DHEA-induced antiproliferative effect in MCF-7 cells is androgen- and estrogen receptor-independent.


Source

Departmento de Biología Celular, Instituto Nacional de Cardiología Ignacio Chávez,, UNAM, Mexico City, Mexico.

Abstract

Dehydroepiandrosterone, an adrenal hormone derived from cholesterol, can be metabolized to estrogens (estradiol) and androgens (testosterone). In this study, we evaluated whether the antiproliferative effect induced by dehydroepiandrosterone in MCF-7 cells (an estrogen-dependent breast cancer cell line) is direct, or indirect, through its conversion to estradiol or testosterone. Although dehydroepiandrosterone had an antiproliferative effect at supraphysiologic concentrations, when it was used at physiologic concentrations, it increased the proliferation of MCF-7 cells. 17Beta-estradiol induced an increase in MCF-7 cell proliferation at physiologic concentrations, whereas testosterone had a weak inhibitory effect at 100 microM. Dehydroepiandrosterone sulfate (its inactive sulfate ester) had no effect upon the cell cycle. Dehydroepiandrosterone-induced antiproliferative and proliferative effects were not blocked by inhibitors of androgen or estrogen receptors, thus indicating that its effect is secondary to a direct interaction with a "putative" receptor rather than a conversion into steroid hormones. These results suggest that dehydroepiandrosterone could be used at supraphysiologic concentrations in the treatment of breast cancer.

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