



The effect of XIAP-Survivin interaction on apoptosis inhibition

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ABSTRACT

Apoptosis has been recognized as an important mode of “programmed” cell death, which involves genetically determined elimination of cells. In order to protect against inadvertent death, cells have evolved several systems such as IAPs (Inhibitor of Apoptosis family of Proteins) to check and balance cell death. IAPs, especially XIAP and survivin have emerged as critical regulators of cell survival in tumors. XIAP inhibits caspases by direct physical interaction in apoptosis pathway. However, survivin is a weak apoptosis inhibitor at physiological concentrations and may exert anti-apoptotic activity through stabilization of XIAP. In this study, HEK293 cell line and a stably transfected HEK293 expressing survivin were both transfected with pcDNA-XIAP. Our results showed that in response to cell death stimulation by doxorubicin (1 μ M), survivin promotes XIAP stability to inhibit apoptosis. Elevated inhibition of apoptosis was observed in HEK293/survivin compared to HEK293 due to changes in the morphological features of the cells. The experiments revealed that HEK293/survivin can prevent apoptosis in the presence of XIAP. XIAP and survivin form a heterocomplex which enhances the stability of XIAP and decreases the rate of apoptosis. This interaction synergistically suppresses mitochondrial cell death induced by drug stimulation *in vivo* and enhances cell survival.

Keywords: Apoptosis; XIAP; Survivin; Doxorubicin.