

TEMPORAL DEPENDENCE OF CHROMOSOMAL ABERRATION ON RADIATION QUALITY AND CELLULAR GENETIC BACKGROUND

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Radiation induced cancer risks are driven by genetic instability. It is not well understood how different radiation sources induce genetic instability in cells with different genetic background. Here we report our studies on genetic instability, particularly chromosome instability using fluorescence in situ hybridization (FISH), in human primary lymphocytes, normal human fibroblasts, and transformed human mammary epithelial cells in a temporal manner after exposure to high energy protons and Fe ions. The chromosome spread was prepared 48 hours, 1 week, 2 week, and 1 month after radiation exposure. Chromosome aberrations were analyzed with whole chromosome specific probes (chr. 3 and chr. 6). After exposure to protons and Fe ions of similar cumulative energy (??), Fe ions induced more chromosomal aberrations at early time point (48 hours) in all three types of cells. Over time (after 1 month), more chromosome aberrations were observed in cells exposed to Fe ions than in the same type of cells exposed to protons. While the mammary epithelial cells have higher intrinsic genetic instability and higher rate of initial chromosome aberrations than the fibroblasts, the fibroblasts retained more chromosomal aberration after long term cell culture (1 month) in comparison to their initial frequency of chromosome aberration. In lymphocytes, the chromosome aberration frequency at 1 month after exposure to Fe ions was close to unexposed background, and the chromosome aberration frequency at 1 month after exposure to proton was much higher. In addition to human cells, mouse bone marrow cells isolated from strains CBA/CaH and C57BL/6 were irradiated with proton or Fe ions and were analyzed for chromosome aberration at different time points. Cells from CBA mice showed similar frequency of chromosome aberration at early and late time points, while cells from C57 mice showed very different chromosome aberration rate at early and late time points. Our results suggest that relative biological effectiveness (RBE) of radiation are different for different radiation sources, for different cell types, and for the same cell type with different genetic background at different times after radiation exposure. Caution must be taken in using RBE value to estimate biological effects from radiation exposure.