P52

Synergistic Effects of Dexamethasone and Genistein on the Expression of Cdk inhibitor p21$^{WAF1/CIP1}$ in Human Hepatocellular and Colorectal Carcinoma Cells

JAE-HONG PARK[1], EUN-JIN OH[1], YUNG HYUN CHOI[2], CHI-DUG KANG[3], HO SUNG KANG[1], DONG-KYOO KIM[4], KWANG IL KANG1 and MI-AE YOO[1]

[1]Department of Molecular Biology, Pusan National University, Pusan 609-735; [2]Department of Biochemistry, College of Oriental Medicine, Dong-Eui University, Pusan 614-714; 3Department of Biochemistry, College of Medicine, Pusan National University, Pusan 602-735; 4Department of Chemistry, Inje University, Kimhae 621-749, Korea

Previous studies have shown that dexamethasone, a synthetic glucocorticoid, can induce a G1 arrest, however, genistein, a natural isoflavonoid phytoestrogen, induces a G2/M arrest in the cell cycle progression in various cancer cell lines. A block of cell cycle checkpoint by dexamethasone and genistein correlates with a selective induction of cyclin-dependent kinase (Cdk) inhibitor p21$^{WAF1/CIP1}$ in a tumor suppressor p53-independent manner and abolishment of Cdk2 phosphorylation. In the present study, the effects of dexamethasone and genistein (both singly and combined) on the expression of p21 in human hepatocellular Hep G2 and colorectal Colo320 HSR carcinoma cells were evaluated. Whereas dexamethasone mildly induced the level of p21 protein, genistein strongly increased the expression of p21 protein in our experimental condition. Both compounds also activated p21 promoter reporter constructs. The combined effects of dexamethasone and genistein on the induction of p21 protein and activation of p21 promoter were synergistic in both cell lines. These findings indicate that dexamethasone and genistein act in a synergistic fashion and have potential for combination chemotherapy for the treatment of liver and colon cancer.