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 137-Cs-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 (NFκB, 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.