82 Preliminary evaluation of brain development in mice prenatally irradiated with fast neutron

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It is well known that radiation induces microcephaly or mental retardation when fetus is irradiated during brain development stage. Several researches have demonstrated that prenatal irradiation of low-LET radiation induced cerebral hypoplasia in rodents. However, little is known about neutrons. So, we examined the effects of prenatal exposure of neutrons on mice brains. B6C3F1 mice were irradiated with fast neutrons (0.1 to 1 Gy) or gamma-rays (0.8, 1.5 Gy) on embryonic day 13.5. At 8 weeks of age, offsprings of both sexes were necropsied. The brains were removed, weighed, and then were fixed in formalin for histopathology. Both types of radiation caused hypoplasia of cerebral cortex and brain absolute weight loss. These changes were remarkable at the highest dose groups. The brain weight loss was still noted at 0.1 Gy of neutrons. Histopathologically, loss of cortical neurons were observed. The degrees of these changes were larger for neutrons, the RBE for brain weight loss was 2 to 3 for both sexes.

83 Effects of DNA-PKcs-targeted siRNA on radio/heat sensitivity in human cancer cells

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It is well known that DNA-PKcs contributes to nonhomologous end-joining of DNA double-strand breaks, forming a complex with Ku70 and Ku80. We examined whether radio/heat sensitivity is enhanced by DNA-PKcs-targeted small interference (si)RNA which degrades DNA-PKcs mRNA. We used *p53*-null human cultured cells (H1299) transfected with wt*p53* (H1299/wt*p53*) or m*p53* gene (H1299/m*p53*) or SAS cells transfected with m*p53* gene to study whether the effect of DNA-PKcs-targeted siRNA on radio/heat sensitivity of cells is *p53*-dependent or not. Colony formation assay showed X-ray sensitivity of those cells was remarkably enhanced by DNA-PKcs-targeted siRNA *p53*-independently but the heat sensitivity was not affected by the siRNA in the H1299 cells. In contrast, the heat sensitivity of SAS cells was slightly enhanced by the siRNA. In addition, heat-induced hsp70 accumulation was increased by the siRNA in the H1299 cells. Therefore, the increased hsp70 accumulation by the siRNA may introduce the no effectiveness about the heat sensitivity of the H1299 cells. These results suggest that DNA-PKcs-targeted siRNA is a strong candidate for *p53*-independent radiation sensitizer.

84 Effects of Mild Temperature Hyperthermia and p53 Status of Tumor Cells on the Size of Hypoxic Cell Fractions in Solid Tumors

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Human head and neck squamous cell carcinoma cells transfected with mutant TP53 (SAS/mp53) or with neo vector as a control (SAS/neo) were inoculated subcutaneously into both hind legs of Balb/cA nude Mice. The mice then received nicotinamide injection or carbogen gas (95% O2, 5% CO2) inhalation with or without mild temperature hyperthermia (MTH, 40 centigrade, 60 min). After each treatment, the mice received a series of test doses of gamma-rays while alive or after tumor clamping to obtain hypoxic fractions (HFs) in the tumors. SAS/mp53 tumors showed significantly larger values in the size of not only the HF but also the diffusion-limited chronically HF than SAS/neo tumors. MTH could efficiently release the chronically HF, irrespective of p53 status. These supported the fact that, in gamma-ray irradiation and cisplatin treatment, the enhancement in combination with MTH was more remarkable in SAS/mp53 cells than SAS/neo cells.

85 Effect of Heavy Ion Exposures on Cell Cycle Progression and related proteins

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We studied the cell cycle progression and the induction of cyclinB1 and p21 in cultured human fibroblasts after irradiation with heavy ion beams at HIMAC of NIRS. Asynchronous human normal fibroblasts (NB1RGB) in monolayer were irradiated with X-rays, carbon ion beam (75 keV/um), Si ion beam (250 keV/um), and Fe ions (200–440 keV/um) at room temperature. Cell cycle distribution and the protein induction were measured by flow cytometory. After irradiation, both G_1 and G_2 block were observed independently on ions. From 30 to 50 percent of NB1RGB cells have accumulated at G_2/M phase. Percentage of cell number at G_2/M phase increased with dose up to 2 Gy. CyclinB1 was expressed only in G_2/M phase cells. The percentage of cells in which cyclin B1 was expressed increased with incubation time after irradiation up to 8 h. No increment of cyclin B1 expression was observed from 2 Gy to 10 Gy. P21 was expressed both in G_1 and G_2/M cells after 3 h and longer incubation after irradiation.