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POSTER ABSTRACTS

501.HEMATOPOIETIC STEM AND PROGENITOR CELLS AND HEMATOPOIESIS: BASIC AND TRANSLATIONAL

A Longitudinal Study to Assess Hematopoietic Stem Cell and Immune Cell Health in Astronauts Pre-, during, and Post-Mission

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The International Space Station (ISS) allows research to be done in low earth orbit (LEO), offering a uniquely accelerating environment to model disease and study human health. Studies done in microgravity can simulate models of stress, inflammation, aging, immune dysfunction, and pre-malignant transformation of stem cells. The NASA Twins Study suggests that extended periods of spaceflight may affect hematopoietic stem cell and immune cell health and function through their multi-omics approach of one ground-based twin, Mark Kelly, and one on board the ISS, Scott Kelly (Garrett-Bakelman et al., Science, 2019). A recent study also suggests an adaptive response to immune cell activity related to pre- and post-flight long-term missions after transcriptomic analysis of astronaut blood samples (Stratis, et al., Frontiers in Immunology, 2023). These studies emphasize the importance of assessing astronaut hematopoietic stem cell and immune cell function to further understand the mechanisms of cellular and molecular changes associated with time spent in LEO.

We designed a longitudinal study to collect (under an IRB-approved protocol) peripheral blood from Axiom Mission 2 (Ax-2) astronauts to assess their hematopoietic stem cell and immune cell health. Timepoints include Launch-45 days, Launch-2 days, inflight, Return+1 day, Return+50 days, and yearly for 5 years. Ax-2 was a 10-day mission which launched on May 21, 2023 and splashed down on May 31, 2023. This was a private crew-tended mission with a sample size of 4 astronauts.

As part of the stem cell health and fitness assessment, we selected for CD34+ hematopoietic stem and progenitor cells (HSPCs) from the 4 private astronauts and performed functional survival and self-renewal assays from each timepoint. Preliminary results suggest that the self-renewal capacity of HSPCs decreases inflight, but upon Return+1 day, HSPCs regain their ability to clone themselves at a higher capacity than pre-flight. Furthermore, we collected HSPCs for whole genome sequencing, 10x Genomics single cell sequencing, and whole transcriptome sequencing, to analyze pre-, during, and post-flight genomic and transcriptomic changes. Analyses will be done to identify mutational burden and mutational signatures associated with each timepoint. These mutational signatures will be compared to previously identified C-to-T mutations to assess the pre-malignant status of HSPCs due to short-term spaceflight (Jiang et al., Cell Reports, 2021). In addition to assessing CD34+ HSPC health, we will also profile the immune landscape by sequencing in parallel the CD34- fraction and performing targeted FACS analysis based on initial sequencing results. We also seek to identify markers of inflammation and anti-viral response through analysis of cytokines from biobanked plasma.

This investigation has the potential to provide valuable insight into stem cell and immune cell health and fitness associated with short-duration missions in LEO.

Disclosures No relevant conflicts of interest to declare.

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