New Developments in NASA’s Rodent Research Hardware for Conducting Long Duration Biomedical and Basic Research in Space

Yasaman Shirazi, Ph.D.
Mission Scientist – Rodent Research
ASGSR
Oct 2017, Seattle, WA

Y. Shirazi-Fard¹, S. Choi², C. Harris², C. Gong², R.J. Fisher¹, J.E. Beegle¹, K.C. Stube², K.J. Martin¹, R.G. Nevitt², R.K. Globus¹

¹ Space Biosciences Division, NASA Ames Research Center, Moffett Field, CA
² KBRWyle, Moffett Field, CA
• Rodent Research Project’s goals:
  • Use of rodents as a translational model
  • To better understand long term adaptation to microgravity
  • To Maximize science return thru BioSpecimen Sharing
  • To expand science capabilities
Rodent Research Hardware

**Rodent Transporter**
- Houses mice during ascent and descent to/from ISS
- Accommodates up to 10 adult mice in each of the 2 compartments

**Rodent Habitat**
- Long-term housing on the ISS
- Accommodates up to 10 mice in one or separate compartments
- Continuous telemetry (%humidity, temperature)
- Video capability to monitor health and behavior

**Animal Access Unit**
- Attaches to Transporter and Habitat
- Used when accessing the animals for transfers, husbandry, or science procedures

**Mouse Transfer Box**
- Holds the animals during transfer to/from Transporter, Habitat, or MSG
- Holds animals in the MSG during science procedures
**Concept of Operations**

1. **Late Load Transporters**
   - Transporter w/ animals (20 mice, 10 days support)

2. **Launch**
   - SpX

3. **Ascent**
   - ~ 3 days

4. **ISS Dock and Animal Transfer**
   - NLT Dock + 48 hours, transfer animals from Transporters to Rodent Habitats (w/ AAU). Stow Transporter for return.

5. **On-Orbit**
   - Rodent Habitat w/o animals (passive transport)

6. **Transfer Remaining Live Animals and samples**
   - Animal Processing System
   - Tissue and Blood Samples
   - Stabilized samples

7. **Descent**
   - (same or next) SpX

8. **Sample Recovery**
   - (same or next) SpX

**On-Orbit ConOps: Animal Processing System**

- Dissections and DXA using the Animal Processing System and Bone Densitometer
- Access Unit
- Mouse Transfer Box
- Rodent Habitat w/ animals (10 mice, 30-45 days support)
- Frozen Samples Refrigerated
- Stabilized Samples
- Bioprocessing and Analysis System
ISS Operations Overview

Habitat

Access Unit

MSG
Rodent Research Capabilities

• Husbandry
  o Supply enrichment
  o Foodbar change out
  o Video health check
  o Group housing

• Environmental Control
  o Telemetry for temperature and % humidity
  o Light cycle
  o Real time alerts

• DXA scanning with anesthesia & recovery

• Sample Recovery and Preservation:
  o Euthanasia & Dissections
  o Cardiac puncture
  o Blood centrifugation
  o Tissue dissection and preservation
  o Fixative swap
  o Grip strength measurements
Capabilities: Video Health Checks

- Daily health checks
  - 1hr per habitat during dark cycle
- Extended video collection for behavioral studies
New Developments: Live Animal Return

Transfer from Habitat to Transporter NET 36hrs before Dragon hatch close

~7hrs

Visual Health Check

Dragon splashdown in Pacific Ocean

~1hr

Transporter/Locker transferred to SeaVan. Telemetry sensors installed.

~48 hrs

NASA delivers Transporter to PI designated lab (within 120 mi). Animals will be checked by PI, attending vet, and NASA science team.

~3-5hrs

NASA receives payload once SeaVan at Pier
New Developments: Enrichment Hut

- Enclosure for rodents to huddle and sleep in
- Supplied as a form of enrichment per animal welfare guidelines
- Made of stainless steel mesh, similar to the cage
- Facilitates animal retrieval by the crew
Maximizing Science Return

Working Microgravity is different than working in a lab on earth

- Investigators are used to processing large numbers of samples in a single day – with large teams, lots of space, no restrictions on time worked, etc.
- We work with Principal Investigators to develop an experiment flow that returns the best possible science results within the constraints for spaceflight research
  - Translates to full crew days and multiple days in a row
  - Time critical operations
- These requirements are captured in our Ground Rules and Constraints
Successfully completed 6 missions to date.
Rodent Research – 1 (SpaceX-4: Sep 21, 2014):

• Objective: Rodent Research Validation Mission

• 20 female C57BL/6J adult mice:
  o 10 (16 week old) for NASA’s validation mission
  o 10 (32 week old) for the National Lab’s science experiment

• Mission duration:
  o 33 days in microgravity (NASA’s Validation)
  o 18 days in microgravity (Novartis)

• Euthanized and dissections performed. Samples returned on SpX5 (Feb 2015)
• Crew times: 75 hrs

