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Estrogen Receptor α Regulates ERK in MCF-7 Cells

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Abstract

Estrogen (E2) signaling significantly affects breast tumorigenesis by enhancing cell growth and preventing apoptosis. The actions of estrogen in MCF-7 breast cancer cells are mediated through a kinase pathway involving CaM KK, CaM KI, and ERK. Current research is examining the involvement of the Estrogen Receptor (ER) alpha (α) and beta (β) as well as G-Protein Coupled Receptor GPR30 in cell growth and proliferation. ERα is suggested to be responsible for ERK and perhaps CaM Kinase activation. Our goal was to evaluate if ERα, rather than GPR30 or ERβ, mediates CaM KI and ERK activation upon treatment of MCF-7 breast cancer cells with E2. E2 treatment of MCF-7 cells led to a significant rise in CaM KI and ERK activation. This effect was blocked by pretreatment with the ERα antagonist MPP; however MPP did not block EGF stimulation of ERK. We then explored the role of ERβ in E2-mediated ERK activation by pretreating cells with the ERβ inhibitor PHTPP. PHTPP did not reduce ERK phosphorylation, suggesting ERβ is not involved in activation of ERK. MCF-7 cells were transfected with siRNA against ERα to further examine the role of ERα in ERK regulation. Knockout of ERα in MCF-7 cells subsequently treated with E2 showed a significant decrease in ERK phosphorylation. To ensure the specificity of the siRNA for ERα, transfected cells were stimulated with EGF. ERK phosphorylation following EGF treatment was not inhibited in ERα-knockout cells. Taken together our data suggests that ERα is capable of rapidly activating both CaM KI and ERK in MCF-7 cells.