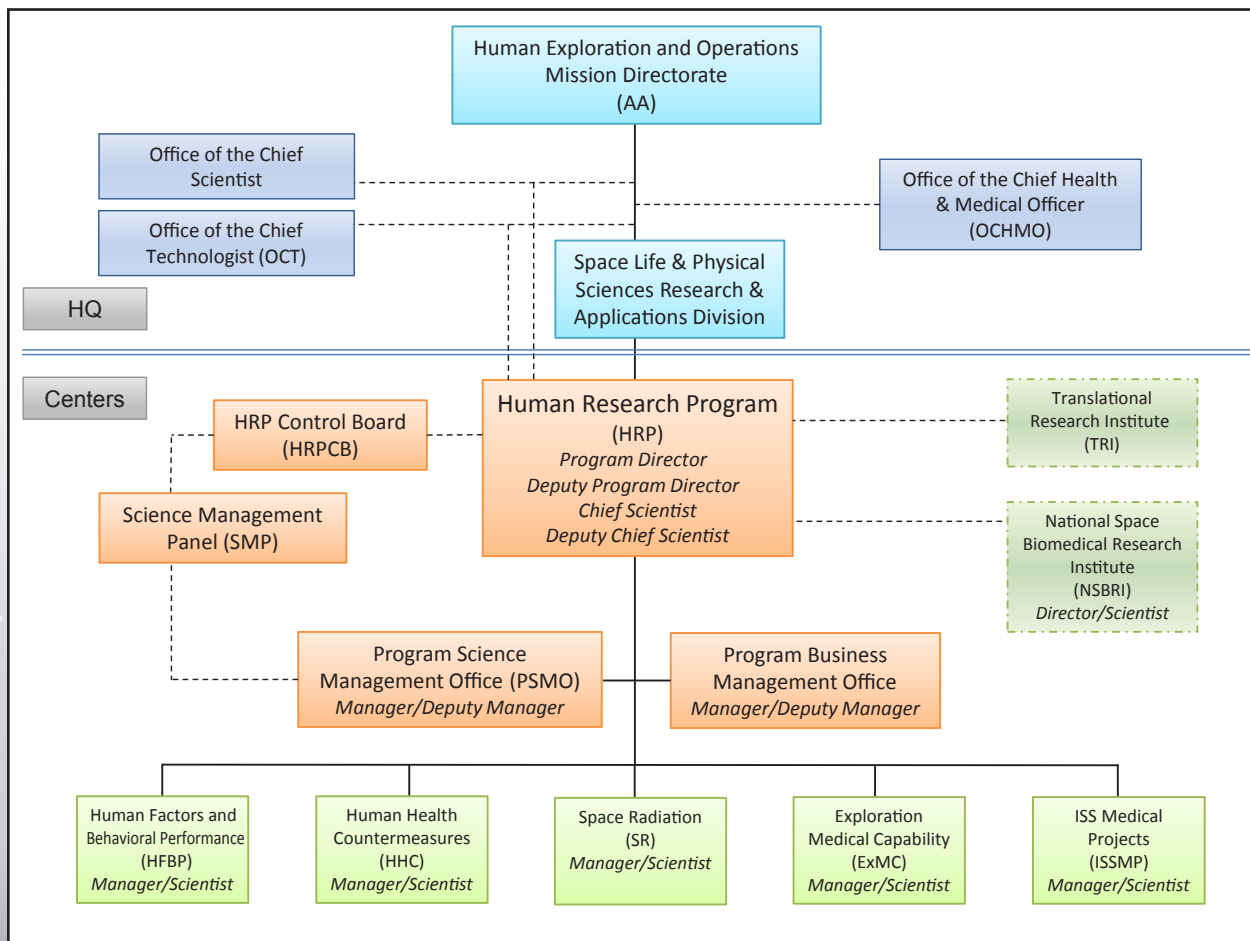
technology that enables the OCHMO to establish and maintain NASA-wide human health and performance standards. Furthermore, HRP provides HEOMD with methods of meeting those standards in the design, development, and operation of space-flight vehicle systems for exploration missions.

Organizationally, HRP resides within the HEOMD; however, the management of HRP is located at the Johnson Space Center (JSC) and work is performed across multiple NASA centers. The HRP Program and Deputy Directors lead all aspects of the program and the HRP Chief and Deputy Chief Scientists lead the science management and coordination.

Program Organization

The HRP's organization is designed to support the goals of the Human Exploration and Operations Mission Directorate (HEOMD) and NASA's Office of the Chief Health and Medical Officer (OCHMO). To that end, HRP conducts research and develops

As shown in the chart below, two offices support program, science and business management and provide integration across the Program.



Overview

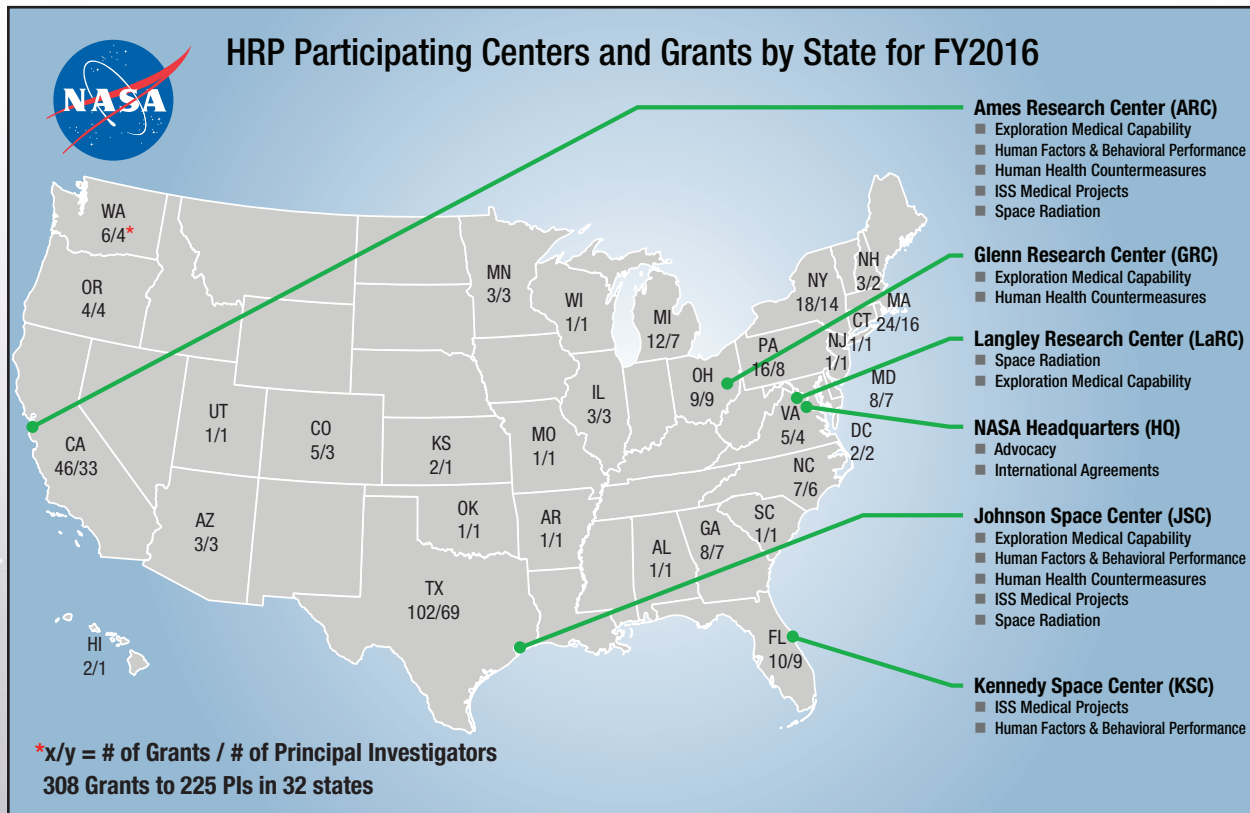
The Program Science Management Office (PSMO) integrates program management science tasks across all elements, communicates research needs to other NASA programs, and cultivates strategic research partnerships with other domestic and international agencies. The Program Business Management Office maintains all business functions for the Program and provides budget planning, integration and coordination with the HEOMD as well as across all program components.

There are five Elements that comprise the Program and are focused to accomplish specific goals for investigating and mitigating the highest risks to astronaut health and performance. Of the five, four are research Elements and one, the International Space Station Medical Projects, is a service element which provides the other Elements access to the ISS and ground-based analogs. The research Elements include: Space

Radiation, Human Health Countermeasures, Exploration Medical Capability, and Human Factors and Behavioral Performance. These Elements provide the HRP's knowledge and capabilities to conduct research to address human health and performance risks of spaceflight, and they advance the readiness levels of technology and countermeasures to the point where they can be transferred to the customer programs and organizations.

As shown below, the HRP is a multi-center program, with research being performed across the nation. Each research Element consists of related portfolios, projects, and research tasks focused toward developing products that reduce the highest risks in that area.

To learn more about the HRP Elements, please visit the website: <http://www.nasa.gov/hrp/elements>.



Overview

Partnerships and Collaborations

The HRP has a long history of collaborative work with universities, hospitals, and federal and international agencies for the purpose of sharing research facilities and multi-user hardware, and cooperation on research tasks of mutual interest.

In October 2015, HRP released a Cooperative Agreement Notice soliciting a Translational Research Institute (TRI) to provide innovative approaches, in cooperation with NASA, to reduce risk to humans during exploration missions. Work began in October 2016 and will run nominally through September 2022 with the potential to operate through the year 2028. The TRI is led by Baylor College of Medicine in Houston and their consortium partners, California Institute of Technology in Pasadena and Massachusetts Institute of Technology in Cambridge. Together the consortium operates the new institute. For more information, please visit: <https://www.bcm.edu/centers/space-medicine/translation-research-institute>.

The National Space Biomedical Research Institute (NSBRI), an institute funded by HRP, investigates the physical and psychological challenges of long-duration human spaceflight. Founded in 1997 through a NASA competition, NSBRI is a nonprofit research

consortium that connects the research, technical, and clinical expertise of the biomedical community with the scientific, engineering, and operational expertise of NASA. NSBRI is located within the Baylor College of Medicine's Center for Space Medicine. For more information, visit www.nsbri.org.

The HRP also maintains collaborative relationships with international partners through various working groups. These relationships enhance the research capabilities of all partners and provide synergism of research efforts. In FY2016, HRP began discussions with Deutsches Zentrum für Luft- und Raumfahrt (DLR) for multi-lateral bed rest studies to be conducted in their new facility—called “:envihab”—located in Cologne, Germany.

Additionally, HRP strives to develop intra-agency agreements and collaborations with agencies such as the Department of Defense (DoD), National Science Foundation (NSF) and the Department of Energy (DoE). For example, the NASA Space Radiation Laboratory (NSRL) at the DoE's Brookhaven National Laboratory in Upton, New York, conducts research using accelerator-based simulations of space radiation. HRP also has agreements with the NSF to facilitate investigations at remote U.S. Antarctic stations.

Partnerships and Collaborations with Universities, Industries, and Government Agencies

| Examples of HRP Partnerships and Collaborations | Benefits to Exploration |
|--|--|
| Translational Research Institute (TRI) | Promotes state-of-the-art research and education related to human spaceflight and NASA's mission |
| National Space Biomedical Research Institute (NSBRI) | Investigates challenges of long-duration human spaceflight and bridges the expertise of biomedical community with the scientific, engineering, and operational expertise of NASA |
| US-Russian Joint Working Group (JWG) | Broadens ISS research and enhances opportunities for collaboration with Russian Space Agency (RSA), Gagarin State Scientific Research-and-Testing Cosmonaut Training Center (GTC), Institute for Biomedical Problems (IMBP). |
| Multilateral Medical Operations Panel (MMOP) | Multilateral hardware and data collaborations between ISS operations and HRP research |

Overview

| Examples of HRP Partnerships and Collaborations | Benefits to Exploration |
|--|--|
| Multilateral Human Research Panel for Exploration (MHRPE) | Permanent steering group for ISS program. Integrates data and strategies from operations and research. Leverages existing processes among implementation groups |
| International Human Space Flight Analog Research Coordination Group (HANA) | Coordinates isolation and confinement research in analog environments across multiple international partners |
| International Space Life Sciences Working Group (Canada, Japan, Germany, Ukraine, France, and the European Space Agency) | Encourages a unified effort among space life sciences communities around the world by coordinating the use of spaceflight and ground research facilities and identifying mutual interests and compatibilities |
| National Institutes of Health (NIH), Department of Energy (DoE) - Brookhaven, Centers for Disease Control and Prevention (CDC), Department of Agriculture (DA), Department of Defense (DoD), National Science Foundation (NSF) | State-of-the-art research facilities, research activities, analogs, and technology development of mutual interest. |
| Cleveland Clinic Center for Space Medicine | Provides collaboration and consultation regarding medical issues experienced during space flight and provides access to a network of more than 2,000 Cleveland Clinic physicians |
| Summa Health Systems | Provides collaborative research for advanced health care delivery to astronauts |
| European Space Agency (ESA) | Collaboration on the utilization of the Pulmonary Function System, MARES, and exercise research |
| Japan Aerospace Exploration Agency (JAXA) | Research on bone-related risks, auscultation capabilities, and utilization of environmental sampling |
| Institute for Biomedical Problems (IBMP) | Coordination of the One-Year Mission and functional performance Field Test Experiment and VIIP research |
| SHAPE America | Collaborating and co-promoting the Mission X (MX): Train Like an Astronaut (TLA) Project |
| University at Buffalo, Dept. of Epidemiology and Environmental Health | Space Act Agreement for collaboration on topics in pediatric obesity and program evaluations for MX and TLA |
| Destination Station and ISS Program | Public dissemination of HRP information on the human challenges of space exploration |
| The Jamestown Resource Center | Collaboration on HREC content used for people with unique needs and their participation in MX:TLA activities |
| Let's Move! Initiative | TLA materials co-branded with this White House Initiative |
| International space agency education support with world-wide community partners, schools, and institutions. | Collaborative partnerships fostering the world-wide dissemination of HREC <i>Mission X: Train Like an Astronaut</i> physical and educational activities encouraging better nutrition and healthier lifestyles for children |



Major Program-Wide Accomplishments

Conclusion of Collaborative One-Year Mission and Ongoing Twins Study Research

The One-Year ISS Mission (1YM) began with the launch of astronaut Scott Kelly and cosmonaut Mikhail Kornienko to the ISS on March 28, 2015, and ended with their Soyuz spacecraft undocking from the ISS on March 2, 2016, marking 340 days in space. The HRP research complement for the 1YM included 18 studies for which a total of 459 biological samples were taken, including about 450 milliliters of blood and 1.3 liters of urine. Information on the 1YM studies can be found in charts on pages 19-21.

The NASA and NSBRI-supported Twins Study, as part of the 1YM, was a collaborative effort involving ten investigations representing multiple research disciplines and research institutions. The study offered a unique opportunity to conduct a longitudinal study of twins and observe how the human body reacts to environmental changes, whether during spaceflight or on Earth.

To prepare for the mission, HRP supported the first-of-its-kind development of the NASA Institutional Review Board interim policy on the collection and

distribution of genetic data and samples, and the formulation of the unique astronaut genetic consent for participation in these studies. The ISS Medical Projects (ISSMP) Element coordinated the Twins Study collection schedule for both Scott Kelly's flight and Mark Kelly's ground data and samples.

Physiologic samples and psychological data collection occurred during the pre-, in-, and postflight mission phases with Scott Kelly onboard the ISS while concurrent sessions were conducted with his identical twin, former astronaut Mark Kelly, on Earth. Frozen samples collected during flight were returned via the SpaceX-8 commercial resupply mission and ambient-temperature samples were returned to Earth via Soyuz landings. Pre- and postflight sessions were performed at multiple locations throughout the U.S., and the biological samples and cognitive data were then sent to the participating investigators for analysis.

Completion of the sample and data analysis will produce a comprehensive portrait of the human physiological response to spaceflight. The integration of these data will demonstrate changes in the body's cellular systems and the potential adaptations of humans in their responses to microgravity.

Major Program-Wide Accomplishments

Twins Study: Investigations

| Principal Investigator/Affiliation | Investigation Title |
|---|---|
| Susan Bailey, PhD Colorado State University/Fort Collins, CO | Differential Effects on Telomeres and Telomerase in Twin Astronauts Associated with Spaceflight |
| Andrew Feinberg, MD Johns Hopkins University School of Medicine/Baltimore, MD | Comprehensive Whole Genome Analysis of Differential Epigenetic Effects of Space Travel on Monozygotic Twins |
| Christopher Mason, PhD Weill Medical College of Cornell University/New York, NY | The Landscape of DNA and RNA Methylation Before, During, and After Human Space Travel |
| Scott M. Smith, PhD NASA JSC/Houston, TX | Biochemical Profile: Homozygous Twin Control for a 12 month Space Flight Exposure |
| Stuart Lee, PhD KBRwyle/Houston, TX | Metabolomic and Genomic Markers of Atherosclerosis as Related to Oxidative Stress, Inflammation, and Vascular Function in Twin Astronauts |
| Brinda Rana, PhD University of California/San Diego, CA | Proteomic Assessment of Fluid Shifts and Association with Visual Impairment and Intracranial Pressure in Twin Astronauts |
| Emmanuel Mignot, MD, PhD Stanford University School of Medicine/Palo Alto, CA | Twin Astronaut Study Consortium (TASC): Immunome Changes in Space |
| Mathias Basner, MD, PhD University of Pennsylvania School of Medicine/Philadelphia, PA | TASC Project: Cognition on Monozygotic Twin on Earth |
| Fred Turek, PhD Northwestern University/Evanston, IL | TASC Project: Metagenomic Sequencing of the Bacteriome in GI Tract of Twin Astronauts |
| Michael Snyder, PhD Stanford University/Palo Alto, CA | TASC Project: Longitudinal Integrated Multi-omics Analysis of the Biomolecular Effects of Space Travel |

Formation of New HFBP Element Allows Research Efficiencies, Enhanced Collaboration

In FY2016, HRP announced the consolidation of the Space Human Factors & Habitability (SHFH) and the Behavioral Health & Performance (BHP) Elements. The new element, named the Human Factors and Behavioral Performance (HFBP) Element, is for 9 of the 12 risks previously covered by BHP and SHFH:

- Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders;
- Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team;
- Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload;
- Risk of an Incompatible Vehicle/Habitat Design;
- Risk of Inadequate Design of Human and Automation/Robotic Integration;
- Risk of Inadequate Mission, Process and Task Design;
- Risk of Performance Errors Due to Training Deficiencies;
- Risk of Inadequate Human-Computer Interaction;

Major Program-Wide Accomplishments

- Risk of Injury from Dynamic Loads (Occupant Protection).

The other three risks were transferred to existing elements; two moved to the Human Health Countermeasures (HHC) Element:

- Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System;
- Risk of Adverse Health Effects Due to Host-Microorganism Interactions.

The remaining risk moved to the Exploration Medical Capability (ExMC) Element:

- Risk of Adverse Health & Performance Effects of Celestial Dust Exposure.

The merger brings together natural synergies between the elements and more closely aligns efforts in these research areas.

HRP and MPCV Programs Select Compact, Efficient Exercise Device for Orion

HRP funded research concepts for compact exercise devices that provide resistive and aerobic exercise capabilities within the limited space available in the Orion capsule. Orion is intended to carry four astronauts on future deep-space missions. These missions will require use of an exercise device that must be about the size of a shoebox, weigh no more than 23 pounds, and provide up to 400 pounds of resistive force and the capability for an aerobic workout.

During FY2016, HRP conducted human-in-the-loop testing on four of the leading exercise candidate devices as part of the final selection process for Orion missions. In February, stakeholders selected the Resistive Overload Combined with Kinetic Yo-Yo (ROCKY) device as the top candidate along with aspects of the Device for Aerobic and Resistive Training (DART). Zin Technologies of Middleburg Heights, Ohio, developed ROCKY, which is current-

ly designed specifically for the constraints required for Orion. DART was developed by TDA Research of Wheatridge, Colorado, and provided motor control algorithms that received the highest rankings during the evaluations.

The HRP and Multi-Purpose Crew Vehicle (MPCV) programs jointly decided to select a device combining the ROCKY packaging with the DART algorithms. ROCKY was chosen for its extensibility to exploration. By using two devices in tandem, a more robust exploration device can be developed. This larger, more robust version of ROCKY, called the Advanced Twin Lifting and Aerobic System, has a resistive capability up to 600 pounds of force. This capability is similar to that of the Advanced Resistive Exercise Device on the ISS, but is in a much more compact package and possesses optimized loading capabilities. This larger version will be developed for exploration and demonstrated on the ISS. HRP will be responsible for the full flight development of the operational hardware,



ROCKY is a robust exercise device that offers multiple workout options while occupying a minimal amount of space.

Major Program-Wide Accomplishments

and ROCKY will be manifested on the Orion vehicle during its first crewed mission planned for 2021.

Over the next several years, HRP will refine and optimize these devices for near-term Orion missions as well as for potential use on future long-duration missions. HRP will continue to investigate ways to expand the capabilities of these devices while keeping mass and volume to a minimum.

HRP Selects Baylor College of Medicine to Lead New Translational Research Institute

In October 2015, HRP released a Cooperative Agreement Notice soliciting for a Translational Research Institute (TRI) to provide innovative approaches, in cooperation with NASA, to reduce risk to humans during exploration missions. NASA received six proposals and, after rigorous assessment, announced the selection of Baylor College of Medicine in July 2016.

TRI joins NASA with Baylor College of Medicine in Houston and their consortium partners, California Institute of Technology in Pasadena, CA and the Massachusetts Institute of Technology in Cambridge, MA to operate the new institute. Work under the TRI Cooperative Agreement, overseen by HRP, began in October 2016 and will run through September 2022 with the potential to operate through the year 2028.

The main purpose of the institute is to deliver cutting-edge research results that accelerate reduction of health risks associated with exploration missions. The TRI implements a “bench-to-spaceflight” model, allowing rapid migration of research methods from laboratory experiments or clinical trials to point-of-care astronaut health and performance applications. The endpoint of this research will be the adoption of promising new approaches, treatments, countermeasures, and technologies with practical applications for spaceflight.

TRI represents a significant departure from the mission of NSBRI, which is closely coordinated with



By forming the TRI, HRP gains access to researchers and technologies from the Baylor College of Medicine and their consortium partners Caltech and MIT.

HRP Elements and intimately connected to the HRP Path to Risk Reduction. Rather, TRI will seek out novel, potentially game-changing approaches to solving risk mitigation challenges from investigators and developers not traditionally associated with NASA. While HRP will continue to implement the Path to Risk Reduction communicated through the Human Research Roadmap (<https://humanresearchroadmap.nasa.gov>), the new institute will invest in research that—while more risky—has the potential to move solutions into practical application much faster than traditional research approaches.

In addition, TRI will provide opportunities for scientists to gain experience in cutting-edge research in laboratories within and outside of NASA, and apply their knowledge and expertise to reducing human exploration risks. This translational workforce may participate in the NASA Space Radiation Summer School, the UTMB Aerospace Medicine Residency Program, faculty exchange, visiting scientist programs, and postdoctoral fellowships to gain experience working within the NASA system. Scientists can apply the knowledge they gain from these programs to their academic research approaches and vice versa, providing more focused solutions that can be readily adapted to the spaceflight environment.

NASA’s collaboration with the consortium partners will provide a pipeline of highly qualified research scientists who will help establish strategic visions for reducing risks to human health and performance from exploration missions. TRI will provide a forum

Major Program-Wide Accomplishments

for the exchange and development of collaborative ideas from terrestrial and spaceflight human health and performance research. TRI constitutes a new approach for NASA and has the potential to tap the intellect of the global scientific community and provide diverse solutions in a more cost-effective and timely manner than traditional independent NASA Research Announcements.

HERA Campaign 3 Introduces 30-Day Missions and International Study Collaboration

In FY2016, longer 30-day missions began in the Human Exploration Research Analog (HERA). These missions—called Campaign 3—extended the length beyond the one or two week duration of previous campaigns. Domestic research studies were conducted and operational tools were tested during the mission encompassing research from four HRP Elements: HHC, HFBP, and ExMC. Additionally, studies funded by the German Space Agency (DLR) were integrated into the HERA campaign.

HERA Campaign 3 hosted 20 studies—the largest complement to date—and marked the first time that non-HRP studies were included. The collaborative effort with DLR was established through an Implementing Arrangement (IA) facilitated by the Office of International and Interagency Relations at NASA Headquarters and approved by NASA and the DLR Microgravity and Life Science Research division. The five-year duration of the IA will enable additional DLR-funded studies to be conducted in future HERA campaigns, further enhancing the Path to Risk Reduction for long-duration exploration missions.

New capabilities for Campaign 3 included the integration of virtual reality (VR) extravehicular activities (EVAs) with the existing flight simulator to support an asteroid exploration mission scenario. Inclusion of the VR EVAs not only increased mission fidelity but also provided complex tasks and team structures that are relevant to HRP researchers. The fidelity of the analog was further improved by including live edu-



HERA crewmembers participated in 20 different research investigations in addition to executing a wide variety of operational tasks during their 30-day missions.

cation outreach events with schools or organizations selected by the crewmembers before the mission.

New Analog Collaborations and Contracts Provide Access to Unique Research Facilities

HRP's path to risk reduction relies on utilizing multiple types of analog environments, such as: Isolated, Confined and Controlled (ICC), Isolated, Confined and Extreme (ICE), Long-Duration ICC, and head-down tilt (HDT) bed rest. In FY2016, the flight analogs team worked with the National Science Foundation (NSF), the DLR Institute of Aerospace Medicine (DLR), and Russia's Institute of Biomedical Problems (IBMP) to obtain access to additional analog environments to support planned HRP research needs.

The NSF operates research stations in Antarctica that represent a prime example of an ICE analog environment. In July 2016, NASA and the NSF signed an agreement that will enable HRP-funded studies to be conducted at one or more of the Antarctic stations. This agreement also includes job rotation opportunities for NASA flight surgeons at these research stations, providing a benefit to the staff at the stations while serving as a training platform for the surgeons.

A high-priority HRP behavioral health and performance study called Characterization of Psychological

Major Program-Wide Accomplishments

Risk, Overlap with Physical Health and Associated Performance in Isolated, Confined, Extreme Environments by Candice Alfano, PhD of the University of Houston is the first to be implemented at the McMurdo and south pole research stations during the upcoming winter season. The research goal is to identify signs and symptoms of potentially adverse psychological and behavioral conditions experienced in isolated, confined and extreme environments, and to develop effective countermeasures.

The DLR Institute of Aerospace Medicine operates the :envihab facility in Cologne, Germany. The :envihab is a state-of-the-art bedrest facility where the effects of diverse environmental conditions on humans can be analyzed and countermeasures developed. The first study will place 12 subjects in HDT for 30 days, in an atmosphere enriched in carbon dioxide. The study seeks to better understand and characterize the vision impairment and intracranial pressure syndrome observed in some ISS astronauts, and determine whether a ground-based analog can be used to develop countermeasures.

Another objective is to investigate neurostructural, neurofunctional, and cognitive function changes during bedrest—with and without the presence of CO₂—a significant risk factor for the behavioral medicine risk of adverse behavioral or cognitive and psychiatric disorders. Five HRP-funded and one DLR-funded research investigations will be conducted in the latter half of 2017.

Longer duration ISS missions—up to one year in length—provide additional opportunities to validate countermeasures. Additionally, these longer missions increase HRP's confidence in extrapolating ISS research results to much longer exploration missions.

The Russian IBMP NEK isolation facility is also being considered for longer duration, one year isolation studies to supplement HRP's operational knowledge. The NEK was used for simulated long-duration missions, including a Russian-sponsored 520-day mis-



NASA Astronaut Christina Koch takes a frozen selfie at the South Pole which is sometimes referred to as “White Mars” due to the extreme isolation and environmental conditions.

sion that was part of a campaign called the Mars500. NASA hopes to collaborate on multilateral isolation missions of 4-, 8-, and 12-months.

Workshop Celebrates HRP 10th Anniversary

The 2016 HRP Investigators' Workshop (IWS) was held February 8-11 in Galveston, Texas. The workshop was the largest to date, with 1,032 participants and 500 abstracts submitted. The meeting is the primary venue for HRP and NSBRI researchers to share their findings. It included 6 plenary sessions, 50 discipline-specific sessions, and 2 poster sessions.

Dava Newman, PhD, NASA Deputy Administrator, and Ellen Stofan, PhD, NASA Chief Scientist, presented opening remarks. Sessions also included a presentation by astronaut Don Pettit, PhD, who demonstrated various chemical and physical processes on the ISS, as well as a panel discussion on applications of 3D printing for exploration spaceflight.

The HRP 10th Anniversary Banquet featured Jeffrey Kluger, editor-at-large of *TIME*® Magazine, who provided his insights into historical perspectives human space exploration. During the banquet, the NSBRI Pioneer Award was bestowed upon David Dinges, PhD and the Post-Doctoral Fellow/Graduate Student and Poster Competition awards were announced.

Major Program-Wide Accomplishments

On the final day, Katherine Wilson, PhD, of the National Transportation Safety Board discussed the role of human factors in the Space Ship Two accident, and John Guidi, Deputy Director of Advanced Exploration Systems, provided details on NASA's Evolvable Mars Campaign. The workshop closed with Mark Shelhamer, ScD, HRP Chief Scientist Emeritus, transferring his duties to John Charles, PhD, current HRP Chief Scientist.

SMARTCAP Provides Grants and Partnerships with U.S. Small Businesses

Transitioning a technology from bench to market or space is an expensive and complex endeavor, requiring specialized expertise in diverse areas of science, medicine, engineering, and business. NSBRI is committed to ensuring that its research investments have the greatest possible impact for the human space program as well as health on Earth. To this end, the NSBRI Industry Forum partnered with the private sector to develop space-compatible healthcare solutions.

Through the Space Medical and Related Technologies Commercialization Assistance Program (SMARTCAP), NASA dollars are matched with private funding. The funding is modest, with total programmatic expenditures equivalent to one single four-year grant typically awarded to a university. Six of SMARTCAP's eight solicitations were open to products addressing any health area, but two focused on two high-priority risks. The "BioShield 4 Mars" solicitation focused on radiation countermeasures and the "Vision 4 Mars" solicitation focused on ocular health.

