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New HDAC inhibitor, IN2001 induces apoptosis/cell cycle arrest in human breast cancer cells

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The acetylation of histone is one of the mechanisms involved in the regulation of gene expression and is tightly controlled by two core enzymes, histone acetyltransferase (HAT) and deacetylase (HDAC). There are several reports that imbalance of HAT and HDAC activity is associated with abnormal behavior of the cells in morphology, cell cycle, differentiation, and carcinogenesis. Recently, an increasing number of structurally diverse HDAC inhibitors have been identified that inhibit proliferation and induce differentiation and/or apoptosis of tumor cells in vivo and in vitro. In this study, we have investigated the effects of novel HDAC inhibitors, IN2001 on ER positive and ER negative human breast cancer cell lines. The growth inhibition, cell cycle arrest and apoptosis of cells by HDAC inhibitors were determined using SRB assay, DNA fragmentation, and flow cytometry. We found that IN 2001 as well as Trichostatin A inhibited cell growth dose-dependently in both ER positive and ER negative human breast cancer cell lines. The growth inhibition with HDAC inhibitors was associated with profound morphological change. The result of cell cycle analysis after 24 h exposure of IN2001 showed G2-M cell cycle arrest in MCF-7 cell and apoptosis in T47D and MDA-MB-231 cell. In summary, IN2001 has antiproliferative effect on human breast cancer cells regardless of the expression of estrogen receptor. These findings heights the possibility of developing HDAC inhibitors as potential anticancer therapeutic agents for the treatment of breast cancer.