cells at G_2/M phase was increased from (18.5±0.87)% to (32.7±1.2)%, and the MDA-MB-231cells at G_2/M phase was increased from (19.9±0.44)% to (30.9±1.89)%. Thus, Our experimental data clearly indicate that genistein arrests the cell cycle at G_2/M phase and exerts an inhibitory effect on the proliferation of both breast cancer cell lines, they may play an important role in cancer prevention.

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3 - 79 Radiation-induced Delayed Microsatellite Instability in Human Normal Liver HL-7702 Cells

Zhao Ting, Ye Fei, Liu Xiongxiong and Li Qiang

The paradigm in which the deleterious effects of ionizing radiations are attributed to chemical alterations of DNA through energy depositions is well established. However, accumulating evidence suggests that other phenomena like heritable phenotype of genomic instability (radiation-induced genomic instability, RIGI) may also occur when cells are irradiated. The manifestation of this instability may be delayed for many cell divisions; it will then show itself in a variety of ways depending on the cell system used. Delayed lethal mutations (delayed reproductive cell death), delayed apoptosis, non-clonal cytogenetically detectable chromosome aberrations, often involving chromatid lesions, microsatellite instability, micronucleus formation and, potentially, transformation, are all well documented end-points[1]. The delayed nature of onset may be of particular relevance to neoplasia, but the relationship is still unclear[2]. In our experiment, human normal liver HL-7702 cells were irradiated with high linear energy transfer (LET) carbon ions (30 keV/(m) and low-LET X rays, respectively. Delayed effect in terms of microsatellite instability (MSI) in progenies of the directly irradiated cells and bystander cells, obtained in the way of medium transfer, at the 8th passage postirradiation was examined. Shown in Figs. 1～3 are the results acquired in our experiment.

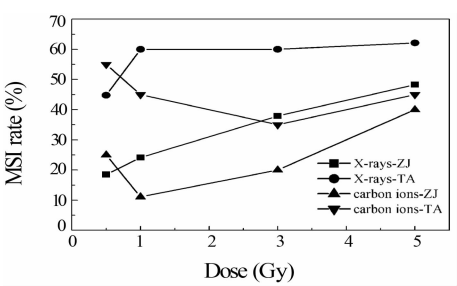

Fig. 1 MSI rate varies with exposure dose and ray type.

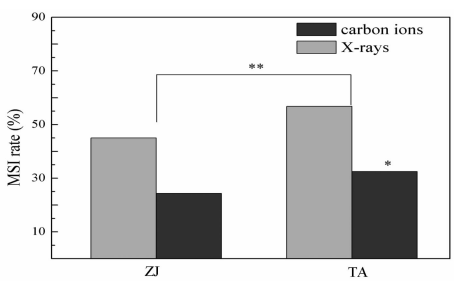

Fig. 2 MSI rate of different ray type and treatment.

These experimental data exhibit that the delayed effect induced by the high-LET carbon ions was different from that induced by the low-LET X rays, and a higher incidence of MSI was observed in the progenies of the cells after exposure to the X-rays than to the carbon ions. We also found that the delayed effect in the progenies of the bystander cells was much more severe than those of the directly irradiated cells. Furthermore, the events of MSI and loss of heterozygosity (LOH) induced by the ionizing radiations were not randomly distributed throughout the genome and specific loci existed indeed. These results imply that the radiation risk to normal tissues is lower in heavy ion therapy than in conventional X-ray radiotherapy. Probably the analysis of microsatellite loci with MSI high-frequency occurrence can be applied to access long-term survival conditions and second cancer risks for the patients after radiotherapy.

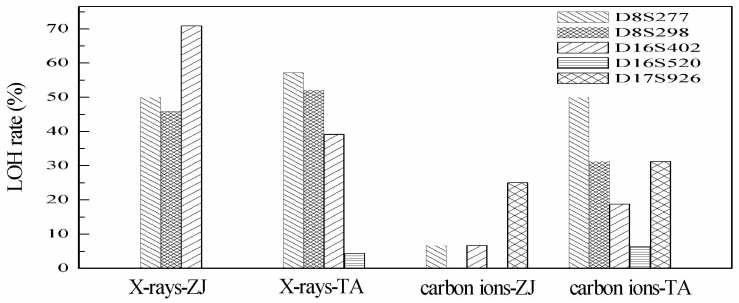

Fig. 3 LOH rates of different microsatellite sites.

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3 - 80 Effect of Carbon-ion Radiation on Mitochondrial DNA

Zhang Hong and Zhou Xin

Heavy-ion radiation is regarded as a significant risk during long-term manned space missions. The genetic damage induced by heavy-ion irradiation has been extensively studied. Although substantial evidence has been provided for the evaluation of mutagenetic effect of heavy-ion radiation, no report investigated mitochondrial DNA (mtDNA) damage and mutation induced by heavy-ion irradiation. MtDNA is a maternally-inheirited, closed-circle, double-strand molecule located within the mitochodnrial matrix. MtDNA encodes 2 rRNAs, 22 tRNAs, and 13 polypeptides, which are essential for nornal mitochondrial function. MtDNA is believed to be more susceptible to oxidative damage and consequently acquires mutations at a higher rate than does nuclear DNA. The differences in its susceptibility could be caused by lack of protective histones, limited DNA repair capacity, and high level of reactive oxygen species produced during oxidative phosphorylation. Heavy-ion radiation therefore could possiblely induced more severe damage in mtDNA than in nuclear DNA.

Several studies were carried out to investigate the effect of carbon-ion radiation on mitochondrial DNA in our group[1,2]. With respect to the mtDNA damage, we found that carbon-ion induced significant and irreversible mtDNA conformation change; Carbon-ion induced mtDNA was more severe than X-ray radiation. While ROS contribute to the most of the mtDNA damage induced by carbon-ion and X-ray irradiation, the direct effect of radiation on mtDNA was different. Direct effect of carbon-ion on mtDNA was irrepairable, while X-ray induced damage were not. Carbon-ion induced mtDNA mutation were investigated in both human cancer cell lines and zebrafish. We found irradiated HeLa cell accumulated D310 mutation and could habor transit mtDNA 4977 deletion. The transgeneration effect of mtDNA mutation induced by carbon-ion was investigated in zebrafish. We found that low dose carbon-ion radiation on female zebrafish could significantly elevate the mtDNA mutation rate in their off springs.

In conclusion, our current findings indicate that carbon-ion radiation could induce severe mtDNA damage and mutations. The deterious effect of carbon-ion radiation on mtDNA is different in nature to the X-ray radiation.

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