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Cellular and Genetic Adaptations Involved in Immune Related Functional Responses in Resting and Activated Human T- Cells in Response to Modeled Microgravity.

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Gravity has been present and it has played an important role during the entire course of evolution on our planet Earth, right from the first organic molecule to mammals and humans. The effects of the spaceflight environment on the immune system have been established for some time now but the functional significance of changes in immune responses remains to be answered. Our knowledge of spaceflight induced alterations in genetic response in human lymphocytes has been enhanced by use of ground based spaceflight analog like high aspect ratio wall vessel bioreactors (RWV). The purpose of this study was to search for microgravity sensitive genes and specifically genes in lymphocytic function influenced by the microgravity environment. The experiments were performed on resting and activated human T-cells. The cells were cultured in 1g and modeled microgravity (NASA rotating wall vessel) for 24 and 72 h. We used Affymetrix DNA microarray chips to assess gene expression. Data were collected and subjected to two-way analysis of variance. Different groups of genes related to immune response were then analyzed. Many molecules related to T- cell activation and second messengers, located both in the cell membrane and cytoplasm, were significantly altered (positive or negative regulation) in modeled microgravity. Previous findings in our laboratory showed lymphocyte activation and locomotion to be significantly suppressed in microgravity. Detailed results from the genetic analysis are presented in this study and we have shown that multiple genes (approximately 3 – 8 % of tested genes) respond to microgravity conditions by two and more fold changes in expression. Among the genes showing reproducible changes in expression in modeled microgravity, several regulated genes involved in apoptosis as well as in immune response were identified in both resting and activated lymphocytes. These are IL-7 receptor, Granzyme B, Beta 3 endonexin, Apo 2 ligand, HSP40, HSP70,90, alpha -2-HS-glycoprotein, MHC class II HLA-DRA, Granulysin (TLA519) and STAT1. Possible functional implications of these changes are discussed. Further analysis at the protein levels of genes involved in these responses could lead to development of therapeutic and preventive strategies to cope successfully with medical problems during space exploration.

Key Words: *microgravity, microgravity analog culture system, high aspect ratio wall vessel bioreactor, modeled microgravity, RNA, T- cell activation, three dimensional cell growth.*