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TRP Channel Regulation of Estrogen Signaling

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Abstract

Calcium regulates numerous cell functions including growth and development. Calcium can enter cells through transient receptor potential channels (TRPCs). Previous studies in MCF-7 cells have suggested that the expression of one particular TRPC, TRPC6, correlates with cell transformation and disease progression. Calcium has several cellular targets including the Calcium/Calmodulin-dependent protein kinases (CaM Ks) and ERK. Previous work has shown that estrogen (E2) may utilize CaM Ks and ERK to promote breast cancer cell proliferation, however the possible involvement of TRPCs in this pathway is currently unknown. Our objective was to understand which E2 receptor is used in our system and if TRPCs participate in the control of CaM Kinase activation of ERK in MCF-7 cells. Specifically, we wanted to explore if E2 may utilize TRPCs particularly, TRPC6, upstream of the ERK pathway in MCF-7 cells. E2 stimulation of MCF-7 cells and the estrogen receptor alpha (α) inhibitor, MPP, completely blocked ERK activity. In contrast, MPP did not block EGF stimulation of ERK. MCF-7 cells express endogenous TRPC6 protein and TRPC inhibitors, APB and SK&F, both blocked ERK activation downstream of E2. In addition, neither APB or SK&F inhibited EGF activation of ERK. Results from these studies suggest that E2 is capable of activating ERK through the specifically through the alpha form of the estrogen receptor and TRPCs.