Mice Exposed to Combined Chronic Low-Dose Irradiation and Modeled Microgravity Develop Long-Term Neurological Sequelae

Eliah G. Overbey1,2, Amber M. Paul2,3, Willian A. da Silveira4, Candice G.T. Tahimic3,4, Sigrid S. Reinsch2, Nathaniel Szewczyk4, Seta Stamboully2, Charles Wang4, Jonathan M. Galazka5, and Xiao Wen Mao6

† These authors contributed equally to this work.

1: Department of Genome Sciences, University of Washington
2: Space Biosciences Division, NASA Ames Research Center
3: Institute for Global Food Security (IGF), School of Biological Sciences
4: Universities Space Research Association
5: KBR, Moffett Field
6: MRC-UKU Centre for Mammalian Aged Research & National Institute for Health Research Nottingham Biomedical Research Centre
7: Division of Biomedical Engineering Sciences (DBES), Department of Basic Sciences, Loma Linda University
8: Center for Geriatrics, School of Medicine, Loma Linda University
9: Department of Basic Sciences, School of Medicine, Loma Linda University
† These authors contributed equally to this work.

Introduction

How rapidly do astronauts recover neurologically from spaceflight? Evidence suggests that astronauts can experience cognitive impairment while in space, but we don’t know how long gene expression changes in brain tissue persist once returned to Earth. This study works towards the long-term goal of uncovering the length of time that astronauts need to in order to re-adapt to Earth after returning from their missions.

In our experiment, mice were exposed to modeled microgravity (hindlimb unloading) and low-dose radiation (cobalt plates). RNA sequencing data was collected from brain tissue and analyzed for differentially expressed genes and their corresponding functions.

Results

Experimental Design

Differentially Expressed Genes Profile for Combination Group

Gene Ontology (GO) and Pathway Analyses

Discussion

• The combination group and each individual conditions do not share any overlapping differentially expressed genes. Each group had a distinct set of differentially expressed genes.
• Differentially expressed genes in the combination group suggest increased transcriptional machinery, increased neurogenesis and neurotrophic production, dysregulated cell structure and cell signaling at the 4 month timepoint.

A combination of spaceflight-relevant factors (fluid-shift and radiation) created a different gene expression profile than either factor individually.

Gene expression differences can persist for at least 4 months after a 21-day exposure to a combination of fluid-shift and radiation in the brain tissue of mice.