SMARTCAP received over 200 applications from small U.S.-based companies, many of which have not previously engaged with NASA. The application process, while rigorous, was streamlined and relatively short in duration. Most importantly, the selected projects integrated well with existing commercialization strategies and enabled the companies to expand their terrestrial market opportunities.

The program funded twelve companies that developed three software tools, seven medical devices, and three nutraceutical or pharmaceutical countermeasures. In many cases, SMARTCAP's timely support was critical for the refinement of a prototype or establishment of proof of efficacy in humans. The circadian re-alignment sleep mask by LumosTech, is one such technology slated for further evaluation by NASA and possible transition to operations. Another, the variable focus glasses, are being evaluated by astronauts as their visual acuity changes during flight. Two of the other technologies have since received regulatory approval.

SMARTCAP deliverables have the potential to reduce human health risks from radiation exposure, circadian misalignment, spaceflight-induced visual impairment and intracranial hypertension, and intervertebral disc damage. The program has also fueled scientific and technological advances, facilitated commercialization, fostered economic growth of small businesses, and educated commercial industry on NASA's needs and the constraints of spaceflight.

HERO Research Solicitations and Selections

The Human Exploration Research Opportunities (HERO) NASA Research Announcement (NRA) is a solicitation process that remains open all year with research opportunities, or appendices, being issued as needed. For the 2015 NRA, HRP issued six appendices including: NASA Flagship Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions; NASA Human Research Program Omnibus Opportunity; NSBRI Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions; Artificial Gravity Opportunity; International Life Sciences Research Announcement; and Physiological and Behavioral Responses in Humans to Intermittent Artificial Gravity during Bed Rest. In response to the 2015 appendices, HRP received 225 Step-1 proposals, 169 invited Step-2 proposals, and issued 36 awards.

Major Program-Wide Accomplishments

In 2016, HRP focused the appendices on more integrated topics. HRP received, and invited all, 125 Step-1 proposals submitted in response to the Flagship and Omnibus appendices. Peer review of proposals will occur in February and March, and final selections will be announced in April.

SBIR Research Solicitations and Selections

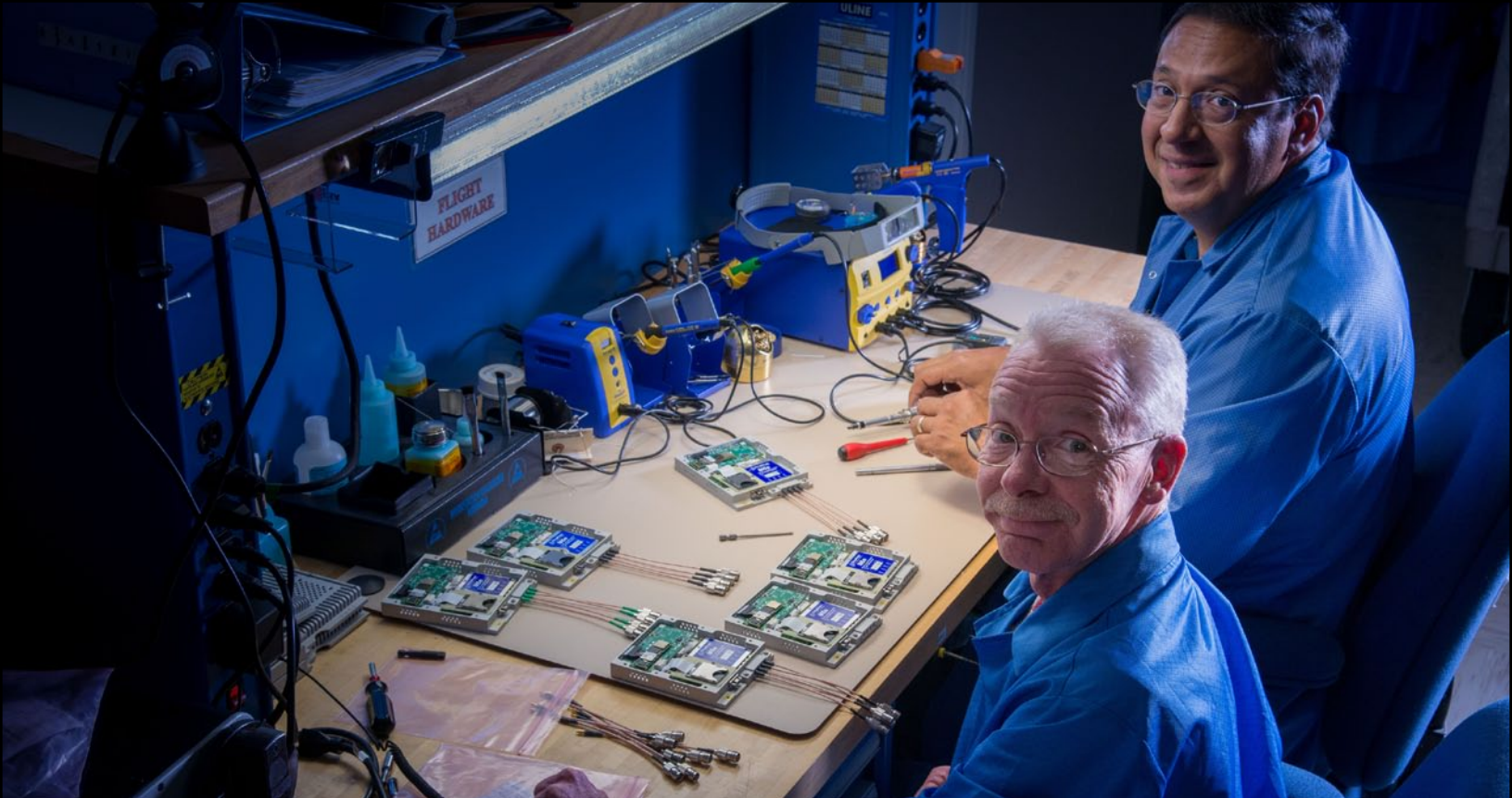
The NASA Small Business Innovation Research (SBIR) Program Management Office released the 2016 SBIR Phase 1 Solicitation in November 2015. HRP topics included in the solicitation were Task Analysis Visualization and Data Management Tool, Passive Vital Sign Monitoring, and Novel Imaging Technologies for Space Medicine. Five HRP 2016 SBIR Phase 1 awards were announced in April 2016: Task Analysis Data Processing and Enhanced Representations (TAPER); 5D Task Analysis Visualization Tool; SpaceDoc-Intelligent Health Management System for Astronauts; Multi-Purpose X-ray System; and Novel Methods for the Flexible Ultrasound System utilizing Augmented Reality Just-In-Time Procedural Guidance.

In addition, two 2015 SBIR Phase 2 awards for HRP were announced in March 2016: Cognitive Assessment and Prediction to Promote Individualized Capability Augmentation and Reduce Decrement (CAPT PICARD) and Optical System for Monitoring Net Ocular Blood Flow.



The SBIR program is a competitive 3-phase award system which provides small businesses with opportunities to propose innovations to meet specific research and development needs.

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International Space Station Medical Projects Element

Overview

The International Space Station Medical Projects (ISSMP) Element provides planning, integration, and implementation services for HRP research studies. ISSMP supports both spaceflight and flight analog research. Through the integration of these efforts, ISSMP offers an innovative way to guide research decisions to meet the unique challenges of understanding the health risks associated with space exploration.

The objectives of ISSMP are to maximize utilization of the ISS and flight analog environments and to develop and verify strategies to ensure optimal crew performance for exploration missions. The ISSMP also enables the development and validation of physical, behavioral, pharmacologic, and nutritional countermeasures, sponsored by HRP research Elements, that influence mission success or crew health.

ISSMP supports HRP flight and flight analog research investigations by integrating pre-, in-, and post-mission activities. Services provided by ISSMP include training of crewmembers and ground controllers; monitoring of real-time experiment and hardware operations; and facilitating the transfer of

data to research investigators. ISSMP also serves as the HRP interface to the ISS Program and external analog providers such as the :envihab bedrest facility and the NEK isolation chamber.

ISSMP provides and sustains the Human Research Facility (HRF) onboard the ISS, which includes hardware that enables human research and is available to investigators who wish to conduct human physiological research. ISSMP also facilitates the development and certification of new flight hardware, manifests consumables to ensure uninterrupted in-flight data collections, and provides complete integration support for multiple flight vehicles including the Russian Soyuz and Progress, Japanese, and commercial launch vehicles. During flight research operations, ISSMP maintains the JSC Telescience Support Center (TSC). The TSC provides a focal point for real-time ISSMP operations and for remote investigators to monitor their experiments and acquire telemetry data.

Additionally, ISSMP coordinates with the International Partners (IP) to develop integrated mission-specific science complements for flight investigations and schedules, usage agreements, and crewmember participation.

International Space Station Medical Projects Element

The ISSMP Flight Analogs (FA) team operates the Human Exploration Research Analog (HERA), located at JSC, in support of HRP-sponsored research. The HERA facility provides a platform for conducting HRP isolation and confinement studies under controlled mission conditions, and ISSMP is responsible for all aspects of mission planning and operations, crew provisioning, and facility maintenance in addition to research integration.

The use of flight analog environments on the ground, such as bed rest and HERA, is essential for HRP research efforts because access to resources required to conduct studies in space is very limited, the expense of ground studies is significantly less than the expense of flight studies, and ground studies allow participation of a greater number of subjects and teams. Flight analog testing will become more and more essential to validate countermeasures, given the few opportunities to use flight platforms such as the ISS and the limited number of crewmembers per ISS Expedition.

The ISSMP flight analogs team assists HRP researchers by characterizing current and potential spaceflight analogs, evaluating their relevance and similarity to spaceflight conditions, and matching the characteristics of analogs to requirements for research. Examples

of analog environments are head-down tilt bed rest, isolation and confinement facilities, altitude chambers, and extreme environments such as remote Antarctic outposts.

To learn more about ISSMP, visit:
<https://www.nasa.gov/hrp/elements/issmp>.

To learn more about flight analogs, visit:
<https://www.nasa.gov/analogs>.

FY2016 Activities and Accomplishments

In FY2016, ISSMP supported the preflight and in-flight operations of the unique NASA Twins Study, the return of the first one-year mission crewmembers as well as joint U.S.-Russian research investigations. Postflight testing will continue in FY2017 for the one-year crew. The ISSMP team also supported ISS Increments 45–48, which included the completion of 8 flight studies, 15 continuing studies and initiation of 3 new studies.

Also in FY2016, four new investigations began experiment development, and four investigations underwent feasibility assessment. Through early September 2016, ISSMP supported 1,394 in-flight crew activities from the TSC, utilizing 693 hours of crew time. ISSMP also coordinated 7 informed consent briefings, conducted 121 crew training sessions, and coordinated 271 preflight and 316 postflight baseline data collection (BDC) sessions. ISSMP also provided support to international partners by assisting with 11 test readiness reviews for their BDC sessions.

In order to provide better service for international partner research at JSC, the ISSMP recently moved into a new Baseline Data Collection Facility. This facility allows extended research time with crewmembers in a controlled environment and includes classrooms for experiment-specific training.



An ISS crewmember adds blood samples to the Minus Eighty-degree Laboratory Freezer for the ISS (MELFI) for storage prior to return to Earth for analysis. ISSMP provides essential logistic support to expedite the return of these samples to PIs.

International Space Station Medical Projects Element

International Space Station Medical Projects Flight Investigations

| Investigation Title | Operations Name | Investigator and Institution | Subject Participation | | |
|---|---------------------------|--|-----------------------|-----------------|--------|
| | | | Req'd. | Through Inc. 48 | In 1YM |
| Investigations That Continued Flight Operations in Fiscal Year 2016 | | | | | |
| NASA Biochemical Profile Project | Biochemical Profile | Scott Smith, PhD NASA JSC | All USOS | 14 | 1 |
| Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss | Bisphosphonates (Control) | Adrian LeBlanc, PhD <i>Universities Space Research Association</i> Toshio Matsumoto, MD, PhD <i>University of Tokushima</i> | 10 | 10 | - |
| Quantification of In-flight Physical Changes – Anthropometry and Neutral Body Posture | Body Measures | Sudhakar Rajulu, PhD NASA JSC | 12 | 8 | - |
| Defining the Relationship Between Biomarkers of Oxidative and Inflammatory Stress and the Risk for Atherosclerosis in Astronauts during and after Long-Duration Spaceflight | Cardio Ox | Stuart Lee, PhD <i>KBRwyle/NASA JSC</i> | 12 | 11 | 1 |
| Recovery of Functional Sensorimotor Performance Following Long Duration Space Flight | Field Test | Millard Reschke, PhD NASA JSC Inessa Kozlovskaya, MD <i>Russian Federation State Research Center, Institute of Biomedical Problems (IBMP)</i> | 15 | 3 | 2 |
| Effects of Long-duration Microgravity on Fine Motor Skills | Fine Motor Skills | Kritina Holden, PhD NASA JSC | 8 | 5 | 2 |
| Fluid Shifts Before, During and After Prolonged Space Flight and Their Association With Intracranial Pressure and Visual Impairment | Fluid Shifts | Michael Stenger, PhD <i>KBRwyle/NASA JSC</i> Scott Dulchavsky, MD, PhD <i>Henry Ford Health System</i> Alan Hargens, PhD <i>University of California, San Diego</i> | 10 | 4 | 2 |

International Space Station Medical Projects Element

| Investigation Title | Operations Name | Investigator and Institution | Subject Participation | | |
|---|-------------------|---|------------------------|-----------------------|--------|
| | | | Req'd. | Through Inc. 48 | In 1YM |
| Habitability Assessment of International Space Station | Habitability | Sherry Thaxton <i>KBRwyle/NASA JSC</i> | 6 | 4 | 1 |
| Risk of Intervertebral Disc Damage (IVD) After Prolonged Spaceflight | IVD | Alan Hargens, PhD <i>University of California, San Diego</i> | 12 | 6 | - |
| Spaceflight Effects on Neurocognitive Performance: Extent, Longevity and Neural Bases | NeuroMapping | Rachel Seidler, PhD <i>University of Michigan</i> | 13 | 5 | 1 |
| NASA Biological Specimen Repository | Repository | Kathleen McMonigal, MD <i>NASA JSC</i> | All | 47 | - |
| Integrated Resistance and Aerobic Training Study | Sprint | Lori Ploutz-Snyder, PhD <i>University of Michigan</i> | 6 Control 12 Active | 5 Control 8 Active | 1 |
| Assessing Telomere Lengths and Telomerase Activity in Astronauts | Telomeres | Susan Bailey, PhD <i>Colorado State University</i> | 10 | 7 | 1 |
| Investigations Completing ISS In-Flight Operations in Fiscal Year 2016 | | | | | |
| Individualized Real-Time Neurocognitive Assessment Toolkit for Space Flight Fatigue | Cognition | Mathias Basner, MD, PhD <i>University of Pennsylvania</i> | 6 | 5 | 2 |
| Physiological Factors Contributing to Changes in Post-Flight Functional Performance | FTT | Jacob Bloomberg, PhD <i>NASA JSC</i> | 13 | 13 | 1 |
| Occupational Risk Surveillance for Bone: Pilot Study-Effects of In-Flight Countermeasures on Sub-Regions of the Hip Bones | Hip QCT | Jean Sibonga, PhD <i>NASA JSC</i> | 10 | 10 | 1 |
| Behavioral Issues Associated with Long Duration Space Expeditions: Review and Analysis of Astronaut Journals | Journals (6 crew) | Jack Stuster, PhD <i>Anacapa Sciences, Inc.</i> | 10 | 10 | 1 |
| Study of the Impact of Long-Term Space Travel on the Astronaut's Microbiome | Microbiome | Hernan Lorenzi, PhD <i>J. Craig Venter Institute, Inc.</i> | 9 | 9 | 1 |
| Prospective Observational Study of Ocular Health in ISS Crews | Ocular Health | Christian Otto, MD <i>Baylor College of Medicine</i> | 12 | 13 | 2 |

International Space Station Medical Projects Element

| Investigation Title | Operations Name | Investigator and Institution | Subject Participation | | |
|---|--------------------|---|-----------------------|-----------------|--------|
| | | | Req'd. | Through Inc. 48 | In 1YM |
| Psychomotor Vigilance Test Self-Test on ISS | Reaction Self Test | David Dinges, PhD <i>University of Pennsylvania</i> | 24 | 24 | 2 |
| The Effects of Long-Term Exposure to Microgravity on Salivary Markers of Innate Immunity | Salivary Markers | Richard Simpson, PhD <i>University of Houston</i> | 6 | 7 | 1 |
| Sleep-Wake Actigraphy and Light Exposure on ISS-12 | Sleep 1YM | Laura Barger, PhD <i>Brigham and Women's Hospital/Harvard Medical School</i> | 20 | 21 | 2 |
| Differential Effects on Homozygous Twin Astronauts Associated with Differences in Exposure to Spaceflight Factors | Twins Study | <i>List of Principal Investigators and their affiliations listed on page 8</i> | 2 | 2 | 1 |

| Investigation Title | Operations Name | Investigator and Institution | Subject Participation | |
|---|------------------------------|--|-----------------------|-----------------|
| | | | Required | Through Inc. 48 |
| Investigations with Initial Operations (pre/in/post flight data collection) in Fiscal Year 2016 | | | | |
| Dose Tracker Application for Monitoring Crew Medication Usage, Symptoms and Adverse Effects During Missions | Dose Tracker | Virginia Wotring, PhD <i>Baylor College of Medicine</i> | 24 | 4 |
| Functional Immune Alterations, Latent Herpesvirus Reactivation, Physiological Stress and Clinical Incidence Onboard the International Space Station | Functional Immune | Brian Crucian, PhD <i>NASA/JSC</i> | 10 | 0 |
| Testing Solid State Lighting Countermeasures to Improve Circadian Adaptation, Sleep, and Performance During High Fidelity Analog and Flight Studies for the International Space Station | Lighting Effects | George Brainard, PhD <i>Thomas Jefferson University</i> | 6 | 0 |
| Investigations Initiating Flight Development Activities in Fiscal Year 2016 | | | | |
| Medical Consumables Tracking | Medical Consumables Tracking | John Zoldak <i>Zin Technologies/ NASA GRC</i> | N/A | N/A |
| One Carbon Metabolism: Expanded Polymorphism Evaluation | One Carbon Poly | Scott Smith, PhD <i>NASA/JSC</i> | Up to 98 subjects | 0 |

International Space Station Medical Projects Element

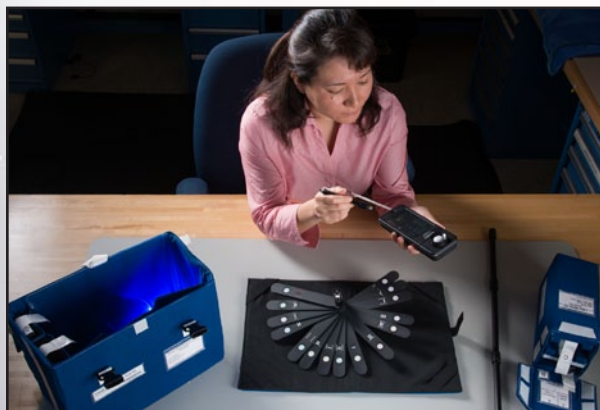
| Investigation Title | Operations Name | Investigator and Institution | Subject Participation | |
|---|-----------------|---|--|-----------------|
| | | | Required | Through Inc. 48 |
| Developing personalized countermeasures for sensorimotor adaptability: A bed rest study | Predictors | Ajitkumar Mulara, PhD KBRwyle/NASA JSC | Up to 29 subjects from previous flown crew | 0 |
| Inflight pharmacokinetic and pharmacodynamic responses to medications commonly used in spaceflight. | RX Metabolism | Virginia Wotring, PhD Baylor College of Medicine | 6 | 0 |

New ISS Hardware Enhances Studies of Cardiovascular Research and Lighting Effects

The ISSMP delivered two new flight hardware systems to the ISS in FY2016 to augment HRP research on the ISS. In support of cardiovascular research, the ISSMP flight-certified and manifested a new hardware system called VeinPress. The VeinPress system gives investigators a way to noninvasively measure venous pressure which, when combined with standard sonographic techniques to measure venous dimensions can be used to measure venous compliance—the ability of a blood vessel wall to expand and contract passively with changes in pressure. This information may contribute to understanding of the etiology of the vision

impairment syndrome. The VeinPress interfaces with the HRF Ultrasound 2 system and cables included with the system add the capability to display real-time data. The VeinPress system was first used as part of the Fluid Shifts investigation during Increment 47/48.

ISSMP also developed new hardware for the ISS Lighting Effects study, which will assess the acceptability, use, and operational impact of the dynamic lighting schedule protocol on astronaut vision, sleep, alertness, circadian rhythms, and general well-being during missions aboard the ISS. Two new kits were developed to support this study: the Light Meter Kit and the Visual Performance Test Kit. The Light Meter Kit collects lighting measurements on orbit for the new Solid-State Light Assemblies, the existing General Luminaire Assemblies, and ambient light in the Cupola and other modules. The Visual Performance Test Kit tests crewmember's color discrimination proficiency and printed contrast acuity.



The Lighting Effects flight hardware system includes storage kits, a visual performance test kit and a light meter.

FLIGHT ANALOGS

FY2016 Activities and Accomplishments

In FY2016, the Flight Analogs team completed the third campaign of HERA research which included the largest group of studies to date. HERA Campaign 3 consisted of 4 identical 30-day missions simulating a voyage to an asteroid, with flight-like mission tasks

International Space Station Medical Projects Element

interspersed with the research activities. Each mission had a crew of four test subjects who met criteria similar to those for the NASA astronaut corps.

Campaign 3 included 17 HRP-funded studies, 2 operational tools, and 3 studies funded by the German Aerospace Center's (DLR's) Microgravity Research and Life Sciences division. The HRP studies included six studies that continued from previous HERA missions, four of which have now completed their required number of subjects. The 20 studies will help inform researchers on a wide array of concerns for long-duration space flight, including team interactions and dynamics; physiological, cognitive, and psychological effects of stress; circadian and sleep

cycles; and the efficacy of wearable technologies.

The Flight Analogs team began the definition phase and integration of 7 new and 12 continuing studies, which represent the complement of studies for HERA Campaign 4 which consists of four 45-day missions.

Similar to FY2015, FA assisted the Astronaut Office with implementing Space Week, a three-day mission in the HERA involving members of the astronaut corps and aimed at providing an opportunity for crewmembers to hone expeditionary skills. Space Week participants evaluated six HRP-provided tools and gave valuable feedback on these tools and the fidelity of the HERA.

Analog Investigations

| Analog | Investigation Name | Investigator and Institution | Subjects Req'd. | Subjects Complete through FY16* |
|--|---|--|-----------------|---------------------------------|
| FY 2016 Flight Analogs Investigations Continuing Operations | | | | |
| HERA | Leadership Followership: Moving Beyond Traditional Leadership to Build Highly Functioning Autonomous Teams (HERA) | Shawn Burke, PhD <i>University of Central Florida</i> | 32 | 32 |
| HERA | Optical Computer Recognition of Stress, Affect and Fatigue in Space Flight | David Dinges, PhD <i>University of Pennsylvania</i> | 40** | 40 |
| HERA | Biomarkers as Predictors of Resiliency and Susceptibility to Stress in Space Flight | Namni Goel, PhD <i>University of Pennsylvania</i> | 32 | 32 |
| HERA | Capturing Teamwork Dynamics – Analogs | Steve Kozlowski, PhD <i>Michigan State University</i> | 64 | 48 |
| HERA | Using Real-Time Lexical Indicators to Detect Performance Decrements in Spaceflight Teams: A Methodology to Dynamically Monitor Cognitive, Emotional, and Social Mechanisms That Influence Performance | Eduardo Salas, PhD <i>Rice University</i> | 48 | 48 |
| HERA | Dynamic Team Role Allocation in Long Duration, Exploration Missions: Identification of Roles, Triggers, and Measurement Tools | Eduardo Salas, PhD <i>Rice University</i> | 48 | 32 |

* Note the final mission of Campaign 3 started in FY 2016 and will complete in FY 2017.

** Only participated in two of the four missions during 2016.

International Space Station Medical Projects Element

| Analog | Investigation Name | Investigator and Institution | Subjects Req'd. | Subjects Complete through FY16* |
|---|---|---|-----------------|---------------------------------|
| HERA | Habitability Ground and Analog Testing (ISHORT) | Sherry Thaxton, PhD <i>Liedos</i> | (Ops Tool) | N/A |
| HERA | Evaluation of the ISS Food Intake Tracker (ISS FIT) App | Sarah Zwart, PhD <i>USRA</i> | (Ops Tool) | N/A |
| FY 2016 Flight Analogs Investigations Initial Operations | | | | |
| HERA | Physical activity for better sleep and psychophysiological state during isolation | Vera Abeln, PhD <i>German Sports University</i> | 32 | 16 |
| HERA | Characterization of Psychological Risk, Overlap with Physical Health, and Associated Performance in Isolated, Confined, Extreme (ICE) Environments | Candice Alfano, PhD <i>University of Houston</i> | 16 | 16 |
| HERA | Low Latency Teleoperation (LLT) Study | Andrew Ambercromby, PhD <i>NASA JSC</i> Harry Litaker <i>Liedos</i> | 32 | 16 |
| HERA | SCALE: Shared Cognitive Architectures for Long-term Exploration & Team Task Switching in Astronaut Crews on the International Space Station: Integrating Multiteam Membership, Multiteam Systems, Multitasking, & Multidimensional Networks to Monitor & Enable Functional Work Shifts in Astronaut Crews & CREWS: Crew Recommender for Effective Work in Space | Leslie DeChurch, PhD <i>Georgia Tech (2)</i> Noshir Contractor, PhD <i>Northwestern University</i> | 48 | 16 |
| HERA | Standardized BHP Measures | David Dinges, PhD <i>University of Pennsylvania</i> | 16 | 16 |
| HERA | Effects on Circadian Rhythm in humans during long-term Isolation and confinement | Hanns-Christian Gunga <i>Center for Space Medicine</i> | 32 | 32 |
| HERA | Evaluation of Crew-Centric Onboard Mission Operations Planning and Execution Tool | Steve Hillenius, MS <i>NASA ARC</i> Jessica Marquez <i>NASA ARC</i> | 32 | 16 |
| HERA | Performance Degradation Precursors in Operational Teams | Jerry Lamb, PhD & Sarah Chabal, PhD <i>Naval Submarine Medical Research Laboratory</i> | 16 | 16 |

International Space Station Medical Projects Element

| Analog | Investigation Name | Investigator and Institution | Subjects Req'd. | Subjects Complete through FY16* |
|---|---|---|-----------------|---------------------------------|
| HERA | Understanding and Preventing Crew Member Task Entrainment | Jeff LePine, PhD <i>Arizona State University</i> | 48 | 16 |
| HERA | STARwatch to Deliver Objective Sleep Measures for Spaceflight Operations | Daniel Mollicone, PhD <i>Pulsar Informatics</i> | 32 | 16 |
| HERA | Meal Replacement Mass Reduction and Integration Acceptability Study | Takiyah Sirmons, PhD <i>NASA JSC</i> | 16 | 16 |
| HERA | Effects of Isolation and Confinement on Hippocampal Volume and Visuo-Spatial Memory | Alexander Stahn MD, PhD <i>Center of Space Medicine Berlin</i> | 32 | 16 |
| HERA | Sleep Electroencephalography and Near-Infrared Spectroscopy Measurements for Spaceflight and Analogs | Gary Strangman, PhD <i>Harvard University</i> | 16 | 16 |
| HERA | Wearable Biosensor Monitor to Support Autonomous Crew Health and Readiness to Perform | William Toscano, PhD <i>NASA ARC</i> | 8 | 8 |
| FY 2016 Flight Analogs Investigations Initial Planning | | | | |
| HERA | A US-Russian Collaborative Proposal for Data Collection in HERA: The Relationship between Composition, Interpersonal Relations, and Team Effectiveness in Space Crews | Suzanne Bell, PhD <i>Depaul University</i> | 32 | 0 |
| HERA | The Integrated Impact of Diet on Human Immune Response, the Gut Microbiota, and Nutritional Status During Adaptation to Spaceflight | Grace Douglas, PhD <i>NASA JSC</i> | 8 | 0 |
| HERA | Real-Time Estimation Of The Effects Of A Simulated Long-Duration Exploration Mission on Flight Performance, Workload, And Situation Awareness | Kevin Duda, PhD <i>Draper Laboratory</i> | 32 | 0 |
| HERA | Evaluation of the Validity, Acceptability and Usability of Bio-Mathematical Models to Predict Fatigue in an Operational Environment | Erin Flynn-Evans, PhD <i>NASA ARC</i> | 16 | 0 |
| HERA | Cardiorespiratory Kinetics during Exercise in Simulated Stressful Missions | Uwe Hoffaman, PhD <i>German Sport University</i> | 16 | 0 |
| HERA | Lighting Protocols for Exploration: HERA Campaign | Steven Lockley, PhD <i>Harvard University</i> | 16 | 0 |
| HERA | Quantifying and Predicting Operationally-Relevant Performance in a Long-Duration Spaceflight Analog | Gary Strangman, PhD <i>Harvard University</i> | 32 | 0 |

International Space Station Medical Projects Element

| Analog | Investigation Name | Investigator and Institution | Subjects Req'd. | Subjects Complete through FY16* |
|----------------------------|--|--|-----------------|---------------------------------|
| ICE-Antarctica (NSF Sites) | Characterization of Psychological Risk, Overlap with Physical Health, and Associated Performance in Isolated, Confined, Extreme (ICE) Environments | Candice Alfano, PhD <i>University of Houston</i> | 110 | 0 |
| :envihab | Omics and biochemical markers of cardiovascular and bone health: Relationship with bedrest and standard physiological | Carl Ade, PhD <i>University of Oklahoma, Norman</i> | 12 | 0 |
| :envihab | Comparing Globe Deformations in Head-Down Bed Rest to those Measured in Astronauts Following Short and Long-Duration | Noam Alperin, PhD <i>University of Miami</i> | 12 | 0 |
| :envihab | Integrative physiology of VIIP: cardiopulmonary, sleep, and cognitive function assessment during hypercapnic bed rest | Steven Laurie, PhD <i>KBRwyle/NASA JSC</i> | 12 | 0 |
| :envihab | Identification of functional metabolomic alterations during the simulated spaceflight environment | Brinda Rana, PhD <i>University of California, San Diego</i> | 12 | 0 |
| :envihab | Bed Rest Combined with 0.5% CO ₂ as a Spaceflight Analog to Study Neurocognitive Changes: Extent, Longevity, and Neural Bases | Rachael Seidler, PhD <i>University of Michigan</i> | 12 | 0 |

FUTURE PLANS

ISSMP will continue to play a critical role in the development, testing, and integration of research investigations and hardware systems on the ISS and in flight analog environments. ISSMP will deliver a new centrifuge to the ISS in FY2017 to support HRP research through the end of the ISS Program as well as an electroencephalography (EEG) system to study crewmember brain activity that may be altered by medications.

