MAIDEN VOYAGE OF THE RODENT HABITAT ON ISS: OPPORTUNITIES FOR INVESTIGATING MOLECULAR MECHANISMS AND BIOMEDICAL CONSEQUENCES OF LONG DURATION SPACEFLIGHT

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Research using rodents is an essential tool for advancing biomedical research on Earth and in space. The National Research Counsel's Decadal survey (1) emphasized the importance of expanding NASAs 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 ARC to support both commercial and government-sponsored research.

In preparation for the maiden voyage of the Rodent Habitat hardware and operations system (Rodent Research-1), and in close consultation with a Science Working Group comprised of veterinarians and experienced spaceflight investigators, we modified existing Animal Enclosure Module hardware, developed new hardware, operations, and science activities, and performed a series of ground-based verification tests.

Preflight, groundbased hardware tests included a simulation of SpaceX Dragon launch conditions (vibration and hypergravity) using the Transporter, and also two long-term biocompatibility tests (32 and 92 days) using the Habitat developed for long term housing on the ISS. The launch simulation test showed that adult mice housed in Transporter hardware adapted well, even if launch simulation was followed by a period of simulated weightlessness (via hindlimb unloading). The biocompatibility tests demonstrated that the Habitat successfully supported animal health and also provided a useful video imaging system that enables frequent monitoring of animal health and behavior by veterinary and scientific experts on the ground, independent of ISS crew intervention. At the conclusion of all tests, mice were deemed healthy and suitable for conducting biological research.

Additional preflight analyses of tissues preserved by freezing or fixation for gene expression analyses revealed that spleen and liver tissues recovered under conditions that simulated on-orbit activities yielded high quality RNA (RIN values 8-10) and liver enzyme activities and protein content (e.g. catalase). In addition, new methods were developed to optimize future science return by dissecting tissues post-euthanasia and storage. Various tissues were harvested from either intact or partially dissected, frozen carcasses after storage for ~2-6 months; most of the tissues (brain, heart, kidney, eye, adrenal glands and skeletal muscle) were of high RNA quality for science return, whereas some tissues (small intestine, bone marrow and bones) were not. These data demonstrated the protocols developed for future flight experiments supported science return despite delayed preservation post-euthanasia or prolonged storage, and furthermore, that high-quality RNA samples from many different tissues can be recovered by dissection following prolonged storage of the tissue *in situ* at -80˚C.

The first flight experiments carrying 20 mice were launched on Sept 21, 2014 in an unmanned Dragon Capsule, SpaceX4; Rodent Research-1 is dedicated to achieving both NASA validation and CASIS science objectives. Groundbased control groups (housed in flight hardware or standard cages) were maintained in environmental chambers at Kennedy Space Center. Crewmembers previously trained in animal handling transferred mice from the Transporter into Habitats under simultaneous veterinary supervision by video streaming and were deemed healthy. Health and behavior of all mice on the ISS was monitored by video feed on a daily basis. The 10 mice for validation (16wk old, female C57Bl6/J) ambulated freely and actively throughout the Habitat, relying heavily on their forelimbs for locomotion. The first on-orbit dissections of mice were performed successfully on Oct 12 and 13, 2014, and the validation mice will reside on ISS for up to 30 days.

In conclusion, new capability for long duration rodent research is under development, including in-flight sample collection (which avoids the complication of reentry); results obtained to date will be described. This new Rodent Research system enables achievement of both basic science and translational research objectives to advance human exploration of space.

REFERENCE

[1] NRC Decadal Survey on Biological and Physical Sciences in Space, (2011)
http://sites.nationalacademies.org/SSB/CompletedProjects/SSB_067720