Microgravity and immunity: Changes in lymphocyte gene expression.
D. Risin (1)**,** N. E. Ward (2), S. A. Risin (3), and N. R. Pellis (1).

(1) NASA/Johnson Space Center, (2) Wyle Life Sciences, Systems and Services, and (3) Department of Pathology and Laboratory Medicine, UT-Houston Medical School, Houston, TX, USA.

(diana.risin-1@nasa.gov / 281-483-7650)

Earlier studies had shown that modeled and true microgravity (MG) cause multiple direct effects on human lymphocytes. MG inhibits lymphocyte locomotion, suppresses polyclonal and antigen-specific activation, affects signal transduction mechanisms, as well as activation-induced apoptosis. In this study we assessed changes in gene expression associated with lymphocyte exposure to microgravity in an attempt to identify microgravity-sensitive genes (MGSG) in general and specifically those genes that might be responsible for the functional and structural changes observed earlier. Two sets of experiments targeting different goals were conducted. In the first set, T-lymphocytes from normal donors were activated with anti-CD3 and IL2 and then cultured in 1g (static) and modeled MG (MMG) conditions (Rotating Wall Vessel bioreactor) for 24 hours. This setting allowed searching for MGSG by comparison of gene expression patterns in zero and 1 g gravity. In the second set - activated T-cells after culturing for 24 hours in 1g and MMG were exposed three hours before harvesting to a secondary activation stimulus (PHA) thus triggering the apoptotic pathway. Total RNA was extracted using the RNeasy isolation kit (Qiagen, Valencia, CA). Affymetrix Gene Chips (U133A), allowing testing for 18,400 human genes, were used for microarray analysis.
The experiments were performed in triplicates with T-cells obtained from different blood donors to minimize the possible input of biological variation in gene expression and discriminate changes that are associated with the exposure to microgravity.
In the first set of experiments MMG exposure resulted in altered expression of 89 genes, 10 of them were up-regulated and 79 - down-regulated. In the second set, changes in expression were revealed in 85 genes, 20 were up-regulated and 65 were down-regulated. All the altered genes were categorized by their function and their structural role. The analysis revealed that significant numbers of MGS genes are associated with signal transduction and apoptotic pathways. Interestingly, that the majority of genes, that responded by up- or down-regulation in the alternative sets of experiments, were not the same, possibly reflecting different functional states of the examined T-lymphocyte populations.
The responder genes (MGSG) might play an essential role in adaptation to MG and/or be responsible for pathologic changes encountered in Space and thus represent potential targets for molecular-based countermeasures (Supported by NRA OLMSA-02 and NSCORT NAG5-4072 grants).