In FY2017, ISSMP also looks forward to starting the fourth campaign of HRP research in the HERA facility, which will feature increased mission durations of 45 days. Efforts will continue to integrate HRP research into new analog environments, with the first campaign using the DLR :envihab facility scheduled to begin in late FY2017, along with ongoing discussions with Russian colleagues regarding use of their NEK isolation chamber.

As NASA transitions to transporting crews to the ISS by commercial vehicles, and expanding the number of crewmembers to seven, the ISSMP is uniquely positioned to support research studies, certify flight hardware, train crewmembers, and integrate the research required for safe space exploration.

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Space Radiation Element

Overview

The Space Radiation (SR) Element is responsible for ensuring that crewmembers can safely live and work in space without exceeding acceptable radiation health risks. Outside the protection of Earth's magnetic field, space radiation is a serious hazard to humans. The main sources of space radiation are solar particle events (SPEs) and galactic cosmic rays (GCRs), which are atomic nuclei, consisting of protons and neutrons trapped in Earth's magnetic field. GCRs permeate interplanetary space and include high-energy, charged nuclei of elements ranging from hydrogen to iron.

At the cellular and tissue levels, space radiation causes damage that is largely different from the damage caused by terrestrial radiation, such as X-rays or gamma-rays, because of the significantly greater ionizing power of space radiation. Because of this difference, large uncertainties exist in quantifying biological response to space radiation. Shielding against GCRs is much more difficult than shielding against terrestrial radiation because of the large masses required to stop primary GCR particles in space and the secondary particles generated in the shield material.

Health risks from space radiation may include an increased risk of cancer, acute radiation syndrome, degenerative tissue damage manifested as health problems such as heart disease and cataracts, and early and late central nervous system (CNS) damage. Cancer risks pose the greatest challenge for exploration. Uncertainties in cancer risk projection have significant impacts on exploration mission design and can affect the ability to accurately assess mitigation measures such as shielding and biological countermeasures. Uncertainties about dose thresholds, the effects of radiation quality, and latency and progression rates for risks involving the CNS and cardiovascular system also affect mission design.

SR study results provide a scientific basis to accurately project and mitigate health risks from space radiation. Research in radiobiology and physics guides and supports risk assessment and protection strategies. The results provide tools for evaluating shielding recommendations for habitats and vehicles, as well as requirements for storm shelters and early warning systems for SPEs.

To read more about SR, please visit: <http://www.nasa.gov/hrp/elements/srpe>.

Space Radiation Element

FY2016 Activities and Accomplishments

SR completed another successful year of high-caliber research through the efforts of many outstanding investigators across the country who conducted ground-based studies at the NASA Space Radiation Laboratory (NSRL). The 27th Annual Investigators' Workshop was completed and included a kick-off of the GCR Simulator Experimental Consortium, whose goal is to support future research using radiation exposure scenarios tailored to more accurately simulate deep space and planetary exploration missions.

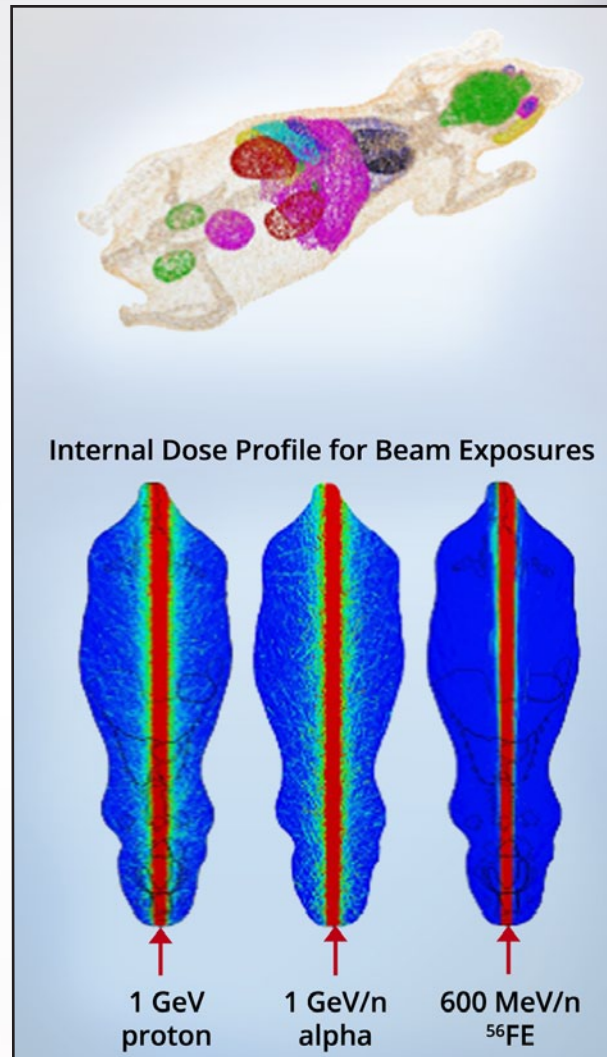
Collaborative efforts with other HRP Elements continued to better understand the combined effects of radiation and other aspects of spaceflight on the CNS, cardiovascular system, and immune function. This cooperation also continued to lay the foundation for selection of future medical countermeasures.

The National Council on Radiation Protection (NCRP) published a report of their Phase I review focused on CNS risks: *NCRP Commentary No. 25, Potential for Central Nervous System Effects from Radiation Exposure during Space Activities. Phase I: Overview*. The Phase I report reviewed the major issues related to the potential short and long-term effects of space radiation exposure on the central nervous system and identified important knowledge gaps in this area. The report provided the foundation for a more comprehensive Phase II review that was initiated in 2016 as an expansion of this important topic.

Finally, collaborative efforts with the NASA Space Biology Program and GeneLab Project, as well as continued development of mechanisms to facilitate tissue sharing are progressing—all of which facilitates cross-discipline research and enhanced scientific output.

NSRL Upgrades, Campaign Statistics, and New GCR Simulator Validation Consortium

Major upgrades to the NSRL that will enable continuation of its cutting-edge ground-based research con-



Simulated dose distribution within phantom mouse model for major GCR particle species.

ducted through SR are scheduled for completion by January 2017. These upgrades will enhance the lab's ability to simulate the radiation environment inside a shielded spacecraft. Specifically, the GCR simulator will generate an accelerator-based spectrum of ions and energies that closely approximate those known to make up the GCR environment in a shielded spacecraft. An initial reference radiation field mimicking the radiation environment inside a shielded spacecraft has been defined and is characterized by hydrogen, helium, oxygen, silicon, and iron ions at multiple energies that are modulated by well-designed radiation absorbers. This design enables the generation of

Space Radiation Element

a spectrum of ions and energies characteristic of primary GCR particles in space and secondary particles generated in shielding material.

The GCR Simulator Experimental Validation Consortium was formed to enhance outcomes from early GCR simulation design experiments to validate results across multiple endpoints. After solicitation of proposals and peer review, three principal investigator (PI) teams were selected to perform the first GCR simulations. Teams tested hypotheses about the additivity of effects on long-term health from exposure to multiple particle types, as would be experienced by crews on exploration missions or on the ISS.

The investigators are studying cancer-relevant endpoints measured in human and mouse cell lines, as well as in animal models, using single and multiple beams of protons, helium, oxygen, silicon, and iron. All studies leverage results from a substantial historical database using single ion beams spanning more than 20 years.

Important questions remain: How to best simulate the lower dose rates found in space? How to simulate the possibility of nonlinear responses due to nontargeted effects? And, what are the impacts of a mixed radiation field for in-flight and late CNS effects on behavior and cognition? These issues will be the focus of future GCR simulator validation studies. Ultimately, the optimized combination of particle types and energies, doses and dose rates determined from these early experiments are required for and will be used for biological countermeasures validation.

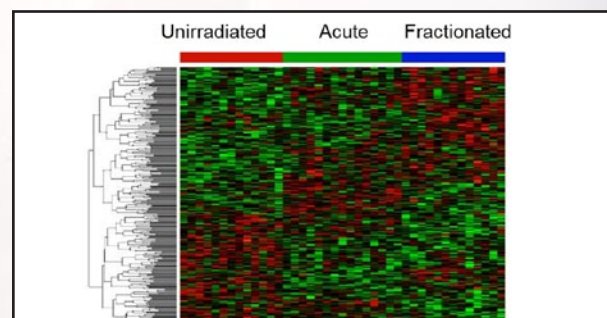
In addition to the significant NSRL upgrades that are underway, the NSRL science team and SR-funded PIs completed three successful beam campaigns in FY2016. During these campaigns, 84 investigator teams conducted experiments on over 9,000 biological specimens, including tissues and cells, and the facility provided more than 1,000 hours of use of those specimens. The results of the scientific research yielded more than 80 peer-reviewed articles in major

journals such as *Cancer Research*, *Oncogene*, *Radiation Research*, *Stem Cells*, *Nature Medicine*, *Oncotarget*, and *Biological Psychiatry*.

Lung Cancer NSCOR Completion Results in More Than 80 Peer Reviewed Articles

SR supports individual PI-driven studies as well as larger collaborative projects known as NASA Specialized Center of Research (NSCORs). An NSCOR consists of a team of investigators who have complementary skills and who work together to answer a closely focused set of research questions with the goal of achieving overall research progress that is greater than the sum of the progress achievable by each project individually.

In FY2016, NSCOR teams at Duke University, led by David Kirsch, PhD; Emory University, led by Ya Wang, MD, PhD; and University of Texas Southwestern Medical Center, led by John Minna, MD, completed major space radiation research efforts. The overarching goal of these three complementary NSCOR teams was to provide a comprehensive approach to improve the understanding and estimation of the risk of radiation-induced lung cancer after exposure to space radiation particles with high atomic number and energy (HZE). The risk of late development of lung cancer is among the largest risks from space radiation exposure that crews will experience after long-duration space travel.



Identification of inflammatory pathways permissive for tumor progression in lung cancer rodent model published in the March 2014 issue of *Clinical Cancer Research*.

Space Radiation Element

Using two-dimensional and advanced 3D cell culture models, sophisticated mouse genetics, innovative studies of lung progenitor cells, and state-of-the-art examination of DNA repair and oxidative stress coupled with quantitative genetic and epigenetic analyses, these teams contributed more than 80 peer-reviewed publications with important information on the mechanistic basis of space radiation carcinogenesis. These results will be used for mission planning and formulation of future medical countermeasures targeting this large space radiation risk.

Human System Risk Board Sets New Likelihood and Consequence Assessment Metrics

The Human System Risk Board (HSRB), under the purview of NASA's Office of the Chief Medical Officer, assesses the status of the major risks to crew health and performance on a continuing basis. Four major risks are identified as part of the SR research portfolio: radiation carcinogenesis, cardiovascular disease, acute radiation syndromes, and in-flight and late effects on the CNS. To establish a consistent, integrated process for managing all of the human system risks, the likelihoods and consequences of about 30 major risk areas must be relatable to each other, as well as to currently accepted health standards. NASA's health standard defines the acceptable level of risk for radia-

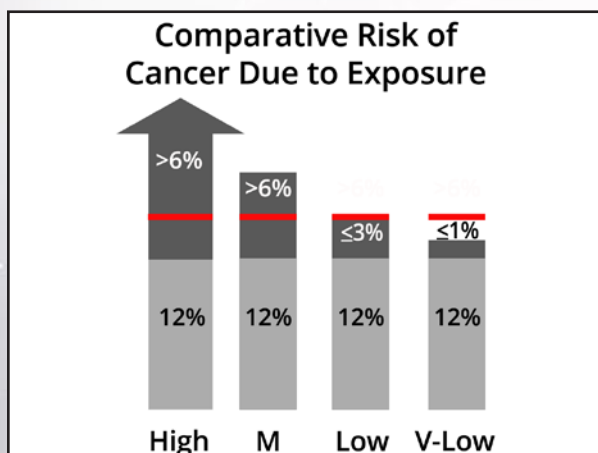
tion carcinogenesis as less than or equal to 3% risk of exposure-induced death, which positions this risk at the highest likelihood of occurrence—greater than 1%—with the highest long-term health consequence of death. This leads to difficulties in assessing the large risk of radiation carcinogenesis, compared with the other HRP identified health risks, using the HSRB risk disposition criteria where the risk of death from space radiation induced cancers would remain as unacceptable even if the permissible exposure limits were met. New and unique metrics were approved by the HSRB in order to better communicate a risk posture that reflects the Agency's position on the level of risk that NASA deems acceptable to the crew.

The new HSRB metrics for rating radiation carcinogenesis are scaled to space radiation Permissible Exposure Limits (PELs), as well as to background cancer mortality rates for those who were 'never-smokers', in the U.S. population sector that is representative of crewmembers. This new rating scale allows HRP to better communicate the impact of mitigation strategies on reducing SR's risk posture for long duration exploration missions.

Additionally, this rationale supports NASA's ability to accept additional risk, using guidance established by the Institute of Medicine Ethics Framework, in considering options when a standard cannot be met. The decision to except health standards for an exposure will be a policy decision made at the highest levels of NASA. The Space Radiation Element continues to implement its rigorously reviewed integrated research plan to understand and mitigate the human health and performance risks to crewmembers from exposure to the chronic high-linear energy transfer (LET) space radiation environment.

Radiation Effects on Cognitive Function Study Completion

NSBRI's neurobehavioral research team at The Johns Hopkins Medical School led by Catherine Davis, PhD, and Robert Hienz, PhD, is assessing the likely



Gray bars depict the baseline risk of ~12% probability of dying from cancer for normal weight never-smoking Americans. The red line indicates NASA Health Standard of 3%. The dark grey bar indicates excess risk due to exposure.

Space Radiation Element



A NEEMO crewmember and rat both perform versions of the PVT to evaluate vigilance, attention and psychomotor speed.

effects of radiation exposure on astronauts during long-duration space explorations. To determine the likely effects of such radiation on an astronaut's cognitive function as well as on the CNS, Drs. Davis and Hienz have developed an animal model of a commonly used human reaction response test, the Psychomotor Vigilance Test, for use in rodents. This test is currently used by astronauts on the ISS, where it is termed the "Reaction Self Test," and is used to assess their current levels of vigilance, attention, and psychomotor speed.

Research findings have shown that exposures to space radiation particles at mission-relevant doses of protons, iron ions, or silicon ions significantly impair cognitive function by increasing lapses in attention and slowing normal reaction times. Importantly, individual strains of rats differ in their susceptibility to radiation—that is, some rat strains are highly sensitive to radiation while others appear more resistant to radiation effects. This differential susceptibility to the cognitive effects of radiation correlates with changes in protein levels related to neurotransmitter function in the CNS dopamine system that are seen only in radiation-sensitive subjects.

The development of this comprehensive and experimentally flexible animal model of astronaut performance provides a useful tool for preclinical research in other domains such as sleep and chronobiology, neuropsychiatric disorders, aging, and cognitive enhancement. In ongoing research, Drs. Davis and Hienz are investigating biomedical countermeasures that may protect or reduce effects of space radiation on human cognitive function, and examining the po-

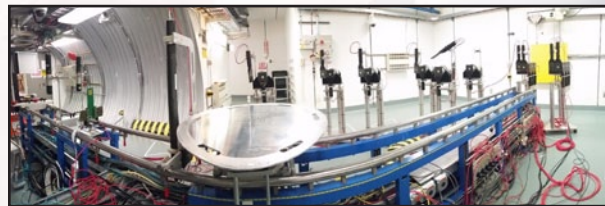
tential effects of space radiation on sleep, fatigue, and normal daily circadian rhythms.

Release of HZETRN2015 Adds 3D Capabilities and Inclusion of New Particles

The ability to model the radiation environment inside spacecraft and habitats is important in planning for the human exploration of space. NASA developed the High Charge and Energy Transport (HZETRN) suite of computational models to efficiently calculate the radiation environment behind complex shielding used in modern spacecraft. The latest version, HZETRN2015, was released for government use in FY2016 and was approved, for the first time, for public release in March 2016. It includes state-of-the-art updates to increase accuracy while maintaining the computational efficiency for which the HZETRN suite is known.

HZETRN2015 now includes the production and transport of pions, muons, electrons, positrons, and photons. Pions are copiously produced in the nuclear reactions of space radiation with shielding materials. Pions can then decay to muons, which can decay further to electrons, positrons, and photons. These particles were neglected in HZETRN and can now be fully accounted for in radiation exposure calculations.

HZETRN was traditionally a one-dimensional model of particle transport. The new version; however, called 3DHZETRN, has the capability to model 3D transport of radiation particles. Computational efficiency was maintained in the development of 3DHZETRN, and the updated model is approximately 100,000



To assist in future validation of HZETRN2015, nuclear cross section measurements were performed at the NSRL at Brookhaven National Laboratory.

Space Radiation Element

times faster than stochastic models—radiation models attempting to account for random events. Additionally, HZETRN2015 includes the latest version of the Badhwar-O’Neill GCR environment model, which was shown to be more accurate than previous versions for human exploration applications.

HZETRN2015 was verified against other transport models and validated against measurements of radiation absorbed dose in Earth’s atmosphere, on the ISS, and on the Mars Science Laboratory. To assist in future validation work, measurements of cross sections of atomic nuclei were performed at the NSRL at Brookhaven National Laboratory. HRP has also collaborated with the Advanced Radiation Protection project in the JSC Space Technology Mission Directorate on measurements of particles resulting from bombardment by radiation beams of thick targets composed of shielding material.

FUTURE PLANS

SR continues to foster collaborations with other HRP Elements, NASA centers, International Partners and government agencies including the National Institutes of Health, and the Armed Forces Radiobiology Research Institute. Additionally, ongoing ground-based research will continue to close the radiation knowledge gaps in cancer, cardiovascular diseases, and CNS risks.

In addition to the ongoing NCRP Phase 2 study addressing the CNS risk area, SR is collaborating with the HFBP element to develop a translational, cognitive, and behavioral test suite focusing on aligning studies conducted in rodents with relevant human tests for assessment of astronaut cognitive health. This effort seeks to identify the links between measurement techniques and possible predictors for future rodent space radiation CNS studies. It will also support the ability to make meaningful inferences and conclusions about the effects of radiation exposure on performance and health uncovered in animal research and the potential impact on humans.

One of the more important questions that remain for quantifying risk and developing mitigation strategies across all of the risk areas is the effect of dose rate. Previous studies have shown varied effects on late disease endpoints according to the order of ion delivery and exposure type, namely, acute exposures versus fractionated exposures—exposures occurring at defined intervals. Because continuous protracted exposures longer than 24 hours are not possible at the NSRL, Space Radiation will develop a GCR simulator irradiation scheme in FY2017.

Several projects conducted through the GCR simulator consortium are underway to evaluate the effects of low dose rates, including chronic neutron exposures and fractionated exposures over longer times. Data from these studies, along with new data on low-dose-rate exposures from epidemiological studies, will help design future GCR chronic studies. Questions about relevant dose rates and fractionation schedules, scaling from rodent to human lifespans, and ion order will be addressed.

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Human Health Countermeasures Element

Overview

NASA uses the term “countermeasures” to describe the strategies to keep astronauts healthy and productive during space travel and return to Earth. The Human Health and Countermeasures (HHC) Element is responsible for understanding the normal physiologic effects of spaceflight and developing countermeasures to those with detrimental effects on human health and performance. HHC provides the biomedical expertise for the development and assessment of medical standards, vehicle and spacesuit requirements, and countermeasures that ensure crew health during all phases of flight.

Preflight countermeasures involve physical fitness and exercise, and physiologic adaptation training. In-flight countermeasures include nutritional health, physical fitness, pharmaceuticals, and sensorimotor training protocols. Postflight countermeasures target rehabilitation strategies. Before they are flight-tested, candidate countermeasures and technologies are developed and refined using ground-based studies.

The HHC is composed of five portfolios: Vision and Cardiovascular, Exercise and Perform-

mance, Multi-System, Bone, and Technology and Infrastructure. To learn more, please visit: <http://www.nasa.gov/hrp/elements/hhc>.

VISION AND CARDIOVASCULAR PORTFOLIO

FY2016 Activities and Accomplishments

A variety of flight and ground studies in HHC’s Vision and Cardiovascular Portfolio continue to explore changes in the eye, brain, and cardiovascular system that are hypothesized to result from spaceflight exposure. The Portfolio’s three active flight studies—Fluid Shifts, Ocular Health, and Cardio Ox—are generating important data for understanding the effects of long-duration space flight. All three studies were also selected for inclusion in the 1YM investigation.

The Fluid Shifts experiment compares body fluid distribution before, during, and after spaceflight, and determines adaptations of the cardiovascular system and the eye to spaceflight. This study also investigates the ability of lower-body negative pressure to temporarily reverse or diminish the vascular and ocular effects of the headward fluid shift that occurs during

Human Health Countermeasures Element

weightlessness. The Ocular Health study documents the time course of observed structural and functional changes in the eyes during and after spaceflight, and seeks to understand the impact of these changes on ocular health. The Cardio Ox study investigates the effects of long-duration spaceflight on measures of arterial structure and function, and determines if they are related to spaceflight-induced changes in stress caused by oxidation and inflammation.

While Cardio Ox addresses adaptations that occur during and immediately after flight, it also is the first study of its kind to monitor the vascular health of astronauts for up to five years after their long-duration spaceflight mission. The study results, together with results from associated ground-based investigations and previous work, represent a significant improvement in understanding of the cardiovascular system during and after long-duration spaceflight, and will lead to an improved understanding for the risks associated with future exploration missions.

International Study Investigates the Effects of Fluid Shifts and Elevated CO₂ on the Brain

The risks of visual impairment or increased intracranial pressure (VIIP) manifests in astronauts as structural and functional changes in the visual system that correlate with time in space. On Earth, similar changes, such as swelling of the optic nerve, are associated with elevated ICP. It is hypothesized spaceflight may increase ICP because body fluid shifts headward in microgravity, and this increased pressure may be exacerbated by the elevated CO₂ environment of the ISS. Postflight spinal taps conducted in astronauts who experienced swelling of the optic nerve suggested ICP was mildly elevated; however, no preflight ICP measures were conducted nor was ICP measured in astronauts who did not have ophthalmic changes.

To study the effects of fluid shifts and elevated CO₂ on brain physiology and to test the new German Aerospace Center (DLR) bed-rest facility, NSBRI conducted an international study called "SPACE-COT:



SPACECOT subject in -12 degree head down tilt performing a battery of cognitive tests while simultaneously being monitored via near infrared spectroscopy for brain oxygenation.

Studying the Physiological and Anatomical Cerebral Effects of Carbon Dioxide and Tilt." This study was designed to investigate the effects of headward fluid shifts and elevated CO₂ on cerebral physiology and function. The integrated study team, consisting of ten separate institutions and companies, measured the effects of headward fluid shifting and elevated CO₂ on brain, eye, cardiac, pulmonary, and cognitive function in six healthy middle-aged males over a 28 hour period using MRI imaging techniques as well as new emerging portable technologies that may be useful during spaceflight. The study was completed on time and under budget with 95% of expected data collected. This demonstrated that the DLR was fully operational and ready for the 30-day bedrest study.

MRI analyses suggested that HDT decreased blood flow to the brain; however, contrary to expectations, the combination of HDT with mildly elevated CO₂ improved blood flow and improved cognitive performance over HDT alone. No notable changes in ICP or ocular structures were detected with either HDT or HDT plus elevated CO₂. Thus, given that the ocular syndrome in astronauts has been observed during long-duration spaceflight, NASA 30-day bed rest with elevated CO₂ levels may be informative.

Human Health Countermeasures Element

Subjects Breathe Elevated CO₂ During Head-Down Tilt to Simulate the ISS Environment

The primary hypothesis explaining vision changes during spaceflight is the headward shift of fluids caused by weightlessness. It is hypothesized this shift elevates intracranial pressure (ICP) and initiates structural changes of the eye. Additional spaceflight factors may also play a role, such as ambient carbon dioxide (CO₂) levels, which are greater on the ISS than on Earth.

To investigate potential effects of elevated CO₂ during long-duration spaceflight, researchers in the Cardiovascular and Vision Laboratory at JSC measured ocular and cardiovascular outcomes resulting from acute exposure of subjects to mildly elevated CO₂ levels combined with a headward fluid shift produced using 6° head-down tilt (HDT). Eight subjects completed laboratory testing in three conditions for 60 minutes each: seated upright, during HDT, and during HDT while breathing 0.5% CO₂. During each experimental condition researchers measured optic nerve sheath diameter using ultrasound; imaged the structures of the back of the eye using optical coherence tomography (OCT); and measured end-tidal CO₂ levels, intraocular pressure (IOP), and intracranial pressure (ICP).

Preliminary results suggest breathing mildly elevated levels of CO₂ during HDT slightly increased CO₂ levels in the subjects, but did not result in significant changes to factors hypothesized to be related to the vision and ocular changes during spaceflight. Those changes included increased ICP and the pressure difference across the back of the eye. Additionally, no structural changes were detected on the OCT images.

While this acute exposure to mildly elevated CO₂ did not cause changes in vision or eye structure, the effects of a chronic exposure, as would be experienced by astronauts, have not yet been investigated. In 2017 many of these same measurements will be conducted during a 30-day HDT bed rest study at the Ger-



A subject breathes a gas mixture of elevated CO₂ through a facemask connected to a breathing reservoir, while ultrasound is used to image the optic nerve behind their eye.

man Aerospace Center (DLR) to determine whether chronic exposure to mild CO₂ levels replicates any of the vision or ocular structural changes that develop during spaceflight.

VeinPress® Device Allows First Noninvasive Measure of Jugular Venous Pressure On-Orbit

Several mechanisms are being investigated as potential contributors to the development of changes in vision and ocular structure that many astronauts experience during long-duration spaceflight. One hypothesis is that the headward fluid shift causes congestion of the veins which drain the head and neck, and this venous congestion may contribute to increased pressure in the head. Until recently this increased pressure could not be quantified. Distension of the jugular vein during spaceflight is visually apparent in some astronauts and has been measured using standard clinical ultrasound, but a noninvasive measure of jugular vein pressure has not been possible until this past year.

The amount of pressure required to compress a vein to the point of closure is directly related to the pressure inside the vein, and this can be measured using the VeinPress device. The VeinPress consists of a small,

Human Health Countermeasures Element



The VeinPress is pressed against the skin overlying the jugular vein to measure venous pressure in the laboratory.

translucent bladder with a pressure sensor and can be attached to the end of an ultrasound probe. The probe is placed over the vein and the pressure in the bladder is increased. Ultrasound is used to visualize compression of the vein while measuring the pressure required to collapse the vessel.

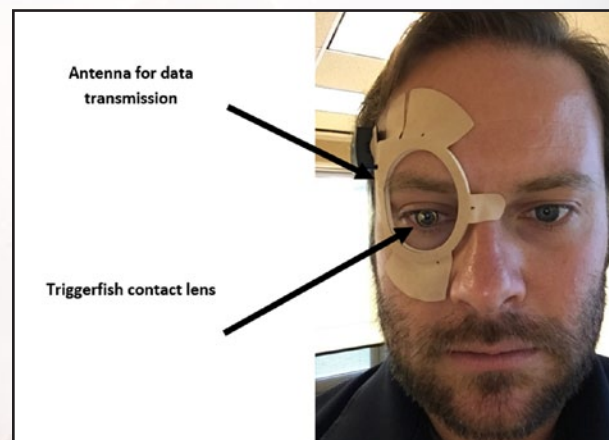
After pilot-testing the VeinPress method extensively in JSC's Cardiovascular and Vision Laboratory, researchers measured internal jugular vein pressures during parabolic flight and bedrest studies. Jugular venous pressure almost doubled during acute exposure to weightlessness and was further elevated during Valsalva breathing maneuvers that are commonly done when performing high-load resistive exercise, similar to those performed during in-flight exercise countermeasures.

This method of measuring jugular vein pressure was recently used on the ISS for the first time as part of the Fluid Shifts spaceflight investigation. Engineers at JSC integrated the venous pressure data into the on-orbit ultrasound system to seamlessly collect data with the two systems simultaneously, thus improving the efficiency of data collection by the crew. Use of this technology to understand changes in venous pressures in the head and neck during spaceflight and spaceflight analogs may provide important clues to the cause of the spaceflight-induced changes in vision and ocular structure.

Influence of Exercise Modality on Cerebral-Ocular Hemodynamics and Pressures

Moderate and high-intensity aerobic and resistance exercise provide clearly identified benefits for cardiac, muscle, and bone health. However, the impact of such exercise—as either a mitigating or an exacerbating factor—on the development of intracranial hypertension and vision changes that are induced during spaceflight is unknown. Given that aerobic and resistance exercise are essential countermeasures used on long-duration missions, it is critical to determine the impact of exercise modality on blood flow and pressure in the head and eye. In FY2016, a study led by Jessica Scott, PhD, in the Exercise Physiology and Countermeasure Laboratory at JSC, characterized the impact of three types of exercise on blood flow and pressure in the head and eye.

During each testing session, subjects lay supine for ten minutes, were then positioned in a 15° HDT for ten minutes, and then performed the exercise during 15° HDT. Blood flow into and out of the head was evaluated using ultrasonography. Several novel technologies were also used, including a hand-held 3D imaging tool to measure facial swelling induced by HDT; a contact lens to measure continuous IOP; and an ultrasound-based tool to measure jugular vein pressure noninvasively.



The Triggerfish® contact lens provides continuous measurement of intraocular pressure and can be worn during exercise.

