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Gynaecology

Oestrogen receptor ligands show promise for treating endometriosis

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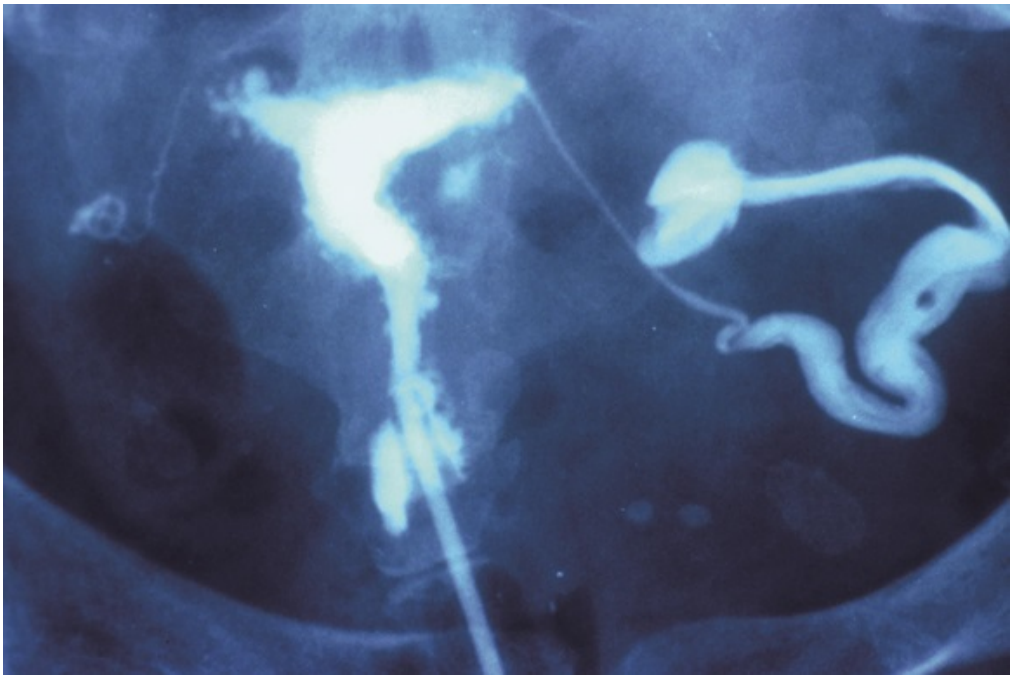
Studies show that two compounds can control endometriosis in mice without affecting fertility.



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Endometriosis creates inflammatory lesions and scar tissue that can cause severe pelvic pain, bowel and bladder problems, fatigue and reduced fertility in patients

Researchers studying endometriosis, a painful gynaecological condition that involves the growth of endometrial cells in areas outside the uterus, have discovered a potential way to treat the disease that avoids many of the side effects seen with existing therapies.

Two compounds, chloroindazole (CLI) and oxabicycloheptene sulfonate (OBHS), which both bind to oestrogen receptors, were shown to control inflammation and reduce lesions in mice models without affecting fertility.

The researchers, led by a team at the University of Illinois at Urbana-Champaign in the United States, say their work, published in *Science Translational Medicine*[1], has also provided greater insight into the causes and progression of the disease.

"While more years of work must be done to test these new compounds in other models, and eventually in human patients, the work demonstrates a new approach to treating endometriosis and other disorders tied to oestrogen signalling and inflammation," says one of the paper's authors, Benita Katzenellenbogen of the University of Illinois.

The paper notes that knowledge gained through the research could be applied to diseases ranging from multiple sclerosis to certain cancers, such as inflammatory breast cancer.

Endometriosis creates inflammatory lesions and scar tissue that can cause severe pelvic pain, bowel and bladder problems, fatigue and reduced fertility in patients. The disorder affects between 10% and 14% of women of reproductive age, totalling about 176 million women worldwide, according to the World Endometriosis Society.

Because the disorder is oestrogen dependent, researchers seeking to develop treatments face a careful balancing act in attempting to suppress oestrogen sufficiently to stop the disease from progressing while maintaining its beneficial effects, the authors note.

Current therapies focus largely on hormone treatments, including contraceptives and testosterone derivatives such danazol and gestrinone. These therapies block or reduce levels of oestrogen in patients in order to curtail further development of the disorder and help relieve pain. However, although hormonal treatments can improve the quality of life for patients, they do not reduce existing lesions and their effects are usually temporary. Moreover, they can cause severe side effects, such as loss of bone density and weight gain, and may further interfere with fertility.

Both CLI and OBHS reduced cell proliferation and blood-vessel density, and destroyed endometrial tissue located outside the uterus, without causing any perceptible damage to normal endometrial tissue.

In an article[2] accompanying the research paper, Warren B. Nothnick of the University of Kansas Medical Center says that the two compounds could represent a new line of attack by targeting disease tissue more directly, thereby sparing the menstrual cycle and improving the likelihood that patients would be able to achieve a pregnancy. However, he adds, "an immediate point of consideration going forward is whether compounds such as CLI or OBHS impact pregnancy establishment, pregnancy maintenance, or offspring well-being".

References:

[1]Zhao, Y, Gong, P, Chen, Y *et al.* Dual suppression of estrogenic and inflammatory activities for targeting of endometriosis. *Science Translational Medicine* 2015, doi: 10.1126/scitranslmed.3010626.

[2]Nothnick, WB. Endometriosis: Bright future for a cloudy past? *Science Translational Medicine* 2015, doi: 10.1126/scitranslmed.aaa5075.

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