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Histone deacetylation effects of the CYP1A1 promoter activity, proliferation and apoptosis of cells in hepatic, prostate and breast cancer cells

K.N. Min, K.E. Joung, M.J. Cho, J.Y. An, D.K. Kim and Y.Y. Sheen

We have studied the mechanism of action of TCDD on CYP1A1 promoter activity in both Hepa I and MCF-7 cells using transient transfection system with p1A1-Luc reporter gene. When HDAC inhibitors, such as trichostatin A, HC toxin and a novel HDAC inhibitor, IN2001 were cotreated with TCDD to the cells transfected with p1A1-Luc reporter gene, the basal promoter activity of CYP1A1 was increased by HDAC inhibitors. Also, in MCF-7 human breast cancer cells, HDAC inhibitors, such as IN2001 and trichostatin A increased the basal activity of CYP1A1 promoter but TCDD stimulated CYP1A1 promoter activity was not changed by HDAC inhibitors. And, in stably-transfected Hepa I cells with p1A1-Luc, HDAC inhibitors increased the basal promoter activity only.

Also, we have investigated the effects of HDAC inhibitors on the human breast and prostate cancer cells in terms of cell proliferation and apoptosis based on SRB assay. IN2001 as well as trichostatin A inhibited the MCF-7, MDA-MB-231, MDA-MB-468, T47D, ZR75-1, PC3 cell growth dose-dependently. The growth inhibition of these cells with HDAC inhibitors was associated with profound morphological change, which suggests the HDAC inhibitors induced apoptosis of cells. The result of cell cycle analysis after 24h exposure of IN2001 showed G2/M cell cycle arrest in MCF-7 cells and apoptosis in T47D and MDA-MB-231 cells.