The German ISS-Experiment Cellular Responses to Radiation in Space (CERASP): The Effects of Single and Combined Space Flight Conditions on Mammalian Cells

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The combined action of ionizing radiation and microgravity will continue to influence future space missions, with special risks for astronauts on the Moon surface or for long duration missions to Mars. Previous space flight experiments have reported additive (neither sensitization nor protection) as well as synergistic (increased radiation effect under microgravity) interactions of radiation and microgravity in different cell systems. Although a direct effect of microgravity on enzymatic mechanisms can be excluded on thermo dynamical reasons, modifications of cellular repair can not be excluded as such processes are under the control of cellular signal transduction systems, which are controlled by environmental parameters, presumably also by gravity. DNA repair studies in space on bacteria yeast cells and human fibroblasts, which were irradiated before flight gave contradictory results: from inhibition of repair by microgravity to enhancement, whereas others did not detect any influence of microgravity on repair. At the Radiation Biology Department of the German Aerospace Center (DLR) recombinant bacterial and mammalian cell systems were developed as reporters for cellular signal transduction modulation by genotoxic environmental conditions. The space experiment CERASP (Cellular Responses to Radiation in Space) to be performed at the International Space Station (ISS) will make use of such reporter cell lines thereby supplying basic information on the cellular response to radiation applied in microgravity. One of the biological endpoints will be survival reflected by radiation-dependent reduction of constitutive expression of the enhanced variant of green fluorescent protein (EGFP), originally isolated from the bioluminescent jellyfish *Aequorea victoria*. A second end-point will be gene activation by space flight conditions in mammalian cells, based on fluorescent promoter reporter systems using the destabilized d2EGFP variant. The promoter element to be investigated reflects the activity of the nuclear factor kappa B (NF-κB) pathway. The NF-κB family of proteins plays a major role in the inflammatory and immune response, cell proliferation and differentiation, apoptosis and tumor genesis. Results obtained with X-rays and accelerated heavy ions imply that densely ionizing radiation has a stronger potential to activate NF-κB dependent gene expression than sparsely ionizing radiation. The correlation of NF-κB activation to negative regulation of apoptosis could favor survival of cells with damaged DNA.