Poster #19

Characterization of Rapid Estrogen Actions in Uterine Smooth Muscle and Leiomyoma Cells

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Leiomyomas, benign tumors originating from uterine smooth muscle, are a significant health concern among reproductive aged women, affecting almost 30% of the population. These tumors are hypersensitive to the mitogenic effects of estrogen but lack differences in expression of estrogen-regulated genes. This finding suggests that nongenomic actions, those that occur too quickly to be the result of transcription, may play an important role in these tissues' sensitivity to estrogen. In order to characterize and further study the rapid effects of estrogen in these tissues, we obtained unique uterine smooth muscle (UtSM) and leiomyoma (UtLM) cell lines. Western blot analyses yielded the following results. Estrogen (E_2) treatment rapidly: (1) increased levels of activated protein kinase C (PKC), an important player in uterine growth during pregnancy, in both cells types, (2) increased levels of activated protein kinase A (PKA), an inhibitor of cell proliferation, in UtSM cells but lowered levels in UtLM cells, and (3) increased levels of ERK1/2, the downstream effector of the proliferative MAPK cascade, in UtLM versus UtSM cells. Proliferation studies demonstrate that the stabilization of cAMP, the activator of protein kinase A, results in reduced proliferation of UtSM but not UtLM cells with E_2 treatment. Estrogen's rapid activation of the proliferative PKC and ERK1/2 proteins combined with lowered activation of the inhibitory PKA may contribute to the formation of leiomyomas. Ongoing studies are being conducted to determine whether rapid activation of PKA and PKC are G-protein and estrogen receptor dependent and the importance of these pathways in fine-tuning uterine smooth muscle's proliferative response to estrogen.

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