The role of heat shock protein 70 (Hsp70) in radiation-induced immunomodulation.

Despite enormous progress in radiation technologies (high precision image-guided irradiation, proton irradiation, heavy ion irradiation) and radiotherapeutic concepts (hypofractionated irradiation schemes), the clinical outcome of radiotherapy in locally advanced and metastasized tumors and in hypoxic tumors which are radiation-resistant remains unsatisfactory. Given their key influence on a number of biological and immunological parameters, this article considers the influence of irradiation-induced stress proteins on radiation-induced immunomodulation. Depending on its location, the major stress-inducible Heat shock protein 70 (Hsp70) has been found to fulfill multiple roles. On the one hand, increased intracellular Hsp70 levels have been found to play a key role in the recovery from stress such as radio(chemo)therapy, and on the other hand extracellular Hsp70 proteins are potent stimulators of the innate immune system and mediators of anti-tumor immunity. Furthermore, if loaded with tumor-derived peptides, members of the Heat Shock Protein 70 (HSP70) and 90 (HSP90) families can stimulate the adaptive immune system via antigen cross-presentation. An irradiation-induced enhancement of the selective expression of a membrane form of Hsp70 on the surface of tumor cells which can act as a recognition structure for activated NK cells might have significant clinical relevance, in that the outcome of irradiation therapy for advanced
tumors could be improved by combining it with cell-based and other immunotherapies that target this membrane form of Hsp70.