# Cell apoptosis induced by a synthetic carbazole compound LCY-2-CHO is mediated through activation of caspase and mitochondrial pathways.

許銘仁

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## 摘要

## Abstract

carbazole derivative identified as an anti-inflammatory compound, were studied. Cell cycle analysis by propidium iodide staining in human THP-1 monocytic leukemia cells showed the ability of LCY-2-CHO to increase cell population in sub-G1 stage with time- and concentration-dependent manners. LCY-2-CHO-mediated cell death was also demonstrated by DNA laddering and was not related to the release of lactate dehydrogenase. Apoptosis in THP-1 cells induced by LCY-2-CHO was accompanied by the Bid cleavage, collapse of mitochondrial transmembrane potential, the release of cytochrome c and the activation of caspase-3. The apoptotic effect of LCY-2-CHO was diminished by the presence of zVEID-fmk (caspase-6 inhibitor), zIETD-fmk (caspase-8 inhibitor), and zVAD-fmk (non-selective caspase inhibitor), but was not altered by several antioxidants, and cathepsin inhibitor. The Bid cleavage and loss of mitochondrial transmembrane potential, but not the cytochrome c release, were reversed by zIETD-fmk. Comparing the cell selectivity of LCY-2-CHO, we found T-cell acute lymphoblastic CEM leukemia cells were sensitive to 1 mM LCY-2-CHO, acute myeloid leukemia HL-60 cells underwent apoptosis at 10 mM, while adherent cancer cells, such as PC3, HT29 and MCF-7, were resistant to 30 mMLCY-2-CHO within 24-h incubation. Taken together in the present study, we demonstrated LCY-2-CHO might be apoptotic for malignant hematopoietic cells but not anchorage-dependent cells. This action is mediated by an intrinsic caspase-dependent apoptotic event involving mitochondria. # 2005 Elsevier Inc. All rights reserved.