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1: Ann Clin Lab Sci. 1998 Nov-Dec;28(6):360-9.

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Progesterone inhibits growth and induces apoptosis in breast cancer cells: inverse effects on Bcl-2 and p53.

Formby B, Wiley TS.

Sansum Medical Research Institute, Santa Barbara, CA 93105, USA.

Progesterone inhibits the proliferation of normal breast epithelial cells in vivo, as well as breast cancer cells in vitro. But the biologic mechanism of this inhibition remains to be determined. We explored the possibility that an antiproliferative activity of progesterone in breast cancer cell lines is due to its ability to induce apoptosis. Since p53 and bcl-2 genetically control the apoptotic process, we investigated whether or not these genes could be involved in the progesterone-induced apoptosis. We found a maximal 90 percent inhibition of cell proliferation with T47-D breast cancer cells after exposure to 10 microM progesterone for 72 hours. Control progesterone receptor negative MDA-231 cancer cells were unresponsive to these two concentrations of progesterone. After 24 hours of exposure to 10 microM progesterone, cytofluorometric analysis of T47-D breast cancer cells demonstrated 43 percent had undergone apoptosis without signs of necrosis. After 72 hours of exposure to 10 microM progesterone, 48 percent of the cells had undergone apoptosis and 40 percent demonstrated "leaky" membranes. Untreated cancer cells did not undergo apoptosis. Evidence proving apoptosis was also demonstrated by fragmentation of nuclear DNA into multiples of oligonucleosomal fragments. After 24 hours of exposure to either 1 microM or 10 microM progesterone, the expression by T47-D cancer cells of bcl-2 was down-regulated, and that of p53 was up-regulated as detected by semiquantitative RT-PCR analysis. These results demonstrate that progesterone at a concentration similar to that seen during the third trimester of pregnancy exhibited a strong antiproliferative effect on at least two breast cancer cell lines. Apoptosis was induced in the progesterone receptor expressing T47-D breast cancer cells.

PMID: 9846203 [PubMed - indexed for MEDLINE]

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Bcl-2, survivin and variant CD44 v7-v10 are downregulated and p53 is upregulated in breast cancer cells by progesterone: inhibition of cell growth and induction of [Apoptosis](#) [Mol Cell Biochem. 1999]

Progesterone induces apoptosis and up-regulation of p53 expression in human ovarian carcinoma [\[Cancer Res. 1997\]](#)

Apoptosis inhibition mediated by medroxyprogesterone acetate treatment [\[Breast Cancer Res Treat. 2001\]](#)

Progesterone induces apoptosis in malignant mesothelioma [\[Anticancer Res. 2001\]](#)

Novel signaling molecules implicated in tumor-associated fatty acid synthase-dependent breast cancer cell proliferation and survival: Role of exogenous dietary fatty acids, p53-p21WAF1/CIP1, ERK1/2 MAPK, p27KIP1, BRCA1, and [\[Mol Cell Biochem. 2004\]](#)

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