Human Health Countermeasures Element

Preliminary results demonstrated several unique findings. First, the 3D imaging tool could accurately evaluate fluid shifts to the head and is a promising method for developing a simple tool for use in space. Co-investigators at MD Anderson Cancer Center use this tool to create dynamic 3D models in patients with thyroid eye disease and orbital tumor producing proptosis—a protrusion of the eyeball. Second, use of the Triggerfish® contact lens made it possible to measure eye pressure during exercise for the first time. Therefore, the Triggerfish could be used to assess eye pressure in astronauts while they performed daily tasks. Third, information on the effects of exercise on head and eye blood flow and pressure might be used to optimize astronaut exercise countermeasures to prevent VIIP on exploration missions.

EXERCISE AND PERFORMANCE PORTFOLIO

FY2016 Activities and Accomplishments

The Exercise and Performance Portfolio encompasses studies to determine how astronauts' ability to pilot a spacecraft is impaired in space, and how sensorimotor changes associated with spaceflight affect crewmembers' ability to exit the vehicle. Additionally, the Portfolio addresses the risk of reduced physical performance due to the diminished aerobic capacity and impaired performance that results from reduced muscle mass, strength, and endurance in space.

In FY2016, the Manual Control flight study revealed that astronauts have significant decreases in performance on the day they return from a long-term spaceflight. In addition, researchers evaluated techniques used in preflight training to mitigate motion sickness during spaceflight. The Field Test study, a functional task performance test conducted shortly after landing, continued in FY2016, and to date six crewmembers have completed this evaluation. Orion capsule egress tests, completed in the Neutral Buoyancy Lab in FY2016, will help inform new physical fitness standards for exploration missions.

Completion of Manual Control Study: Assessment of Postflight Sensorimotor Deficits

Evidence from the Space Shuttle Program suggested that even short-term exposure to microgravity impairs an astronaut's ability to pilot a spacecraft. This is a critical issue for future exploration missions—how does long-term exposure to weightlessness affect an astronaut's ability to perform landing maneuvers and other postflight tasks? A combined study, led by Steven Moore, PhD of Icahn School of Medicine at Mount Sinai and Scott Wood, PhD of Azusa Pacific University, was conducted at JSC to answer this question by assessing the ability of astronauts to perform full-motion simulations, as well as a battery of tasks that assessed sensorimotor and cognitive function, after they return from six months aboard the ISS.

Significant decrements in the ability to operate vehicles were observed in eight astronauts within 24 hours of their return from the ISS. Compared to preflight performance, the ability to maintain lane position when driving a simulated car was significantly impaired. In six astronauts, simulated piloting performance of landing a T-38 jet was compromised, and included one crash at the runway threshold. Variability in performance during a simulated Mars rover docking maneuver was also significantly increased. Performance in a group of schedule-control subjects



A test subject attempts to maintain lane position on a twisting road. The Manual Control study assessed complex sensorimotor tasks such as landing a spacecraft or operating a rover.

Human Health Countermeasures Element

and a sleep-deprived cohort, tested after 30 hours of sleep deprivation, was unchanged – showing that the deficits observed in astronaut proficiency were due to spaceflight.

On the day of the astronauts' return, they had subtle but significant changes in cognitive and sensorimotor performance. Manual dexterity and perception of tilt were diminished, suggesting general postflight deficits in motor function and perception. Although tracking a moving target was unaffected, adding a distracting task significantly impaired performance, indicating a lack of cognitive reserve when faced with multitasking. These changes were not observed in the schedule-control or sleep-restricted groups.

Performance on all tasks returned to baseline approximately four days after landing. Taken together, the results suggest that subtle physiological changes in spaceflight leave astronauts vulnerable to performance decrements on the day of landing. Suggested countermeasures include “just-in-time” training, displays showing vehicle tilt, self-assessments to gauge fitness before attempting challenging tasks, and limitation of multitasking involving manual controls.

AFTE Preflight Training May Help Mitigate Spatial Disorientation During Spaceflight

NASA has identified a potential risk to future astronauts during reentry of the Earth's atmosphere on some vehicles such as the Multi-Purpose Crew Vehicle (MPCV) Orion, which is intended to take a crew of four beyond low Earth orbit and return them to Earth. Orion's reentry can produce extreme gyroscopic movements that will significantly affect the crew, and may affect their ability to operate and exit the vehicle.

The potential risk is that medications to control symptoms of dizziness or nausea will not be effective for all crewmembers and will lead to adverse side effects. A recent study, led by Patricia Cowings, PhD of Ames Research Center, attempted to determine



Rotating chair simulates Orion re-entry while subject uses a keypad for tests of manual dexterity and mental arithmetic.

whether a six-hour physiological training procedure, called Autogenic-Feedback Training Exercise (AFTE), could help astronauts adapt to spaceflight and readapt to Earth.

Twenty subjects were randomly assigned to either a control group or AFTE, and subjects were matched by sex and susceptibility to motion sickness. Physiological measures recorded were: heart rate (HR), respiration, muscle activity of arms and legs, skin conductance, blood pressure, peripheral blood flow, cardiac output, and stroke volume. All subjects were evaluated using a standard rotating-chair test to determine initial susceptibility to motion sickness. Subjects then performed four simulated Orion reentry tests in the chair once a week as well as three sessions involving a manual performance task. In addition, some subjects were given AFTE training before the simulated Orion reentry test. A standard diagnostic scale was used to evaluate the severity of motion sickness symptoms in all tests.

Results showed that four hours of AFTE significantly reduced the symptoms of motion sickness during a simulated Orion reentry. During the third and fourth Orion simulations, AFTE subjects were also able to maintain lower HRs and more constant breathing

Human Health Countermeasures Element

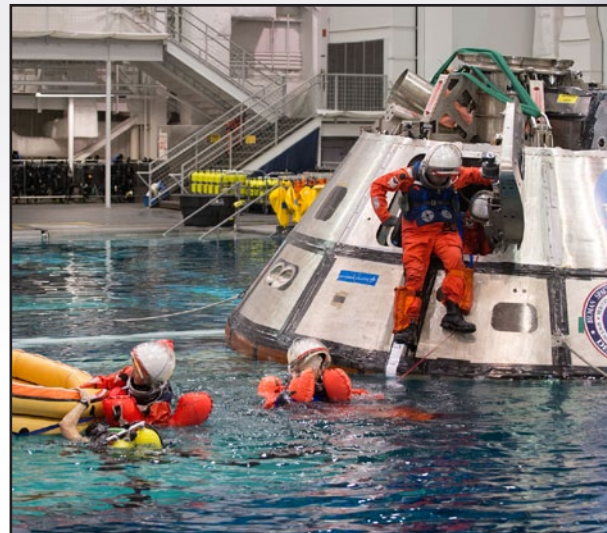
rate and volume than the control group. The control subjects showed higher respiration rates on all simulations. Trends showed that performance measures were less degraded for AFTE subjects. The results of this study and earlier investigations on AFTE indicate that astronauts could benefit from receiving at least four hours of preflight training, and during missions they could practice physiologic self-regulations using small mobile feedback devices.

Orion Capsule Egress Tests and Quantification of Workload in Neutral Buoyancy Lab

Researchers from the JSC Exercise Physiology and Countermeasures Laboratory and the Crew Survival Engineering and Orion Program measured heart rates (HR) in test subjects as they were exiting the side hatch of the Orion spacecraft and entering the inflatable life raft. These tests, conducted in the Neutral Buoyancy Laboratory, showed that unaided exit through the Orion side hatch is a relatively short-duration activity that increases HR for several minutes.

Average HRs were 108 beats per minute (BPM) during cabin operations, 137 BPM while entering the capsule through the side hatch, 147 BPM while moving to the life raft, and 153 BPM while entering the raft. The highest HRs were seen after raft entry and ranged from 72-99% of peak HR. The HR data from this initial series of evaluations will inform a larger NASA project that seeks to develop fitness for-mission standards based on the physiologic demands of critical mission tasks. Such standards will inform the development and use of effective exercise countermeasures for the ISS and exploration missions.

Although all test subjects successfully completed the activity, adding variables such as high seas, poor visibility, an incapacitated crewmember, neurovestibular perturbation, and neuromuscular deconditioning, may increase the physiologic demand or may decrease physiologic capacity. Furthermore, landing conditions may require crewmembers to exit from the top hatch, which is expected to be even more physiologi-



Test subject's physiological data was monitored during egress from the Orion capsule during a crew egress study at the NBL.

cally demanding. This egress scenario will be evaluated in subsequent collaborative testing with the Crew Survival Engineering Team.

Field Test Study Continues Data Collection Immediately After Vehicle Egress

Crewmembers experience changes in multiple physiological systems as a result of spaceflight. Changes include sensorimotor disturbances, cardiovascular deconditioning, and loss of muscle mass and strength. These disruptions may cause significant impairment of the ability to perform tasks immediately after landing, when a crewmember is reintroduced to a gravitational environment after prolonged travel in weightlessness. For instance, an astronaut's ability to exit the spacecraft without assistance may be impaired after landing on a planetary surface during an exploration-class mission.

In the past, functional task tests—tests of the ability to perform mission-like activities—were performed on the second day after landing. Thus, neither the immediate response after landing nor a true characterization of the entire recovery time has been investigated or established for long-duration flights.

Human Health Countermeasures Element



Returning crewmembers often need assistance immediately after landing. The field test study seeks to quantify physiological decrements and assess performance on a battery of tasks.

The Field Test study represents a joint effort between Millard Reschke, PhD of the Neuroscience Laboratory at JSC and Inessa Kozlovskaya, MD, PhD from the Sensorimotor Laboratory at the Institute of Biomedical Problems in Moscow, Russia. The study's primary goal is to determine crewmembers' ability to perform functional tasks representative of the critical mission requirements that crews must perform after landing following long-duration missions.

A battery of functional performance tests are conducted on crewmembers before they fly, and as soon after landing as possible. Two follow-up postflight assessments are conducted later on the day of landing, and a final assessment is conducted about one week later. Findings from this investigation will provide information needed for planning future Mars or other deep-space missions that include unassisted landings. Preliminary data for a subset of the protocol has been collected on 18 crewmembers, and 6 crewmembers have completed the full protocol, including 2 crewmembers who flew on the one-year mission. A total of 30 crewmembers—15 cosmonauts and 15 astronauts—are scheduled to participate in the study.

MULTISYSTEM PORTFOLIO

FY2016 Activities and Accomplishments

The Multisystem Portfolio encompasses research on a diverse set of physiological risks, including the effects of nutrition, immunology, pharmacology, extravehicular activity (EVA), decompression sickness (DCS), and exploration atmosphere. Each discipline team strives to identify specific effects of spaceflight that contribute to the unified picture of intersystem dynamics, with the goal of developing countermeasures to increase the quality of human health and performance during spaceflight. About 15 new studies were selected this year, ranging across the multisystem disciplines.

This year the EVA team brought the Active Response Gravity Offload System (ARGOS) facility into operation and completed the initial pilot tests for the microgravity-based EVA Human Health and Performance Benchmarking Study. This study will develop a standard protocol for assessing performance of humans wearing EVA suits—the foundation of the EVA risk research plan.

The Immune Team saw the completion of the Salivary Markers flight study which successfully characterized dysregulation within components of the immune system during spaceflight. New endeavors this year included a new study which will assess the potential of wintering over in Antarctica as an appropriate analog for long-duration spaceflight with respect to changes in the immune system. This work was completed by Richard Simpson, PhD of the University of Houston.

Ocular Health Study Produces Compelling Results Regarding Vision Loss in Space

Ophthalmic changes were recently identified in some astronauts during and after return from ISS missions. Biochemical evidence from the Nutritional Status Assessment Project revealed differences in blood chemistry between the affected astronauts and those

Human Health Countermeasures Element

who were unaffected. Specifically, the astronauts with ophthalmic changes had higher concentrations of chemicals produced by an important metabolic pathway in the body, which is known as the “one-carbon metabolism” pathway and depends on B-vitamins. Not only were the concentrations of these metabolites higher during and after spaceflight, they were also higher before flight, suggesting these astronauts may have had a predisposition to ophthalmic changes.

A follow-on study led by Scott Smith, PhD, in collaboration with university and industry laboratories, was conducted to evaluate genetic differences—known as polymorphisms or multiple forms—that occur within a population. This was NASA’s first attempt at examining individual genetic data that might be related to a health issue. Seventy astronauts agreed to participate in the study. The results revealed that genetics, along with B-vitamin and hormone status, significantly predicted the incidence of ophthalmic issues. In other words, some astronauts are predisposed to spaceflight ophthalmic issues.

Although this work establishes an association in some astronauts between the development of ophthalmic issues on one hand and genetics of the one-carbon pathway and B-vitamin status on the other, how or why this happens is still not known. The results of the study were published in the January 2016 issue of *The FASEB Journal*, a publication of the Federation of American Societies for Experimental Biology.

Studies are underway to understand these results in more detail, and ideally will lead to an understanding of why these eye changes occur and how to prevent or treat them. The results could have significant implications for NASA, and for terrestrial medicine. The ISS Program Scientist described these findings as one of the most important findings from the ISS this year, and the team received the Compelling Results in Human Health in Space award for 2015.

BONE & OCCUPANT PROTECTION PORTFOLIO

FY2016 Activities and Accomplishments

The Bone and Occupant Protection Portfolio continues to pursue innovative methods to increase understanding of musculoskeletal adaptation to space by optimizing the use of modeling capabilities for fracture assessment and bone mass, maximizing the use of preclinical studies and exploring new measures of bone quality.

This year saw the conclusion of several ongoing studies including research conducted by Ariel Anbar, PhD of Arizona State University that validated the double spike technique for measuring calcium isotopes. This new technique produces data that is significantly more precise and accurate than the previous method.

Because this is more operationally feasible than previous clinically-established methods, it could lead to new techniques for simultaneously monitoring the relative impact of countermeasures on bone formation and bone resorption during spaceflight. Retrospective analyses to verify and validate the clinical utility of



Human Health Countermeasures Element

the calcium isotope data are planned in collaboration with clinical researchers in the osteoporosis arena.

Additionally, results from a study that developed a reproducible method for performing cervical and lumbar ultrasonography to evaluate the accuracy of inflight ultrasound IVD measurements were presented to the medical operations community. This work by Scott Dulchavsky, MD, PhD of the Henry Ford Health System, demonstrated that ultrasound could provide real time monitoring of spinal changes during spaceflight and could be correlated to MRI results. It was recommended and accepted by the bone researchers as a potential inflight tool to characterize spinal status.

Bone Loss and Renal Stone Risk on the ISS

Bone loss and increased risk of renal stone formation are long-standing concerns for astronauts. Bone breakdown brought on by spaceflight elevates urinary calcium and the risk of renal stone formation. Loss of bone calcium leads to concerns about fracture risk and increased long-term risk of osteoporosis. Bone health is a balance of bone formation and bone breakdown, and this process is affected by many factors, including diet, exercise, and gravity.

In late 2015, the journal *Bone* published results from the HRP Nutritional Status Assessment Project, reporting bone biochemistry and renal stone risk data from 23 astronauts who participated in 4- to 6-month missions. Results included evaluation of different exercise regimens and pharmacologic countermeasures.

The regulation of bone and calcium homeostasis seems to be intact during spaceflight, and the body is simply responding to—and trying to adapt to—its new environment. Bone breakdown increases during flight, regardless of the type of exercise, but heavy resistance exercise using the ISS exercise device, the Advanced Resistance Exercise Device (ARED), led to a greater bone formation response. This increase in both breakdown and formation allows bone density

to be maintained, but raises concerns about bone architecture given higher rates of both processes. Bone architecture, strength, and fracture risk are being further studied in ongoing HRP experiments.

Kidney stone risk is increased during spaceflight, and is largely related to urine volume. That is, crewmembers need to consume more fluid to produce urine that is more dilute, which will reduce the risk of stone formation. This has importance not only for crews on ISS missions, but also for future exploration missions, where water generation will need to support the higher intakes.

TECHNOLOGY & INFRASTRUCTURE PORTFOLIO

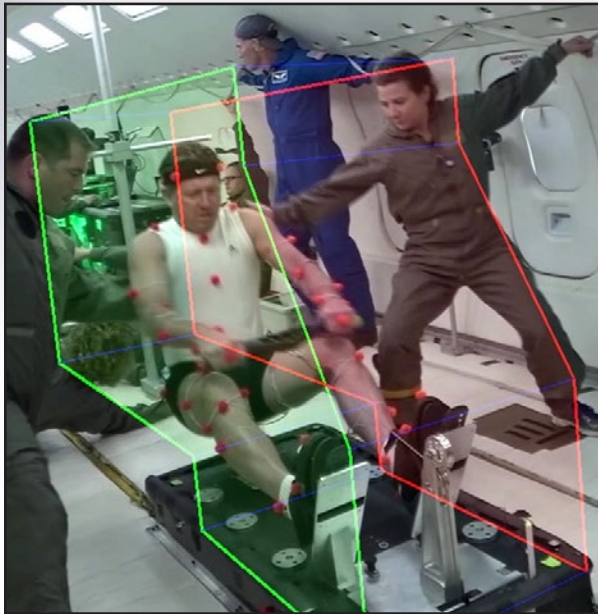
FY2016 Activities and Accomplishments

The Technology and Infrastructure Portfolio consists of three projects that augment the risk mitigation and countermeasure development of HHC. These three projects are the Advanced Exercise Concepts (AEC) Project, the Digital Astronaut Project (DAP), and the Artificial Gravity (AG) Project. The AG Project continues to expand by pursuing ground, parabolic, and flight studies to characterize and validate the use of AG as an effective countermeasure for multiple physiological risks. An International AG Workshop, held in January 2016, developed a collaborative path forward, and initial steps have been taken to pursue the workshop recommendations. Future collaborations with ISS International Partners and next-generation vehicle developers are underway, paving the path for implementing AG as a countermeasure for spaceflight. The AG project also released its first solicitation for evaluating the effects of centrifugation on rodents and selected its first two research investigations.

Digital Astronaut Project Informing Orion Operational Volume Assessments

In FY2016, DAP performed an Exercise Operational Volume analysis to evaluate whether crewmembers could perform aerobic and resistance exercises within

Human Health Countermeasures Element



Motion data from aerobic rowing during a reduced gravity research flight was used to determine if the exercise could be performed within the allocated volume of the Orion vehicle.

the relatively limited volume of the Orion exploration-mission vehicle. Using biomechanical models and data obtained from ground-based and parabolic flight evaluations, the DAP team analyzed resistive exercises, including upright row, bent-over row, shoulder press, squat, power clean, single cable thrust, and deadlift for males in the 99th and 50th percentiles. The team also analyzed a 0g aerobic rowing exercise with a 50th-percentile male biomechanical model.

The initial assessment is that for the 99th- and 50th-percentile males performing resistive exercises, most exercises remained within the volume if the exerciser was oriented facing the tail of the vehicle and a foot plate was available to angle the exerciser into the allocated volume. For the 50th-percentile male performing the aerobic rowing exercise, the exercise remained within the volume with the least amount of interference when the exerciser was oriented facing the nose of the vehicle.

Further evaluations of operational volume will be completed in FY2017 using the Miniature Exercise Device (MED2) on the ISS. This data will also be

modeled and will inform the design of the Orion exercise device, the Resistive Overload Combined with Kinetic Yo-Yo (ROCKY), as well as the Preliminary Design Review for Orion's first crewed mission.

FUTURE PLANS

HHC plans for FY2017 include further implementation of research studies on the ISS, such as testing of an integrated group of countermeasures to mitigate sensorimotor disturbances immediately after landing on a planetary surface; final characterization of spaceflight effects on the immune system; and continuation of the Fluid Shifts study to determine how vision changes occur during spaceflight, in light of new and surprising preliminary data.

HHC will continue collaborations with NASA engineers to develop and test the optimal exercise countermeasure devices for short- and long-duration deep-space missions. New studies will also be selected to determine the thresholds and efficiencies of AG as a countermeasure against the physiological deconditioning of long-duration space missions.

In addition, a ground-based investigation will be initiated to evaluate and recommend shorter oxygen prebreathing protocols that can mitigate decompression sickness during EVA. Other planned studies will define the muscle and sensorimotor performance standards for mission-related tasks. HHC also plans to test a balance plate on the ISS as part of an integrated group of countermeasures to sensorimotor effects of microgravity.



Exploration Medical Capability Element

Overview

Human exploration of the moon, Mars, and other destinations beyond Earth's orbit will present significant new challenges to crew health. During exploration missions, crews will need medical capabilities to diagnose and treat injuries and address medical conditions such as the increased risk of renal stones. Providing capabilities that overcome these challenges will require new health care systems, procedures, and technologies to ensure the safety and success of exploration missions.

The Exploration Medical Capabilities (ExMC) Element develops medical technologies for in-flight diagnosis and treatment, as well as data systems to maintain and protect patients' private medical data. These data systems also aid in the diagnosis of medical conditions, and act as repositories of information that support relevant NASA life science experiments.

ExMC physicians and scientists develop models to quantify the probability that a medical event will occur during a mission. Personnel also define procedures for treating an ill or injured crewmember without having access to an emergency room and

with limited communications with ground-based personnel for consultation and diagnostic assistance. To read more about the ExMC Element, visit <http://www.nasa.gov/hrp/elements/exmc>

FY2016 Activities and Accomplishments

In FY2016, ExMC delivered research and technology to help NASA better manage medical risk during an exploration-class mission. ExMC partnered with the Canadian Space Agency (CSA) to test their Astroskin wearable monitoring system during Human Exploration Research Analog (HERA) Campaign 3. The Astroskin technology augments NASA's capabilities to wirelessly monitor astronaut health. A next-generation ultrasound device was delivered to researchers, enabling them to provide clinical-grade imaging and ultrasound-based therapeutics on one common platform. The Medical Consumable Tracking (MCT) system, which uses radio frequency identification (RFID) technology to determine usage rates for medical consumables, was rebuilt after the original was lost on SpaceX-7, and was delivered for launch on the Japanese cargo mission HTV-6.

The NSBRI Industry Forum partnered with the

Exploration Medical Capability Element

private sector to develop space-compatible health-care solutions via the Space Medical and Related Technologies Commercialization Assistance Program (SMARTCAP). This partnership provided several innovative products.

ExMC also completed a variety of medical risk assessment tools that will one day be a part of JSC Medical Operations. The Medical Optimization Network for Space Telemedicine Resources (MONSTR), a database of resources required for diagnosis and treatment of anticipated medical conditions, was delivered and used to inform the continued work on the Medical Operations Concept of Operations. Finally, ExMC completed an external review of the Integrated Medical Model (IMM), a necessary step in using the model for Medical Operations.

Astroskin Wearable, Non-Invasive Sensors Tested During HERA Campaign 3

In collaboration with the CSA, ExMC supported a study during HERA Campaign 3 to evaluate and validate a prototype wearable biosensor monitoring system, called Astroskin. CSA and NASA have mutual interests in promoting the use of biosensors to monitor aspects of health. These new data streams will allow analytic capabilities to support decision making



HERA crewmembers wore the non-invasive Astroskin physiologic monitoring device during Campaign 3 missions.

based on medically relevant data from biosensors and other sources.

Astroskin is an autonomous medical monitoring system, developed by CSA, that consists of an intelligent garment for the upper body; a headband fitted with sensors; and associated software and technology that measure vital signs such as blood pressure, skin temperature, heart rate, breathing rate, blood oxygen levels, sleep quality, and activity level of the wearer.

ExMC and CSA trained HERA crewmembers to operate the hardware and collected baseline data for all participants. In FY2016, 12 HERA crewmembers collected data over 6 mission days. Early results show that Astroskin is able to collect vital signs, sleep quality, and activity levels in a noninvasive manner during HERA missions. ExMC will continue to process the data and generate a final report on the study. This effort provides foundational work for exploration missions in the areas of international collaboration, medical data architecture, clinical decision support, and biosensor systems development.

Flexible Ultrasound System Provides Additional Capabilities for Exploration Missions

The Flexible Ultrasound System (FUS) is a technology development project that enhances medical imaging for crews on future exploration missions. Ultrasound is currently the best internal imaging modality for space because it is portable, consumes less power than other methods, and does not use ionizing radiation. Crews on the ISS have access to excellent ultrasound equipment, but it still cannot meet all of NASA's needs for medical imaging.

The FUS increases medical capability by extending ultrasound beyond its typical use. It is both a state-of-the-art clinical ultrasound scanner and a development platform for creating new advanced ultrasound methods. It is also a pathway toward creating reliable ultrasound equipment that will survive in the harsher radiation environment of deep space.

Exploration Medical Capability Element

General Electric's Global Research Center delivered three FUS units to Glenn Research Center and NASA established loan agreements to make the FUS available to developers of advanced ultrasound modalities. These units will be used as development platforms by research teams at the University of Washington, Stony Brook University, and KBRwyle in Houston.

Using FUS, researchers can now develop new scanning methods and therapies to meet the unique medical challenges of long-duration space flight, while maintaining a traditional, clinical-grade ultrasound. The FUS project will ultimately demonstrate that many different new ultrasound modes can reside on a single scanner alongside state-of-the-art traditional modes serving crews on exploration-class missions. FUS also provides medical benefits here on Earth, as these new ultrasound methods become more and more accepted in a clinical setting.

FUS Enhancements Provides Renal Stone Treatment Options During Spaceflight

Urinary stones afflict one in eleven Americans at an annual treatment cost of \$10 billion. The risk to astronauts is even higher as minerals are concentrated in the kidney due to bone demineralization and dehydration. At least 15 events of urinary stones have occurred after return from space, and one Russian crew initiated emergency evacuation procedures because a crewmember was in extreme pain before a stone passed naturally. A growing stone obstructs urine flow from the kidney and causes unbearable pain and could potentially result in an unplanned emergency return to Earth.

The work of Michael Bailey, PhD, at the University of Washington, sponsored by NSBRI, provides a capability to manage renal stones during spaceflight where there currently is not an option. Bailey demonstrated that his image processing algorithms allow physicians to identify stones when they are still very small and treatable with non-surgical medical interventions. Additionally, Bailey established that when combined



A researcher demonstrates use of an ultrasound wand to reposition kidney stones on a mannequin.

with the sensitive imaging, the ultrasound waves can be used to reposition small stones to exit the kidney so they will pass into the urinary tract with less resistance, or in the case of a large obstructing stone, tuck it back into the kidney to avoid emergency situations.

NSBRI and the National Institutes of Health's National Institute of Diabetes and Digestive and Kidney Diseases have sponsored successful clinical trials of this technology. There are applications for this technology in military, veteran, and civilian populations.

Bone Assessment and Fracture Healing Capabilities Using Quantitative Ultrasound

Musculoskeletal deterioration and associated complications, such as osteopenia and stress fracture, pose significant threats to astronauts during long-term space missions. Both the structure and strength of bone are considered critical for skeletal tissues to resist fracture. Early diagnosis of these bone disorders can lead to prompt and optimized treatment that will dramatically reduce the risk of fracture and have long-term crew health benefits.

Exploration Medical Capability Element



Former astronauts view a demonstration of the SCAN which can be used for fracture healing and assessment of bone quality.

Noninvasive assessment of trabecular bone strength and density is extremely important in predicting the risk of fracture in space. Quantitative ultrasound has the potential to directly detect trabecular bone strength, and NSBRI has funded Yi-Xian Qin, PhD, of Stony Brook University to address these issues.

Dr. Qin developed an image-based Scanning Confocal Acoustic Navigation (SCAN) system that increases resolution, sensitivity, and accuracy in diagnosing osteoporosis. Dr. Qin also developed and demonstrated a system that uses ultrasound waves to accelerate healing after fracture. He is currently working to develop a portable rapid SCAN system combined with imaging and therapeutic capability, for noninvasive bone loss assessment in space that is integrated into the FUS.

RFID Technology Enhances On-Orbit Medical Consumable Tracking

The ISS is supplied with medical equipment and consumables for the treatment of acute and traumatic injuries. Tracking of these medical supplies can be difficult and time-consuming which often results in medical kits being returned after missions with more resources consumed than were reported. This is not an issue for ISS missions because frequent resupply occurs; however, frequent resupply will not be possible during exploration missions. To address this



Sensors inside the locker detect RFID tags on items in medical kits. When items are removed, the inventory is updated.

challenge, a study will be conducted on the ISS to determine whether these consumables can be tracked more effectively and efficiently.

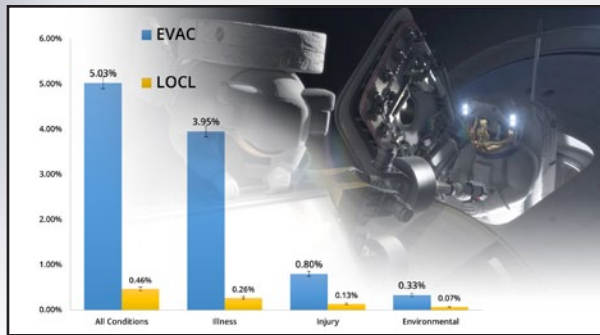
The MCT system uses an electronic identification system composed of an RFID reader and an RFID transponder or tag that can read and write data to track medicines and medical consumables. The system transmits a radio signal which is read by RFID tags attached to each item. The tag sends its own signal, which is registered by the system and records which supplies are consumed. This newly enhanced MCT was destroyed in-transit to the ISS during the SpaceX-7 launch. A new system was engineered and will be manifested for launch on HTV- 6.

External Review Validates IMM as a Tool for Assessing and Mitigating Mission Risks

The Integrated Medical Model (IMM) helps capture and use knowledge obtained from space medicine, training, operations, engineering, and research domains and uses this knowledge to forecast the health risk for crew members and risks to mission success. The model is most helpful in comparing the risk of two or more mission profiles, and is not used as a tool for predicting absolute risk.

In FY2016, IMM version 4.0 underwent an extensive

Exploration Medical Capability Element



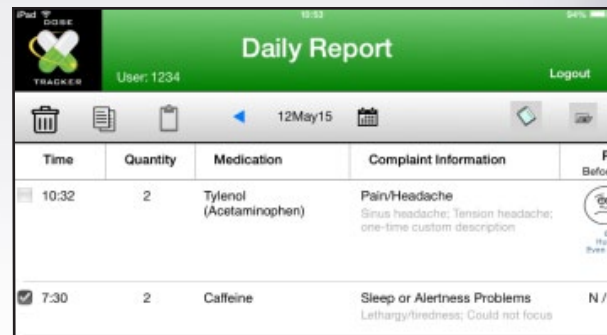
A chart generated with IMM data showing the percentage of missions with at least one evacuation (EVAC) or loss of crew life (LOCL). Data generated from 100,000 simulated missions.

external review in preparation for its transition to an operational status. The Systems Review Office at NASA Goddard Space Flight Center conducted the review to ensure impartiality in the review process. The external review team covered compliance with NASA software standards, the pedigree of clinical data input, and the model's overall performance.

