

Radioadaptive Cytoprotective Pathways in the Mouse Retina

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Exposure to cosmic radiation implies a risk of tissue degeneration. Radiation retinopathy is a complication of radiotherapy and exhibits common features with other retinopathies and neuropathies. Exposure to a low radiation dose elicits protective cellular events (radioadaptive response), reducing the stress of a subsequent higher dose. To assess the risk of radiation-induced retinal changes and the extent to which a small priming dose reduces this risk, we used a mouse model exposed to a source of ¹³⁷Cs- γ radiation. Gene expression profiling of retinas from non-irradiated control C57BL/6J mice (C) were compared to retinas from mice treated with a low 50 mGy dose (LD), a high 6 Gy dose (HD), and a combined treatment of 50 mGy (priming) and 6 Gy (challenge) doses (LHD). Whole retina RNA was isolated and expression analysis for selected genes performed by RTqPCR. Relevant target genes associated with cell death/survival, oxidative stress, cellular stress response and inflammation pathways, were analyzed. Cellular stress response genes were upregulated at 4 hr after the challenge dose in LHD retinas (Sirt1: 1.5 fold, Hsf1: 1.7 fold, Hspa1a: 2.5 fold; Hif1a: 1.8 fold, Bag1: 1.7). A similar trend was observed in LD animals. Most antioxidant enzymes (Hmox1, Sod2, Prdx1, Cygb, Cat1) and inflammatory mediators (NF κ B, Ptgs2 and Tgfb1) were upregulated in LHD and LD retinas. Expression of the pro-survival gene Bcl2 was upregulated in LD (6-fold) and LHD (4-fold) retinas. In conclusion, cytoprotective gene networks activation in the retina suggests a radioadaptive response to a priming irradiation dose, with mitigation of the deleterious effects of a subsequent high dose exposure. The enhancement of these cytoprotective mechanisms has potential value as a countermeasure to ocular alterations caused by radiation alone or in combination with other factors in spaceflight environments.