Ionizing radiation and nitric oxide donor sensitize Fas-induced apoptosis via up-regulation of Fas in human cervical cancer cells

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Abstract

Fas/CD95/Apo1 is a transmembrane receptor known to trigger apoptotic cell death in several cell types. In the present study, we showed that ionizing radiation (IR) and NO donor, S-nitroso-N-acetyl-penicillamine (SNAP), sensitized Fas-induced apoptotic cell death of HeLa human cervical cancers. Suboptimal dose of IR and SNAP up-regulated cell-surface Fas antigen, detected by FACScan using FITC-anti-Fas antibody. When combined with IR or SNAP, agonistic anti-Fas antibody CH-11 resulted in marked enhancement of apoptosis. This sensitization was completely abrogated by anti-Fas neutralizing antibody ZB4. During the IR and SNAP sensitized Fas-induced apoptosis, mitochondria permeabilization, cytochrome c release, and DNA fragmentation were detected. Furthermore, combined treatment of IR and SNAP additively up-regulated the surface Fas protein expression and sensitized Fas-induced apoptosis. Our finding demonstrate that sensitization of HeLa cervical cells to Fas-mediated apoptosis by IR and NO donor is most likely due to the up-regulation of Fas expression and also provides a means with which to sensitize tumors to the killing effects of cancer therapy via the Fas receptor.