Low-LET and High-LET Radiation Action of 125I Decays in DNA: Effect of Cysteamine on Micronucleus Formation and Cell Killing

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Chinese hamster ovary cells were pulse-labels with 125I-iodo-deoxyuridine during early S phase, and cell samples were harvested 30 min or 5 h after labeling. The samples were frozen (with or without 25 mM cysteamine) and stored at -196˚C for accumulation of 125I decays. X-ray control experiments were performed at 37˚C and -196˚C. Aliquots of cells were plated for evaluating micronucleus formation and cell survival. The results demonstrated a striking shift in micronucleus formation an sell death with time after labeling. Cells frozen 30 min after labeling exhibited effects typical of low-Let radiation, but cells frozen 5 h after labeling showed a response characteristic of high-LET radiation. Cysteamine provided protection against the effects of 125I during the initial phase of effects characteristic of low-LET radiation, but no protection was seen during the phase characteristic of high-LET radiation. When cell survival was evaluated as a function of micronucleus frequency rather than dose in decays/cell, the survival curves for all treatment groups became superimposed. Previous work using the same experimental system had failed to show a direct link between 125I-induced DNA double-strand breaks and cell death. These findings are consistent with the hypothesis that DNA damage may not be the sole mechanism for cell killing and that damage to higher-order structures in the cell nucleus may contribute to (or modify) radiation-induced cell death.

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