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Modulation of Cell Cycle Control by Histone Deacetylase Inhibitor Trichostatin A in A549 Human Non-small Cell Lung Cancer Cells

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Histone deacetylase (HDAC) inhibitors target key steps of tumor development. They inhibit proliferation, induce differentiation and/or apoptotic cell death, and exhibit potent antimetastatic and antiangiogenic properties in cancer cells *in vitro* and *in vivo*. Although they are emerging as a promising new treatment strategy in malignancy, how they exert their effect on human non-small cell lung cancer cells is as yet unclear. The present study was undertaken to investigate the underlying mechanism of a HDAC inhibitor trichostatin A (TSA)-induced growth arrest and its effect on the cell cycle control gene products in a human lung carcinoma cell line A549. TSA treatment induced the growth inhibition and morphological changes in a concentration-dependent manner. Treatment of A549 cells with TSA resulted in a concentration-dependent increased G1 (under 100 ng/ml) and/or G2/M (200 ng/ml) cell population of the cell cycle as determined by flow cytometry. Moreover, 200 ng/ml TSA treatment significantly induced the population of sub-G1 cells (23.0 fold of control). This anti-proliferative effect of TSA was accompanied by a marked inhibition of cyclins, positive regulators of cell cycle progression, and cyclin-dependent kinases (Cdks) expression and concomitant induction of tumor suppressor p53 and Cdk inhibitors such as p21 and p27. Although further studies are needed, these findings provide important insights into the possible molecular mechanisms of the anti-cancer activity of TSA in human lung carcinoma cells.