

6. Summary

Exposure of astronauts to space radiation, together with the reduced gravity level, represents the limiting factor for long-term human space missions. Experiments on the interaction of microgravity and radiation in mammalian cells can be performed only insufficiently on Earth. The International Space Station, as the most important space-based research platform, offers the possibility to perform relevant experiments. One of the first experiments to be flown on the European laboratory module COLUMBUS will be the experiment CERASP (and its successor experiment *Cellpath*). Aim of these experiments is to investigate the modulation of gene expression changes of damage-inducible genes under simultaneous exposure to microgravity and radiation. For that, a cellular test system, which is based on receptor-reporter-principles, was developed. It makes use of a host cell line and a stably integrated vector which controls EGFP expression as reporter protein by a DNA damage responsive element as a sensor. To identify a candidate gene promoter/enhancer, suitable to act as a regulatory element, gene expression studies of damage-inducible genes, whose products are operating in different DNA repair-pathways, were performed in a series of human cell lines using a quantitative real time RT-PCR based approach. The results of these studies showed the p53R2 gene to fulfil the requirements set for the establishment of such an inducible test system. The vector system was designed by inserting the p53 binding site located in the first intron of the gene coding for the inducible form of the Ribonucleotide Reductase (p53R2) in the MCS of the promoterless EGFP-1 vector. The radiation-biological characterisation of the examined cell lines (MCF-7, A549, AGS, NHF, and HEK) identified A549 cells as best suited for hosting the test system. After selection of EGFP expressing cell clones, the recombinant clone A549-RRM2b was chosen for further experiments based on its highly inducible reporter gene expression. This cell line was tested using different experimental treatment conditions. Exposure experiments with various radiation qualities (UV, X-rays, and accelerated carbon and argon ions) revealed the high suitability and significance of the cellular test system for future use in space experiments.