Effect of vorinostat on INK4 family and HDACs 1, 2, and 3 in pancreatic cancer and hepatocellular carcinoma

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Abstract

Background and purpose: In mammalian cells, several distinct surveillance systems, named cell cycle checkpoints, can interrupt normal cell-cycle progression. The cyclin-dependent kinases are negatively regulated by proteins of cyclin-dependent kinases inhibitors comprising INK4 and Cip/Kip families. Histone deacetylation induced by histone deacetylases (HDACs) inactivates the INK4 and Cip/Kip families lead to cancer induction. HDAC inhibitors (HDACIs) have been indicated to be potent inducers of differentiation, growth arrest, and apoptotic induction. Vorinostat (suberoylanilide hydroxamic acid, SAHA), as an HDACI, is reported to be useful in various cancers. Previously, we reported the effect of trichostatin A on hepatocellular carcinoma and also vorinostat on colon cancer cell lines. The current study was aimed to investigate the effect of vorinostat on p16INK4a, p14ARF, p15INK4b, and class I HDACs 1, 2, and 3 gene expression, cell growth inhibition, and apoptosis induction in pancreatic cancer AsPC-1 and hepatocellular carcinoma LCL-PI 11 cell lines.

Experimental approach: The AsPC-1 and LCL-PI 11 cell lines were cultured and treated with vorinostat. To determine, viability, apoptosis, and the relative expression level of p16INK4a, p14ARF, p15INK4b, class I HDACs 1, 2, and 3 genes, MTT assay, cell apoptosis assay, and RT-qPCR were performed, respectively.

Findings/Results: Vorinostat significantly inhibited cell growth, induced apoptosis, increased p16INK4a, p14ARF, p15INK4b, and decreased class I HDACs 1, 2, and 3 gene expression.

Conclusion and implications: Vorinostat can reactivate the INK4 family through inhibition of class I HDACs 1, 2, and 3 genes activity.

Keywords

Author Keywords: Cyclin-dependent kinase inhibitors; Neoplasms; Vorinostat
KeyWords Plus: HISTONE DEACETYLASE INHIBITORS; SUBEROYLANILIDE HYDROXAMIC ACID; APOPTOSIS INDUCTION; VALPROIC ACID; METHYLATION; P16(INK4A); EXPRESSION; GROWTH; P16INK4A; INACTIVATION