# The effect of valproic acid on intrinsic, extrinsic, and JAK/STAT pathways in neuroblastoma and glioblastoma cell lines

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## Abstract

Background and purpose: Epigenetics has been defined as the study of mitotically heritable alterations in gene expression that are not caused by changes in DNA sequence. Epigenetic-mediated silencing of a gene includes genomic imprinting, histone deacetylation, DNA methylation, and RNA-associated silencing. Cell growth and cell proliferation are inhibited by some histone deacetylase and histone inhibitors. This study was designed to investigate the effect of valproic acid (VPA) on extrinsic, intrinsic, and the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathways in neuroblastoma and glioblastoma cell lines.

Experimental approach: The neuroblastoma and glioblastoma cells were cultured and treated with VPA. MTT assay was done to determine cell viability. Besides, a flow cytometry assay was performed to determine apoptotic cells and finally, the relative gene expression level was evaluated by qRT-PCR.

Findings / Results: VPA changed the expression level of the genes of the extrinsic, intrinsic, and JAK/STAT pathways which induced cell apoptosis and inhibited cell growth in the neuroblastoma and glioblastoma cells. In the neuroblastoma cell lines, VPA upregulated the expression level of FAS, FAS-L, DR4, DR5, and TRAIL genes significantly. Additionally, it significantly up-regulated the expression level of Bak, Bax, and Bim genes and down-regulated the expression level of Bcl-xL, Bcl-2, and Mcl-1 genes in both neuroblastoma and glioblastoma cell lines.

Conclusion and implications: VPA induced cell apoptosis through extrinsic, intrinsic, and JAK/STAT pathways.

**Keywords:** Apoptosis; Gene Expression; Neoplasms; Valproic acid.