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# FUNCTION AND SIGNAL TRANSDUCTION IN CELLS OF THE INNATE IMMUNE SYSTEM IN MICROGRAVITY – RESULTS FROM COORDINATED SPACE AND PARABOLIC FLIGHT EXPERIMENTS

**Abstract**

Sensitivity of cells of the human immune system to reduced gravity has been supposed since the first Apollo missions and was demonstrated during several space missions in the past. However, it is not understood if and how human cells respond rapidly to reduced gravity and how reduced gravity is sensed by a human cell. However, their sensitivity to altered gravity renders cells of the immune system an ideal model system to understand if and how gravity on Earth is required for normal mammalian cell function. In search of rapid-responsive molecular alterations in mammalian cells, short term microgravity provided by parabolic flight maneuvers is an ideal way to elucidate such initial and primary effects, whereas access to space is an instrument to elucidate long-term and functional effects of microgravity.

In a sequence of projects we investigated the effect of microgravity on key functions of monocytic/macrophageal cells, the antigen-presenting, phagocytosing immuno effector cells of the immune system. Such cells belong to the the innate immune system that plays a key role in defending the organism in early phases of infections and diseases and in execution of immune reactions.

During the TEXUS-49 sounding rocket mission in March 2011 (Signal Transduction in Cells of the Immune System, part 1, acronym: SITI-1), we achieved a systematic overview of microgravity-related gene-expression in a human cell line of the monocyte-macrophage system (U937 cells) using genome-wide expression arrays and found gravi-sensitive gene expression in the proteasome system, in the cell-cycle-regulation and in the p53 system. The effects of long-term microgravity were investigated during the first Sino-German space life sciences mission on board the Shenzhou-8 spaceship (SIMBOX mission) in November 2011 (Signal Transduction in Cells of the Immune System, part 2, acronym: SITI-2), where we detected a severe disruption of the actin cytoskeleton and a loss of CD86 and ICAM-1 expression in

macrophageal differentiated human U937 cells during several days in microgravity. During the 19th DLR Parabolic Flight Campaign in February 2012 (Signal Transduction in Cells of the Immune System, part 3, acronym: SITI-3), we analysed gravity-related expression of genes and of immunologically relevant surface molecules after 22s altered gravity in the human monocyte/macrophage cell line U937 and in primary human macrophages. Therefore, the combination of the results from TEXUS-49, SIMBOX/SHENZHOU-8 and the 19th DLR Parabolic Flight Campaign provided an unique overview about initial (seconds), mid-term (minutes) and long-term (days) alterations in cells of the monocyte-macrophage system in microgravity.