Systemic Microgravity Response: Utilizing GeneLab to Develop Hypotheses for Spaceflight Risks

Afshin Beheshti[1,2], Homer Fogle[1], Jonathan Galaska[3], Yared Kidane[1], Kaushik Chakravarty[1], Daniel Berrios[4], Sylvain V. Costes[3]

[1]WYLE, NASA Ames Research Center, Moffett Field CA

[2]Division of Hematology/Oncology, Molecular Oncology Research Institute, Tufts Medical Center, Boston, MA

[3]NASA Ames Research Center, Space Biosciences Division, Moffett Field, CA

[4]USRA, NASA Ames Research Center, Moffett Field, CA

Biological risks associated with microgravity is a major concern for space travel. Although determination of risk has been a focus for NASA research, data examining systemic (i.e., multi- or pan-tissue) responses to space flight are sparse. The overall goal of our work is to identify potential “master regulators” responsible for such responses to microgravity conditions. To do this we utilized the NASA GeneLab database which contains a wide array of omics experiments, including data from: 1) different flight conditions (space shuttle (STS) missions vs. International Space Station (ISS); 2) different tissues; and 3) different types of assays that measure epigenetic, transcriptional, and protein expression changes. We have performed meta-analysis identifying potential master regulators involved with systemic responses to microgravity. The analysis used 7 different murine and rat data sets, examining the following tissues: liver, kidney, adrenal gland, thymus, mammary gland, skin, and skeletal muscle (soleus, extensor digitorum longus, tibialis anterior, quadriceps, and gastrocnemius). Using a systems biology approach, we were able to determine that p53 and immune related pathways appear central to pan-tissue microgravity responses. Evidence for a universal response in the form of consistency of change across tissues in regulatory pathways was observed in both STS and ISS experiments with varying durations; while degree of change in expression of these master regulators varied across species and strain, some change in these master regulators was universally observed. Interestingly, certain skeletal muscle (gastrocnemius and soleus) show an overall down-regulation in these genes, while in other types (extensor digitorum longus, tibialis anterior and quadriceps) they are up-regulated, suggesting certain muscle tissues may be compensating for atrophy responses caused by microgravity. Studying these organ/tissue-specific perturbations in molecular signaling networks, we demonstrate the value of GeneLab in characterizing potential master regulators associated with biological risks for spaceflight.