The review found that the IMM is a scientifically sound, comprehensive approach for identifying the health risks facing astronauts, and an excellent communication tool for engineers and physicians. The review board recommended that the IMM team develop a sustainable process to augment, peer review, and maintain the information used in the IMM as medical knowledge continues to evolve. IMM v4.0 will be released at the end of FY2017 after the review findings are addressed. Once delivered, IMM will provide additional support to assess the health risks to astronauts and estimate the medical capabilities required to ensure mission success.

ExMC Develops Multiple Database and Application Tools for Spaceflight Research

As medical systems for space exploration missions are developed, the ability to evaluate trade-offs between medical and other spacecraft resources is critical to ensure adequate medical care is available during these missions. In FY2016, ExMC developed MONSTR, a database that identifies medical resources required for



The Dose Tracker app allows crewmembers to document medication usage, dosage and any side effects while on-orbit.

a variety of exploration-relevant medical conditions. ExMC will use MONSTR to prioritize research, develop resources for a medical system, and for quantitative risk analyses.

In FY2016, ExMC also began development of their Concept of Operations (ConOps). The current ConOps document will assist with planning, designing, and prototyping of an integrated medical system for exploration missions to Mars. This document helps define how NASA will provide medical care for human spaceflight in the exploration paradigm and defines the requirement of a system that must fulfill medical needs.

ExMC collaborated with Virginia Wotring, PhD from BCM to develop and deploy Dose Tracker, a native iPad app that documents the medication usage of crewmembers before, during, and after their missions. The app captures previously unrecorded data regarding medication use during spaceflight, including symptoms, frequencies, and severities of side-effects of the medicine. Dose Tracker started data collection in FY2016 and will continue collection through FY2020.

FUTURE PLANS

ExMC will continue to develop and advance the medical technologies needed to ensure the health and performance of crewmembers. Efforts will focus on high-impact technologies such as diagnostic imag-

Exploration Medical Capability Element

ing and blood analysis, and overall integration of the technologies into an exploration vehicle. The Element will also continue to research and develop the medical data architectures necessary to execute a seamless transfer of information between crew, medical, flight, and ground systems.

ExMC will employ Model Based System Engineering (MBSE) concepts to develop a well-integrated System Modeling Language (SysML) model for an exploration medical system. The model is composed of a variety of sequence diagrams, user interactions, functional decompositions, and system block diagrams.

The goal is to take a deliberate, MBSE approach to medical system development, specifically to develop functional requirements for medical systems and expose high-impact interfaces between the vehicle and medical system. ExMC will collaborate with international partners to ensure the capabilities of future medical systems are well integrated across the stakeholders and appropriately documented into ExMC's ConOps and overall SysML Medical System Model.

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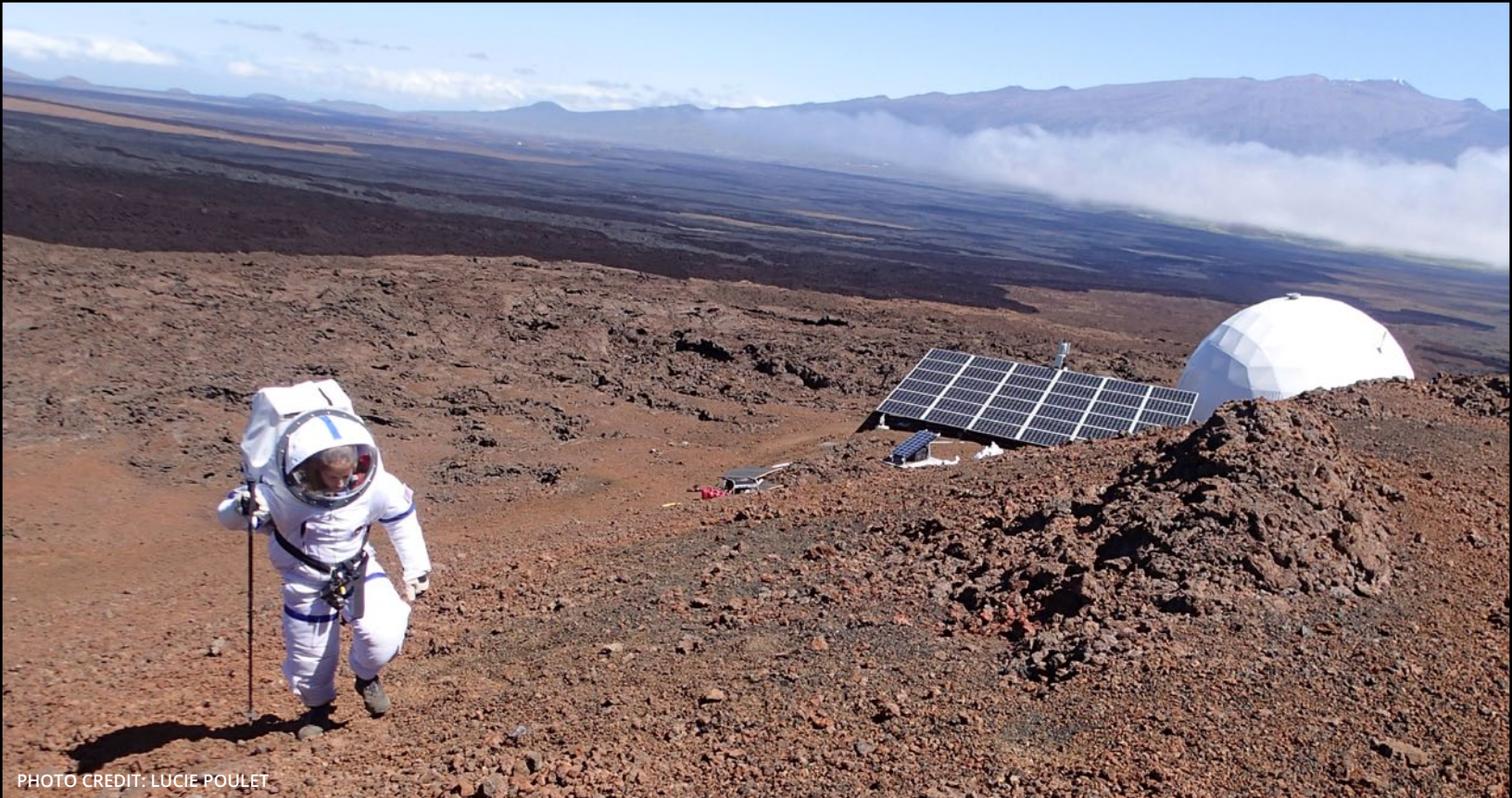


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Human Factors and Behavioral Performance

Overview

In FY2016, HRP announced the consolidation of the Space Human Factors & Habitability Element and the Behavioral Health & Performance Element into a newly formed Human Factors and Behavioral Performance (HFBP) Element. This new Element manages three research portfolios focused on characterizing and mitigating human health and performance risks: the Behavioral Medicine and Sleep Risk Portfolio, Team Risk Portfolio, and Space Human Factors and Engineering Portfolio.

Long-duration missions beyond low Earth orbit will require crews to adapt to increasingly autonomous operations in isolated, confined, and extreme environments. The distance and duration of these missions will be unprecedented; crews will face challenges such as prolonged separation from home, communication loss or delay, loss of the view of Earth, and confinement in a small vehicle. Other risk factors such as radiation and reduced sensory stimulation and monotony may further lead to adverse behavioral and performance outcomes.

The safety net of mission control for cross-checking

data, answering questions, and assisting or controlling spacecraft systems from the ground will not be available or will be time-delayed. It is critically important that interfaces between the crew and their habitat, tools, and systems are well designed. Additionally, the spacecraft habitat should be tailored to maintain and promote behavioral health and performance of individuals and the crew as a whole.

HFBP uses a combination of laboratory, analog, and flight studies to conduct research that addresses the relevant risks and solutions. To read more, please visit <https://www.nasa.gov/hrp/elements/hfbp>.

FY2016 Activities and Accomplishments

In FY2016, HFBP accomplishments furthered progress on the HFBP risk mitigation research strategy, specifically in the areas of analog and spaceflight research. To adequately test and validate countermeasures that address HFBP space exploration risks, it is essential to provide an analog environment that mimics the psychological environment of an exploration mission and includes an aspect of extended duration, isolation, confinement, or danger. Antarctic research stations provide a remote location ideal for conduct-

Human Factors and Behavioral Performance

ing such research. Several NASA-funded studies are underway at international Antarctic stations such as Concordia and Neumayer to evaluate cognitive monitoring tools and to examine new hybrid exercise countermeasures which combine virtual reality and exercise. NASA also recently established a Memorandum of Understanding with the National Science Foundation so that investigations may be implemented at U.S. Antarctic stations. The first such study seeks to characterize the incidence of psychological and behavioral conditions in winter-over cohorts which are important for future exploration missions to prevent disturbances in mood and degradation of cognitive function.

Research that addresses risks to team well-being and performance requires a different analog that allows greater throughput—or participation of more teams—in high-fidelity simulations and includes capabilities for delayed communication. The Human Exploration Research Analog (HERA) at JSC offered a venue to implement multiple studies that assessed team-related monitoring tools and countermeasures in four 30-day simulations.

HFBP also focused on the challenges of providing a long-duration space habitat that optimizes livability and supports crew performance and well-being. Accordingly, HFBP research was initiated to understand the effects of long-duration microgravity on habitability, determining the best methods and tools for calculating and assessing net habitable volume (NHV) and determining NHV and internal layout requirements for future exploration habitats. Two human factors studies were part of the ISS one-year mission: “ISS Habitability” and “Fine Motor Skills.” Mission attributes for a future Mars mission were drafted, and work on a computational model to estimate NHV began to mature.

BEHAVIORAL MEDICINE & SLEEP RISK PORTFOLIO

FY2016 saw several major HFBP accomplishments addressing the risk of adverse cognitive or behavioral

conditions and psychiatric disorders, and the risk of adverse health and performance decrements resulting from sleep loss, circadian desynchronization, and work overload. A comprehensive report was published that included a qualitative analysis of the journal entries that astronauts completed during their stay on the ISS. Notably, four HFBP studies were part of the ISS one-year mission: a continuation of “Astronaut Journals,” “Reaction Self-Test on ISS,” “Cognition” and “Sleep-Wake.”

The first of the new flexible, LED-based solid-state lighting assemblies was launched to the ISS in continued support of a study on the use of light as a countermeasure for maintaining circadian entrainment and promoting sleep and alertness.

Six experiments assessing performance and other relevant factors were part of four 30-day HERA missions, which included the first simulated spacewalks and telerobotics operations. In addition, increased integration with other elements continued and led to a joint SR and HFBP assessment of standard measures for evaluating central nervous system effects resulting from radiation exposure. This effort will be important for formulating more accurate astronaut risk profiles for future exploration missions.

‘Astronaut Journals’ Study Issues Final Report with Data Spanning 10-Person Years

The “Astronaut Journals” flight experiment began in 2003 and has provided the first quantitative data derived from space operations on which to base an understanding of the behavioral issues associated with long-duration isolation and confinement. The study was conducted in two phases. The first phase involved ten astronauts who were members of two- and three-person crews on the ISS. The second phase consisted of ten astronauts who were members of six-person crews. The final report documents more than ten person-years of living and working in space and provides unique insight into factors that contribute to and degrade adjustment to the conditions.

Human Factors and Behavioral Performance



Astronauts who participated in the Journals Experiment used laptops to record their experiences, observations, and feelings.

The study was based on the assumption that the more a subject writes about a specific topic, the more important that topic is at the time. Astronauts' journal entries were parsed into statements and were coded for category, tone, and mission day. The first level of analysis identified the relative salience of 24 major categories of issues. The top ten categories were the same during both phases of the study, but had slightly different orders of importance; the order of salience during phase two was adjustment, work, outside communications, group interaction, equipment, recreation and leisure, food, event, exercise, and organization and management. During the first phase, work and outside communication were primary.

The second level of analysis identified more than 100 subcategories and calculated their frequency, temporal distribution, and tone. The third level of analysis focused on the tone of entries as an indicator of specific problems and general morale; results of this analysis support hypotheses concerning a "third-quarter phenomenon," which is a decline in morale during the third quarter of a mission, regardless of its total duration.

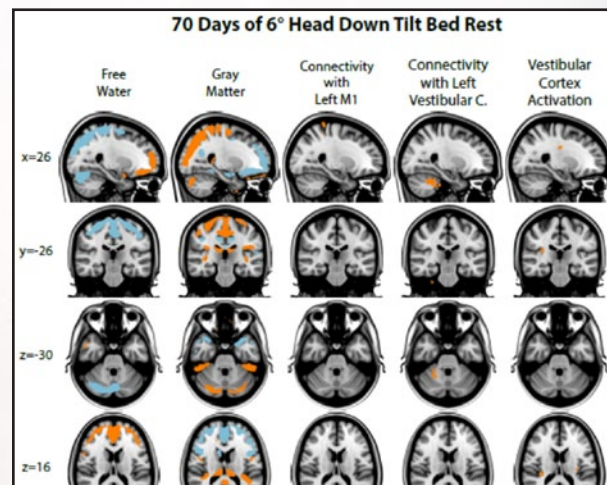
Responses to questions asked before, during, and after the expeditions suggested that living and work-

ing onboard the ISS is not as difficult as anticipated. Astronauts reported they benefited from writing in their journals and recommended continuation of the research. Operational implications of study results are presented in the final report as recommendations to facilitate living and working in space, whether on the ISS or other long-duration missions.

A PDF of the final report is available here: <https://ston.jsc.nasa.gov/collections/TRS/listfiles.cgi?DOC=TM-2016-218603>

Final Results of 'Bed Rest as a Spaceflight Analog to Study Neurocognitive Changes'

Head-down tilt bed rest (HDBR) is used as a ground-based analog to study the effects of microgravity exposure on human physiology. An NSBRI project, led by Rachael Seidler, PhD, of the University of Michigan, followed an interdisciplinary approach using cutting-edge neuroimaging techniques and a broad-ranging battery of sensory, motor, and cognitive assessments to investigate changes in brain and behavior after a 70-day exposure to 6° HDBR. Structural and functional MRI data, as well as behavioral data, were collected at seven sessions before, during, and after HDBR. Control subjects were tested on the same measures in four sessions.



Changes in grey matter volume after 70-day bed rest in measures of brain structure, function, and network integrity, correlating with indices of cognitive, sensory, and motor function.

Human Factors and Behavioral Performance

After long-duration bed rest, participants exhibited reduced balance and mobility. Moreover, the volume of gray matter in the brain increased in regions that process sensory information, but was reduced in the front part of the brain. Brain fluid followed the opposite pattern. Recovery was observed after bed rest but remained incomplete 12 days later. Larger increases in gray matter volume and reductions in fluid in brain regions that control movement were associated with small balance impairments. Additionally, there was more communication between brain regions controlling movement and those processing sensory information. Greater brain region interactivity was seen in participants who exhibited the smallest balance impairments upon exiting bed rest.

In summary, observed, recoverable HDBR-related changes in measures of brain structure, function, and network integrity correlated with indices of cognitive, sensory, and motor function. These findings could help to predict changes during spaceflight.

Circadian Misalignment Affects Sleep and Medication Use During Spaceflight

Astronauts often have trouble sleeping while in space and sleep loss causes many problems, such as fatigue diminished cognitive function and impaired decision making. There are many possible reasons for these sleep issues such as adaptation, noise, uncomfortable temperature, and irregular or overly-intrusive schedules. On Earth, the daily light-dark cycle promotes sleep during the night and wakefulness during the day; however, the space station rotates around the Earth every 90 minutes, which creates sunrises and sunsets too rapidly for human adaptation. These rapid changes in schedule and light exposure induce jet lag-like symptoms because the innate circadian rhythm promotes sleep during waking. The researchers hypothesized this combination of irregular schedules and lighting might contribute to reduced sleep duration during spaceflight.

A team of investigators at NASA Ames Research Cen-



ISS crewmembers emerge from their sleep quarters. Sleeping in space can be problematic due to irregular day/night schedules.

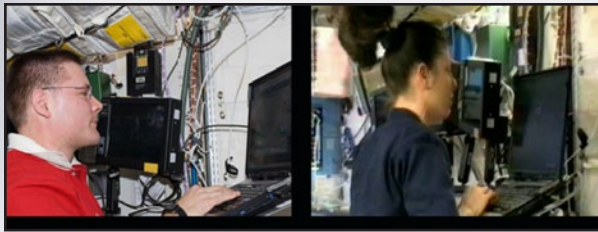
ter, led by Erin Flynn-Evans, PhD, studied 21 astronauts living and working on the ISS. These astronauts wore activity and light monitors and logged information about their sleep, alertness, and medication use during long-duration missions. A mathematical model was used to determine when astronauts were likely sleeping in a circadian-misaligned state.

The study found that astronauts slept out of synchrony with their circadian rhythm on about 20% of nights during spaceflight. On the nights when they were circadian misaligned, they obtained about an hour less sleep and took more medication to help them sleep than they did when their circadian rhythm was aligned with their sleep schedule. These findings suggest that promoting measures to help keep astronaut schedules and lighting patterns stable may lead to astronauts obtaining more sleep and consuming less sleep medication during spaceflight as reaction time is related to arousal, vigilance, and directed attention. This measure may be useful to monitor individual well-being and performance for future exploration missions.

'Reaction Self-Test on ISS' Study Data Collection Complete

The "Reaction Self-Test on ISS" study led by David Dinges, PhD, of the University of Pennsylvania evalu-

Human Factors and Behavioral Performance



ISS astronauts perform the Reaction-Self Test which objectively measures neurobehavioral changes during spaceflight.

ated 24 astronauts before, during, and after 6-month missions on the ISS using a computer program named the “Reaction Self Test” (RST). The RST is a portable five-minute task that enables astronauts to monitor the daily effects of fatigue on their performance while in space. For the study, astronauts volunteered to take the test every four days in the morning and evening while they were on the ISS, as well as in the weeks before and after their missions.

Each evaluation was designed to quickly determine the effects of spaceflight on behavioral alertness using a reaction-time test. Contributors to alertness could include the duration and quality of sleep, the degree of fatigue, stress, and medications they used. A total of 2,856 RST evaluations were obtained—2,109 were completed on-orbit and the remaining 747 RST tests were completed before and after flight.

Analyses of RST data revealed reaction-time performance was sensitive to the effects of sleep duration on the ISS, with RST scores declining as sleep duration declined. Astronaut sleep times were often in the range of 5.5 to 6.5 hours on workdays, which was less than they acquired in space on weekends, and much less than after returning to Earth.

Ratings of sleep quality revealed poor sleep quality was often associated with physical exhaustion, tiredness, and ratings of stress increased with mission duration for many astronauts. There were considerable individual differences among astronauts in the degree to which their RST performance and sleep were decreased and their stress increased. Collectively the results demonstrated the utility of the RST to ob-

jectively detect and track important neurobehavioral changes in astronauts during spaceflight.

SMARTCAP Funds Help LumosTech Develop a Sleep Mask for Circadian Realignment

On Earth, misalignment of the circadian system is common and regularly experienced during travel across time zones, in shift work, the elderly, teenagers and infants. The use of continuous bright light to shift circadian rhythm is well established, but disrupts daily activities and misses the circadian clock’s peak sensitivity—which most often occurs during sleeping hours. Through an NSBRI-sponsored Space Medical and Related Technologies Commercialization Assistance Program (SMARTCAP) grants, LumosTech is building a smart, wearable eye mask that could improve sleep for astronauts in space.

Using proof-of-concept research results from Stanford University, LumosTech is developing a personalizable sleep mask that emits short pulses of light while the user is sleeping to adjust circadian phase. This technology can help astronauts optimize their sleep schedules in the absence of natural light, assist ground crewmembers adjusting to sleep changes, and increase alertness after wake-up. The technology is effective during sleep without causing sleep disruptions and reduces side effects from continuous bright light therapy, such as headaches and strained eyes.

During the project, the investigator team, led by Vanessa Burns, developed 30 advanced sleep mask



LumosTech wearable technology is a sleep mask to help circadian alignment by emitting short light pulses.

Human Factors and Behavioral Performance

prototypes and performed user testing in individuals with circadian disruptions. Specifically, they targeted frequent travelers journeying at least 2000 miles, which results in about three hours of circadian misalignment. Mask features were tested including light therapy efficacy, and user interface with the companion smartphone app.

User interviews were also conducted with shift workers and teens to determine if the product could be useful to the general consumer. On the basis of user feedback, a comprehensive feature list was developed for the engineering and textile components, and LumosTech is working on validation testing of sleep mask production. With this newer model, the goal is to offer a solution to easily shift sleep cycles in multiple environments, including the ISS and those of consumers on Earth.

TEAM RISK PORTFOLIO

The Team Risk Portfolio ended another year of spaceflight analog research and completed three studies using HERA and the ISS. Studies included an investigation of communication delays on team performance and well-being. For the HERA analog study, the DebriefNow tool facilitated a self-assessment of the team and created a discussion guide which enhanced communication within the team and increased resilience in these isolated crews.

Eight studies were included in HERA's third campaign which examined team cohesion, shared mental models, leadership and autonomy, team composition and roles, task switching, and team resilience during four 30-day missions. Six new grants were awarded in FY2016 to fund data collection in analogs and analogous populations.

Notably, a partnership with DePaul University and Russian colleagues from the Institute for Biomedical Problems will share analog data as part of a recently awarded International Life Sciences Research Announcement study focused on team composition.



Recent studies simulate communication delays to investigate methods to mitigate risks associated with delays inherent in exploration-class missions such as a Mars mission.

Several technical publications were also completed during FY2016 including the Team Risk Evidence Report, which was fully revised from the 2009 version and included on the HRP roadmap website. In preparation for future research solicitations and other research efforts, six research requirements reports provided recommendations in the areas of team adaptation and resilience, member selection, multi-team systems, team habitability, training needs, and team performance and functioning benchmarks.

Completion of Communication Delay Studies Researching Protocols and Team Dynamics

Researchers led by Lawrence A. Palinkas, PhD, of the University of Southern California, used the ISS to assess impacts of communication delays on individual and team performance and well-being. Three ISS astronauts and 18 mission support personnel performed tasks with and without 50-second one-way communication delays during a 166-day mission. Assessments of individual and team performance and mood, communication quality, and task autonomy were obtained after each task. Qualitative data from post-mission astronaut interviews were used to validate and expand on quantitative data, and to elicit recommendations for countermeasures.

Results indicated that crew well-being and communication quality were significantly reduced, and

Human Factors and Behavioral Performance

individual stress and frustration increased, during tasks performed with the communication delay relative to tasks performed without it. Qualitative data suggested that communication delays affected operational outcomes, teamwork processes, and mood. This was particularly evident when activities involved numerous task-related communication demands, either because of poor communication strategies or low crew autonomy.

These issues were further examined in research by Ute Fischer, PhD, of the Georgia Institute of Technology, and Kathleen Mosier, PhD, of San Francisco State University. In several laboratory and space-analog studies the investigators identified communication issues in space-ground interactions that were associated with transmission delays and communication protocols were developed to mitigate these issues. Protocols are structured templates designed to counteract human's innate communication proximity bias and help remote team members efficiently keep track of conversational threads and the sequence of messages during asynchronous communications.

Effectiveness of the protocols were assessed during two previous NEEMO missions and six HERA missions. Participants received training highlighting the challenges of asynchronous communication and the elements of the protocols and conventions were explained. Acceptance and compliance in using the protocols was high and surveys administered throughout a mission indicated that participants considered protocols to be effective in supporting interactions with mission control. The protocols have the potential of mitigating the known communication quality decrements caused by communication delays.

Study Suggests Differences in Maintaining Team Performance on Long-Duration Missions

Owned and operated by the University of Hawaii at Manoa, the Hawai'i Space Exploration Analog and Simulation (HI-SEAS) program is led by principal investigator Kim Binsted, PhD. HI-SEAS is a Mars



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The HI-SEAS habitat is home to a six person crew where researchers can conduct studies investigating social, interpersonal, and cognitive factors affecting team performance over time.

analog hybrid in terms of an Isolated, Confined and Controlled (ICC) and an Isolated Confined and Extreme (ICE) environment and simulates long-duration planetary surface missions to investigate crew composition and cohesion. A crew of six 'astronaut-like' individuals, monitored by an experienced mission support team, perform geological field work and life systems management while isolated on the Mars-like lava fields of Mauna Loa, 8200 feet above sea level. Conditions such as habitat, mission profile, communication delay, and high crew autonomy are explicitly designed to emulate a planetary surface exploration mission. Rigorous mission routines support innovative behavioral and psychological tests and tasks performed by the crew.

In FY2016, HI-SEAS finished its first one-year isolation mission, and completed several studies comparing 4-, 8-, and 12-month mission durations. These studies focus on identifying psychological and psychosocial factors, measures, and combinations that can be used to compose highly effective self-directing teams for long-duration exploration missions. The studies include team performance, continuous monitoring of face-to-face interactions, mitigation of the effects of isolation using virtual reality, measurement of emotional and affective states, and multiple stress and cognitive monitoring studies. Most studies have components that are incorporated into other space simulation environments such as HERA.

Human Factors and Behavioral Performance

Preliminary data analysis from the 4- and 8-month missions suggests that some team processes predict the next day's team processes, with differing impact. For instance, one study found that the previous day's cohesion positively predicted the next day's performance, but no reciprocal relationship was found. Analysis of crew task briefings by another study suggested that openness used to defuse conflict can have an opposite effect in a confined environment, prompting the crew to apply different strategies to promote social resilience.

A final report will be completed in FY2017. HI-SEAS is preparing for two additional 8-month missions starting in 2017 to develop effective team composition strategies for long-duration space exploration.

SPACE HUMAN FACTORS ENGINEERING PORTFOLIO

Major SHFE Portfolio accomplishments in FY2016 included the completion of data collection for two human factors studies that were part of the first ISS one-year mission: "ISS Habitability" and "Fine Motor Skills." Near-real-time observations from the habitability study brought attention to issues on the ISS, and also improved the information quality of postflight crew debriefs. Habitability work products were also used to support planning for new cis-lunar habitat work. Research on the Fine Motor Skills study garnered the attention of several university healthcare organizations interested in exploring the software as a diagnostic or rehabilitation tool. Both studies will complete six-month mission data collection near the end of FY2017.

Other SHFE projects completed in FY2016 include research of lighting effects, automation of procedures, and multimodal augmented displays. A Phase II Small Business Innovative Research grant was awarded for unobtrusive workload measurement, and two Phase I grants were awarded for task analysis visualization techniques. SHFE also held a Human Factors Standard Measures workshop jointly coordinated with NSBRI and held at the "Space 4 Biomedicine," which

included university and Department of Defense participation. Research is continuing in the areas of habitat space utilization, net habitable volume modeling, electronic procedures design, training retention, task analysis, and crew self-scheduling tools. New research tasks were awarded in the areas of human-robot function allocation, cognitive aids, training, automation, and vertebral strength imaging.

Habitability Tools Help Determine Volume and Layout Requirements for Spacecraft

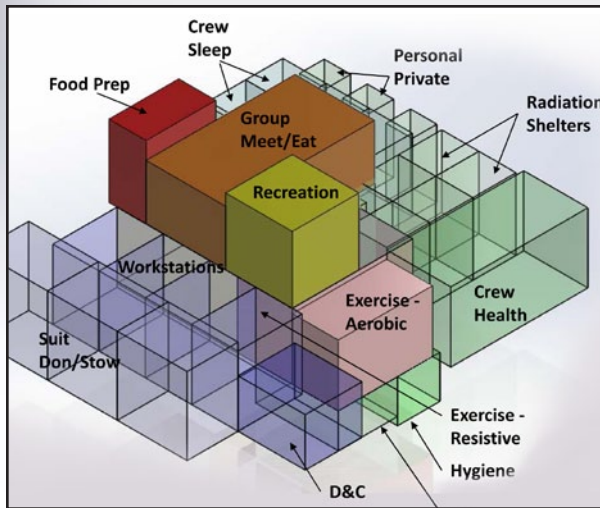
HFBP funds projects which provide tools for establishing habitable volume and layout of future-generation spacecraft. It is essential the design of space vehicles and habitats incorporate appropriate dimensions and layout, particularly for long-duration exploration missions.

The Habitability Working Group (HWG) is a key component of HFBP's strategy to better understand habitable volume and layout needs. This group, formed in 2015, is composed of NASA subject matter experts, as well as experts from industries such as maritime shipping and terrestrial architecture.

The HWG has contributed to and vetted a Mission Attributes Matrix, which is a template that enables mission planners to succinctly document key mission parameters that will have a direct impact on habitable volume and layout needs. In addition, they have provided insight into the use of agile development as a potential tool for the design of vehicles and habitats. The HWG is a resource for continued reviews and provides expert knowledge consensus for ongoing HFBP work, including efforts to document a dataset of the amounts of spacecraft interior volume needed to complete critical mission tasks.

HFBP is also currently funding a NASA Research Announcement grant for work led by principal investigator Sherry Thaxton, PhD, of Leidos, to develop the Spacecraft Optimization Layout and Volume (SOLV) model. This model will take an optimization-

Human Factors and Behavioral Performance



SOLV assesses various algorithm-generated task volume layouts against habitability scoring concepts.

based approach to calculate habitable volume needs based on mission-specific parameters. SOLV uses a bottom-up, task-driven approach for estimating volume needs and align them with human-centered design principles. The developed tool, which will make use of internal work such as the Mission Attributes Matrix and the task volume dataset, will support the iterative design process and help to reduce design and human health and safety mission risks such as the risk of adverse behavioral or cognitive conditions and psychiatric disorders.

Human-Centered Design in an Agile Process

Despite its challenges, agile development—a method for software development—is becoming more popular and is used in many NASA and commercial software development efforts. The agile method is a product of the software development process, and it is unclear how human factors and human-centered design principles can best be integrated into agile efforts. In many cases, it may not be incorporated at all.

