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Characterization of the cellular response of HUVECs and EA.hy926 cells following exposure to low dose acute X-irradiation

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High radiation doses (> 5 Gy) are known to increase the risk of cardiovascular diseases. In recent years, epidemiological data support the fact that lower radiation doses increase the risk of cardiovascular diseases as well (cfr. Atomic bomb survivors). However, lack of statistical power in the epidemiological studies requests a better understanding of the underlying biological and molecular mechanisms for an accurate low dose risk assessment.

The endothelium is believed to be a critical target in the development of radiation-related cardiovascular diseases. Hence, we used primary Human Umbilical Vein Endothelial Cell (HUVEC) and the immortalized derivative endothelial cell line EA.hy926 as models to characterize the endothelial response to acute low and medium doses (0.05 - 5 Gy) of X-irradiation (250 keV, 15mA, 1mm Cu). The dose rate was 0.25 ± 0.01 Gy/min. Investigated endpoints included DNA damage, cell cycle changes and associated apoptosis. In addition, the production of reactive oxygen species (ROS), an important player in both cardiovascular diseases and cellular radiation response, was assessed. DNA damage and repair were studied by means of immunostaining for γH2AX-foci and quantitative fluorescence microscopy respectively 30 min and 24 h post irradiation (p.i.). Apoptosis, cell cycle changes and the production of ROS was assessed by flow cytometry. Apoptosis was investigated 24, 48 and 72 h p.i. using Annexin-V/propidium iodide (PI) costaining. Cell cycle changes were studied 8, 24, 48 and 72 h p.i. via PI staining. Production of ROS was examined 30 min p.i. using the ROS sensitive dye CM-H2DCFDA.

Our results indicate that both in HUVECs and EA.hy926 cells, fundamental cell cycle changes due to G2 arrest is limited to higher dose irradiation (5 Gy). A significant increase of apoptotic cells was observed after 0.1 Gy and higher, but results were not consistent over multiple experiments. The production of ROS was significantly increased after exposure to 0.1 Gy and higher. More subtle, but significant effects such as DNA damage could be observed down to the lowest tested dose of 0.05 Gy. In conclusion, HUVECs elicited in general a less pronounced response compared to EA.hy926 cells as shown by smaller γH2AX-foci number, smaller percentage of apoptotic cells, and a less pronounced G2 arrest.

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