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Chronic low dose rate γ-irradiation of HUVECs: a high throughput gene expression analysis

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Seeing the increasing use of nuclear power, planning of long term space missions, occupational and medical exposures, knowledge about health effects related to chronic low dose exposure are of importance. Recent epidemiological studies indicate an increased risk of cardiovascular diseases at low doses, however a comprehensive understanding of the underlying biological and molecular mechanisms is still lacking. The endothelium plays a pivotal role in normal vascular functioning. Therefore, within the DoReMi Network of Excellence (Task 7.3), we have chosen to assess the effect of chronic low dose rate γ-radiation exposure on Human Umbilical Vein Endothelial Cells (HUVECs) with a particular focus, in our laboratory, on the transcriptomic level by means of whole genome microarray analysis.

The set-up of the irradiation experiments (performed in triplicate) is shown in the table:

week 1	week 3	week 6
0 mGy/h	0 Gy	0 Gy	0 Gy
1.4 mGy/h	0.24 Gy	0.71 Gy	1.41 Gy
4.1 mGy/h	0.96 Gy	2.07 Gy	4.13 Gy

Microarrays were performed in biological triplicates using the Affymetrix Human Gene 1.0 ST Arrays. Analysis of the obtained data was performed using the Partek Genomics Suite v6.5. Single gene analysis showed that the number of differentially expressed genes ($P < 0.05$ and $FC > 1.5$; < -1.5) between control and irradiated cells was in general quite small at all weeks suggesting that low dose rate exposure induces a rather subtle response. Therefore, Gene Set Enrichment Analysis (based on Kegg and Reactome databases) was used to see if predefined gene sets, instead of individual genes, were significantly enriched ($FDR < 0.05$). In general it was observed that after one week, both dose rates activate a broad range of cellular pathways including DNA repair, cell cycle and gene translation and transcription. Also, many gene sets related to cellular metabolism were significantly enriched after one week of exposure. Interestingly, after three weeks, enrichment of gene sets involved in inflammation and immune response was observed in the irradiated cells. After six weeks only a small number of gene sets were enriched in the irradiated compared to control cells. The complete data analysis has revealed interesting pathways that are specifically involved in the chronic low dose rate radiation response of HUVEC.

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