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## Growth and EGFR Regulation in Breast Cancer Cells by Vitamin D and Retinoid Compounds.

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The effect of 1,25-dihydroxyvitamin D(3), analog C (1,25-(OH)(2)-16-en-23-yn-26,27-F(6)-vitamin D(3)), 9- cis retinoic acid, and all- trans retinoic acid on the growth and expression of EGFR in MCF7, T47D, BT474, and BT549 breast cancer cells was examined. Significant growth inhibition was noted in MCF7, T47D, and BT474 cells by 8 days of treatment, while BT549 cells showed none. MCF7, T47D, and BT549 cells treated with 1,25-dihydroxyvitamin D(3) demonstrated a 50% decrease in EGFR mRNA within 2 h which was sustained to 72 h, while BT474 cells demonstrated a 200-500% increase. EGFR protein levels correlated with these mRNA changes in BT474 and BT549 cells. Measurement of mRNA stability in vitamin D treated BT474 cells indicated that there was no change in EGFR mRNA half-life. Transfection of an EGFR promoter containing reporter plasmid demonstrated vitamin D induced changes in reporter gene activity that paralleled the changes observed in EGFR mRNA and protein. Electrophoretic mobility shift assays using a putative vitamin D response element within this region of the EGFR promoter demonstrated specific VDR binding. These results indicate that the vitamin D effect on EGFR expression in breast cancer cells has a transcriptional component likely mediated through a vitamin D responsive promoter sequence. They also suggest that growth inhibition and EGFR down-regulation by vitamin D and retinoids may be related events in some breast cancer cells, but not in all.