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Oral Communication

DIFFERENTIAL EFFECTS OF PROTON- AND γ-RADIATION ON CELL SURVIVAL AND PROLIFERATION

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Abstract

We discuss several effects of proton- and γ-radiation on cell survival, proliferation, and delayed luminescence (DL), in various cell types. For wild-type *Saccharomyces cerevisiae* yeast cells, at an applied dose of 200 Gy, γ-irradiated cells were able to maintain the G_2/M checkpoint active and arrest proliferation for a significant time after irradiation, whereas proton-irradiated cells continued to proliferate at a slightly slower rate than non-irradiated cells. However, clonogenic survival under similar conditions was virtually identical, which provided the relative yield of lethal DNA lesions of about 0.63 for both types of radiations. We estimated the relative yield of DNA lesions that cannot be repaired by the cellular repair systems neither by recovery in the G_0 phase or during growth in normal cell culture medium. The yield of irreparable DNA lesions was 0.31 in proton-irradiated cells as compared to 0.001 in γ-irradiated cells. On a simple account regarding the ionization density in multiply damaged sites on DNA, we estimated that the number of DNA double-strand breaks (dsbs) per cell produced by protons is at least 1.42 higher than that produced by γ rays. Our results are consistent with the idea that radiation-induced cell death could be determined quantitatively by the number of ionization clusters produced in DNA rather than by the total number of dsbs. For both radiation types, the total number of DL 645 nm- photons emitted by irradiated cells remained similar to the control for about 120 min. and 200 min. after γ- and proton-irradiation, respectively, and increased non-monotonically thereafter, with a maximal increase of 2.5-fold with respect to non-irradiated cells. Our results suggest that DL enhancement might be correlated with activation of molecular species involved in cellular repair after irradiation, but not to radiation-induced damage on DNA or microtubules.

We also investigated the relation between calcium homeostasis and apoptosis induction by 10 Gy proton-irradiation in human prostate cancer cells PC-3. By spectrofluorimetric measurements, we observed a maximal increase of 23% in the intracellular Ca^{2+} on PC-3 cell suspensions, at about 7 h after irradiation, which was correlated to the maximal degree of apoptosis, of about 12%. We estimated that over a 10-h window following irradiation, the

cytosolic Ca^{2+} concentration in apoptotic cells remains at high levels, of about 3 times higher than in non-irradiated cells.

We assessed clonogenic survival and delayed luminescence of two other cell types, human Jurkat T-lymphocytes and human glioma cells U87, after treatment with 10 Gy protons. There was a clear difference in cell morphology even at short time after irradiation (2 h). Irradiated Jurkat cells did not display significant differences from their regular morphology, whereas U87 cells presented dramatic changes immediately after proton-treatment. These observations correlated well to the differences in the DL emission, which was unchanged in Jurkat cells but showed a consistent increase in U87 cells.

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