The DHEA metabolite 7β-hydroxy-epiandrosterone exerts anti-estrogenic effects on breast cancer cell lines.


Source
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Abstract
7β-Hydroxy-epiandrosterone (7β-OH-EpiA), an endogenous androgenic derivative of dehydroepiandrosterone, has previously been shown to exert anti-inflammatory action in vitro and in vivo via a shift from prostaglandin E2 (PGE2) to 15-deoxy-Δ(12,14)-PGJ2 production. This modulation in prostaglandin production was obtained with low concentrations of 7β-OH-EpiA (1-100nM) and suggested that it might act through a specific receptor. Inflammation and prostaglandin synthesis is important in the development and survival of estrogen-dependent mammary cancers. Estrogen induced PGE2 production and cell proliferation via its binding to estrogen receptors (ERs) in these tumors. Our objective was to test the effects of 7β-OH-EpiA on the proliferation (by counting with trypan blue exclusion), cell cycle and cell apoptosis (by flow cytometry) of breast cancer cell lines MCF-7 (ERα+, ERβ+, G-protein coupled receptor 30: GPR30+) and MDA-MB-231 (ERα-, ERβ+, GPR30+) and to identify a potential target of this steroid in these cell lineages (by transactivations) and in the nuclear ER-negative SKBr3 cells (GPR30+) (by proliferation assays). 7β-OH-EpiA exerted anti-estrogenic effects in MCF-7 and MDA-MB-231 cells associated with cell proliferation inhibition and cell cycle arrest. Moreover, transactivation and proliferation with ER agonists assays indicated that 7β-OH-EpiA interacted with ERβ. Data from proliferation assays on the MCF-7, MDA-MB-231 and SKBr3 cell lines suggested that 7β-OH-EpiA may also act through the membrane GPR30 receptor. These results support that this androgenic steroid acts as an anti-estrogenic compound. Moreover, this is the first evidence that low doses of androgenic steroid exert antiproliferative effects in these mammary cancer cells. Further investigations are needed to improve understanding of the observed actions of endogenous 7β-OH-EpiA.

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