Biological effects of 12C - heavy ions on tumor cells

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We investigated the induction of chromosome aberrations by carbon ions of different energies in tumor cells of different intrinsic radiosensitivities: MCF-7, an extremely radiosensitive human breast adenocarcinoma cell line and WiDr, an extremely radioresistant colon carcinoma cell line. The aberration yields evaluated in cells in their first postirradiation metaphase (BrdU-method) were constant independently on the culture time. Carbon ions were in general more efficient with respect to the aberration induction than 200 kV X-rays. The frequencies of dicentric chromosomes and excess acentric fragments were always higher for carbon ions as compared with X-rays in both tumor cell lines. However, in the radioresistant WiDr-cells, a pronounced yield of dicentric chromosomes (about 1 dicentric per cell) could be observed just after irradiation with D = 4 Gy in Bragg peak. Representative aberration data for carbon ions in comparison with X-rays, as observed after irradiation with a dose of 1 Gy are shown in fig. 1



Figure 1: Frequency of dicentric chromosomes (a) and extra acentric fragments (b) per cell scored in first post-irradiation metaphases after irradiation with carbon ions (D=1 Gy) with energies of 400, 100 MeV/u and in Bragg peak, in comparison with 200 kV X-rays.

Using the FISH-method, we scored the radiation-induced simple reciprocal translocations as well as complex exchange aberrations. Since tumor cells are genomically unstable, we first analyzed various chromosomes in both cell lines with respect to their stability. Solely chromosomes No. 2, 4 and 5 were suitable for a FISH-analysis: these chromosomes showed in both unirradiated cell lines either no aberrations or one (or two) stable translocations. The

translocation induction was strongly increased for carbon ions as compared with X-rays. Partial translocation yields in WiDr cells irradiated with carbon ions or 200 kV X-rays, as evaluated for chromosome No. 2, are shown as a representative example in fig. 2. Similar results were obtained for chromosomes No. 4 and 5, too. After irradiation with D = 4 Gy, a beginning saturation in the translocation yield could be observed; this is caused by a strong increase in the yield of complex exchanges, as shown in the next figure. Fig. 3 shows the relative proportions of cells containing complex exchanges after irradiation with two different doses of carbon ions or X-rays. Up to 50% of cells irradiated in Bragg peak contained different types of complex exchanges resulting mostly from interactions among 3 different chromosomes.

In summary, a strongly increased biological efficiency of heavy ions is thus confirmed in tumor cells of different intrinsic radiosensitivities with respect to the induction of unstable and stable chromosome aberrations. Moreover, carbon ions induce very efficiently complex exchange aberrations, especially in Bragg peak.



Figure 2: Partial reciprocal translocation yields in WiDr cells, evaluated for chromosome No. 2, irradiated with carbon ions of different energies or 200 kV X -rays.



Figure 3: The relative proportions of WiDr cells containing complex exchanges after irradiation with two different doses D=1 Gy and D=4 Gy with carbon ions (100 MeV/u or Bragg peak) in comparison with 200 kV X-rays.