Effects of trichostatin A on the intrinsic and extrinsic apoptotic pathway, cell viability, and apoptosis induction in hepatocellular carcinoma cell lines

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The current study investigated the effect of trichostatin A (TSA) on mitochondrial/intrinsic [pro- (Bax, Bak, and Bim) and anti- (Bcl-2, Bcl-xL, and Mcl-1) apoptotic genes] and cytoplasmic/extrinsic (DR4, DR5, FAS, FAS-L, and TRAIL genes) pathways, histone deacetylase 1, 2, and 3, p53, p73, cell viability, and apoptosis in hepatocellular carcinoma (HCC) HCCLM3, MHCC97H, and MHCC97L cell lines.

Modulation of the acetylation status of histones, histones modification, plays an important role in regulating gene transcription and expression. Histone deacetylation controlled by histone deacetylases (HDACs) leads to gene downregulation. Histone deacetylase inhibitors (HDACIs) are an emerging class of therapeutics with potential anticancer effects. They can induce apoptosis by activating both extrinsic and intrinsic apoptotic pathways

HCCLM3, MHCC97H, and MHCC97L cells were cultured and treated with TSA. To determine viability, apoptosis, and the relative expression level of the mentioned genes, MTT assay, cell apoptosis assay, and qRT-PCR, respectively, were conducted.

TSA up-regulated Bax, Bak, Bim, DR4, DR5, FAS, FAS-L, TRAIL, p53, and p73 and down-regulated Bcl-2, Bcl-xL, Mcl-1, histone deacetylases 1, 2, and 3 significantly, resulting in apoptosis induction. Maximal and minimal apoptosis was seen in the MHCC97H and HCCLM3 cell lines (93.94% and 39.68%, respectively) after 24 and 48 h. Therefore, the MHCC97H cell line was more sensitive to TSA.

The current findings demonstrated that the HDAC inhibitor TSA can induce apoptosis and inhibit cell growth through both mitochondrial/intrinsic and cytoplasmic/extrinsic apoptotic pathways in hepatocellular carcinoma HCCLM3, MHCC97H, and MHCC97L cell lines.

Keywords: Trichostatin A, Extrinsic, Intrinsic, Pathway, Apoptosis