7 CHROMOSOMAL DAMAGE OBSERVED IN FIRST POSTIRRADIATION METAPHASES OF REPAIR-PROFICIENT AND -DEFICIENT CELL LINES

S. Ritter, W. Kraft-Weyrather, K. Fussel, E. Kehr, G. Kraft

Investigation of radiation induced damage in mutant strains of mammalian cells which show a defect in the rejoining of DNA double strand breaks provides an unique opportunity to examine the role of double strand breaks and the mechanisms of double strand break rejoining in the production of chromosome aberrations. This is particularly important, because there is increasing evidence that the DNA double strand break is the major lesion responsible for the formation of chromosome aberrations. To address this issue, we studied the induction of chromosome aberrations in xrs-5 cells, a X-ray sensitive strain of a Chinese hamster ovary cell line, which shows a defect in the rejoining of double strand breaks and their wild-type parent CHO-cells. Because radiosensitivity depends strongly on cellular age, the experiments were performed with synchronous cells.

Both cell lines were synchronised by mitotic shake off and were irradiated in G1-phase with 780 MeV/u Au ions (LET: 50 keV/μm) at the SIS, Darmstadt. For comparison an experiment with 250 kV X-rays was performed. The amount of aberrant cells and aberrations was determined at serial, multiple sampling times following exposure, because recent experiments have shown that the amount of chromosomal damage varies with sampling time (2). By the use of the Fluorescence-plus-Giemsa technique it was assured that the analysis of chromosomal damage was restricted to first postirradiation metaphases. After X-ray exposure xrs-5 cells showed a five fold excess of aberrant cells and a twelve fold excess of aberrations/cell compared to CHO cells (fig 1a, b). After high LET radiation these differences were diminished. The number of aberrant cells was only slightly higher in xrs-5 cells (fig. 1c) and the aberration frequency/cell was only 2 times higher in the mutant strain compared to the wild-type parent (fig. 1d).

Furthermore, the comparison of the aberration types which were induced by densely and sparsely ionizing radiation in both cell lines showed that in CHO cells the distribution of aberration types changes as LET increases, but not in xrs-5 cells. In CHO cells the number of chromosomal breaks was found to rises from 45% after X-ray exposure to 58cells, another repair-proficient Chinese hamster cell line (3). In xrs-5 cells the frequency of X-ray induced breaks was higher than in CHO-cells, i.e. 75% of all aberrations were chromosomal breaks, but there was no further increase following Au ion exposure.

Based on these observations as well as on other studies investigating the rejoining kinetics of radiation induced DNA strand breaks it is evident that X-ray induced lesions are repaired with a high efficiency in CHO cells and only a small amount of these lesions appears cytogenetically as aberrations. In xrs-5 cells however, which show a defect in DNA double strand repair similar doses of X-rays result in a much higher number of aberrant cells and aberrations/cell as shown in fig. 1 indicating that DNA double strand breaks are causal in the production of chromosome aberrations. When the wild-type cells and the mutant cells are exposed to high LET radiation these differences in the amount of chromosomal damage are diminished. Probably, even for repair-proficient cells the lesions induced by densely ionizing radiation are more severe and less rejoinable than those induced by sparsely ionizing radiation. Moreover, densely ionizing radiation seems to inactivate the mechanisms, which are responsible for the formation of exchange type...
aberrations in CHO cells. In xrs-5 cells however, these processes are probably not present or work less efficiently, because there was no increase in the frequency of chromosomal breaks among the total number of aberrations with LET.

Further experiments are in progress to investigate in both cell lines the dependence of the pattern of radiation induced cytogenetical damage from radiation quality.

References

