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The effect of dominant negative EGR-1 and hyperbaric oxygen on immune cell apoptosis

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Abstract

The ultimate means of limiting the influence of an individual cell on the physiology of a multicellular organism is to induce the death of that cell. Apoptosis is a genetically regulated form of cell death that removes cells that are malfunctioning, unnecessary or damaged. During development, cells are produced in excess and those that are not optimal in form, location or function are removed via apoptosis. In the adult organism, apoptosis allows for the turnover of cells that have carried out specialized functions and maintains tissue homeostasis. ^ Negative selection is the developmental process by which immature T cells that have inappropriate reactivity to self antigen are induced to undergo apoptosis. During work in the lab confirming the requirement for the orphan nuclear hormone receptor, Nur77, for thymocyte apoptosis, an upregulation of the early growth response 1 gene (*egr-1*) was observed. This thesis investigates the requirement for transcriptional activation mediated by EGR-1 during the apoptosis of DO11.10, a cell line model of thymocyte negative selection. A dominant negative form of EGR-1, WT1EGR1, was expressed in DO11.10. The ability of these transfectants to undergo apoptosis in response to a variety of stimuli was measured. ^ Another important function of apoptosis is to limit the life span of activated immune cells. The inception of the second part of this work was the clinical observation that exposure of non-healing wounds to hyperbaric oxygen (HBO), 100% oxygen at elevated atmospheric pressures, aids in the healing of these wounds. The hypothesis tested here is that HBO enhances the apoptosis of immune cells. Such an enhancement would promote the resolution of chronic inflammation and aid in wound healing. It is demonstrated that HBO enhances apoptosis of immune cells in response to stimuli relevant to both the regulation of the immune system and the application of HBO as an adjuvant to anti-cancer therapy. ^ This study provides a new approach for studying the role of oxygen and its derivatives in apoptosis. The findings also support the continued investigation of expanding the clinical application of HBO. ^

Subject Area

Molecular biology|Cellular biology

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