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Gene expression and cYtokine Monitoring for Biodosimetry and RAdiation Sensitivity Screening (GYMBRASS)

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One of the major hurdles for manned interplanetary space exploration is the increased cancer risk due to long-term exposure to cosmic radiation and solar particle events. However, besides cancer, also other adverse health effects may arise in astronauts as a result of exposure to cosmic radiation. In order to better understand and define the biological risks of cosmic radiation, it is important to identify biomarkers for exposure and for predicting individual sensitivity to radiation-induced biological damage.
Based on preliminary experiments in which human peripheral blood mononuclear cells (PBMCs) from 10 different donors were X-irradiated (Pentak HF420 RX machine; 250 keV, 15 mA; dose rate= 0,25 Gy/min) with doses of 0 (control), 0.1 and 1 Gy, we have found evidence that gene expression signatures can be used to predict exposure to doses as low as 0.1 Gy, and possibly to even lower doses. Furthermore, our data show that the use of single exon expression signatures further enhances the sensitivity of the prediction analysis. Both at low and high doses, mainly genes involved in p53-related pathways (cell cycle arrest, DNA repair, apoptosis) were affected, although most of these genes showed a clear dose-dependent response. Finally, our data show that several genes expressed different transcript variants after irradiation. Some of these genes showed marked differences between different donors, indicating that the regulation of radiation-induced transcript variation may be important for the individual response to radiation.
In our project we aim at identifying biomarkers (genes, exons, secreted proteins) for exposure of PBMCs to low (0.05 and 0.1 Gy) and moderate (1 Gy) doses of high-LET (linear energy transfer) heavy ions such as can be encountered in cosmic radiation. Concomitantly, the individual radiosensitivity of blood donors will be assessed using ⍻-H2AX staining. These data will then be integrated with the results from microarrays and protein assays (multiplex array system) to identify markers for individual radiosensitivity screening. All results will be compared to similar doses of low-LET X-ray irradiations in order to obtain more insight into the differences of the biological effects of different radiation qualities.

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