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MUSCLE ATROPHY TRANSCRIPTOME PHENOTYPE IS LINKED TO LIVER LIPID METABOLIC PROCESSES GENES EXPRESSION IN MICE DURING SPACEFLIGHT

Abstract

Humans have permanently inhibited space for the last twenty years and outer space settlement is the new goal of the next ongoing decades. During spaceflight, astronauts, and other living organisms cope with several space stressors such as space radiation, microgravity, isolation and confinement, impaired day/light cycles, hostile conditions, and distance from Earth. Theses stressors induce physiological changes that can become deleterious during both spaceflight and gravity re-exposure thus impairing our planetary goal. Mitochondrial stress is a central biological hub for spaceflight impact and abnormal metabolic feature are consistently found in biological tissues exposed to space conditions. The muscle and the liver are two master organs of the metabolism and are among the most affected tissues during spaceflights. An intricated role of both the liver and the muscle is often demonstrated on Earth metabolic diseases. However, the molecular dynamics of the two organs in response to space exposure has been poorly, if never, yet studied. In the present study, we compared the transcriptome response in the liver and in the quadriceps of mice from the NASA Rodent Research 1, after 37 days sojourn in space. Using GeneSet Enrichment Analysis, Over Representation Analysis and the R- MixOmics package, we found that lipid metabolism is the most commonly affected biological process between the two organs (p-value ¡ 0.05, FDR ¡ 0.05). Moreover, liver lipid metabolic processes strongly correlate with a hyperglycemic transcriptomic response in the muscle, mostly affecting glucose import (p-value ¡ 0.05, FDR ¡ 0.05). Consistently energy demand processes as DNA Repair, Autophagy, and Translation are downregulated and correlate with liver lipid metabolic processes (p-value ¡ 0.05, FDR ¡ 0.05). We identified a specific gene cluster expression pattern correlating with muscle atrophy phenotype genes. Together our results strongly suggest that a metabolic alteration and a bioenergetic stress are key events in spaceflight-induced muscle atrophy and liver dysfunction, by promoting energy saving, glucose use avoiding, and proteins decrease in the muscle. Exercises improve the conditions of patients with Non-Alcoholic Fatty Liver, Obesity, Diabetes, with without sarcopenia. Thus, exercises and lifestyle modifications are still currently the strongest and easiest countermeasures against spaceflight-induced physiological changes. Energy challenge is an overall humanity challenge both on Earth and beyond, and as such, this study concerns a large part of the worldwide population.