

Investigating altered liver metabolic function following spaceflight

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Microgravity induces deleterious effects, including muscle atrophy. However, little is known about the effect of spaceflight on liver function and a metabolic profile of liver has not been characterized. We obtained liver tissue from $n = 6$ mice flown aboard STS-135, with age-matched ground and baseline controls. Analysis of the samples was performed by Metabolon, and a total of 298 metabolites were identified. 38 metabolites were significantly downregulated in spaceflight and 21 were significantly upregulated with spaceflight. Using the Human Metabolome Database, a list of enzymes correlating to the metabolites was compiled. 229 enzymes correlated with downregulated metabolites, 297 correlated with upregulated metabolites and 23 enzymes correlated with both up and downregulated metabolites. Analysis using EGAN software (akt.ucsf.edu) for genes correlating with downregulated metabolites suggested that the most highly enriched KEGG pathways were metabolic pathways (2.69 E-79) and fat digestion and absorption (3.7 E-36). Fatty acid and amino acid metabolic pathways were also highly enriched. Nicotinate and nicotinamide metabolic pathways were among the most highly enriched KEGG pathways for genes correlated with upregulated metabolites (6.92 E-21). Analysis of gene ontology (GO) terms showed that lipid metabolic processes, including lipase and oxidoreductase activity, were the most enriched for downregulated metabolites. In contrast, functions correlating to upregulated metabolites included ligase and transferase activities; among them, NAD+ADP-ribosyltransferase activity was enriched (3.33 E-09). Continued analysis of these results will provide more insight on the role of microgravity in altering liver metabolism that may contribute to pronounced muscle atrophy in long-term spaceflight.

Biography

Karen R Jonscher earned her Ph.D. in Applied Physics in 1996 from the California Institute of Technology pioneering mass spectrometry instrumentation and large-scale analytical methods for proteomics applications. She directed a proteomics facility at the University of Colorado and has published over 30 papers. She recently transitioned from core facility direction to biomedical research, and has focused on metabolomic analyses. Her lab seeks to characterize the effect of maternal obesity on offspring liver and kidney mitochondrial function, and with collaborators at the University of Colorado Boulder and Loma Linda University, is also interested in effects of microgravity on cellular metabolism.

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