NEW DEVELOPMENTS IN NASA'S RODENT RESEARCH HARDWARE FOR CONDUCTING LONG DURATION BIOMEDICAL AND BASIC RESEARCH IN SPACE

Abstract

Animal models, particularly rodents, are the foundation of pre-clinical research to understand human diseases and evaluate new therapeutics, and play a critical role in translating biotechnologies both on Earth and in space. The National Research Council's Decadal survey emphasized the importance of expanding NASA's life sciences research to perform long duration, rodent experiments on the International Space Station (ISS) to accomplish this objective, flight hardware, operations, and science capabilities were developed at NASA Ames Research Center (ARC) to enhance science return for both commercial (CASIS) and government-sponsored rodent research. The Rodent Research program at NASA ARC has pioneered a new research capability on the International Space Station and has progressed toward translating research to the ISS utilizing commercial rockets, collaborating with academia and science industry, while training crewmembers to assist in performing research on orbit.

Starting with a validation mission in 2014, the Rodent Research team has successfully completed four missions to the International Space Station (ISS). In collaboration with commercial, academic, and government entities, the Rodent Research Habitat is capable of supporting researchers to study the effects of spaceflight on the musculoskeletal and neurological systems of mice as well as develop new animal models of human health and disease, particularly in areas of muscle atrophy, bone loss, and fracture healing. Results from these studies contribute to the science community via both the primary investigators and banked samples that are shared in publicly available database such as GeneLab. Following each flight, through the Biospecimen Sharing Program (BSP), numerous tissues and thousands of samples will be harvested, and distributed from the Space Life and Physical Sciences (SLPS) to Principal Investigators (PIs) through the Ames Life Sciences Data Archive (ALSDA). Every completed mission sets a foundation to build and design greater complexity into future research and answers questions about common human diseases.

Approach

Live Animal Return: Concept of Operations

- To support long duration flight experiments with mice as a translational model for human risks in space
- Maximize science return through biospecimen collection and sharing
- Expand science capabilities with each mission, including recent advances to enable live animal return, cage enrichment, male mice as study subjects

Introduction

- Animal studies are a valuable translational model because they facilitate extensive experimentation and application of techniques that cannot be applied to human subjects (e.g. extensive tissue sampling)
- To better understand how mammals adapt to long duration habitation in space, a system for performing rodent experiments on the ISS has been validated by the RR-1 mission and expanded in 4 subsequent missions that included on-orbit animal support and tissue preservation
- To maximize science return, we developed methods to recover multiple tissue types from frozen carcasses following prolonged storage of carcasses that are now being applied to multiple ISS missions

Objectives

- To support long duration flight experiments with mice as a translational model for human risks in space
- Maximize science return through biospecimen collection and sharing
- Expand science capabilities with each mission, including recent advances to enable live animal return, cage enrichment, male mice as study subjects

Materials

Rodent Transporter

- accommodates up to 10 adult mice in each of the 2 compartments

Animal Access Unit

- used by crew to move mice between: Transporter and Habitat OR Habitat and Microgravity Science Glove Box for on-orbit operations, including euthanasia and dissection

Rodent Habitat

- houses mice long-term on the ISS
- accommodates up to 5 adult mice in each of the 2 compartments
- continuously records humidity, temperature, and video capability to monitor health and behavior

Mouse Transfer Box

- used to transport mice between: Transporter and Habitat OR Habitats and Microgravity Science Glove Box (MSGB) OR also used to hold mice during on-orbit activities including injection, food bar changes, dissection, and other activities requiring temporary restraint

Mouse Habitat

- 20 mice

Animal Models

- Multiple Mammalian species from testing to developed standards, and we are able to modify and customize our procedures and operations for mission specific requirements. The Rodent Research Habitat is capable of providing a living environment for animals on ISS according to standard animal welfare requirements. Using the cameras in the Habitat, the Rodent Research team has the ability to perform daily health checks on animals, and further analyze the collected videos for behavioral studies. A recent development of the Rodent Research hardware is inclusion of enrichment, to provide the animals the ability to rest and hide. The Enrichment Hut is designed carefully for adult mice (up to 35 week old) within animal welfare, engineering, and operations constraints. The Hut is made out of the same stainless steel mesh as the cage interior, it has an ingress and egress to allow animals move freely, and a hinge door to prevent animals from escaping. Using the cameras in the Habitat, the Rodent Research team has the ability to develop Live Animal Return (LAR) capability, which will be implemented during Rodent Research 5 mission for the first time. The animals will return through the Habitat, which will return on the Dragon capsule and splash down in the Pacific Ocean. Once Spacecraft retrieves the Dragon, all powered payloads will be transferred to a Sea Van and transferred to the Long Beach pier. The NASA team then receives the Habitat and delivers to a PI designated laboratory within 120 miles radius of Long Beach. This is a significant improvement allowing researchers to examine animals within 72 hours of return to conduct recovery experiments.

Together, the hardware improvements and experience that the Rodent Research team has gained working with principal investigators and ISS crew to conduct complex experiments on orbit are expanding capabilities for long duration rodent research on the ISS to achieve both basic science and biomedical objectives.

Experimental Groups of Mice

- Samples recovered by on-orbit dissection or after return of frozen carcasses post-euthanasia, then distributed to PI or retained in via Life Sciences Data Archive for later distribution to and additional investigators (Russian IBMP, academic and government scientists)

On-orbit video collection

- 5 mice per compartment, 10 per Habitat
- Video feed to the ISS, stored locally
- Air flow to eat up waste in filters
- Video stored in form of avatars
- Water supply (not in image)
- Lighting (dark-light cycle)
- Video cameras (infrared)

Summary of Missions Completed to Date

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Biospecimen Sharing

- Biospecimen sharing enhances science outcome.

RR1 BSS (April 2015)
- 32 tissues from 40 RR-1 Validation mice
- 550-500 tissues stored in microgravity

RR2 BSS (April 2016)
- 35 tissues from 20 untreated mice (10 mice each from the basal, untreated control, and flight groups)
- 1-200 tissues stored in microgravity

RR3 BSS (September, 2016)
- 25 tissues from 30 untreated mice (10 mice each from the basal, untreated control, and flight groups)
- 1-200 tissues stored in microgravity

RR4 BSS (April, 2017)
- 18 tissues from 20 sham operated mice (5 mice each from the basal, untreated control, and flight groups)
- 1-200 tissues stored in microgravity

Summary & Conclusions

Comparison of results between the experimental group (Flight) and various other possible control groups (basal, vivarium, ground control) facilitates interpretation of which independent variable accounts for observed differences.

Acknowledgements