

Involvement of Heme Oxygenase I in the apoptotic pathway.

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HO catalyzes the degradation of heme to produce biliverdin, CO and free iron. HO-1, an inducible isoform of HO, is induced by a wide variety of stress-inducing stimuli. Accumulating evidences suggest a vital role for HO-1 in both cell growth and cell death. Although most evidences corroborate the cytoprotective (anti-apoptotic) effect of HO-1, this is not a universal finding. HO-1 may exert different effects in cell survival, including a pro-apoptotic effect, depending on the level of HO-1 expression and the cell type. The pre-monocytic cell line, U937, and the lymphoblastic cell line Jurkat were submitted to serum starvation plus hemin 20uM (inductor of HO). Cells extracts were prepared and assayed for caspase 3/7 activity using Ac-DEVD-MCA substrate, at different time points. After 12 hours, both cell lines showed an increase in the activity of caspase 3/7 (U937, 135 pmol/min/mg protein, and Jurkat, 384 pmol/min/mg protein) when compared with the controls. On the other hand, with the the addition of an inhibitor of HO-1, zinc protoporphyrin (ZnPP), the activity of caspase 3/7 was downregulated (U937, 70 pmol/min/mg protein, and Jurkat, 150 pmol/min/mg protein). These findings indicate that activity of HO-1 is important to keep the high levels of caspase 3/7. Therefore, in these stress systems the HO-1 are acting like a positive regulator of apoptosis.

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