Distinct radioprotective activities of major heat shock proteins in irradiated mammalian cells

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Abstract

Several years ago we have suggested that heat shock proteins (Hsps) can be involved in cellular and tissue mechanisms of protection from ionizing radiation. At present, the accumulated experimental data do allow us to characterize three major mammalian Hsps, Hsp70, Hsp27 and Hsp90, as specific endogenous radioprotectors which are able to prevent or minimize cell death resulting from the radiation exposure. It follows from the many findings that the radioprotective effect of these Hsps is particularly manifested in their ability to attenuate apoptosis in various normal and tumor cells irradiated in vivo or in vitro.

The obtained data already enable to suggest three main mechanisms of the radioprotection conferred by the excess Hsps: (i) modulation of the intracellular signaling so that the apoptotic signal transduction is blocked, whereas the 'cell survival' signal transduction is stimulated; (ii) suppression of the radiation-associated free radical generation and apoptosis induced by reactive oxygen species (ROS); (iii) attenuation of the genotoxic impact of ionizing radiation.

The latter suggested mechanism seems particularly intriguing and implies that the excess Hsps can somehow contribute to protection/repair of genomic DNA from radiation-induced damage. According to our recent results, Hsp90 is indeed involved in the post-irradiation repair of nuclear DNA, while excess Hsp70 can beneficially affect the p53-mediated DNA damage response in irradiated cells to ensure their long-term survival and recovery. As for Hsp27, we found that its accumulation in target cells increases their radioresistance by enhancing the irradiation-responsive activation of antiapoptotic pathways. While the Hsp70 and Hsp27 seem to perform different functions in irradiated cells, the synergistic enhancement of radioprotection was clearly observed in the cells enriched by the both the Hsps.

In vivo, such radioprotective activities of the major mammalian Hsps may play a role in radiogenic carcinogenesis; also, the high levels of Hsp expression taking place in some human tumors may contribute to the tumor cell resistance to radiotherapy.

KEYWORDS: apoptosis; stress-proteins; cellular radioresistance; DNA damage/repair.

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