

# **Cadmium-induced apoptosis in the BJAB human B cell line: Involvement of PKC/ERK1/2/JNK signaling pathways in HO-1 expression**

**Auteur:** Nemmiche, Said; Chabane-Sari, Daoudi; Kadri, Malika; Guiraud, Pascale

**Abstract/Résumé :** Heme oxygenase-1 (HO-1, EC 1.14.99.3) is a key enzyme in the cellular response to tissue injury and oxidative stress. It oxidizes heme, a pro-oxidant and toxic species, to biliverdin, CO, and free iron. Cytoprotection during the heat shock response is a complex phenomenon involving multiple inducible mechanisms. Several important pathways involving serine/threonine kinases mediate the induction of HO-1 in response to external stimuli. The objective of the present study was to investigate the mechanism of HO-1 induction during cadmium (Cd)-induced oxidative stress and apoptosis in the lymphocyte B cell line BJAB. To examine the signal pathways involved in HO-1 expression, cells were pre-treated with various inhibitors of key signaling molecules. Increased DNA fragmentation and caspase-3 activity were observed in BJAB cells exposed to 5-40  $\mu$  M CdCl<sub>2</sub> revealing that Cd induced apoptosis in these cells. Our results indicate that Cd also induces HO-1 expression which is modulated by the thiol redox status, tyrosine kinase and PI3-kinase. The inhibitory effect of calphostin C suggests that Cd induction of HO-1 expression could be mediated by the PKC pathway in the BJAB cells together with the involvement of ERK 1/2 and JNK in a dose-dependent manner. The molecular and cellular pathways should not be considered separately. They should be viewed as an array of interconnecting signals, all contributing to the final outcome, thereby allowing fine control of the duration and extent of HO-1 induction. (C) 2012 Elsevier Ireland Ltd. All rights reserved.

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