

### 3 - 59 Radiosensitization to X-ray Radiation by Telomerase Inhibitor MST-312 in Human Hepatoma HepG2 cells\*

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Telomerase inhibitor MST-312 is a new compound derived from epigallocatechin gallate (EGCG)<sup>[1]</sup>. Our results demonstrated that 4  $\mu$ M MST-312 not only showed lower cytotoxicity, but also inhibited telomerase activity in HepG2 cells. Therefore, in our experiments, 4  $\mu$ M MST-312 was chosen to study radiosensitization and related mechanisms.  $\gamma$ -H2AX foci are considered as an indicator of DNA damages<sup>[2]</sup>. The immunofluorescence staining results showed the number of  $\gamma$ -H2AX foci in the pretreatment with MST-312 followed by 2 Gy X-ray irradiation group. However, as shown in Fig. 1, the formation of Rad51 foci in the combined treatment group was blocked outside the nuclear of HepG2 cells, when compared with the irradiation alone group. JC-1 staining showed that MST-312 pretreatment, followed by X-ray irradiation, caused increase of the green/red fluorescence intensity ratio ( $\Delta\Psi_m$ ) compared with X-ray irradiation alone. Meanwhile, MST-312 pretreatment followed by X-ray irradiation elevated expression of p53 protein and decreased expression of caspase-3 as well as fraction of Bcl-2 / Bax.

Summarizing our results, it can be concluded, the telomerase inhibitor MST-312 pretreatment enhanced the radiosensitivity of HepG2 cells to X-ray irradiation. This increased radiosensitivity was due to inhibition of telomerase activity that could result in telomerase dysfunction, and was related to impaired HR repair processes. MST-312 not only increased irradiation-induced DNA damages, but impaired DNA repair, which led to HepG2 cells apoptosis through p53-dependent mitochondrial pathway.

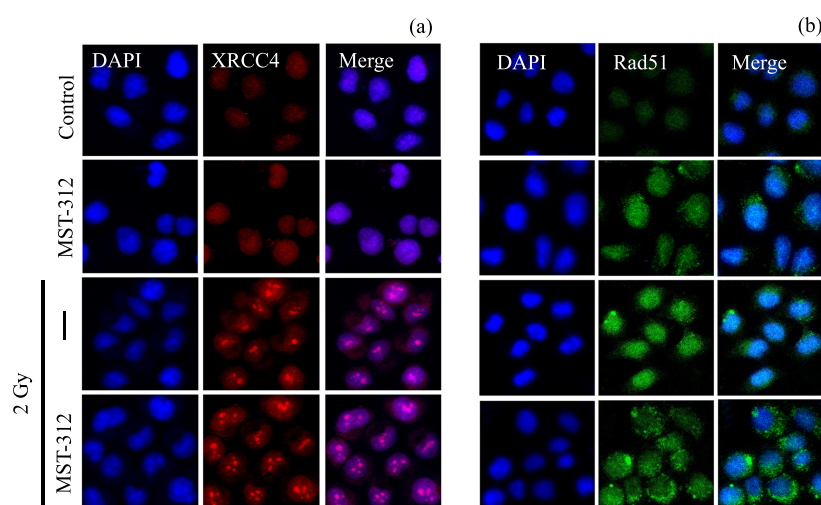


Fig. 1 (color online) Effects of MST-312 pretreatment followed by X-ray irradiation, on the DNA repair of HepG2 cells. Nuclear staining was done with DAPI (blue) while XRCC4 (a) and Rad51 (b) staining appeared as red foci and green foci, respectively.

#### References

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- [2] A. Munshi, T. Tanaka, M. L. Hobbs, et al., Mol. Cancer. Ther, 5(2006)1967.

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