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Cytokine secretion profiles and signaling pathways analysis of endothelial cells exposed to high doses of ionizing radiation

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Vascular injury is one of the most common effects of ionizing radiation on normal tissues due to the high radiation sensitivity of endothelial cells.
The knowledge of molecular mechanisms involved in endothelium dysfunction following radiation exposure is needed to identify therapeutic targets and to develop strategies to prevent and/or reduce effects of irradiation.

Methods : To clarify some molecular mechanisms involved in this response, we examined irradiation-responsive proteins in cultured primary human umbilical vein endothelial cells (HUVEC) using multiplex suspension bead arrays (Bio-Plex suspension array system). In an attempt to study the long term response of irradiated endothelial cells, protein secretion and signaling pathways were studied after exposure of HUVEC to doses of 0, 2 and 20 Gy. The secretion of 27 cytokines (interleukines, chemokines, growth factors) and the levels of 5 intracellular phosphoproteins (Akt, ERK1/2, JNK, P38 MAPK, P53), with their respective total forms, were assayed 1, 2 and 3 weeks after ionizing radiation exposure.

Results : Out of the 27 cytokines, 4 proteins (IP-6, Eotaxin, IL-6 and RANTES) were clearly overexpressed in the culture medium after 21 days. On the other hand, the levels of the intracellular phosphoproteins were all overexpressed 21 days post-irradiation, suggesting that signaling pathways were continuously activated in long-term cultured irradiated HUVECs.

Conclusion : These results clearly indicate that the survival fraction of irradiated HUVEC always display a modified phenotype 3 weeks after ionizing radiation exposure. This phenotype could reflect the continuous expression of stress and inflammatory signals in the survival fraction of irradiated HUVECs.

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