A project led by Angelia Sebok of Alion Science and Technology investigated the integration of agile development processes with human-centered design (HCD) principles, and the relevance of this hybrid process for safety- and mission-critical systems.

The team conducted a literature review and 12 interviews with personnel from industry and government to identify lessons learned and best practices. Several important findings were identified. First, an integrated agile/HCD process is currently used by some industries for software development in safety and mission-critical systems, such as medical devices, aerospace systems, and intelligence information and security systems.

Second, this process requires the traditional agile cyclical process to be adapted for use with these systems. The adaptations include significant data gathering at the beginning of the process, planning for and integrating the HCD and developer perspectives, identifying and integrating relevant requirements into the process, including representative end users and surrogate users in the process, and performing relevant user-based testing. The process requires considerably more documentation than a typical agile process.

Third, the process requires HCD specialists to work one to several cycles ahead of the development team in developing prototype design concepts, to work in parallel with the development team by providing day-to-day feedback on design issues, and to include usability testing as part of a unit of development, or sprint cycle.

Study Assesses Impact Displays and Indicator Lights Have on Vehicle Ambient Lighting

Current NASA spacecraft standards and requirements do not limit the impact that light sources—such as displays and indicators—have on the ambient light spectrum. Nor do they address the impact these sources may have on health-related lighting countermeasures used in spaceflight. The goal of a modeling project, led by Toni Clark with Leidos, was to identify how these light sources affect the operational environment, and to recommend solutions.

The project team used computational modeling and real-world lighting mockups to document the

Human Factors and Behavioral Performance

amount of light that sources other than the ambient lighting system contribute to the lighting environment. The team focused on the impacts of these light sources on performance of long-term tasks which were conducted near avionics or computer displays. They then analyzed options for changing the ambient light spectrum as a lighting countermeasure. The project used a variety of physical and computer-based simulations to determine direct relationships between system implementation and light spectrum.

Analysis of the computer model and real-world data showed vehicle architecture and avionics can have a measurable impact on the spectrum of light that reaches the retina. The data showed obvious design techniques that can be used to adjust the ambient light spectrum closer to a more desirable spectrum for the operating environment.

The impact of software-implemented display graphics is dependant on the red-green-blue pixel output of the display. Additionally, the undesirable spectrum increases when smaller operational areas include highly reflective surfaces. Finally, vehicle architecture, combined with ambient light source placement, had a direct impact on the light spectrum to which the crew was exposed. These findings will be important for the design of future exploration habitats.

Study Suggests Speech and Tone Alarms More Effective Than Tone Only Alarms

Speech alarms—alarms that use spoken words rather than a tone—are heavily used in aviation and are recommended for use in other domains as well. In industry, the combination of a tone alarm and voice instructions is considered safer than tone only for evacuating crowds during an emergency because it helps people remain calm and provides additional information about evacuation routes.

In a study led by Aniko Sandor, PhD, with KBRwyle, researchers investigated tone and speech alarms in controlled conditions as well as in HERA. Identifi-



Speech alarms, used in addition to tone alarms, were tested in HERA and found to be more effective than tone alarms alone.

cation and detection times were measured and comments from HERA participants were recorded. The study showed speech alarms were identified faster and more accurately than tone alarms. In situations where it is important to identify both the problem and related details, speech alarms—which include that detail—may provide advantages.

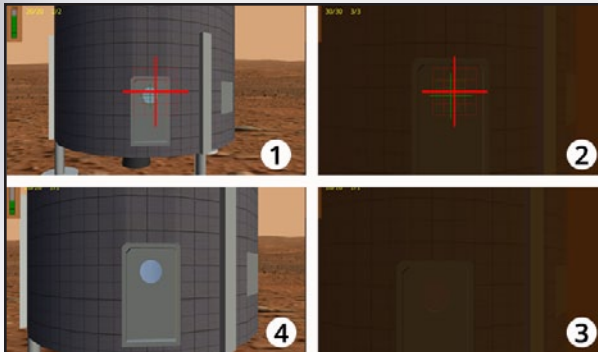
The speech alarms generated for this study are currently used in the HERA facility. In light of the positive results, these alarms should be considered for both current ISS and future space exploration missions since they are detected and identified faster and more accurately than tone alarms.

The results of this study were published in an article in *New Scientist*, a UK-based weekly international science magazine. The research was also presented, along with an overview of NASA alert design and related requirements, at the Ocean Energy Safety Institute Forum for Dialogue.

Study Suggests Combining Auditory and Visual Cues Improve EVA and Telerobotic Tasks

During planetary or lunar surface exploration missions, crew sensory inputs may be degraded or absent, communication time delays are expected to affect human teleoperations, and astronauts may be required to perform multiple tasks simultaneously. These cir-

Human Factors and Behavioral Performance



A simulated docking task for visual or bimodal (top panels) and auditory (bottom panels) aids under both high and low visibility conditions (left and right respectively). Subjects attempt to align red and green crosshairs or match auditory cues.

cumstances could increase visual workload, reduce situational awareness, and negatively affect astronaut performance. Researchers led by Elizabeth Wenzel, PhD, at NASA Ames Research Center evaluated the benefit of augmented displays using visual and spatial auditory modalities as potential countermeasures to improve performance during surface extravehicular activities (EVAs) in an exploration environment.

The investigator team simulated EVAs on the Mars surface to examine performance on an orientation and localization task with three types of display aids: a 3D spatial auditory navigation aid, a 2D north-up visual map, and a combined visual and auditory cue or bimodal aid. Workload was increased by requiring subjects to simultaneously perform a second monitoring task and in environments with variable visibility and ambiguity. The results showed that the bimodal aid enabled the subjects to more accurately judge orientation and respond faster.

A second study simulated the docking of a remotely controlled rover to a surface habitat under different time delays and visibility conditions, using three types of docking aids: a 2D visual targeting reticle, an auditory sonification, and a combined bimodal aid. Results indicate that accurate docking could be performed using all three types of aids, and quantified how adding control response latency decreased accuracy and increased reaction time.

These results demonstrate the potential value of integrating 3D audio to aid EVAs on planetary surfaces for tasks as diverse as orientation, localization, and docking. When auditory cues are provided in synergy with visual information, bimodal performance for tasks such as orientation and localization can exceed that of the best unimodal performance.

FUTURE PLANS

International research studies will continue in HERA, as a group of 18 studies are planned for FY2017—with an emphasis on lighting, nutrition, and exercise interventions over the course of four 45-day missions. A long-duration investigation is planned at the National Science Foundation Antarctic bases, with an emphasis on developing methods to systematically assess neurobehavioral conditions. HFBP will also strengthen its partnerships with military agencies, including the Army War College and the Naval Submarine Medical Research Laboratory. These collaborations will focus on issues such as human-robotic interactions and cognitive changes related to carbon dioxide exposure.

HFBP is on target to complete current flight experiments on the ISS addressing habitability concerns and examining changes in body size and volume. HFBP expects to increase participation and contribution to cis-lunar activities as well as development and planning of flight test objectives an assessment of potential exploration-class habitat designs.

In summary, HFBP plans to enhance its risk-reduction research strategy in FY2017 through collaborations with international partners, military and other federal agencies. The Element will continue to increase the use of ISS and ground analogs in order to answer key questions regarding the spaceflight risks inherent with long duration missions.



Engagement and Communications

Overview

The Human Research Program supported a number of education and communication initiatives in FY2016 across multiple NASA centers and the National Space Biomedical Research Institute (NSBRI). Additionally, HRP Elements helped support education initiatives including research internships, post-doctoral programs, and summer institutes for interns. Within HRP, the Human Research Engagement and Communications (HREC) Project is committed to engaging and informing the general public about NASA's human health and performance research and technology development.

Collaboration with Time Magazine Leads to Special Edition on Historic One Year Mission

During the HRP Investigators' Workshop (IWS), Jeffrey Kluger, Editor at Large for *TIME*® Magazine, conducted a session on "Communicating Space Medicine in the Popular Imagination." As an avid space enthusiast and communications professional, Kluger emphasize how important it is for researchers to tell NASA's story and convey the message in versatile ways to increase the public's understanding of spaceflight

research. The session was standing room only, and Kluger answered questions and autographed a media poster that was designed by the HREC team. Kluger also served as the IWS banquet keynote speaker. His speech, titled "Historical Lessons Across Time," highlighted historic space events and examined the media coverage of those events.



Kluger from TIME magazine was a featured speaker during the IWS and produced a special edition featuring the 1YM.

Engagement and Communications

After the workshop, Kluger produced a 95-page *TIME* Magazine special edition titled “A Year in Space: Inside Scott Kelly’s Historic Mission – Is Travel to Mars Next?” Interviews conducted at the IWS contributed to approximately 15 pages highlighting human spaceflight research. Kluger also participated in the IWS by retweeting and conveying IWS media coverage.

MX Continues Global Effort to Address Childhood Obesity with Exercise and Nutrition

NASA’s Mission X: Train Like an Astronaut (MX) international challenge completed its sixth consecutive year with over 53,000 participants in 30 countries. MX encourages children and their families to “train like an astronaut” by performing activities based on astronaut fitness training and nutrition while learning about the challenges of human spaceflight. Some students participated during physical education or science classes, while others participated after-school.

European Space Agency astronaut Tim Peake, the MX16 Astronaut Ambassador, began the challenge by hosting “Peake Liftoff,” MX’s first-ever astronaut-led activity. He also recorded numerous videos while he was aboard the ISS. MX participants and the JSC Exercise Physiology Laboratory team supported Tim’s running of the London Marathon in the first mini activity, “26.2 with Tim.”

New teams joined returning teams, and growth was seen in several states to make a total of 4,900 Team



Elementary school students celebrate the Mission X awards ceremony at Ars Electronica Center in Linz, Austria.

USA participants. Due to the overwhelming number of countries seeking to participate, Mission X was expanded into two challenges: “Walk Around the Earth Challenge” and “Walk to the Moon Challenge.” The program is expecting similar growth in FY2017 with projections for 55,000 participants, 36 countries, and 19 languages.

A team of adults with unique needs participated for a second year. This composition of participants is an advantage because the program can be adapted to various implementations. MX17 anticipates participation from an additional adult unique needs program located near JSC.

A new approach for the 2016 Team USA closing event involved filming a behind-the-scenes tour of JSC. The film provided solutions to challenges of funding and the need for more flexible scheduling for the schools, which have rigid schedules. HREC decided the best scheduling solution would be a video that could be watched when convenient. Response was positive, and the video was featured on JSC social media pages as well as the website: <http://trainlikeanastronaut.org>.

New Omics Videos and Stories Facilitate Understanding of Complex Genetic Studies

One of HREC’s goals is to take complex human research topics and make them more comprehensible to the general public. In FY2016 the team developed and released an ‘-omics’ video and story series coinciding with National DNA Day and National Twins Days. The videos were posted to JSC’s YouTube, Facebook, and Twitter sites, and the HRP website features the series: <http://www.nasa.gov/hrp>.

The team prepared for the series by interviewing NASA subject matter experts and Twins Study investigators and then developing scripts. The series was filmed with Michael Snyder, PhD, Professor and Chair of Genetics and Director of the Stanford Center for Genomics and Personalized Medicine. After filming and editing, a review process ensued with Dr.

Engagement and Communications



Astronaut Kjell Lindgren promotes HRP 'omics' video series through Reddit's Ask-Me-Anything event.

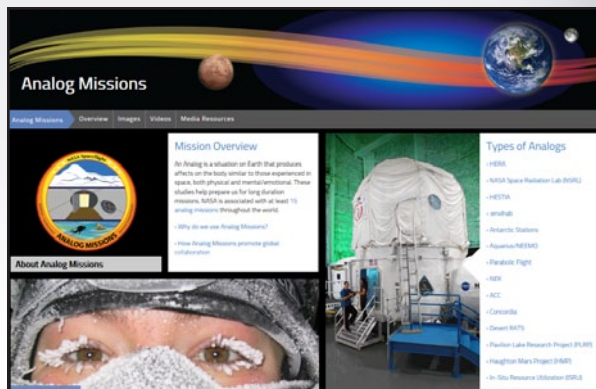
Snyder's staff to ensure timely release of the materials.

HREC teamed up with astronauts Kate Rubins, PhD, and Kjell Lindgren, MD, to help promote the series. Dr. Rubins, a molecular biologist who sequenced DNA in space for the first time, filmed a message from the ISS to promote the microbiomics video. Dr. Lindgren participated in a Reddit Ask-Me-Anything (AMA) event hosted by JSC and NASA Headquarters on National DNA Day.

New NASA Website Consolidates Information on Fifteen Spaceflight Analogs

NASA is associated with numerous space flight analogs throughout the world. An analog is an environment on Earth that mimics effects on the body similar to those experienced in space such as physical, mental, and emotional stressors. The NASA Analog Missions website, <http://www.nasa.gov/analogs>, was created to inform the public about ground and space research activities NASA is conducting to prepare astronauts for long-duration space missions. It explains why analogs are used and how they promote global collaboration.

The site features stories and links about HRP analogs, information on how to become an analog crewmember for a mission, and information for researchers. Each link directs the reader to a description page that has photographs of the analog as well as



The NASA Analogs webpage provides researchers and potential crewmembers with information about each spaceflight analog.

a link to the analog's homepage. The HRP Human Exploration Research Analog (HERA) site includes a 360-degree view of the HERA habitat.

Phase I of the website was released in late July 2016 and is being used by potential crewmembers, and by principal investigators during personal appearances and other outreach events. Future phases will upgrade each analog's homepage to include research conducted, images, infographics, and a blog site.

NSRL Summer School: Training the Next Generation of Radiation Investigators

The 13th annual Space Radiation Summer School was held at the NASA Space Radiation Laboratory (NSRL), located at the Brookhaven National Laboratory in Upton, NY, in June 2016. Sixteen students and one auditor were selected from about 50 applicants. Students came from the United States and other countries, including Germany, Italy, Canada, Japan, and South Korea.

Lectures were presented on topics such as radiation interactions with matter, accelerators, radiation dosimetry, apoptosis, systems biology, leukemia, mutagenesis, and dose-rate effects. Approximately 30 visiting experts gave several lectures and engaged with students. The summer school also included an intensive hands-on experimental program at the NSRL and the Brookhaven National Lab Medical Facility.

Engagement and Communications



Future space radiation investigators participate in NASA's 13th annual Radiation Summer School at the NSRL.

Extensive training occurred on preparing cell cultures and mouse models for experimental irradiation using the high-energy heavy ion beams at the facility. Instruction was given in using the gamma-H2AX assay as a marker of double-strand breaks, use of flow cytometry techniques for cell counting, measurement of cell survival curves and the physics of beam interactions with materials using the NSRL beams.

One of the unique aspects of this year's school was the high level of enthusiasm concerning the new galactic cosmic ray simulator facility now available at NSRL. Also of interest was the topic concerning the substantial contribution of neutrons and light ions to dose-equivalent from realistic distributions of shielding thicknesses for spacecraft. Students were made aware that these recent developments represent a significant shift from past space radiation studies and represent important growth areas for new space radiation research.

NSBRI's Mentored Research Program

NSBRI's Mentored Research Program in Space Life Sciences is conducted at both Texas A&M University (TAMU) and the Massachusetts Institute of Technology (MIT) through the Harvard-MIT Division of Health Sciences and Technology (HST) enabling students to work toward a PhD focusing on space life

sciences. The program offers modules to strengthen current graduate curricula—offering students advanced courses in biomedical science and engineering and the opportunity to engage with NASA's space research programs.

At MIT, NSBRI sponsors a PhD program in bioastronautics, which trains graduate students in space life sciences, biomedical engineering, medical sciences, and space medicine for a broad range of possible career opportunities. The program provides students with a combination of science and engineering course work, clinical experiences, space-related research apprenticeships, and thesis research options at MIT, Harvard, and associated hospitals. The bioastronautics training program is part of HST's Medical Engineering and Medical Physics PhD program. The program is led by Laurence Young, ScD, MIT's Apollo Program Professor of Astronautics.

At TAMU, students who participate in the PhD Mentored Research Program in Space Life Sciences earn a Certificate in Space Life Sciences while obtaining a doctoral degree in various fields such as kinesiology, nutrition, genetics, or biomedical engineering. The program is led by Nancy Turner, PhD, who is a NASA-funded research professor in the Department of Nutrition and Food Science at TAMU.

During FY2016, scientists from the program participated in a ten-week summer enrichment program which included a week of lectures followed by a nine-week assignment in a NASA JSC laboratory. To date, sixteen PhDs had been awarded in the Mentored Research Program, nine at MIT and seven at TAMU.

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FY2016 Publications

Human Factors and Behavioral Performance (HFBP)

Basner, Mathias, Sarah Mcguire, Namni Goel, Hengyi Rao, and David F. Dinges. "A New Likelihood Ratio Metric for the Psychomotor Vigilance Test and Its Sensitivity to Sleep Loss." *Journal of Sleep Research* 24, no. 6 (December 2015): 702–13.

Basner, Mathias, Adam Savitt, Tyler M. Moore, Allison M. Port, Sarah McGuire, Adrian J. Ecker, Jad Nasrini, et al. "Development and Validation of the Cognition Test Battery for Spaceflight." *Aerospace Medicine and Human Performance* 86, no. 11 (November 2015): 942–52.

Bell, Suzanne T., David M. Fisher, Shanique G. Brown, and Kristin E. Mann. "An Approach for Conducting Actionable Research With Extreme Teams." *Journal of Management*, June 20, 2016, 0149206316653805.

Bendrick, Gregg A., Scott A. Beckett, and Elizabeth B. Klerman. "Human Fatigue and the Crash of the Airship Italia." *Polar Research* 35, no. 0 (July 29, 2016).

Bermudez, Eduardo B., Elizabeth B. Klerman, Charles A. Czeisler, Daniel A. Cohen, James K. Wyatt, and Andrew J. K. Phillips. "Prediction of Vigilant Attention and Cognitive Performance Using Self-Reported Alertness, Circadian Phase, Hours since Awakening, and Accumulated Sleep Loss." *PLoS One* 11, no. 3 (March 28, 2016): e0151770.

Bernier, Matthew C., Rosana M. Alberici, Joel D. Keelor, Prabha Dwivedi, Stephen C. Zambrycki, William T. Wallace, Daniel B. Gazda, et al. "Microplasma Ionization of Volatile Organics for Improving Air/Water Monitoring Systems On-Board the International Space Station." *Journal of the American Society for Mass Spectrometry* 27, no. 7 (July 2016): 1203–10.

Chang, Anne-Marie, Andrew C. Bjonnes, Daniel Aeschbach, Orfeu M. Buxton, Joshua J. Gooley, Clare Anderson, Eliza Van Reen, et al. "Circadian Gene Variants Influence Sleep and the Sleep Electroencephalogram in Humans." *Chronobiology International* 33, no. 5 (June 2016): 561–73.

Davis, Catherine M., Kathleen L. DeCicco-Skinner, and Robert D. Hienz. "Deficits in Sustained Attention and Changes in Dopaminergic Protein Levels Following Exposure to Proton Radiation Are Related to Basal Dopaminergic Function." *PLoS One* 10, no. 12 (December 2015): e0144556.

Davis, Catherine M., Peter G. Roma, and Robert D. Hienz. "A Rodent Model of the Human Psychomotor Vigilance Test: Performance Comparisons." *Journal of Neuroscience Methods* 259 (February 2016): 57–71.

Faghih, Rose, Munther Dahleh, Gail Adler, Elizabeth Klerman, and Emery Brown. "Quantifying Pituitary-Adrenal Dynamics and Deconvolution of Concurrent Cortisol and Adrenocorticotrophic Hormone Data by Compressed Sensing." *IEEE Transactions on Bio-Medical Engineering* 62, no. 10 (October 2015): 2379–88.

Feder, Toni. "NASA Mars Mockup Explores Team Cohesion and Performance." *Physics Today* 68, no. 12 (December 2015): 29.

Flynn-Evans, Erin E., Laura K. Barger, Alan A. Kubey, Jason P. Sullivan, and Charles A. Czeisler. "Circadian Misalignment Affects Sleep and Medication Use before and during Spaceflight." *npj Microgravity* 2 (January 7, 2016): 15019.

Goel, Namni. "Probing Personalized Genetic Platforms for Novel Molecular Clues for Circadian Chronotype." *Annals of Translational Medicine* 4, no. 10 (May 2016): 207.

Hong, Mee Young, Nancy D. Turner, Mary E. Murphy, Raymond Carroll, Robert S. Chapkin, and Joanne R. Lupton. "In Vivo Regulation of Colonic Cell Proliferation, Differentiation, Apoptosis and P27Kip1 by Dietary Fish Oil and Butyrate in Rats." *Cancer Prevention Research (Philadelphia, Pa.)* 8 (November 2015): 1076–83.

Hughes, Ashley M., Megan E. Gregory, Dana L. Joseph, Shirley C. Sonesh, Shannon L. Marlow, Christina N. Lacerenza, Lauren E. Benishek, Heidi B. King, and Eduardo Salas. "Saving Lives: A Meta-Analysis of Team Training in Healthcare." *Journal of Applied Psychology* 101, no. 9 (September 2016).

Hursh, Steven R., and Peter G. Roma. "Behavioral Economics and the Analysis of Consumption and Choice." *Managerial and Decision Economics*, July 2016.

Kennedy, Deanna M., Lauren Blackwell Landon, and M. Travis Maynard. "Extending the Conversation: Employee Resilience at the Team Level." *Industrial and Organizational Psychology* 9, no. 02 (June 2016): 466–75.

Klerman, Elizabeth B., Scott A. Beckett, and Christopher P. Landrigan. "Applying Mathematical Models to Predict Resident Physician Performance and Alertness on Traditional and Novel Work Schedules." *BMC Medical Education* 16, no. 1 (September 13, 2016): 239.

Kozlowski, Steve W. J. "Advancing Research on Team Process Dynamics: Theoretical, Methodological, and Measurement Considerations." *Organizational Psychology Review* 5, no. 4 (November 1, 2015): 270–99.

Kozlowski, Steve W. J., Stanton Mak, and Georgia T. Chao. "Team-Centric Leadership: An Integrative Review." *Annual Review of Organizational Psychology and Organizational Behavior* 3, no. 1 (March 2016): 21–54.

Lane, Jacqueline M., Anne-Marie Chang, Andrew C. Bjonnes, Daniel Aeschbach, Clare Anderson, Brian E. Cade, Sean W. Cain, et al. "Impact of Common Diabetes Risk Variant in MTNR1B on Sleep, Circadian, and Melatonin Physiology." *Diabetes* 65, no. 6 (June 2016): 1741–51.

Lee, Michael L., Mark E. Howard, William J. Horrey, Yulan Liang, Clare Anderson, Michael S. Shreeve, Conor S. O'Brien, and Charles A. Czeisler. "High Risk of near-Crash Driving Events Following Night-Shift Work." *Proceedings of the National Academy of Sciences of the United States of America* 113, no. 1 (January 2016): 176–81.

Lerchl, Kathrin, Natalia Rakova, Anke Dahlmann, Manfred Rauh, Ulrike Goller, Mathias Basner, David F. Dinges, et al. "Agreement Between 24-Hour Salt Ingestion and Sodium Excretion in a Controlled Environment." *Hypertension* 66, no. 4 (October 2015): 850–57.

Massa, G.D., R.M. Wheeler, R.C. Morrow, and H.G. Levine. "Growth Chambers on the International Space Station for Large Plants." *Acta Horticulturae*, no. 1134 (May 2016): 215–22.

Mullington, Janet M., Sabra M. Abbott, Judith E. Carroll, Christopher J. Davis, Derk-Jan Dijk, David F. Dinges, Philip R. Gehrman, et al. "Developing Biomarker Arrays Predicting Sleep and Circadian-Coupled Risks to Health." *Sleep* 39, no. 4 (April 2016): 727–36.

Ott, C. Mark, Thomas H. Marshburn, and Cheryl A. Nickerson. "ASMScience | The International Space Station: An Extreme Environment for Key Host-Microbe Discoveries." *Microbe Magazine* 11, no. 6 (June 2016): 253–61.

Palmer, Cara A., and Candice A. Alfano. "Sleep and Emotion Regulation: An Organizing, Integrative Review." *Sleep Medicine Reviews* 0, no. 0 (January 14, 2016).

Peleg, Micha, Amy D. Kim, and Mark D. Normand. "Predicting Anthocyanins' Isothermal and Non-Isothermal Degradation with the Endpoints Method." *Food Chemistry* 187 (November 2015): 537–44.

Peleg, Micha, and Mark D. Normand. "Simulating Shelf Life Determination by Two Simultaneous Criteria." *Food Research International* 78 (December 2015): 388–95.

FY2016 Publications

Peleg, Micha, Mark D. Normand, and Timothy R. Goulette. "Calculating the Degradation Kinetic Parameters of Thiamine by the Isothermal Version of the Endpoints Method." *Food Research International* 79 (January 2016): 73–80.

Perlis, Michael L., Michael A. Grandner, Gregory K. Brown, Mathias Basner, Subhajit Chakravorty, Knashawn H. Morales, Philip R. Gehrman, Ninad S. Chaudhary, Michael E. Thase, and David F. Dinges. "Nocturnal Wakefulness as a Previously Unrecognized Risk Factor for Suicide." *The Journal of Clinical Psychiatry* 77, no. 6 (June 2016): e726–33.

Roma, Peter G., Steven R. Hursh, and Stanton Hudja. "Hypothetical Purchase Task Questionnaires for Behavioral Economic Assessments of Value and Motivation." *Managerial and Decision Economics*, July 2016.

Sá, Rui Carlos, Kirby L. Zeman, William D. Bennett, G. Kim Prisk, and Chantal Darquenne. "Effect of Posture on Regional Deposition of Coarse Particles in the Healthy Human Lung." *Journal of Aerosol Medicine and Pulmonary Drug Delivery* 28, no. 6 (December 2015): 423–31.

Shaw, Natalie D., Andrew W. McHill, Michele Schiavon, Tairmae Kangarloo, Piotr W. Mankowski, Claudio Cobelli, Elizabeth B. Klerman, and Janet E. Hall. "Effect of Slow-Wave Sleep Disruption on Metabolic Parameters in Adolescents." *Sleep* 39, no. 8 (August 1, 2016): 1591–99.

Simpson, Richard J., Austin B. Bigley, Guillaume Spielmann, Emily C. P. LaVoy, Hawley Kunz, and Catherine M. Bollard. "Human Cytomegalovirus Infection and the Immune Response to Exercise." *Exercise Immunology Review* 22 (January 2016): 8–27.

Spaeth, Andrea M., David F. Dinges, and Namni Goel. "Phenotypic Vulnerability of Energy Balance Responses to Sleep Loss in Healthy Adults." *Scientific Reports* 5 (October 8, 2015): 14920.

Spaeth, Andrea M., David F. Dinges, and Namni Goel. "Resting Metabolic Rate Varies by Race and by Sleep Duration." *Obesity (Silver Spring, Md.)* 23, no. 12 (December 2015): 2349–56.

Wickens, Christopher Dow, Robert S. Gutzwiller, Alex Vieane, Benjamin A. Clegg, Angelia Sebok, and Jess Janes. "Time Sharing Between Robotics and Process Control: Validating a Model of Attention Switching." *Human Factors* 58, no. 2 (March 2016): 322–43.

Exploration Medical Capability (ExMC)

Bloomfield, Susan A., Daniel A. Martinez, Ramon D. Boudreaux, and Anita V. Mantri. "Microgravity Stress: Bone and Connective Tissue." *Comprehensive Physiology* 6, no. 2 (March 2016): 645–86.

Cabahug-Zuckerman, Pamela, Dorra Frikha-Benayed, Robert J. Majeska, Alyssa Tuthill, Shoshana Yakar, Stefan Judex, and Mitchell B. Schaffler. "Osteocyte Apoptosis Caused by Hindlimb Unloading Is Required to Trigger Osteocyte RANKL Production and Subsequent Resorption of Cortical and Trabecular Bone in Mice Femurs." *Journal of Bone and Mineral Research: The Official Journal of the American Society for Bone and Mineral Research* 31, no. 7 (July 2016): 1356–65.

Dunmire, Barbrina, Jonathan D. Harper, Bryan W. Cunitz, Franklin C. Lee, Ryan Hsi, Ziyue Liu, Michael R. Bailey, and Mathew D. Sorensen. "Use of the Acoustic Shadow Width to Determine Kidney Stone Size with Ultrasound." *The Journal of Urology* 195, no. 1 (January 2016): 171–77.

Grover, Kartikey, Liangjun Lin, Minyi Hu, Jesse Muir, and Yi-Xian Qin. "Spatial Distribution and Remodeling of Elastic Modulus of Bone in Micro-Regime as Prediction of Early Stage Osteoporosis." *Journal of Biomechanics* 49, no. 2 (January 25, 2016): 161–66.

Harper, Jonathan D., Bryan W. Cunitz, Barbrina Dunmire, Franklin C. Lee, Mathew D. Sorensen, Ryan S. Hsi, Jeff Thiel, Hunter Wessells, James E. Lingeman, and Michael R. Bailey. "First-in-Human Clinical Trial of Ultrasonic Propulsion of Kidney Stones." *The Journal of Urology* 195, no. 4 (April 2016): 956–64.

Hu, Gang, Quan Zhang, Vladimir Ivkovic, and Gary E. Strangman. "Ambulatory Diffuse Optical Tomography and Multimodality Physiological Monitoring System for Muscle and Exercise Applications." *Journal of Biomedical Optics* 21, no. 9 (September 2016): 091314.

Hurst, Victor W., Sean Peterson, Kathleen Garcia, Douglas Ebert, David Ham, David Amponsah, and Scott Dulchavsky. "Concept of Operations Evaluation for Using Remote-Guidance Ultrasound for Exploration Spaceflight." *Aerospace Medicine and Human Performance* 86, no. 12 (December 2015): 1034–38.

Kassemi, Mohammad, and David Thompson. "Prediction of Renal Crystalline Size Distributions in Space Using a PBE Analytic Model. 1. Effect of Microgravity-Induced Biochemical Alterations." *American Journal of Physiology - Renal Physiology* 311, no. 3 (September 1, 2016): F520–30.

Kassemi, Mohammad, and David Thompson. "Prediction of Renal Crystalline Size Distributions in Space Using a PBE Analytic Model. 2. Effect of Dietary Countermeasures." *American Journal of Physiology - Renal Physiology* 311, no. 3 (September 1, 2016): F531–38.

