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Anti-Proliferation Effects of Ginsenoside Rh_2 on Normal Mammary Epithelial Cells and Cancer Cells

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The effects of ginsenosides on the growth and differentiation of normal mammary epithelial cells and mammary cancer cells were studied. Ginsenosides, especially G-Rh_1 and G-Rh_2, increased the population of differentiated structures both in plate and Matrigel culture of normal mammary organoids from the intact glands of female F344 with serum free medium. Moreover, cell-cell communicaton was increased after treatment with G-Rh_2. In mammary cancer cells, G-Rh_2 inhibited the growth of MCF-7 cells. Flow cytometric analysis showed that G-Rh_2 arrested the cell cycle at the G_1/S transition phase while the results from DAPI staining show no special change of nuclear form (no apoptotic cell). The cyclin-E dependent kinase cdk 2 activity which had been immunoprecipitated with cyclin-E specific antibody or cdk 2 specific antibody was down-regulated in the cells treated with G-Rh_2. Western blot analyses showed that G-Rh_2 induced the expression of p21 and reduced the levels of cyclin D, especially D_3, whereas it had no effect on the levels of cdk 2, cdk 4, and cyclin E. Collectively, these data suggest that G-Rh_2 induced differentiation of normal mammary epithelial cells and inhibited the growth of MCF-7 cells, by inducing protein expression of p21 and reducing the protein levels of cyclin D, and as a consequence, down-regulating cyclin E, D-dependent kinases activity, decreasing phosphorylation of RB, and inhibiting E2F releasing. These results suggest that Rh2 has differentiation inducing and/or cytostatic effects on normal or mammary cancer cells.