EXPERIMENTAL DESIGN FOR PRE-CLINICAL ANIMAL MODEL STUDY IN MICROGRAVITY

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Abstract

The Rodent Research program at NASA's Ames Research Center (ARC) has pioneered a new research capability on the International Space Station in less than four years and has progressed toward translating research to the ISS utilizing commercial rockets, collaborating with academia and science industry, and training crew for research purposes on-orbit. Animal models are the foundation of pre-clinical research to understand human diseases and evaluate new therapeutics. Advancement in alleviating ground diseases such as muscle atrophy and osteoporosis can come from the study of similar conditions that are known to occur as a result of exposure to the spaceflight environment. During the completion of the flight phase of two missions, our practices, hardware and operations evolved from tested to developed standards, which successfully translated the studies from ground to space. Results from these studies contribute to the science community via both the primary investigation and banked samples that are shared in publicly available data repository such as GeneLab. Every completed mission sets a foundation to build and design greater complexity into future research and answer questions about common human diseases on ground and in space. Here, we present methods developed for the translation of a rodent experiment to the ISS including a description of hardware and kits available for investigators and a discussion of operational constraints.

Introduction

Aging diseases are more prevalent as the population rises and quality of life extends life expectancy. Unmet medical needs of diseases such as muscle atrophy and osteoporosis can be modeled and studied in spaceflight as physiologic and systemic functions progress four times faster than on ground. The Rodent Research payload aims to maximize the science return by expanding technical capabilities. The materials, reagents, and methods are carefully examined and developed into hardware, kits and operations for the experiment. These hardware, kits and operations must meet standards that are safe to Space Station and crew, compatible with microgravity, and minimize the use of crew time.

www.nasa.gov/ames/research/space-biosciences

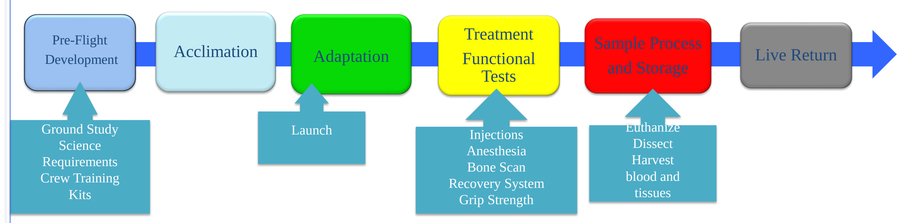
Rodent Research Experiment Timeline

20-G Human Centrifuge, ARC, Moffett Field, CA. Use for pre-flight ground study and live return Ground Controls in the future.

SpaceX, Cape Canaveral, FL. Only Life Science Launch vehicle for RR up to date.

ISS, Low Earth Orbit. Rodent Research Operations.

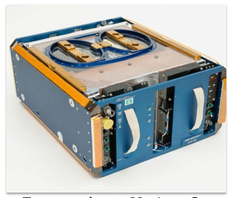
Sample Return, Long Beach, CA.



Hardware

Hardware developed to be compatible for microgravity and meet safety of Space Station.

Animal Enclosure Module

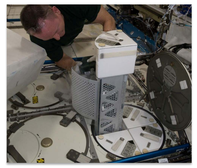


- Transporter houses 20 mice or 5 rats for ascent, water and food compartments, powered for ascent. Can be used for live return capability in descent in the future.
- Habitat houses 10 mice for on-orbit operations, water and food compartments. Equipped with cameras, telemetry outputs, thermal and power sensors.

Microgravity Science Glovebox

Workbench equipped with power outlet and air circulation, holds dissection table, back panel for kits, velcro to anchor dissection tools, racks, cold storage, biohazard sharps container, mouse transfer box, RFID reader, anesthesia recovery system, grip strength meter and more. Can accommodate more capabilities.

MELFI



Three standalone (with 4ºC, -35ºC and-80ºC setpoints) racks on ISS. Sample storage for post-flight OMICS study.

GLACIER

4ºC to -160ºC on ISS in EXPRESS rack. Up to -95ºC on visiting vehicle upon launch or return.

Anesthesia Recovery System

Thermal support for mice to aid recovery from anesthesia.

