3 - 85 Quantitative Analysis of Mitochondrial DNA Mutations Caused by Heavy-ion Radiation

He Yang, Zhou Xin and Zhang Hong

There are two types of mitochondrial DNA mutations: mitochondrial DNA large fragment missing and mitochondrial DNA point mutation (SNPs)[1]. To investigate the mitochondrial DNA mutations caused by heavy-ion radiation, human breast cancer cell line MCF-7 was irradiated by X-ray or heavy-ion, mtDNA 4977 bp deletion was quantificated by real-time PCR and D310 point mutations were quantificated by clone sequencing. The results shows that heavy-ion irradiation induced mtDNA 4977 bp deletion, the mtDNA 4977 bp deletion was not dose-dependent after 2～8 Gy irradiation and could be temperally detected in irradiated MCF-7 cells after 6 Gy irradiation. Clonogenetic assay shows that the cellular inactivation effect of heavy-ion irradiation was greater than X-ray, there are more D310 mutations in heavy-ion irradiated cells than that in X-ray irradiated cells (Table. 1), and the mutations accumulated stably in survived cells.

Table 1 D310 polymorphism distribution in survival clones of MCF-7 cell after two treament

D310 C-track	Unirradiated	X-ray	Carbon ions
C6	8%	16%	24%
C6/C7	4%	0	0
C7	74%	70%	58%
C8	12%	14%	18%
C7/C8	2%	0	0

Reference

[1] P. Parrella, D. Seripa, M. G. Matera, et al. ,Cancer letters, 190, 1(2003)73.

3 - 86 Radiation Biology Effect of Rosmarinic Acid on Normal and Tumor Cells

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Rosmarinic acid (RA) is a water-soluble polyphenolic component isolated from many medicinal plants. It has been reported to have anti-oxidative, anti-inflammatory and protective activity on lipopolysaccharide induced liver injury[1-2]. The study is to compare the radiation biology effect of RA on normal with that of tumor cells. Those cells were treated with X-ray in dose of 2 Gy. Our preliminary result has shown that the irradiation of X-ray in dose of 2 Gy can inhibit both normal and tumor cells growth. RA can promote

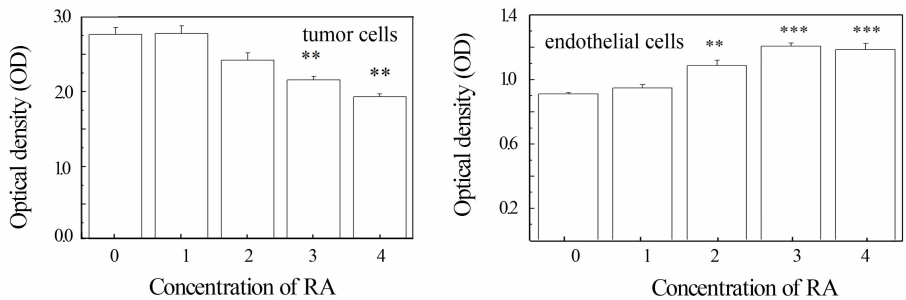

Fig. 1 The effect of rosmarinic acid on normal and tumor cells growth in dose of 2 Gy. The WST-1 was performed to test the effect of RA on different cells proliferation for 24 h after pretreatment by X-ray. The cells were irradiated by X-ray in dose of 2 Gy. RA was added into 96-well plates in concentration of 9, 18, 36, 72 μg/ml.

the normal cells proliferation after treatment of X-ray, however, it can enhance the potential damage effect of X-ray on tumor cells. It suggested that RA have a radioprotective effect on normal cells and can kill the tumor cells as well. In further study, we will investigate its related mechanism at the molecular and genetic level to demonstrate the different effect of RA on tumor and normal cells by low LET radiation.

References

[1] J. Youn, Lee. K. H, Won. J, et al., J. Rheumatol, 30(2003)1203.
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3 - 87 In Vivo Evidence of Localization of DNA Damage Proteins within Apoptotic Bodies

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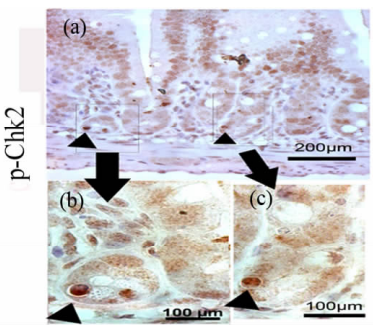

Fig. 1 p-Chk2 (Thr 68) is also localized in apoptotic bodies.

Previous studies have revealed that H2AX is phosphorylated in chromatin flanking DNA double strand breaks DSBs induced by ionizing radiation and is required for the recruitment of the repair machinery to the damaged foci. Therefore, the function of H2AX is believed to be associated primarily with DNA damage repair. In addition to its role in DDR, γ-H2AX was recently identified as an early marker of apoptosis in TNF-related apoptosis-inducing ligand (TRAIL)-treated tumor cell lines[1,2]. In this report, we provide in vivo evidence of H2AX phosphorylation in apoptotic crypt cells that is morphologically distinct from the DNA damage response (DDR) focal pattern. Activated DNA damage response proteins were also identified in apoptotic bodies showed in Fig. 1, where, arrow head indicate apoptotic bodies in crypts that strong positive for p-Chk2 at 1 d after irradiation. The DNA damage response is dramatically enhanced in apoptotic cells compared with non-apoptotic cells.

References

[1] E. P. Rogakou, et al., J. Biol. Chem., 275,13(2000)9390.
[2] S. Solier, Y. Pommier, Cell Cycle, 8,12(2009)1853.