• BSP dissection:
  o First thaw: April 2015
  o Second thaw: March 2016
Rodent Research – 2 (SpaceX-6: April 14, 2015):

- Objective: Evaluate muscle atrophy in microgravity and identify molecular pathways and targets that could be used to develop novel therapies for muscle disease.
- PI: Samuel Cadena, Ph.D. (Novartis, CASIS sponsored)
- 20 female C57BL/6J adult mice:
  - 16 weeks old at launch
- Mission duration:
  - 50 days in microgravity
- On-orbit measurements:
  - Bone densitometry scan
- Euthanized and dissections performed. Samples returned on SpX-?
- Crew times: 157 hrs
Rodent Research – 3 (SpaceX-8: April 8, 2016):

- Objective: Evaluate effects of a drug (anti-myostatin) aimed at preventing muscle loss.

- PI: Rosamund Smith, Ph.D. (Elli Lilly, CASIS sponsored)

- 20 female BALB/c adult mice:
  - 12 weeks old at launch

- Mission duration:
  - 45 days in microgravity

- On-orbit measurements:
  - Bone densitometry scan
  - Grip assessment

- Euthanized and dissections performed. Samples returned on SpX-9

- Crew times: 125 hrs

- BSP dissection:
  - September 2016

- **Objective:** Characterize events associated with bone healing/tissue regeneration in a microgravity environment.

- **PI:** Rasha Hammamieh, Ph.D. (Dept. of Defense, sponsored by US Army Center for Environmental Health Research)

- **40 male C57BL/6 adult mice – First Male Mouse Mission**
  - 10 weeks old at launch

- **Mission duration:**
  - 22 days in microgravity

- **Pre-flight procedure:**
  - Bone defect surgery
  - DXA scan

- Euthanized and dissections performed. Samples returned on SpX-10

- **Crew times:** 101 hrs

- **BSP dissection:**
  - May 2017
Rodent Research – 5 (SpaceX-11: June 3, 2017):

• Objective: Systemic Therapy of NELL1 for Spaceflight-Induced Osteoporosis

• PI: Chia Soo, Ph.D. (UCLA, CASIS sponsored)

• 40 female BALB/c adult mice – First Live Animal Return
  o 32 weeks old at launch
  o 20 for Live Animal Return on SpX-11 (LAR)
  o 20 for ISS Terminal (IT)

• Mission duration:
  o 30 days in microgravity (LAR)
  o 60 days in microgravity (IT)

• On-orbit Operations:
  o Bone densitometry scan
  o IP injections

• Euthanized and dissections performed (20). Samples returned on SpX-12

• Crew times: 130 hrs

• BSP dissection:
  o August 2017
Rodent Research – 9 (SpaceX-12: Aug 14, 2017):

• Objective: Effects of Spaceflight on Musculoskeletal and Neurovascular Systems, Cerebral Arterial, Venous and Lymphatic Function: Implications for Elevated Intracranial Pressure.

• PI: Michael Delp, Ph.D. (Florida State University, SLPS sponsored)

• 20 male C57BL/6 adult mice – *New Habitat Configuration*
  o 10 weeks old at launch

• Mission duration:
  o 35 days in microgravity

• Pre-flight measurement:
  o Gait assessment
  o Intraocular pressure

• All 20 mice returned live on SpX-12

• Crew times: 25 hrs

• BSP dissection:
  o Flight group: September 2017
  o Control group: March 2017
Rodent Research – 6 (SpaceX-13, NET Dec 4, 2017):

- **Objective:** To test the efficacy of sustained subcutaneous delivery of formoterol (FMT) released from nanochannel implants in the microgravity mouse model of muscle atrophy.

- **PI:** Alessandro Grattoni, Ph.D. (Houston Methodist, Novartis, CASIS sponsored)

- **40 male C57BL/6 adult mice:**
  - 30-40 weeks old at launch
  - 20 for Live Animal Return on SpX-13 (LAR)
  - 20 for ISS Terminal (IT)

- **Mission duration:**
  - ~30 (LAR) or ~60 (ISS Terminal) days in microgravity

- **Pre-flight procedure:**
  - Nanochannel Delivery System (nDS) implants
  - Tail vein blood collection

- **Euthanasia and dissections to be performed (20). Samples to be returned on SpX-14**

- **Crew times:** ~145 hrs

- **BSP dissection:**
  - TBD
Summary

• Continuously expanding science capabilities, and refining sample collection and preservation methods
• Achieving both basic and translational research objectives.
• Maximizing science return through the Biospecimen Sharing Program (BSP), sponsored by NASA’s Space Biology Program
• Increased frequency of missions allowing for more science investigations
Acknowledgements

Rodent Research Science Team
• Yi-Chun Chen
• Vandana Verma, Ph.D.
• America Reyes
• Marie Dinh

Rodent Research Mission Integration & Operations Team

Rodent Research Engineering Team

Rodent Research Crew Training

Science Working Group