

Effect of Decitabine (5-aza-2-deoxycytidine, 5-aza-CdR) in Comparison with Vorinostat (Suberoylanilide Hydroxamic Acid, SAHA) on DNMT1, DNMT3a and DNMT3b, HDAC1-3, SOCS 1, SOCS 3, JAK2, and STAT3 Gene Expression in Hepatocellular Carcinoma HLE and LCL-PI 11 Cell Lines

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Epigenetic alterations play an important role in tumorigenesis. Hypermethylation of CpG islands within the promoter regions of tumor suppressor genes (TSGs) and histone deacetylation lead to the silencing of the genes resulting in cancer induction. The suppressor of cytokine signaling (SOCS) family is an important negative regulator of cytokine signaling and deregulation of this family has been reported in several cancers, the protein of the SOCS family inhibit the cytokine-activated Janus kinase/signal transducers and activators of transcription (JAK/STAT) signaling pathway to modulate cellular responses. Previously, we evaluated the effects of DNA demethylating agents and histone deacetylase inhibitors on hepatocellular carcinoma (HCC). The current study aimed to investigate the effect of decitabine (5-aza-2'-deoxycytidine, 5-aza-CdR) in comparison to vorinostat (suberoylanilide hydroxamic acid, SAHA) on DNMT1, DNMT3a and DNMT3b, HDAC 1-3, SOCS 1, SOCS 3, JAK2, and STAT3 gene expression, cell growth inhibition, and apoptosis induction of HCC HLE and LCL-PI 11 cell lines.

Material and methods: The HLE and LCL-PI 11 cells were treated with 5-aza-CdR and SAHA and then the MTT assay, flow cytometry assay, and quantitative real-time RT-PCR were achieved to determine cell viability, cell apoptosis, and relative gene expression respectively.

Results: The result indicated that both compounds inhibited cell growth, induced apoptosis, and down-regulated DNMT1, DNMT3a DNMT3b, HDAC 1-3, JAK2, and STAT3 and up-regulated HDAC 1-3, SOCS 1, and SOCS 3 genes expression significantly. The apoptotic effect of SAHA was stronger than that of 5-Aza-CdR.

Conclusion: 5-Aza-CdR and SAHA can induce cell growth inhibition and apoptosis induction through the JAK/STAT pathway.

Keywords: Decitabine, vorinostat, SOCS, JAK/STAT, HCC