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## Real men need oestrogen

› 23 May 1998 by **Nell Boyce**, Washington DC  
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THE gender gap between the sex hormones oestrogen and testosterone is not so huge after all. Researchers say oestrogen can bind to the same receptor as testosterone, and may play a role in normal male development.

Testosterone binds to androgen receptors in cells, turning on genes that control the development of the male reproductive system. Androgen receptors in prostate cancer cells sometimes respond to oestrogen, but most researchers had assumed that these malignant cells had a mutant form of androgen receptor.

Now Chawshang Chang and his colleagues at the University of Rochester in New York have shown that oestrogen can activate normal androgen receptors in the presence of a substance called ARA70, which exists naturally in the body (Proceedings of the National Academy of Sciences, vol 95, p 5527).

Oestrogen may contribute to normal reproductive development in men, the researchers say. They cite the case of a patient with an unusual form of ARA 70 who also had genital abnormalities, presumably because oestrogen was unable to bind to his cells' androgen receptors.

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## Estrogen Plays Role In Male Development

REUTERS  
Health Information Services

May 19, 1998

NEW YORK (Reuters) - While estrogen is often thought of as a female hormone, a surprising new study suggests that it may play a key role in the formation and function of the male reproductive system. The estrogen-androgen receptor pathway discovered by US researchers may lead to new therapies for prostate cancer, according to a report in the Proceedings of the National Academy of Sciences.

female

For the first time, a study has shown that the hormone can activate a receptor for androgens - hormones such as testosterone that produce male characteristics. A "coactivator" - a molecule that turns on genes in response to receptor binding - was affected by estrogen, increasing 30-fold the activation of genes linked to the androgen receptor, according to study authors Dr. Shuyuan Yeh, Dr. Chawnsang Chang and colleagues from the University of Rochester in Rochester, New York.

In laboratory studies using both yeast and human prostate cancer cells, the team demonstrated that only naturally produced estrogen, known as estradiol (E2), induced an interaction between the androgen receptor and the coactivator, ARA70. Diethylstilbestrol and other synthetic estrogens did not.

The findings have several implications, say the researchers. One is that estrogen plays a role in development of the male reproductive system, because an androgen-insensitivity syndrome that results in genital malformation can be traced to failure of the E2-ARA70-androgen receptor pathway.

Another implication relates to the treatment of prostate cancer. Testosterone can spur the growth of prostate cancer cells, and synthetic estrogens are used to block the process. However, the naturally occurring estradiol is generally a poor blocking agent for prostate cancer.

"Many clinical trials have suggested that E2 would be less effective than (diethylstilbestrol)... when used to treat prostate cancer," the authors add. "Our findings that E2, but not (diethylstilbestrol), can activate androgen-target genes in the prostate may, therefore, provide one explanation for this observation."

The study team also notes that a drug that can block the ARA70 coactivator from binding to the androgen receptor "could have significant therapeutic and perhaps preventative value."

A third implication of the pathway discovery lies in the theory that estrogen-like compounds in the environment may cause disease -- "it will be interesting to know whether any environmental pollutants-estrogenic compounds also have some androgenic activity that may contribute to the disruption of the endocrine system," write the researchers.

SOURCE: Proceedings of the National Academy of Sciences (1998;95:5527-5532)



## HEALTH NEWS

## Estrogen activates androgen receptor on prostate cells

Mon, 18 May 1998 23:53:01 GMT

WESTPORT, May 18 (Reuters) - Presenting evidence that estrogen has a role in the male reproductive system, researchers at the University of Rochester, New York, report that 17-beta-estradiol can activate androgen-receptor target genes.

In previous research, Dr. Shuyuan Yeh and Dr. Chawnsang Chang identified a coactivator, which they designated ARA70, that is relatively specific for the androgen receptor. In the May 12th issue of the Proceedings of the National Academy of Sciences USA, Drs. Yeh and Chang and two colleagues report that estrogen activates the androgen receptor in the presence of ARA70.

In laboratory studies using both yeast and human prostate cancer cells, the team demonstrated that naturally produced estrogen, 17-beta-estradiol (E2), induced an interaction between the androgen receptor and ARA70. Diethylstilbestrol and other estrogens did not. Furthermore, only in the presence of ARA70 did E2 start to activate the androgen receptor.

The Rochester team concludes that not only testosterone but also estrogen are natural ligands of the androgen receptor. The findings has several implications. One is that estrogen plays a role in maturation of the male reproductive system, because an androgen-insensitivity syndrome that results in genital malformation can be traced to failure of the E2-ARA70-androgen receptor pathway

Another implication relates to the treatment of prostate cancer. Dr. Yeh's group comments that "...ARA70 is a key factor for the E2- and androgen-mediated induction of androgen target genes in prostate. Therefore, a drug designed to block the interaction of [the androgen receptor] and ARA70 could have significant therapeutic and perhaps preventative value."

"Many clinical trials have suggested that E2 would be less effective than [diethylstilbestrol]...when used to treat prostate cancer," the authors add. "Our findings that E2, but not [diethylstilbestrol], can activate androgen-target genes in the prostate...may, therefore, provide one explanation for this observation."

Proc Natl Acad Sci USA 1998;95:5527-5532.

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