Radiation combined with hyperthermia induces HSP70-dependent maturation of dendritic cells and release of pro-inflammatory cytokines by dendritic cells and macrophages.

Abstract:

Hyperthermia (HT) treatment of cancer patients was revived over the last years and has been proven to be beneficiary for many cancer entities when applied temperature controlled in multimodal treatments. We examined whether a combination of ionizing irradiation (X-ray) and HT (41.5°C; 1 h) can induce the release of heat shock protein (HSP) 70 by tumor cells and thereby lead to the activation of dendritic cells and macrophages. Extracellular HSP70 was detected in supernatants (SN) of treated colorectal tumor cells by ELISA. Maturation of dendritic cells (DC) after contact with the SN was measured by flow-cytometry. Phagocytosis assays were conducted to get hints about the immune stimulating potential of the tumor cells after the respective treatments. An increased surface expression of HSP70 was observed after X-ray or X-ray plus HT while the amount of extracellular HSP70 was only increased when HT was given additionally. A high up-regulation of the co-stimulation molecule CD80 and the chemokine receptor CCR7 on DC was measured after contact with SN of X-ray plus HT treated cells. This was dependent on extracellular HSP70. Combined treatments further led to significantly increased phagocytosis rates of macrophages and DC and increased pro-inflammatory cytokine (IL-8 and IL-12) secretion. X-ray
combined with HT induces HSP70 dependent activation of immune cells and might generate a tumor microenvironment beneficial for cure.