Effects of Trichostatin A on the Histone Deacetylases (HDACs), Intrinsic Apoptotic Pathway, p21/Waf1/Cip1, and p53 in Human Neuroblastoma, Glioblastoma, Hepatocellular Carcinoma, and Colon Cancer Cell Lines

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Abstract

Background: The aberrant and altered patterns of gene expression play an important role in the biology of cancer and tumorigenesis. DNA methylation and histone deacetylation are the most studied epigenetic mechanisms. Histone deacetylase inhibitors (HDACIs) such as valproic acid (VPA) and trichostatin A (TSA) are a group of anticancer compounds for the treatment of solid and hematological cancers. Previously, we reported the effect of two HDACIs, valproic acid (VPA) and TSA, on colon cancer and hepatocellular carcinoma (HCC), respectively. The aim of the current in vitro study is to investigate the effects of TSA on the intrinsic apoptotic pathway, p21/Waf1/Cip1 (p21), p53, and histone deacetylases (HDACs) 1, 2 and 3 in human neuroblastoma LAN-1, glioblastoma GBM-29, HCC SMMC7721, and colon cancer COLO 201 cell lines.

Materials and methods: In this lab-trial study, all three cell lines were seeded at the density of 3 × 105 cells per well and incubated for 24 hours. Then, the cells were treated with TSA based on IC50 values for 24 hours except in the control groups; the control cells were treated with the equal amounts of the DMSO solvent. Subsequently, cell viability, cell apoptosis and gene expression were determined by three techniques including MTT assay, flow cytometry assay, and qRT-PCR.

Results: The result of qRT-PCR indicated that TSA could increase the expression levels of Bid, BimEL, Noxa, p21, and p53 genes and decrease those of Bcl-xL, RIP, Mcl-1, XIAP, HDACs 1, 2 and 3 significantly ($P < 0.0001$) by which it inhibited cell growth and induced significant cell apoptosis in LAN-1, GBM-29, SMMC7721, and COLO 201 cell lines (p value<0.001).

Conclusion: TSA can affect cell apoptotic via the intrinsic apoptotic pathway in LAN-1, GBM-29, SMMC7721, and COLO 201 cell lines.

Keywords: *Apoptosis, Histone deacetylase, Mitochondrial, Trichostatin A*