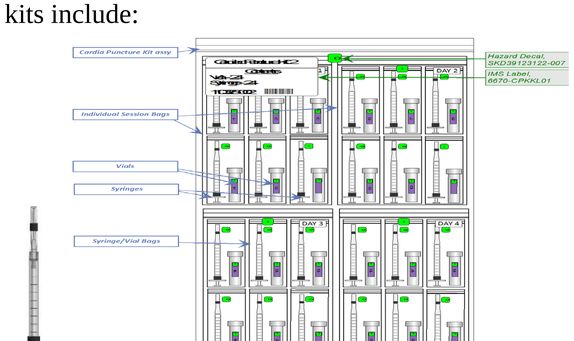
Grip Strength Meter

Measures limb and body strength.

Kits

Kits are developed according to the needs and requirements of the experiment. Syringes customized with silicone plugs at needle end and can endure storage temperatures from -120ºC to ambient. Chemicals used up to Toxicity level 1. Previous and upcoming mission kits include:

Cardiac Puncture Kit
Anesthesia Kit
Tissue Fixation Kit
Ambient and Refrigerated Syringe Kits



Operations

Pre-flight ground studies are developed and tested at Ames, the laboratory of the PI, or other NASA centers.. For flight, the Ground Control experiment is conducted at Kennedy Space Center. In preparation for flight, animals are RFID microchipped, tested for pathogens, and acclimated to a flight-like cage environment under the supervision of trained Animal Care Facility staff. Designated groups for Flight (FL) and Ground Controls (GC) are housed in Transporters for ascent to the ISS. During flight, Flight and Ground Controls are housed in Habitats. Experiment conditions are matched for Flight and Ground Controls groups, with Ground Controls being performed or a time delay (typically 3-4 days) after the Flight groups. On-orbit sessions are performed during crew work hours in GMT. Animal welfare is monitored via a video feed from the Habitats. Current procedures onboard the ISS include:

Injections
Bone Scan
Grip Strength
Anesthesia Recovery
Dissection
Blood Centrifuge
Tissue Preservation
Carcass Preservation

ISSES for Ground Controls, Kennedy Space Center, FL

Science Operations Center for Flight Ames, CA

Conclusion

Our progress in expanding the technical capabilities for Rodent Research and translating ground science to spaceflight provides breakthroughs for science in microgravity. The advantages of microgravity research are to advance the understanding of aging diseases using animal models, to contribute to creating new medicines on ground, and to expand the science in conjunction with innovative technology. The disadvantages are the large-scale cost of up mass, crew time and safety that limit the current animal group size and unaddressed experiment variables. Moreover, the Rodent Research program strives to create more science return in developing more capabilities for upcoming missions.

Acknowledgments

We would like to thank many Rodent Research team members who helped and supported our work.

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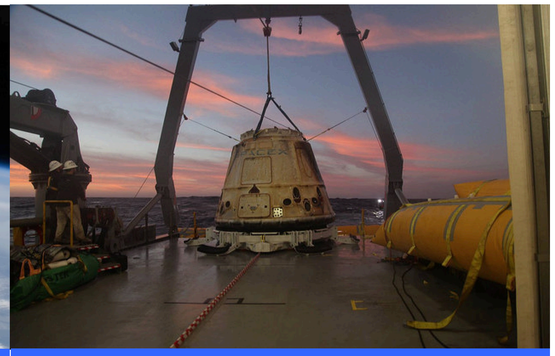

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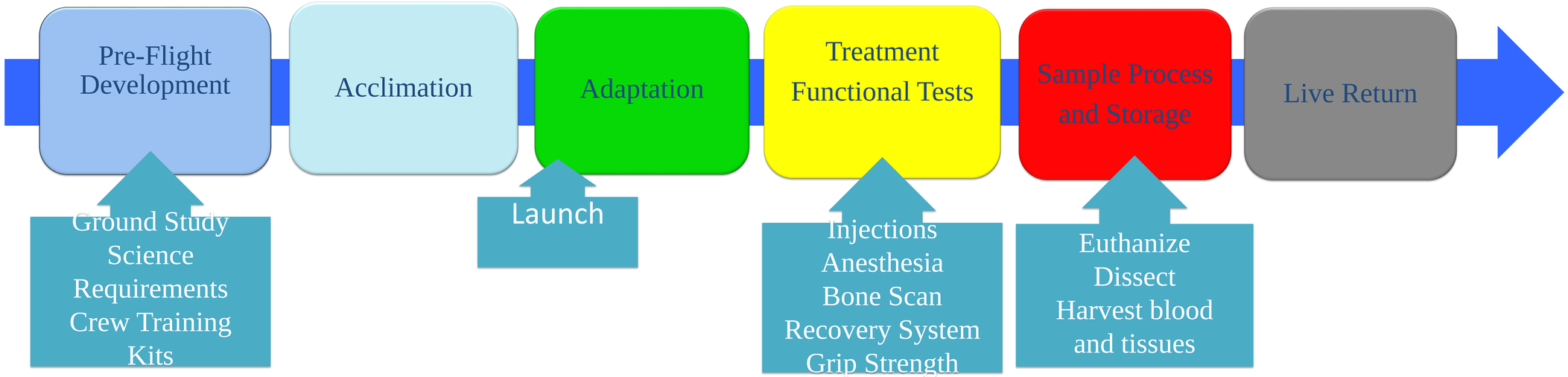

