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Author: Dr. Cora S. Thiel
University of Zurich, Switzerland

Dr. Svantje Tauber
University of Zurich, Switzerland
Mrs. Swantje Hauschild
University of Zurich, Switzerland
Dr. Beatrice Lauber
University of Zurich, Switzerland
Mrs. Jennifer Polzer
University of Zurich, Switzerland
Dr. Katrin Paulsen
University of Zurich, Switzerland
Dr. Liliana E. Layer
University of Zurich, Switzerland
Prof. Oliver Ullrich
University of Zurich, Switzerland

ADAPTATION TO MICROGRAVITY IN CELLS OF THE IMMUNE SYSTEM

Abstract

The immune system is one of the most affected systems of the human body during space flight, which raises questions about the cellular capacity for adaptation to a new gravitational environment. During the International Space Station (ISS) experiment TRIPLE LUX A, we measured the oxidative burst reaction in mammalian macrophages (NR8383 rat alveolar macrophages) exposed to a centrifuge regime of internal 0g and 1g controls and step-wise increase or decrease of the gravitational force in four independent experiments and found that these macrophages adapted to microgravity in an ultra-fast manner within seconds, after an immediate inhibitory effect on the oxidative burst reaction. We further investigated the dynamics of gene expression response to different gravitational environments in human Jurkat T lymphocytic cells during a parabolic flight and a suborbital rocket experiment for 44,699 protein coding genes and 22,829 non-protein coding genes and identified a total number of 279 differentially expressed transcripts after 20 s of microgravity (parabolic flight) and 1873 differentially expressed transcripts after 5 min of microgravity (TEXUS). After 20 s microgravity, the transcript differences were detected mostly in regulatory RNAs. We also identified three gravity-regulated genes which could be cross-validated in both completely independent experiment missions: ATP6V1A/D, a vacuolar H+-ATPase (V-ATPase) responsible for acidification during bone resorption, IGHD3-3/IGHD3-10, diversity genes of the immunoglobulin heavy-chain locus participating in V(D)J recombination, and LINC00837, a long intergenic non-protein coding RNA. During the ISS experiment CELLBOX-PRIME, we investigated long-term alterations in primary human macrophages. Surprisingly, we found neither quantitative nor structural changes of the actin and vimentin cytoskeleton after 11 days in microgravity when compared to 1g controls. The analysis of 74 metabolites in the cell culture supernatant by GC–TOF–MS, revealed eight metabolites with significantly different quantities when compared to 1g controls. The surprisingly ultra-fast adaptation of the oxidative burst reaction to microgravity, the extensive and rapid alteration of gene expression associated with regulatory

RNAs, and the cytoskeletal stability after long-term microgravity exposure suggest the existence of a highly efficient adaptation potential to a low gravity environment in cells of the human system.