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. Sorry There are no reviews yet. August 9, 2005 . A new role for estrogen in metastatic breast cancer: estrogen receptor-independent growth by 17beta-estradiol in human breast cancer cells is regulated by extracellular calcium. Since estrogens have been shown to be critical for the growth of breast cancer cells in vitro and in vivo, this study addressed the effects of 17beta-estradiol (17beta-E2) on the growth of breast cancer cells in comparison with that of human nonmalignant mammary epithelial cells. As shown by in vitro proliferation assays, the growth of all breast cancer cells and nonmalignant mammary cells studied was stimulated by 17beta-E2 in a dose- and time-dependent manner. Growth of MDA-MB-231, MDA-MB-468, and SKBr3 cells was estrogen receptor (ER)-dependent, whereas that of MCF-7 cells was ER-independent. 17beta-E2 significantly enhanced [3H]thymidine incorporation in all breast cancer cell lines but did not influence the growth of nonmalignant mammary cells. Furthermore, growth of MDA-MB-231, MDA-MB-468, and SKBr3 cells was stimulated by 17beta-E2 in a dose- and time-dependent manner and was completely abolished by the pure antiestrogen ICI 182,780. Although the growth of MDA-MB-468 cells was completely inhibited by estradiol depletion, ICI 182,780, or the phosphoinositide 3-kinase (PI-3-kinase) inhibitor LY294002, MCF-7 cells were insensitive to 17beta-E2 or ICI 182,780 treatment. These findings suggest that in ER+ breast cancer cells, 17beta-E2 enhances growth via its own high-affinity ER and through other receptor mechanisms. Because MDA-MB-231 and MDA-MB-468 cells express wild-type ER and PI-3-kinase is aberrantly activated in these cells, we propose that the growth-promoting effect of 17beta-E2 in these cells can be attributed to
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