Deep Profiling of the Spaceflight Plasma Proteome reveals Changes in Reactive Oxygen Species, Extracellular Matrix and Lipid Metabolism

INTRODUCTION

The radiation landscape present in space combined with the interstitial fluid and blood volume shifts that occur in microgravity creates a unique set of factors that influence human health. To better understand these changes, we profiled plasma from circulating blood of the Inspiration4 crew (n=4 astronauts) collected via venipuncture at three time points before and after their 3-day spaceflight.

Longitudinal deep profiling of the proteome

Plasma was isolated from BD cell processing tubes (CPTs) containing sodium heparin. Crew plasma samples were processed using Seer’s 5 nanoparticle (NP) sample processing to generate purified peptides for LC-MS/MS analysis. Peptides were analyzed by DIA LC-MS/MS using a 20 min gradient for each of the 5 nanoparticles of each sample, on a Bruker timsTOF Pro 2 followed by data upload and DIA/NN data processing in Seer’s Proteograph Analysis Suite.

Materials and methods

Sample collection

Proteomic changes in Postflight vs Preflight samples

• We identified a total of 2,992 unique protein groups at a cutoff of 1% false discovery rate.
• Each sample had on average 2,104 proteins and 1,154 were common to all samples.

Temporal dynamics of affected proteins

Conclusions

• We identified 22 upregulated proteins and 28 downregulated proteins when comparing postflight to preflight.
• These proteins were enriched in oxidative stress pathways, collagen and ECM and lipoprotein and lipid metabolism.

• Using deep whole proteome profiling, we identified 50 differentially abundant proteins (adj p-value <0.1 and |log2FC| > 1) in all postflight vs all postflight samples.
• When comparing proteins dysregulated immediately postflight (R+1 days), we found that some proteins returned to preflight levels by R+82 days while others were still dysregulated at R+82 days.
• Even short-term spaceflight can have an impact on human physiology which needs further investigation and monitoring.