Involvement of proapoptotic Bcl-2 family members in terbinafine-induced mitochondrial dysfunction and apoptosis in HL60 cells.

李文森

Yang KC;Wu CC;Wu CH;Chen JH;CHu CH;Chen CH;Chou YH;Wang YJ;Lee WS;Tseng H;Lin SY

Abstract

Terbinafine (TB, lamisil), a promising world widely used oral-anti-fungal agent, has been used in the treatment of superficial mycosis. In this study, we found that apoptosis but not cell growth arrest was induced by TB (1 lM, for 24 h) in human promyelocytic leukemia (HL60) cells. The apoptotic effect induced by TB in the HL60 cell was not through the general differentiation mechanisms evidenced by evaluation of three recognized markers, including CD11b, CD33, and morphological features. In addition, our results also revealed that TB-induced apoptosis was not through the cellular surface CD 95 receptor-mediated signaling pathway. We found that the mitochondria membrane in the TB-treated HL60 cells was dissipated by decreasing of the electrochemical gradient (DWm) led to leakage of cytochrome c from mitochondria into cytosol. Such effects were completely blocked by in vitro transfection of the HL60 cells with Bcl-2 overexpression plasmid (HL60/Bcl-2). However, our data found that TB-mediated apoptosis could not be completely prevented in the Bcl-2 over expressed (HL60/Bcl-2) cells. Such results implied that additional mediators (such as caspase-9) other than mitochondria membrane permeability might contribute to the TB-induced cellular apoptosis signaling. This hypothesis was supported by the evidence that administration of caspases-9 specific inhibitor (z-LEHD-fmk) blocked the TB-induced apoptosis. Our studies highlight the molecular mechanisms of TB-induced apoptosis in human promyelocytic leukemia (HL60) cells.