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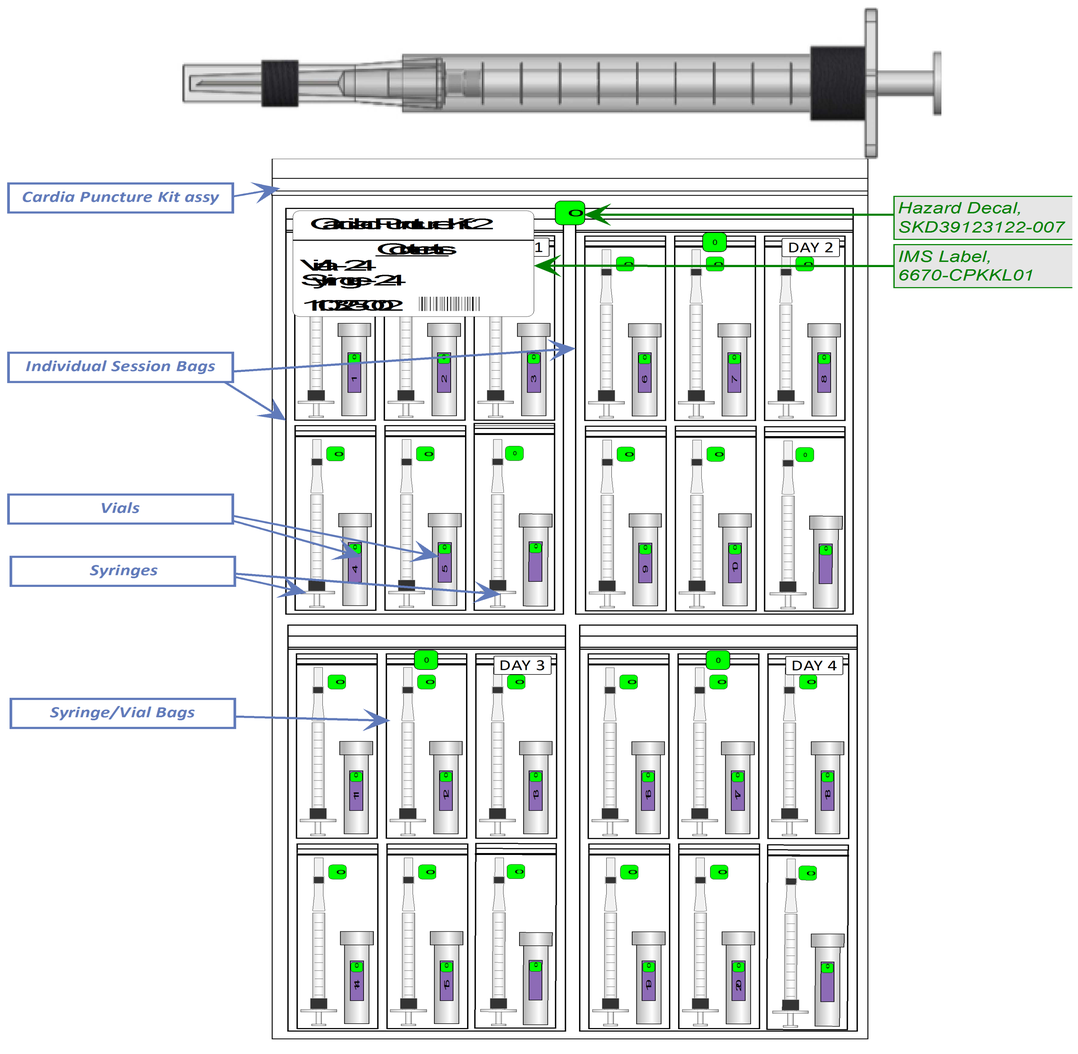

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