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Estrogen Regulation of Jun and Fos in MCF-7 Cells

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Abstract

C-Fos and c-Jun are transcription factors that form the dimer Activator Protein 1 (AP-1) and bind DNA to initiate transcription. C-Fos, c-Jun are targets of the Extracellular Signal-Regulated Kinase (ERK) in multiple cell types, including MCF-7 breast cancer cells. The hormone estrogen (E2) can increase intracellular calcium levels which activates calcium/calmodulin-dependent kinase (CaM Kinase) proteins, which control ERK and gene transcription. Our goal was to evaluate the ability of E2 to activate c-Fos and c-Jun and induce their dimerization, via CaM KK and ERK, in MCF-7 cells. Interestingly, E2 stimulation of MCF-7 cells triggered phosphorylation of c-Jun and c-Fos an effect that was blocked with STO-609 and U0126, which target CaM KK and ERK, respectively. siRNA inhibition of CaM KK and ERK blocked E2-stimulated c-Jun and c-Fos phosphorylation. Additionally, E2 triggered AP-1 directed luciferase activity in MCF-7 cells that was blocked by inhibiting either CaM KK or ERK with siRNA. In summary, our data suggests that E2 utilizes both CaM KK and ERK to phosphorylate c-Jun and c-Fos and regulate their transcriptional activity in breast cancer cells.