

A novel class I histone deacetylase inhibitor, I-7ab, induces apoptosis and arrests cell cycle progression in human colorectal cancer cells

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Epigenetic mutations are closely associated with human diseases, especially cancers. Among them, dysregulations of histone deacetylases (HDACs) are commonly observed in human cancers. Recent years, HDAC inhibitors have been identified as promising anticancer agents; several HDAC inhibitors have been applied in clinical practice. In this study, we synthesized a novel N-hydroxyacrylamide-derived HDAC inhibitor, I-7ab, and examined its antitumor activity. Our investigations demonstrated that I-7ab exerted cytotoxicity toward and inhibited the growth of human cancer cell lines at micromolar concentrations. Among tested cells, HCT116 was the most sensitive one to the treatment of I-7ab. However, I-7ab displayed far less cytotoxicity in human normal cells. In HCT116 cells, I-7ab inhibited the expression of class I HDACs, especially that of HDAC3 and suppressed EGFR signaling pathway. With respect to the cytotoxic effect of I-7ab, it induced apoptosis via increasing the Bax/Bcl-2 ratio and suppressing the translocation of NF- κ B. Other than inducing apoptosis, I-7ab inhibited the expression of cyclin B1 and thereby arrests cell cycle progression at G2/M phase. Further analyses revealed potential role of p53 and p21 in I-7ab-induced apoptosis and cell cycle arrest. According to our findings, I-7ab may serve as a lead compound for potential antitumor drugs.

Biography

Kecheng Lei is pursuing her Doctor's degree in Jianwen Liu's Lab. She has published a paper in Tumor Biology in 2015.

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