Lee, Franklin C., Ryan S. Hsi, Mathew D. Sorensen, Barbrina Dunmire, Ziyue Liu, Michael R. Bailey, and Jonathan D. Harper. "Renal Vasoconstriction Occurs Early During Shockwave Lithotripsy in Humans." *Journal of Endourology / Endourological Society* 29, no. 12 (December 2015): 1392–95.

Macaulay, Timothy R., Brandon R. Macias, Stuart Mc Lee, Wanda L. Boda, Donald E. Watenpaugh, and Alan R. Hargens. "Treadmill Exercise within Lower-Body Negative Pressure Attenuates Simulated Spaceflight-Induced Reductions of Balance Abilities in Men but Not Women." *npj Microgravity* 2 (June 2016): 16022.

May, Philip C., Michael R. Bailey, and Jonathan D. Harper. "Ultrasonic Propulsion of Kidney Stones." *Current Opinion in Urology* 26, no. 3 (May 2016): 264–70.

May, Philip C., Yasser Haider, Barbrina Dunmire, Bryan W. Cunitz, Jeff Thiel, Ziyue Liu, Matthew Bruce, Michael R. Bailey, Mathew D. Sorensen, and Jonathan D. Harper. "Stone-Mode Ultrasound for Determining Renal Stone Size." *Journal of Endourology* 30, no. 9 (September 2016): 958–62.

Wong, Julielynn, and Andreas Pfahnl. "3D Printed Surgical Instruments Evaluated by a Simulated Crew of a Mars Mission" 87, no. 9 (September 9, 2016): 806–10.

Human Health Countermeasures (HHC)

Ade, Carl J., Ryan M. Broxterman, Jesse C. Craig, Susanna J. Schlup, Samuel L. Wilcox, and Thomas J. Barstow. "Standardized Exercise Tests and Simulated Terrestrial Mission Task Performance." *Aerospace Medicine and Human Performance* 86, no. 11 (November 1, 2015): 982–89.

Ade, Carl J., Ryan M. Broxterman, Jesse C. Craig, Susanna J. Schlup, Samuel L. Wilcox, Steve Warren, Phillip Kuehl, Dana Gude, Chen Jia, and Thomas J. Barstow. "Prediction of Lunar- and Martian-Based Intra- and Site-to-Site Task Performance." *Aerospace Medicine and Human Performance* 87, no. 4 (April 2016): 367–74.

Anderson, Allison P., and Dava J. Newman. "Pressure Sensing for in-Suit Measurement of Space Suited Biomechanics." *Acta Astronautica* 115 (October 2015): 218–25.

FY2016 Publications

Anderson, Allison P., Jacob G. Swan, Scott D. Phillips, Darin A. Knaus, Nicholas T. Kattamis, Christine M. Toutain-Kidd, Michael E. Zegans, Abigail M. Fellows, and Jay C. Buckley. "Acute Effects of Changes to the Gravitational Vector on the Eye." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 8 (April 2016): 939–46.

Arentson-Lantz, Emily, Kirk L. English, Douglas Paddon-Jones, and Christopher S. Fry. "14 Days of Bed Rest Induces a Decline in Satellite Cell Content and Robust Atrophy of Skeletal Muscle Fibers in Middle-Aged Adults." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 8 (April 2016): 965–75.

Arvedsen, Sine Kongsbak, Ola Eiken, Roger K leg rd, Lonnie Grove Petersen, Peter Norsk, and Morten Damgaard. "Body Height and Arterial Pressure in Seated and Supine Young Males during +2 G Centrifugation." *American Journal of Physiology, Regulatory, Integrative and Comparative Physiology* 309, no. 9 (November 2015): R1172–77.

Belavy, Daniel L., Michael Adams, Helena Brisby, Barbara Cagnie, Lieven Danneels, Jeremy Fairbank, Alan R. Hargens, et al. "Disc Herniations in Astronauts: What Causes Them, and What Does It Tell Us about Herniation on Earth?" *European Spine Journal*, January 2016, 1–11.

Berg-Johansen, Britta, Ellen C. Liebenberg, Alfred Li, Brandon R. Macias, Alan R. Hargens, and Jeffrey C. Lotz. "Spaceflight-Induced Bone Loss Alters Failure Mode and Reduces Bending Strength in Murine Spinal Segments." *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society* 34, no. 1 (January 2016): 48–57.

Bergouignan, Audrey, T Peter Stein, Caroline Habold, Veronique Coxam, Donal O' Gorman, and St phane Blanc. "Towards Human Exploration of Space: The THESEUS Review Series on Nutrition and Metabolism Research Priorities." *npj Microgravity* 2 (August 18, 2016): 16029.

Bershad, Eric M., Aashish Anand, Stacia M. DeSantis, Ming Yang, Rosa A. Tang, Eusebia Calvillo, Leslie Malkin-Gosdin, et al. "Clinical Validation of a Transcranial Doppler-Based Noninvasive Intracranial Pressure Meter: A Prospective Cross-Sectional Study." *World Neurosurgery* 89 (May 2016): 647–53.

Bigley, Austin B., Katayoun Rezvani, Mira Pistillo, Justin Reed, Nadia Agha, Hawley Kunz, Daniel P. O'Connor, Takuya Sekine, Catherine M. Bollard, and Richard J. Simpson. "Acute Exercise Preferentially Redeploys NK-Cells with a Highly-Differentiated Phenotype and Augments Cytotoxicity against Lymphoma and Multiple Myeloma Target Cells. Part II: Impact of Latent Cytomegalovirus Infection and Catecholamine Sensitivity." *Brain, Behavior, and Immunity* 49 (October 2015): 59–65.

Bigley, Austin B., Katayoun Rezvani, Nina Shah, Takuya Sekine, Natasja Balnegger, Mira Pistillo, Nadia Agha, et al. "Latent CMV Infection Enhances Anti-Tumor Cytotoxicity through Accumulation of NKG2C+ NK-Cells in Healthy Humans." *Clinical and Experimental Immunology* 185, no. 2 (August 2016): 239–51.

Bigley, Austin B., Guillaume Spielmann, Nadia Agha, Daniel P. O'Connor, and Richard J. Simpson. "Dichotomous Effects of Latent CMV Infection on the Phenotype and Functional Properties of CD8+ T-Cells and NK-Cells." *Cellular Immunology* 300 (February 2016): 26–32.

Bigley, Austin B., Guillaume Spielmann, Nadia Agha, and Richard J. Simpson. "The Effects of Age and Latent Cytomegalovirus Infection on NK-Cell Phenotype and Exercise Responsiveness in Man." *Oxidative Medicine and Cellular Longevity* 2015 (October 2015): 979645.

Chartrand, Thomas, Gin McCollum, Douglas A. Hanes, and Richard D. Boyle. "Symmetries of a Generic Utricular Projection: Neural Connectivity and the Distribution of Utricular Information." *Journal of Mathematical Biology* 72, no. 3 (February 2016): 727–53.

Clarke, Andrew H., and Uwe Sch nfeld. "Modification of Unilateral Otolith Responses Following Spaceflight." *Experimental Brain Research* 233, no. 12 (December 2015): 3613–24.

Cl ment, Gilles R., John B. Charles, and William H. Paloski. "Revisiting the Needs for Artificial Gravity during Deep Space Missions." *REACH - Reviews in Human Space Exploration* 1 (March 2016): 1–10.

Cl ment, Gilles, and Scott J. Wood. "Translational Otolith-Ocular Reflex during off-Vertical Axis Rotation in Humans." *Neuroscience Letters* 616 (March 2016): 65–69.

Cl ment, G., W. H. Paloski, J. Rittweger, D. Linnarsson, M. P. Baille, E. Mulder, F. L. Wuyts, and J. Zange. "Centrifugation as a Countermeasure during Bed Rest and Dry Immersion: What Has Been Learned?" *Journal of Musculoskeletal & Neuronal Interactions* 16, no. 2 (June 7, 2016): 84–91.

Conkin, Johnny. "Equivalent Air Altitude and the Alveolar Gas Equation." *Aerospace Medicine and Human Performance* 87, no. 1 (January 2016): 61–64.

Crucian, Brian, Smith Johnston, Satish Mehta, Raymond Stowe, Peter Uchakin, Heather Quiariarte, Duane Pierson, Mark L. Laudenslager, and Clarence Sams. "A Case of Persistent Skin Rash and Rhinitis with Immune System Dysregulation Onboard the International Space Station." *The Journal of Allergy and Clinical Immunology. In Practice* 4, no. 4 (August 2016): 759–62.e8.

Delp, Michael D., Jacqueline M. Charvat, Charles L. Limoli, Ruth K. Globus, and Payal Ghosh. "Apollo Lunar Astronauts Show Higher Cardiovascular Disease Mortality: Possible Deep Space Radiation Effects on the Vascular Endothelium." *Scientific Reports* 6 (July 2016): 29901.

Deymier-Black, Alix C., Jill D. Pasteris, Guy M. Genin, and Stavros Thomopoulos. "Allometry of the Tendon Enthesis: Mechanisms of Load Transfer Between Tendon and Bone." *Journal of Biomechanical Engineering* 137, no. 11 (November 1, 2015).

Diaz Artiles, Ana, Thomas Heldt, and Laurence R. Young. "Effects of Artificial Gravity on the Cardiovascular System: Computational Approach." *Acta Astronautica, Space Flight Safety*, 126 (September 2016): 395–410.

Eikema, Diderik Jan A., Jung Hung Chien, Nicholas Stergiou, Sara A. Myers, Melissa M. Scott-Pandorf, Jacob J. Bloomberg, and Mukul Mukherjee. "Optic Flow Improves Adaptability of Spatiotemporal Characteristics during Split-Belt Locomotor Adaptation with Tactile Stimulation." *Experimental Brain Research* 234, no. 2 (February 2016): 511–22.

English, Kirk L., Stuart M. C. Lee, James A. Loehr, Robert J. Ploutz-Snyder, and Lori L. Ploutz-Snyder. "Isokinetic Strength Changes Following Long-Duration Spaceflight on the ISS." *Aerospace Medicine and Human Performance* 86, no. 12 Suppl (December 2015): A68–77.

English, Kirk L., Joni A. Mettler, Jennifer B. Ellison, Madonna M. Mamerow, Emily Arentson-Lantz, James M. Pattarini, Robert Ploutz-Snyder, Melinda Sheffield-Moore, and Douglas Paddon-Jones. "Leucine Partially Protects Muscle Mass and Function during Bed Rest in Middle-Aged Adults." *The American Journal of Clinical Nutrition* 103, no. 2 (February 2016): 465–73.

Evans, Joyce M., L. Christine Ribeiro, Fritz B. Moore, Siqi Wang, Qingguang Zhang, Vladimir Kostas, Connor R. Ferguson, et al. "Hypovolemic Men and Women Regulate Blood Pressure Differently Following Exposure to Artificial Gravity." *European Journal of Applied Physiology* 115, no. 12 (December 2015): 2631–40.

FY2016 Publications

Feger, Bryan J., J. Will Thompson, Laura G. Dubois, Reddy P. Kom-maddi, Matthew W. Foster, Rajashree Mishra, Sudha K. Shenoy, et al. "Microgravity Induces Proteomics Changes Involved in Endoplasmic Reticulum Stress and Mitochondrial Protection." *Scientific Reports* 6 (September 27, 2016): 34091.

Feola, Andrew J., Jerry G. Myers, Julia Raykin, Lealem Mulugeta, Emily S. Nelson, Brian C. Samuels, and C. Ross Ethier. "Finite Element Modeling of Factors Influencing Optic Nerve Head Deformation Due to Intracranial Pressure." *Investigative Ophthalmology & Visual Science* 57, no. 4 (April 2016): 1901–11.

Fiuzza-Luces, C., R. J. Simpson, M. Ramírez, A. Lucia, and N. A. Berger. "Physical Function and Quality of Life in Patients with Chronic GvHD: A Summary of Preclinical and Clinical Studies and a Call for Exercise Intervention Trials in Patients." *Bone Marrow Transplantation* 51, no. 1 (January 2016): 13–26.

Florian, John P., Friedhelm J. Baisch, Martina Heer, and James A. Pawelczyk. "Caloric Restriction Diminishes the Pressor Response to Static Exercise." *Extreme Physiology & Medicine* 5 (January 2016): 2.

Gadomski, Benjamin C., Zachary F. Lerner, Raymond C. Browning, Jeremiah T. Easley, Ross H. Palmer, and Christian M. Puttitz. "Computational Characterization of Fracture Healing under Reduced Gravity Loading Conditions." *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society* 34, no. 7 (July 2016): 1206–15.

Ghosh, Payal, Brad J. Behnke, John N. Stabley, Cody R. Kilar, Yoonjung Park, Anand Narayanan, Joshua S. Alwood, et al. "Effects of High-LET Radiation Exposure and Hindlimb Unloading on Skeletal Muscle Resistance Artery Vasomotor Properties and Cancellous Bone Microarchitecture in Mice." *Radiation Research* 185, no. 3 (March 2016): 257–66.

Globus, Ruth K., and Emily Morey-Holton. "Hindlimb Unloading: Rodent Analog For Microgravity." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 10 (May 2016): 1196–1206.

Goodwin, Thomas J., Maureen McCarthy, Randall J. Cohrs, and Benedikt B. Kaufer. "3D Tissue-like Assemblies: A Novel Approach to Investigate Virus-Cell Interactions." *Methods (San Diego, Calif.)* 90 (November 2015): 76–84.

Govey, Peter M., Yuka Imamura Kawasawa, and Henry J. Donahue. "Mapping the Osteocytic Cell Response to Fluid Flow Using RNA-Seq." *Journal of Biomechanics* 48, no. 16 (December 2015): 4327–32.

Hackney, Kyle J., Meghan E. Downs, and Lori Ploutz-Snyder. "Blood Flow Restricted Exercise Compared to High Load Resistance Exercise During Unloading." *Aerospace Medicine and Human Performance* 87, no. 8 (August 1, 2016): 688–96.

Hackney, Kyle J., Jessica M. Scott, Andrea M. Hanson, Kirk L. English, Meghan E. Downs, and Lori L. Ploutz-Snyder. "The Astronaut-Athlete: Optimizing Human Performance in Space." *Journal of Strength and Conditioning Research / National Strength & Conditioning Association* 29, no. 12 (December 2015): 3531–45.

Hargens, Alan R., and Laurence Vico. "Long-Duration Bed Rest as an Analog to Microgravity." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 8 (April 2016): 891–903.

Hirsiger, Sarah, Vincent Koppelmans, Susan Méritat, Franziskus Liem, Burak Erdeniz, Rachael D. Seidler, and Lutz Jäncke. "Structural and Functional Connectivity in Healthy Aging: Associations for Cognition and Motor Behavior." *Human Brain Mapping* 37, no. 3 (March 2016): 855–67.

Holt, Jacquelyn A., Brandon R. Macias, Suzanne M. Schneider, Donald E. Watenpaugh, Stuart M. C. Lee, Douglas G. Chang, and Alan R. Hargens. "WISE 2005: Aerobic and Resistive Countermeasures Prevent Paraspinal Muscle Deconditioning during 60-Days Bed Rest in Women." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 10 (May 2016): 1215–22.

Jain, Varsha, and Virginia E. Wotring. "Medically Induced Amenorrhea in Female Astronauts." *npj Microgravity* 2 (April 2016): 16008.

Jeong, Youngjae, Stephanie M. Carleton, Bettina A. Gentry, Xiaomei Yao, J. Andries Ferreira, Daniel J. Salamango, MaryAnn Weis, et al. "Hindlimb Skeletal Muscle Function and Skeletal Quality and Strength in +/G610C Mice With and Without Weight-Bearing Exercise." *Journal of Bone and Mineral Research: The Official Journal of the American Society for Bone and Mineral Research* 30, no. 10 (October 2015): 1874–86.

Judex, S., W. Zhang, L. R. Donahue, and E. Ozcivici. "Genetic and Tissue Level Muscle-Bone Interactions during Unloading and Reambulation." *Journal of Musculoskeletal & Neuronal Interactions* 16, no. 3 (September 7, 2016): 174–82.

Kramer, Larry A., Khader M. Hasan, Ashot E. Sargsyan, Jerry S. Wolinsky, Douglas R. Hamilton, Roy F. Riascos, William K. Carson, et al. "MR-Derived Cerebral Spinal Fluid Hydrodynamics as a Marker and a Risk Factor for Intracranial Hypertension in Astronauts Exposed to Microgravity." *Journal of Magnetic Resonance Imaging: JMIRI* 42, no. 6 (December 2015): 1560–71.

Krishnan, Manickam, Preethi Janardhanan, Linda Roman, Robert L. Reddick, Mohan Natarajan, Rien van Haperen, Samy L. Habib, Rini de Crom, and Sumathy Mohan. "Enhancing eNOS Activity with Simultaneous Inhibition of IKK β Restores Vascular Function in Ins2(Akita+/-) Type-1 Diabetic Mice." *Laboratory Investigation: a Journal of Technical Methods and Pathology* 95, no. 10 (October 2015): 1092–1104.

Lawley, Justin Stevan, Benjamin D. Levine, Michael A. Williams, Jan Malm, Anders Eklund, David M. Polaner, Andrew W. Subudhi, Peter H. Hackett, and Robert C. Roach. "Cerebral Spinal Fluid Dynamics: Effect of Hypoxia and Implications for High-Altitude Illness." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 2 (January 2016): 251–62.

Lee, Andrew G., William J. Tarver, Thomas H. Mader, Charles Robert Gibson, Stephen F. Hart, and Christian A. Otto. "Neuro-Ophthalmology of Space Flight." *Journal of Neuro-Ophthalmology: The Official Journal of the North American Neuro-Ophthalmology Society* 36, no. 1 (March 2016): 85–91.

Lee, Stuart M.C., Alan H. Feiveson, Sydney Stein, Michael B. Stenger, and Steven H. Platts. "Orthostatic Intolerance After ISS and Space Shuttle Missions." *Aerospace Medicine and Human Performance* 86, no. 12 (December 2015): A54–67.

Lloyd, Shane A., Sean E. Morony, Virginia L. Ferguson, Steven J. Sim-ske, Louis S. Stodieck, Kelly S. Warmington, Eric W. Livingston, David L. Lacey, Paul J. Kostenuik, and Ted A. Bateman. "Osteoprotegerin Is an Effective Countermeasure for Spaceflight-Induced Bone Loss in Mice." *Bone* 81 (December 2015): 562–72.

Loerch, Linda H. "Exercise Countermeasures on ISS: Summary and Future Directions." *Aerospace Medicine and Human Performance* 86, no. 12 Suppl (December 2015): A92–93.

Macaulay, Timothy R., Brandon R. Macias, Stuart M.C. Lee, Wanda L. Boda, Donald E. Watenpaugh, and Alan R. Hargens. "Treadmill Exercise within Lower-Body Negative Pressure Attenuates Simulated Spaceflight-Induced Reductions of Balance Abilities in Men but Not Women." *npj Microgravity* 2 (June 2016): 16022.

FY2016 Publications

- Macias, B. R., F. Lima, J. M. Swift, Y. Shirazi-Fard, E. S. Greene, M. R. Allen, J. Fluckey, et al. "Simulating the Lunar Environment: Partial Weightbearing and High-LET Radiation-Induce Bone Loss and Increase Sclerostin-Positive Osteocytes." *Radiation Research* 186, no. 3 (September 2016): 254–63.
- Madansingh, S., and J. J. Bloomberg. "Understanding the Effects of Spaceflight on Head–trunk Coordination during Walking and Obstacle Avoidance." *Acta Astronautica* 115 (October 2015): 165–72.
- Manske, Sarah L., Surabhi Vijayaraghavan, Alyssa Tuthill, Olivier Brutus, Jie Yang, Shikha Gupta, and Stefan Judex. "Extending Rest between Unloading Cycles Does Not Enhance Bone's Long-Term Recovery." *Medicine and Science in Sports and Exercise* 47, no. 10 (October 2015): 2191–2200.
- Mao, Clifford P., Brandon R. Macias, and Alan R. Hargens. "Shoulder Skin and Muscle Hemodynamics during Backpack Carriage." *Applied Ergonomics* 51 (November 2015): 80–84.
- Merfeld, Daniel M., Torin K. Clark, Yue M. Lu, and Faisal Karmali. "Dynamics of Individual Perceptual Decisions." *Journal of Neurophysiology* 115, no. 1 (January 2016): 39–59.
- Moore, Alan D., Peggy A. Lynn, and Alan H. Feiveson. "The First 10 Years of Aerobic Exercise Responses to Long-Duration ISS Flights." *Aerospace Medicine and Human Performance* 86, no. 12 Suppl (December 2015): A78–86.
- Morris, Christopher J., Joanna I. Garcia, Samantha Myers, Jessica N. Yang, Noortje Trienekens, and Frank A. J. L. Scheer. "The Human Circadian System Has a Dominating Role in Causing the Morning/Evening Difference in Diet-Induced Thermogenesis." *Obesity (Silver Spring, Md.)* 23, no. 10 (October 2015): 2053–58.
- Morris, Christopher J., Taylor E. Purvis, Kun Hu, and Frank A. J. L. Scheer. "Circadian Misalignment Increases Cardiovascular Disease Risk Factors in Humans." *Proceedings of the National Academy of Sciences of the United States of America* 113, no. 10 (March 2016): E1402–11.
- Morris, Christopher J., Taylor E. Purvis, Joseph Mistretta, and Frank A. J. L. Scheer. "Effects of the Internal Circadian System and Circadian Misalignment on Glucose Tolerance in Chronic Shift Workers." *The Journal of Clinical Endocrinology and Metabolism* 101, no. 3 (March 2016): 1066–74.
- Mukherjee, Mukul, Diderik Jan A. Eikema, Jung Hung Chien, Sara A. Myers, Melissa Scott-Pandorf, Jacob J. Bloomberg, and Nicholas Stergiou. "Plantar Tactile Perturbations Enhance Transfer of Split-Belt Locomotor Adaptation." *Experimental Brain Research* 233, no. 10 (October 2015): 3005–12.
- Natarajan, Mohan, Natarajan Aravindan, Eugene A. Sprague, and Sumathy Mohan. "Hemodynamic Flow-Induced Mechanotransduction Signaling Influences the Radiation Response of the Vascular Endothelium." *Radiation Research* 186, no. 2 (August 2016): 175–88.
- Owerkowicz, Tomasz, Joshua A. Cotter, Fadia Haddad, Alvin M. Yu, Marinelle L. Camilon, Theresa N. Hoang, Daniel J. Jimenez, et al. "Exercise Responses to Gravity-Independent Flywheel Aerobic and Resistance Training." *Aerospace Medicine and Human Performance* 87, no. 2 (February 2016): 93–101.
- Petersen, Nora, Patrick Jaekel, Andre Rosenberger, Tobias Weber, Jonathan Scott, Filippo Castrucci, Gunda Lambrecht, et al. "Exercise in Space: The European Space Agency Approach to in-Flight Exercise Countermeasures for Long-Duration Missions on ISS." *Extreme Physiology & Medicine* 5 (August 2016): 9.
- Pietrofesa, Ralph A., Anastasia Velopoulou, Stacey L. Lehman, Evguenia Arguiri, Pantelis Solomides, Cameron J. Koch, Om P. Mishra, Constantinos Koumenis, Thomas J. Goodwin, and Melpo Christofidou-Solomidou. "Novel Double-Hit Model of Radiation and Hyperoxia-Induced Oxidative Cell Damage Relevant to Space Travel." *International Journal of Molecular Sciences* 17, no. 6 (June 16, 2016).
- Ploutz-Snyder, Lori L. "Evaluating Countermeasures In Spaceflight Analogs." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 8 (April 2016): 915–21.
- Prisby, Rhonda D., Joshua S. Alwood, Bradley Jon Behnke, John N. Stabley, Danielle J. McCullough, Payal Ghosh, Ruth K. Globus, and Michael D. Delp. "Effects of Hindlimb Unloading and Ionizing Radiation on Skeletal Muscle Resistance Artery Vasodilation and Its Relation to Cancellous Bone in Mice." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 2 (January 2016): 97–106.
- Rizzardi, Lindsay F, Hawley Kunz, Kathleen Rubins, Alexander Chouker, Heather Quiariarte, Clarence Sams, Brian E Crucian, and Andrew P Feinberg. "Evaluation of Techniques for Performing Cellular Isolation and Preservation during Microgravity Conditions." *npj Microgravity* 2 (July 14, 2016): 16025.
- Roberts, D. R., X. Zhu, A. Tabesh, E. W. Duffy, D. A. Ramsey, and T. R. Brown. "Structural Brain Changes Following Long-Term 6° Head-Down Tilt Bed Rest as an Analog for Spaceflight." *AJNR. American Journal of Neuroradiology* 36, no. 11 (November 2015): 2048–54.
- Safikhani, Zhaleh, Nehme El-Hachem, Rene Quevedo, Petr Smirnov, Anna Goldenberg, Nicolai Juul Birkbak, Christopher Mason, et al. "Assessment of Pharmacogenomic Agreement." *F1000Research* 5 (May 9, 2016): 825.
- Schmidt, Michael A., Thomas J. Goodwin, and Ralph Pelligra. "Incorporation of Omics Analyses into Artificial Gravity Research for Space Exploration Countermeasure Development." *Metabolomics: Official Journal of the Metabolomic Society* 12 (February 2016): 36.
- Schneider, Suzanne M., Stuart M. C. Lee, Alan H. Feiveson, Donald E. Watenpugh, Brandon R. Macias, and Alan R. Hargens. "Treadmill Exercise within Lower Body Negative Pressure Protects Leg Lean Tissue Mass and Extensor Strength and Endurance during Bed Rest." *Physiological Reports* 4, no. 15 (August 5, 2016).
- Schreurs, A.-S., Y. Shirazi-Fard, M. Shahnazari, J. S. Alwood, T. A. Truong, C. G. T. Tahimic, C. L. Limoli, N. D. Turner, B. Halloran, and R. K. Globus. "Dried Plum Diet Protects from Bone Loss Caused by Ionizing Radiation." *Scientific Reports* 6 (February 2016): 21343.
- Shelhamer, Mark. "Parabolic Flight as a Spaceflight Analog." *Journal of Applied Physiology (Bethesda, Md.: 1985)* 120, no. 12 (June 2016): 1442–48.
- Sibonga, Jean D., Elisabeth R. Spector, Smith L. Johnston, and William J. Tarver. "Evaluating Bone Loss in ISS Astronauts." *Aerospace Medicine and Human Performance* 86, no. 12 Suppl (December 2015): A38–44.
- Simpson, Richard J., Austin B. Bigley, Guillaume Spielmann, Emily C. P. LaVoy, Hawley Kunz, and Catherine M. Bollard. "Human Cytomegalovirus Infection and the Immune Response to Exercise." *Exercise Immunology Review* 22 (January 2016): 8–27.
- Smith, Scott M., Martina Heer, Linda C. Shackelford, Jean D. Sibonga, Jordan Spatz, Robert A. Pietrzyk, Edgar K. Hudson, and Sara R. Zwart. "Bone Metabolism and Renal Stone Risk during International Space Station Missions." *Bone* 81 (December 2015): 712–20.
- Smith, Scott M., and Sara R. Zwart. "Magnesium and Space Flight." *Nutrients* 7, no. 12 (December 2015): 10209–22.

FY2016 Publications

Spielmann, Guillaume, Catherine M. Bollard, Hawley Kunz, Patrick J. Hanley, and Richard J. Simpson. "A Single Exercise Bout Enhances the Manufacture of Viral-Specific T-Cells from Healthy Donors: Implications for Allogeneic Adoptive Transfer Immunotherapy." *Scientific Reports* 6 (May 2016): 25852.

Tahimic, Candice G. T., Roger K. Long, Takuo Kubota, Maggie Yige Sun, Hashem Elalieh, Chak Fong, Alicia T. Menendez, Yongmei Wang, Jean-Pierre Vilardaga, and Daniel D. Bikle. "Regulation of Ligand and Shear Stress-Induced Insulin-like Growth Factor 1 (IGF1) Signaling by the Integrin Pathway." *The Journal of Biological Chemistry* 291, no. 15 (April 2016): 8140–49.

Taibbi, Giovanni, Ronita L. Cromwell, Susana B. Zanella, Patrice O. Yarbough, Robert J. Ploutz-Snyder, Bernard F. Godley, and Gianmarco Vizzeri. "Ocular Outcomes Comparison Between 14- and 70-Day Head-Down-Tilt Bed Rest." *Investigative Ophthalmology & Visual Science* 57, no. 2 (February 2016): 495–501.

Theriot, Corey A, Christian M Westby, Jennifer L L Morgan, Sara R Zwart, and Susana B Zanella. "High Dietary Iron Increases Oxidative Stress and Radiosensitivity in the Rat Retina and Vasculature after Exposure to Fractionated Gamma Radiation." *npj Microgravity* 2 (May 2016): 16014.

Uzer, Gunes, Clinton T. Rubin, and Janet Rubin. "Cell Mechanosensitivity Is Enabled by the LINC Nuclear Complex." *Current Molecular Biology Reports* 2, no. 1 (March 2016): 36–47.

Uzer, Gunes, Robyn K. Fuchs, Janet Rubin, and William R. Thompson. "Concise Review: Plasma and Nuclear Membranes Convey Mechanical Information to Regulate Mesenchymal Stem Cell Lineage." *Stem Cells (Dayton, Ohio)* 34, no. 6 (June 2016): 1455–63.

Vijay, Priyanka, Alexa B. R. McIntyre, Christopher E. Mason, Jeffrey P. Greenfield, and Sheng Li. "Clinical Genomics: Challenges and Opportunities." *Critical Reviews in Eukaryotic Gene Expression* 26, no. 2 (April 2016): 97–113.

Wallace, Ian J., Gabriel M. Pagnotti, Jasper Rubin-Sigler, Matthew Naeher, Lynn E. Copes, Stefan Judex, Clinton T. Rubin, and Brigitte Demes. "Focal Enhancement of the Skeleton to Exercise Correlates to Mesenchymal Stem Cell Responsivity rather than Peak External Forces." *The Journal of Experimental Biology* 218, no. 19 (October 2015): 3002–9.

