

## Advances in Rodent Research Missions on the International Space Station

S.Choi\*, A. Ronca, D. Leveson-Gower, Cynthia Gong, D. Pletcher, C. Wigley, J. Beegle, R. Globus

\*presenting author

Space Biosciences Division, NASA Ames Research Center

A Research platform for rodent experiment on the ISS is an essential tool for advancing biomedical research in space. The Rodent Research allows for experiments of much longer duration than experiments on the Shuttle. NASA's Rodent Research (RR)-1 mission was successfully completed, including post-flight analysis and achieved a number of objectives including validation of flight hardware, on-orbit operations, and science capabilities that were developed at the NASA Ames Research Center. Briefly, twenty C57BL/6J adult female mice were launched on the SpX4 Dragon vehicle, which thrived for up to 37 days in microgravity. Daily health checks of the mice were performed during the mission via downlinked video; all animals were healthy and displayed normal behavior without any significant signs of stress. Behavioral analysis demonstrated that Flight and Ground Control mice exhibited the same range of behaviors, including eating, drinking, exploratory behavior, self- and allo-grooming, and social interactions indicative of healthy animals.

The animals were euthanized and select tissues were collected from some of the mice on orbit to assess the long-term sample storage capabilities of the ISS. The data obtained from the flight mice were comparable to those from the 3 groups of control mice (baseline, vivarium and ground controls), suggesting that the ISS has adequate capability to support long-duration rodent experimentations.

We recovered over 35 tissues from 40 RR1 frozen carcasses, yielded over 3200 aliquots of tissues, and distributed to the scientific community, including NASA's GeneLab and scientists in the U.S. through Biospecimen Sharing Program via Ames Life Science Data Archive. Tissues were also distributed to Russian research colleagues at the Institute for Biomedical Problems. The expression levels of select genes including albumin, catalase, GAPDH, HMGC0A Reductase, and IGF1 were determined using RNA isolated from the livers by qPCR and no significant differences by one factor ANOVA were found between flight and ground control groups. In addition, some of the liver samples were subject to transcriptomics, epigenomics and proteomics. The data are now available to the scientific community through GeneLab's open science data website.

Since the RR1 mission, another long duration mission (Rodent Research-2) was completed on the ISS in 2015 in which 20 female C57 BL/6J mice were successfully maintained on the ISS for varying time points, with the last group of 5 animals being on-orbit for 54 days. This second Rodent Research flight expanded the program's capabilities with the introduction of new technologies including blood collection and separation and bone densitometry scanning. Furthermore, we have continued to expand the ISS's capabilities by running a series of ground-based verification testing using male mice. Our next step is to fly male mice for Rodent Research-4 on SpaceX-10 to study the effects of microgravity on bone healing and regeneration. It will be the first long-duration mission using male mice using Rodent Hardware. In addition, the number of mice will increase from 20 mice (on RR-1 and RR-2) to 40 for RR-4. When samples return to Earth, a number of tissues will be dissected from the frozen carcasses and select tissue samples will become available to the scientific community via BSP. Altogether, we have continued to expand our capabilities for performing long-duration missions on the ISS as emphasized in the National Research Council's Decadal Survey released in 2011 and to maximize science return from each mission.