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# THE INFLUENCE OF ALTERED GRAVITY ON GENE EXPRESSION IN HUMAN CELLS OF THE IMMUNE SYSTEM

**Abstract**

Immunological problems of spaceflight were already discovered since the first Apollo missions, and were subsequently demonstrated during several space missions in the past. However, so far the underlying mechanisms are not revealed and it is still an open question if and how human cells respond to reduced gravity and what is the nature of the gravity sensing machinery. We were using different platforms to investigate the effect of microgravity on key functions of the immune system. During the 19th DLR parabolic flight campaign and the TEXUS-49 sounding rocket mission, we investigated the effect of microgravity on the gene expression pattern of the human monocyte/macrophage cell line U937 representing the antigen-presenting, phagocytosing effector cells of the immune system. Gravity-dependent gene clusters were discovered in both missions. During the 19th DLR parabolic flight campaign, we analyzed gravity-related expression of genes and of immunologically relevant surface molecules after 20s altered

gravity compared to 1g. The expression data showed that most of the genes that were up-regulated in 1.8g were subsequently down-regulated in 0g and vice versa. The genome-wide gene expression analysis during the TEXUS-49 sounding rocket mission confirmed that specific cellular pathways were affected by altered gravity and we could identify gravi-sensitive gene expression of cytoskeleton-associated proteins, NADPH oxidase subunits, the cell-cycle regulation, transmembrane proteins and ion channels. The comparison of the two data sets (20s parabolic flights and 5min sounding rocket) indicates that cells are able to sense altered gravity already after 20 seconds and that a counterbalance program is immediately initiated by a modified gene expression profile. However, in the investigated human monocytic cell line U937, for certain proteins, groups of molecules, and pathways an immediate adaptation program to altered gravity was lacking and differences in gene expression levels were still prominent after 5min for G-protein coupled receptor signaling, p53 signaling and the oxidative stress response. Our results indicate that adaptation on the gene expression level to altered gravity is a basic biological principle and that the prevailing gravity conditions on Earth could be an important requirement for the homeostasis of gene expression regulation in mammalian cells.