E119 Comparative Studies on the Polyamine Involvement in Human Breast Cancer Cell Proliferation

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Estradiol(E_2) exerted the growth promoting effect on MCF-7 cells and the maximum proliferation effect was achieved at 0.1 nM with 146% of the control during 48 hrs incubation. But no growth stimulatory effect of E_2 was found in MDA-MB-231 cells. The growth inhibitory effect of DFMO was quite noticeable in hormone-dependent MCF-7 cells but that effect was not significant in hormone-independent MDA-MB-231 cells. MCF-7 cells were very sensitive to nonsteroidal antiestrogen 4-hydroxytamoxifen(HO-TAM) at as low as 0.1 μM concentration but MDA-MB-231 cells were resistant to that drug. At higher concentration of HO-TAM, almost no cell multiplication was detected in both cell lines. E_2 administration induced a dramatic increase of putrescine(32-fold) and spermidine(180%) in MCF-7 cell line. Spermine content was not much influenced by E_2. In MDA-MB-231 cells, however, polyamine(PA) levels were not affected by E2. DFMO suppressed PA levels in both cell lines. In MCF-7 cells treated with 5 mM DFMO, the level of each putrescine, spermidine, and spermine dropped to 39%, 28%, and 47% of the untreated control, respectively. In MDA-MB-231 cells, intracellular levels of putrescine and spermidine dropped to 59% and 39% of the control. HO-TAM at 1 μM totally blocked PA synthesis in MCF-7 cells. But, in MDA-MB-231 cells, HO-TAM slightly increased intracellular spermidine and spermine levels without any change in putrescine level.

E120 Reduced Protein Phosphorylation in Polyamine-Starved Human Breast Cancer Cells

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Estrogens stimulate the proliferation of human breast cancer cells through autocrine and paracrine regulations. MCF-7 human breast cancer cell is known to release growth factors by estradiol(E_2) treatment. Growth signal transduction is directly associated with rapid activation of ornithine decarboxylase(ODC) activity. Here we report that treatment of MCF-7 cells with DFMO, an irreversible inhibitor of ODC, decrease the amount of phosphorylation in several membrane-associated proteins. Among the many membrane-associated proteins investigated, mid-to-low range size (51, 48, 46, 43.8, 42, 38, 34, and 31 kDa) of proteins were most sensitive to 5 min treatment of E_2, TGF-α or EGF in the amount of phosphorylation in *in vitro* phosphorylation experiments. The degree of protein phosphorylation induction was in the order of EFG, TGF-α, and E_2. When the membrane fragments pretreated with 5 mM DFMO for 5 min were incubated along with each stimulants, a severe decrease in phosphorylation was detected in most of the mid-to-low range size of proteins. Our results suggest that polyamines may influence the extent of cell proliferation, perhaps by modulating the rate of phosphorylation of proteins.