Westby, Christian M., David S. Martin, Stuart M. C. Lee, Michael B. Stenger, and Steven H. Platts. "Left Ventricular Remodeling during and after 60 Days of Sedentary Head-Down Bed Rest." *Journal of Applied Physiology (Bethesda, Md.: 1985)*, October 2015, jap – 00676.

White, Olivier, Gilles Clément, Jacques-Olivier Fortrat, Anne Pavy-LeTraon, Jean-Louis Thonnard, Stéphane Blanc, Floris L. Wuyts, and William H. Paloski. "Towards Human Exploration of Space: The THESEUS Review Series on Neurophysiology Research Priorities." *npj Microgravity* 2 (August 18, 2016): 16023.

Wilcox, Samuel L., Ryan M. Broxterman, and Thomas J. Barstow. "Constructing Quasi-Linear VO₂ Responses from Nonlinear Parameters." *Journal of Applied Physiology (Bethesda, Md.: 1985)*, January 15, 2016, jap.00507.2015.

Wotring, Virginia E. "Chemical Potency and Degradation Products of Medications Stored Over 550 Earth Days at the International Space Station." *The AAPS Journal* 18, no. 1 (January 2016): 210–16.

Wotring, Virginia E. "Medication Use by U.S. Crewmembers on the International Space Station." *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology* 29, no. 11 (November 2015): 4417–23.

Xie, Aris, Melinda D. Wu, Gabriella Cigarroa, J. Todd Belcic, Azzidine Ammi, Federico Moccetti, and Jonathan R. Lindner. "Influence of DNA-Microbubble Coupling on Contrast Ultrasound-Mediated Gene Transfection in Muscle and Liver." *Journal of the American Society of Echocardiography: Official Publication of the American Society of Echocardiography* 29, no. 8 (August 2016): 812–18.

Yuan, Peng, Vincent Koppelmans, Patricia A. Reuter-Lorenz, Yiri E. De Dios, Nichole E. Gadd, Scott J. Wood, Roy Riascos, et al. "Increased Brain Activation for Dual Tasking with 70-Days Head-Down Bed Rest." *Frontiers in Systems Neuroscience* 10 (August 23, 2016): 71.

Zook, Justin M., David Catoe, Jennifer McDaniel, Lindsay Vang, Noah Spies, Arend Sidow, Ziming Weng, et al. "Extensive Sequencing of Seven Human Genomes to Characterize Benchmark Reference Materials." *Scientific Data* 3 (June 7, 2016): 160025.

Zwart, Sara R., Jesse F. Gregory, Steven H. Zeisel, Charles R. Gibson, Thomas H. Mader, Jason M. Kinchen, Per M. Ueland, Robert Ploutz-Snyder, Martina A. Heer, and Scott M. Smith. "Genotype, B-Vitamin Status, and Androgens Affect Space Flight-Induced Ophthalmic Changes." *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology* 30, no. 1 (January 2016): 141–48.

Space Radiation (SR)

Adams, Cassandra J., Jennifer S. Yu, Jian-Hua Mao, Kuang-Yu Jen, Sylvain V. Costes, Mark Wade, Jocelyn Shoemaker, et al. "The Trp53 Delta Proline (Trp53ΔP) Mouse Exhibits Increased Genome Instability and Susceptibility to Radiation-Induced, but Not Spontaneous, Tumor Development." *Molecular Carcinogenesis* 55, no. 9 (September 2016): 1387–96.

Allen, Antiño R., Jacob Raber, Ayanabha Chakraborti, Sourabh Sharma, and John R. Fike. "(56)Fe Irradiation Alters Spine Density and Dendritic Complexity in the Mouse Hippocampus." *Radiation Research* 184, no. 6 (November 2015): 586–94.

Almeida-Porada, Graça, Anthony Atala, and Christopher D. Porada. "In Utero Stem Cell Transplantation and Gene Therapy: Rationale, History, and Recent Advances toward Clinical Application." *Molecular Therapy. Methods & Clinical Development* 5 (March 2016): 16020.

Azzam, Edouard I., Nicholas W. Colangelo, Jason D. Domogauer, Neha Sharma, and Sonia M. de Toledo. "Is Ionizing Radiation Harmful at Any Exposure? An Echo That Continues to Vibrate." *Health Physics* 110, no. 3 (March 2016): 249–51.

Barcellos-Hoff, Mary Helen, and Jian-Hua Mao. "HZE Radiation Non-Targeted Effects on the Microenvironment That Mediate Mammary Carcinogenesis." *Frontiers in Oncology* 6 (March 2016): 57.

Baulch, Janet E., Munjal M. Acharya, Barrett D. Allen, Ning Ru, Nicole N. Chmielewski, Vahan Martirosian, Erich Giedzinski, et al. "Cranial Grafting of Stem Cell-Derived Microvesicles Improves Cognition and Reduces Neuropathology in the Irradiated Brain." *Proceedings of the National Academy of Sciences of the United States of America* 113, no. 17 (April 2016): 4836–41.

Beheshti, Afshin, Justin Wage, J. Tyson McDonald, Clare Lamont, Michael Peluso, Philip Hahnfeldt, and Lynn Hlatky. "Tumor-Host Signaling Interaction Reveals a Systemic, Age-Dependent Splenic Immune Influence on Tumor Development." *Oncotarget* 6, no. 34 (November 2015): 35419–32.

Benzekry, Sebastien, Afshin Beheshti, Philip Hahnfeldt, and Lynn Hlatky. "Capturing the Driving Role of Tumor-Host Crosstalk in a Dynamical Model of Tumor Growth." *Bio-Protocol* 5, no. 21 (November 2015).

FY2016 Publications

Bhagwandin, Vikash J., J. Michael Bishop, Woodring E. Wright, and Jerry W. Shay. "The Metastatic Potential and Chemoresistance of Human Pancreatic Cancer Stem Cells." *PLoS One* 11, no. 2 (February 2016): e0148807.

Boerma, Marjan, Gregory A. Nelson, Vijayalakshmi Sridharan, Xiao-Wen Mao, Igor Koturbash, and Martin Hauer-Jensen. "Space Radiation and Cardiovascular Disease Risk." *World Journal of Cardiology* 7, no. 12 (December 2015): 882–88.

Britten, Richard A., Jessica S. Jewell, Vania D. Miller, Leslie K. Davis, Melissa M. Hadley, and Andrew J. Wyrobek. "Impaired Spatial Memory Performance in Adult Wistar Rats Exposed to Low (5–20 cGy) Doses of 1 GeV/n 56Fe Particles." *Radiation Research* 185, no. 3 (March 2016): 332–37.

Britten, Richard A., Vania D. Miller, Melissa M. Hadley, Jessica S. Jewell, and Evangeline Macadat. "Performance in Hippocampus- and PFC-Dependent Cognitive Domains Are Not Concomitantly Impaired in Rats Exposed to 20cGy of 1GeV/n 56Fe Particles." *Life Sciences in Space Research* 10 (August 2016): 17–22.

Chang, Jianhui, Yi Luo, Yingying Wang, Rupak Pathak, Vijayalakshmi Sridharan, Tamako Jones, Xiao Wen Mao, et al. "Low Doses of Oxygen Ion Irradiation Cause Acute Damage to Hematopoietic Cells in Mice." *PLoS One* 11, no. 7 (July 1, 2016): e0158097.

Chang, Polly Y., Francis A. Cucinotta, Kathleen A. Bjornstad, James Bakke, Chris J. Rosen, Nicholas Du, David G. Fairchild, Elidedonna Cacao, and Eleanor A. Blakely. "Harderian Gland Tumorigenesis: Low-Dose and LET Response." *Radiation Research* 185, no. 5 (May 2016): 449–60.

Chen, Hongxin, Zhao Zhong Chong, Sonia M. De Toledo, Edouard I. Azzam, Stella Elkabes, and Nizar Souayah. "Delayed Activation of Human Microglial Cells by High Dose Ionizing Radiation." *Brain Research* 1646 (September 1, 2016): 193–98.

Chmielewski, Nicole N., Chongshan Caressi, Erich Giedzinski, Vipan K. Parihar, and Charles L. Limoli. "Contrasting the Effects of Proton Irradiation on Dendritic Complexity of Subiculum Neurons in Wild Type and MCAT Mice." *Environmental and Molecular Mutagenesis* 57, no. 5 (June 2016): 364–71.

Coleman, Matthew A., Sharath P Sasi, Jillian Onufrak, Mohan Natarajan, Krishnan Manickam, John Schwab, Sujatha Muralidharan, et al. "Low Dose Radiation Affects Cardiac Physiology: Gene Networks and Molecular Signaling in Cardiomyocytes." *American Journal of Physiology. Heart and Circulatory Physiology* 309, no. 11 (December 1, 2015): ajpheart.00050.2015.

Datta, Kamal, Shubhankar Suman, Santosh Kumar, and Albert J. Fornace. "Colorectal Carcinogenesis, Radiation Quality, and the Ubiquitin-Proteasome Pathway." *Journal of Cancer* 7, no. 2 (January 2016): 174–83.

Domogauer, Jason D., Sonia M. de Toledo, and Edouard I. Azzam. "A Mimic of the Tumor Microenvironment: A Simple Method for Generating Enriched Cell Populations and Investigating Intercellular Communication." *Journal of Visualized Experiments: JoVE*, no. 115 (September 20, 2016).

El-Ashmawy, Mariam, Melissa Coquelin, Krishna Luitel, Kimberly Batten, and Jerry W. Shay. "Organotypic Culture in Three Dimensions Prevents Radiation-Induced Transformation in Human Lung Epithelial Cells." *Scientific Reports* 6 (August 19, 2016).

Elkin, Sarah R., Nawal Bendris, Carlos Reis, Yunyun Zhou, Yang Xie, Kenneth E. Huffman, John D. Minna, and Sandra L. Schmid. "A Systematic Analysis Reveals Heterogeneous Changes in the Endocytic Activities of Cancer Cells." *Cancer Research* 75, no. 21 (November 1, 2015): 4640–50.

Fleener, Courtney J., Kelly Higa, Michael M. Weil, and James DeGregori. "Evolved Cellular Mechanisms to Respond to Genotoxic Insults: Implications for Radiation-Induced Hematologic Malignancies." *Radiation Research* 184, no. 4 (October 2015): 341–51.

Gao, Xuefeng, Brock J. Sishc, Christopher B. Nelson, Philip Hahnfeldt, Susan M. Bailey, and Lynn Hlatky. "Radiation-Induced Reprogramming of Pre-Senescent Mammary Epithelial Cells Enriches Putative CD44(+)/CD24(-/low) Stem Cell Phenotype." *Frontiers in Oncology* 6 (June 14, 2016): 138.

George, Kerry A., Megumi Hada, and Francis A. Cucinotta. "Biological Effectiveness of Accelerated Protons for Chromosome Exchanges." *Frontiers in Oncology* 5 (October 2015): 226.

Graillot, Vanessa, Inge Dormoy, Jacques Dupuy, Jerry W. Shay, Laurence Huc, Gladys Mirey, and Julien Vignard. "Genotoxicity of Cytolethal Distending Toxin (CDT) on Isogenic Human Colorectal Cell Lines: Potential Promoting Effects for Colorectal Carcinogenesis." *Frontiers in Cellular and Infection Microbiology* 6 (March 2016): 34.

Grygoryev, Dmytro, Stacey Gauny, Michael Lasarev, Anna Ohlrich, Amy Kronenberg, and Mitchell S. Turker. "Charged Particle Mutagenesis at Low Dose and Fluence in Mouse Splenic T Cells." *Mutation Research* 788 (June 2016): 32–40.

Hadley, Melissa M., Leslie K. Davis, Jessica S. Jewell, Vania D. Miller, and Richard A. Britten. "Exposure to Mission-Relevant Doses of 1 GeV/n (48)Ti Particles Impairs Attentional Set-Shifting Performance in Retired Breeder Rats." *Radiation Research* 185, no. 1 (January 2016): 13–19.

Huang, Lin, Samantha I. Wickramasekara, Tunde Akinyeke, Blair S. Stewart, Yuan Jiang, Jacob Raber, and Claudia S. Maier. "Ion Mobility-Enhanced MS(E)-Based Label-Free Analysis Reveals Effects of Low-Dose Radiation Post Contextual Fear Conditioning Training on the Mouse Hippocampal Proteome." *Journal of Proteomics* 140 (May 2016): 24–36.

Impey, Soren, Carl Pelz, Amanuel Tafessu, Tessa Marzulla, Mitchell S. Turker, and Jacob Raber. "Proton Irradiation Induces Persistent and Tissue-Specific DNA Methylation Changes in the Left Ventricle and Hippocampus." *BMC Genomics* 17, no. 1 (March 2016): 273.

Jafri, Mohammad Alam, Syed Kashif Zaidi, Shakeel Ahmed Ansari, Mohammed Hussein Al-Qahtani, and Jerry W. Shay. "MicroRNAs as Potential Drug Targets for Therapeutic Intervention in Colorectal Cancer." *Expert Opinion on Therapeutic Targets* 19, no. 12 (December 2015): 1705–23.

Kennedy, Ann R., Amit Maity, and Jenine K. Sanzari. "A Review of Radiation-Induced Coagulopathy and New Findings to Support Potential Prevention Strategies and Treatments." *Radiation Research* 186, no. 2 (August 2016): 121–40.

Kim, S. B., R. G. Bozeman, A. Kaisani, W. Kim, L. Zhang, J. A. Richardson, W. E. Wright, and J. W. Shay. "Radiation Promotes Colorectal Cancer Initiation and Progression by Inducing Senescence-Associated Inflammatory Responses." *Oncogene* 35, no. 26 (June 2016): 3365–75.

Koturbash, Igor, Isabelle R. Miousse, Vijayalakshmi Sridharan, Etienne Nzabarushimana, Charles M. Skinner, Stepan B. Melnyk, Oleksandra Pavliv, Martin Hauer-Jensen, Gregory A. Nelson, and Marjan Boerma. "Radiation-Induced Changes in DNA Methylation of Repetitive Elements in the Mouse Heart." *Mutation Research* 787 (May 2016): 43–53.

Kugelman, Tara, Damian G. Zuloaga, Sydney Weber, and Jacob Raber. "Post-Training Gamma Irradiation-Enhanced Contextual Fear Memory Associated with Reduced Neuronal Activation of the Infralimbic Cortex." *Behavioural Brain Research* 298, no. Pt B (February 2016): 1–11.

FY2016 Publications

Larsen, Jill E., Vaishnavi Nathan, Jihan K. Osborne, Rebecca K. Farrow, Dhruva Deb, James P. Sullivan, Patrick D. Dospoy, et al. "ZEB1 Drives Epithelial-to-Mesenchymal Transition in Lung Cancer." *The Journal of Clinical Investigation* 126, no. 9 (September 1, 2016): 3219–35.

Latchney, Sarah E., Yindi Jiang, David P. Petrik, Amelia J. Eisch, and Jenny Hsieh. "Inducible Knockout of Mef2a, -C, and -D from Nestin-Expressing Stem/progenitor Cells and Their Progeny Unexpectedly Uncouples Neurogenesis and Dendritogenesis in Vivo." *FASEB Journal: Official Publication of the Federation of American Societies for Experimental Biology* 29, no. 12 (December 2015): 5059–71.

Li, Sheng, Francine E. Garrett-Bakelman, Stephen S. Chung, Mathijs A. Sanders, Todd Hricik, Franck Rapaport, Jay Patel, et al. "Distinct Evolution and Dynamics of Epigenetic and Genetic Heterogeneity in Acute Myeloid Leukemia." *Nature Medicine* 22, no. 7 (July 2016): 792–99.

Liu, Min, Hongyan Wang, Solah Lee, Bailong Liu, Lihua Dong, and Ya Wang. "DNA Repair Pathway Choice at Various Conditions Immediately Post Irradiation." *International Journal of Radiation Biology*, September 13, 2016, 1–11.

Liu, Xinjian, Yujun He, Fang Li, Qian Huang, Takamitsu A. Kato, Russell P. Hall, and Chuan-Yuan Li. "Redefining the Roles of Apoptotic Factors in Carcinogenesis." *Molecular & Cellular Oncology* 3, no. 3 (May 2016): e1054550.

Locke, Paul A., and Michael M. Weil. "Personalized Cancer Risk Assessments for Space Radiation Exposures." *Frontiers in Oncology* 6 (February 2016): 38.

Loucas, Bradford D., Igor Shuryak, and Michael N. Cornforth. "Three-Color Chromosome Painting as Seen through the Eyes of mFISH: Another Look at Radiation-Induced Exchanges and Their Conversion to Whole-Genome Equivalency." *Frontiers in Oncology* 6 (March 2016): 52.

McConnell, Alicia M., Bindu Konda, David G. Kirsch, and Barry R. Stripp. "Distal Airway Epithelial Progenitor Cells Are Radiosensitive to High-LET Radiation." *Scientific Reports* 6 (September 23, 2016): 33455.

McFadden, Conor H., Timothy M. Hallacy, David B. Flint, Dal A. Granville, Aroumougame Asaithamby, Narayan Sahoo, Mark S. Akselrod, and Gabriel O. Sawakuchi. "Time-Lapse Monitoring of DNA Damage Colocalized With Particle Tracks in Single Living Cells." *International Journal of Radiation Oncology, Biology, Physics* 96, no. 1 (September 1, 2016): 221–27.

Mendoza, Matthew L., Ethan M. Anderson, Saïd Kourrich, and Amelia J. Eisch. "A NAc for Spinal Adjustments After Cocaine or Stress." *Biological Psychiatry* 79, no. 11 (June 2016): 872–74.

Menon, Smrithi S., Medha Uppal, Subeena Randhawa, Mehar S. Cheema, Nima Aghdam, Rachel L. Usala, Sanchita P. Ghosh, Amrita K. Cheema, and Anatoly Dritschilo. "Radiation Metabolomics: Current Status and Future Directions." *Frontiers in Oncology* 6 (February 2, 2016): 20.

Mishra, Birendra, Laura Ortiz, and Ulrike Luderer. "Charged Iron Particles, Components of Space Radiation, Destroy Ovarian Follicles." *Human Reproduction (Oxford, England)* 31, no. 8 (August 2016): 1816–26.

Moding, Everett J., Hooney D. Min, Katherine D. Castle, Moiez Ali, Loretta Woodlief, Nerissa Williams, Yan Ma, Yongbaek Kim, Chang-Lung Lee, and David G. Kirsch. "An Extra Copy of p53 Suppresses Development of Spontaneous Kras-Driven but Not Radiation-Induced Cancer." *JCI Insight* 1, no. 10 (July 2016).

Morris, Christelle, Nozomi Tomimatsu, Sandeep Burma, and Pierre Jalinet. "INT6/EIF3E Controls the RNF8-Dependent Ubiquitylation Pathway and Facilitates DNA Double-Strand Break Repair in Human Cells." *Cancer Research*, September 30, 2016.

Muralidharan, Sujatha, Sharath P. Sasi, Maria A. Zuriaga, Karen K. Hirschi, Christopher D. Porada, Matthew A. Coleman, Kenneth X. Walsh, Xinhua Yan, and David A. Goukassian. "Ionizing Particle Radiation as a Modulator of Endogenous Bone Marrow Cell Reprogramming: Implications for Hematological Cancers." *Frontiers in Oncology* 5 (October 2015): 231.

Nelson, Gregory A. "Space Radiation and Human Exposures, A Primer." *Radiation Research* 185, no. 4 (April 2016): 349–58.

Norbury, John W., Walter Schimmerling, Tony C. Slaba, Edouard I. Azzam, Francis F. Badavi, Giorgio Baiocco, Eric Benton, et al. "Galactic Cosmic Ray Simulation at the NASA Space Radiation Laboratory." *Life Sciences in Space Research* 8 (February 2016): 38–51.

Nzabarushimana, Etienne, Sara Prior, Isabelle R. Miousse, Rupak Pathak, Antiño R. Allen, John Latendresse, Reid H. J. Olsen, et al. "Combined Exposure to Protons and ⁵⁶Fe Leads to Overexpression of Il13 and Reactivation of Repetitive Elements in the Mouse Lung." *Life Sciences in Space Research* 7 (November 2015): 1–8.

Pathak, Rupak, Abdel Bachri, Sanchita P. Ghosh, Igor Koturbash, Marjan Boerma, Regina K. Binz, Jeffrey R. Sawyer, and Martin Hauer-Jensen. "The Vitamin E Analog Gamma-Tocotrienol (GT3) Suppresses Radiation-Induced Cytogenetic Damage." *Pharmaceutical Research* 33, no. 9 (September 2016): 2117–25.

Pathak, Rupak, Junru Wang, Sarita Garg, Nukhet Aykin-Burns, Karl-Uwe Petersen, and Martin Hauer-Jensen. "Recombinant Thrombomodulin (Solulin) Ameliorates Early Intestinal Radiation Toxicity in a Preclinical Rat Model." *Radiation Research* 186, no. 2 (August 2016): 112–20.

Peterson, Leif E., and Tatiana Kovyryshina. "Adjustment of Lifetime Risks of Space Radiation-Induced Cancer by the Healthy Worker Effect and Cancer Misclassification." *Heliyon* 1, no. 4 (December 22, 2015): e00048.

Petrik, David, Sarah E. Latchney, Irene Masiulis, Sanghee Yun, Zilai Zhang, Jiang I. Wu, and Amelia J. Eisch. "Chromatin Remodeling Factor Brg1 Supports the Early Maintenance and Late Responsiveness of Nestin-Lineage Adult Neural Stem and Progenitor Cells." *Stem Cells (Dayton, Ohio)* 33, no. 12 (December 2015): 3655–65.

Plante, Ianik. "Calculation of the Second Term of the Exact Green's Function of the Diffusion Equation for Diffusion-Controlled Chemical Reactions." *Computer Physics Communications* 198 (January 2016): 41–46.

Porada, Christopher D., Anthony J. Atala, and Graça Almeida-Porada. "The Hematopoietic System in the Context of Regenerative Medicine." *Methods (San Diego, Calif.)* 99 (April 2016): 44–61.

Raber, Jacob, Antiño R. Allen, Sourabh Sharma, Barrett Allen, Susanna Rosi, Reid H. J. Olsen, Matthew J. Davis, Massarra Eiwaz, John R. Fike, and Gregory A. Nelson. "Effects of Proton and Combined Proton and (⁵⁶Fe) Radiation on the Hippocampus." *Radiation Research* 185, no. 1 (January 2016): 20–30.

Raber, Jacob, Antiño R. Allen, Sydney Weber, Ayanabha Chakraborti, Sourabh Sharma, and John R. Fike. "Effect of Behavioral Testing on Spine Density of Basal Dendrites in the CA1 Region of the Hippocampus Modulated by (⁵⁶Fe) Irradiation." *Behavioural Brain Research* 302 (April 2016): 263–68.

Raber, Jacob, Tessa Marzulla, Amy Kronenberg, and Mitchell S. Turker. "16Oxygen Irradiation Enhances Cued Fear Memory in B6D2F1 Mice." *Life Sciences in Space Research* 7 (November 2015): 61–65.

FY2016 Publications

Raber, Jacob, Sydney Weber, Amy Kronenberg, and Mitchell S. Turker. "Sex- and Dose-Dependent Effects of Calcium Ion Irradiation on Behavioral Performance of B6D2F1 Mice during Contextual Fear Conditioning Training." *Life Sciences in Space Research* 9 (June 2016): 56–61.

Ramadan, Samy S., Vijayalakshmi Sridharan, Igor Koturbash, Isabelle R. Miousse, Martin Hauer-Jensen, Gregory A. Nelson, and Marjan Boerma. "A Priming Dose of Protons Alters the Early Cardiac Cellular and Molecular Response to 56Fe Irradiation." *Life Sciences in Space Research* 8 (February 2016): 8–13.

Rithidech, Kanokporn Noy. "Health Benefits of Exposure to Low-Dose Radiation." *Health Physics* 110, no. 3 (March 2016): 293–95.

Rithidech, Kanokporn Noy, Witawat Jangiam, Montree Tungjai, Chris Gordon, Louise Honikel, and Elbert B. Whorton. "Induction of Chronic Inflammation and Altered Levels of DNA Hydroxymethylation in Somatic and Germinal Tissues of CBA/CAJ Mice Exposed to (48)Ti Ions." *Frontiers in Oncology* 6 (June 2016): 155.

Sishc, Brock J., Christopher B. Nelson, Miles J. McKenna, Christine L. R. Battaglia, Andrea Herndon, Rupa Idate, Howard L. Liber, and Susan M. Bailey. "Telomeres and Telomerase in the Radiation Response: Implications for Instability, Reprograming, and Carcinogenesis." *Frontiers in Oncology* 5 (November 2015): 257.

Slaba, Tony C., Steve R. Blattinig, John W. Norbury, Adam Rusek, and Chiara La Tessa. "Reference Field Specification and Preliminary Beam Selection Strategy for Accelerator-Based GCR Simulation." *Life Sciences in Space Research* 8 (February 2016): 52–67.

Slaba, Tony C., John W. Wilson, Francis F. Badavi, Brandon D. Reddell, and Amir A. Bahadori. "Solar Proton Exposure of an ICRU Sphere within a Complex Structure Part II: Ray-Trace Geometry." *Life Sciences in Space Research* 9 (June 2016): 77–83.

Sridharan, Deepa M., Aroumougama Asaithamby, Steve R. Blattinig, Sylvain V. Costes, Paul W. Doetsch, William S. Dynan, Philip Hahnfeldt, et al. "Evaluating Biomarkers to Model Cancer Risk Post Cosmic Ray Exposure." *Life Sciences in Space Research* 9 (June 2016): 19–47.

Straume, T., L. A. Braby, T. B. Borak, T. Lusby, D. W. Warner, and D. Perez-Nunez. "Compact Tissue-Equivalent Proportional Counter for Deep Space Human Missions." *Health Physics* 109, no. 4 (October 2015): 277–83.

Suman, Shubhankar, Santosh Kumar, Albert J. Fornace, and Kamal Datta. "Decreased RXR α Is Associated with Increased β -Catenin/TCF4 in (56)Fe-Induced Intestinal Tumors." *Frontiers in Oncology* 5 (October 2015): 218.

Suman, Shubhankar, Santosh Kumar, Albert J. Fornace, and Kamal Datta. "Space Radiation Exposure Persistently Increased Leptin and IGF1 in Serum and Activated Leptin-IGF1 Signaling Axis in Mouse Intestine." *Scientific Reports* 6 (August 25, 2016): 31853.

Suman, Shubhankar, Santosh Kumar, Bo-Hyun Moon, Steve J. Strawn, Hemang Thakor, Ziling Fan, Jerry W. Shay, Albert J. Fornace, and Kamal Datta. "Relative Biological Effectiveness of Energetic Heavy Ions for Intestinal Tumorigenesis Shows Male Preponderance and Radiation Type and Energy Dependence in APC(1638N/+) Mice." *International Journal of Radiation Oncology, Biology, Physics* 95, no. 1 (May 2016): 131–38.

Villasana, Laura E., Sydney Weber, Tunde Akinyeke, and Jacob Raber. "Genotype Differences in Anxiety and Fear Learning and Memory of WT and ApoE4 Mice Associated with Enhanced Generation of Hippocampal Reactive Oxygen Species." *Journal of Neurochemistry*, August 19, 2016.

Wang, Jian, Alton B. Farris, Kaiming Xu, Ping Wang, Xiangming Zhang, Duc M. Duong, Hong Yi, Hui-Kuo Shu, Shi-Yong Sun, and Ya Wang. "GPRC5A Suppresses Protein Synthesis at the Endoplasmic Reticulum to Prevent Radiation-Induced Lung Tumorigenesis." *Nature Communications* 7 (June 2016): 11795.

Wang, Jian, Xiangming Zhang, Ping Wang, Xiang Wang, Alton B. Farris III, and Ya Wang. "Lessons Learned Using Different Mouse Models during Space Radiation-Induced Lung Tumorigenesis Experiments." *Life Sciences in Space Research* 9 (June 2016): 48–55.

Wang, Yingying, Marjan Boerma, and Daohong Zhou. "Ionizing Radiation-Induced Endothelial Cell Senescence and Cardiovascular Diseases." *Radiation Research* 186, no. 2 (August 2016): 153–61.

Werner, Erica, Huichen Wang, and Paul W. Doetsch. "Role of Pro-Inflammatory Cytokines in Radiation-Induced Genomic Instability in Human Bronchial Epithelial Cells." *Radiation Research* 184, no. 6 (December 2015): 621–29.

Wilson, John W., Tony C. Slaba, Francis F. Badavi, Brandon D. Reddell, and Amir A. Bahadori. "3DHZETRN: Neutron Leakage in Finite Objects." *Life Sciences in Space Research* 7 (November 2015): 27–38.

Wilson, John W., Tony C. Slaba, Francis F. Badavi, Brandon D. Reddell, and Amir A. Bahadori. "Solar Proton Exposure of an ICRU Sphere within a Complex Structure Part I: Combinatorial Geometry." *Life Sciences in Space Research* 9 (June 2016): 69–76.

Wilson, Paul F. "Magnification of Inter-Individual Variation in Biological Responses After Low Doses and Dose-Rates of Ionizing Radiation." *Health Physics* 110, no. 3 (March 2016): 296–98.

Wu, Yuehan, Suk-Hee Lee, Elizabeth A. Williamson, Brian L. Reinert, Ju Hwan Cho, Fen Xia, Aruna Shanker Jaiswal, et al. "EPPD1 Rescues Stressed Replication Forks and Maintains Genome Stability by Promoting End Resection and Homologous Recombination Repair." *PLoS Genetics* 11, no. 12 (December 2015): e1005675.

Wyrobek, Andrew J., and Richard A. Britten. "Individual Variations in Dose Response for Spatial Memory Learning among Outbred Wistar Rats Exposed from 5 to 20 cGy of (56) Fe Particles." *Environmental and Molecular Mutagenesis* 57, no. 5 (June 2016): 331–40.

Yun, Sanghee, Michael H. Donovan, Michele N. Ross, Devon R. Richardson, Robin Reister, Laure A. Farnbauch, Stephanie J. Fischer, et al. "Stress-Induced Anxiety- and Depressive-Like Phenotype Associated with Transient Reduction in Neurogenesis in Adult Nestin-CreERT2/Diphtheria Toxin Fragment A Transgenic Mice." *PLoS One* 11, no. 1 (January 2016): e0147256.



Human Research Program

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