

New relief for gynecological disorders

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The creation of new blood vessels in the body, called "angiogenesis," is usually discussed in connection with healing wounds and tumors. But it's also an ongoing process in the female reproductive tract, where the growth and breaking of blood vessels is a normal part of the menstrual cycle. But abnormal growth of blood vessels can have painful consequences and resultant pathologies.

Now, Prof. Ruth Shalgi and research associate Dr. Dana Chuderland of Tel Aviv University's Sackler Faculty of Medicine have found a potential treatment for this [abnormal growth](#) in a potent physiological anti-angiogenic factor, PEDF. Administered by simple injection, this protein reverses the symptoms of related diseases without compromising

fertility, according to pre-clinical studies.

These new findings, which have been reported in the *Journal of Clinical Endocrinology and Metabolism*, Human Reproduction and Molecular Human Reproduction, could provide relief for millions of women worldwide. This work was done in collaboration with Prof. Rafael Ron-El and Dr. Ido Ben-Ami from Assaf Harofeh Hospital.

Dangers of angiogenesis

There are two primary pathologies associated with angiogenesis in the female reproductive system. One is endometriosis, characterized by the passage of uterine cells to other locations in the body during menstruation, which causes [severe pain](#) and reduced fertility. The other is ovarian hyperstimulation syndrome (OHSS), a possible side effect of IVF treatments. This is a potentially life-threatening disease with symptoms including [abdominal pain](#) and swelling.

Approximately 170 million women suffer from endometriosis worldwide, and about 10 percent of women receiving IVF treatment develop OHSS. Because no treatment currently exists for either of these conditions, affected women have no choice but to suffer through the symptoms.

In the past few decades, scientists have conducted extensive research on both pro-angiogenic factors such as VEGF and anti-angiogenic factors including PEDF. The effect of PEDF in decreasing abnormal angiogenesis has been extensively investigated in the eye and in tumors. Prof. Shalgi and Dr. Chuderland hypothesized that the same protein could play a role in diseases of the [female reproductive system](#) related to [blood vessels](#) growth.

In both OHSS and endometriosis, rampant VEGF levels allow for the

abnormal vascularization that characterises both diseases. To counteract this effect and restore a healthy angiogenic balance in the reproductive system, the researchers turned to PEDF as a replacement therapy agent. In the lab, Prof. Shalgi and Dr. Chuderland developed mouse models of both endometriosis and OHSS. After preparing the PEDF protein, they injected the mice with it.

The researchers noted a "perfect reversal" of all symptoms, including reduced abdominal swelling in OHSS-induced mice and eradicated lesions in endometriosis. When evaluating whether this protein might affect fertility, they confirmed that PEDF had no negative impact on ovulation or pregnancy rate. In fact, it increased the number of ovulated eggs in the endometriosis model, suggesting improved fertility.

Easing the pain

The next step is to commercialize the protein for therapeutic use, say the researchers, who were the first to prove that this anti-angiogenic protein is active in the reproductive system. This discovery has been patent protected and is currently undergoing commercialization by Ramot, the technology transfer company of TAU.

There are currently no treatment options for women suffering from these diseases, explains Dr. Chunderland, who believes that endometriosis, in particular, is under-diagnosed and usually dismissed as severe menstrual pain. This new treatment could bring long-awaited relief from painful and seemingly uncontrollable symptoms, including severe abdominal pain and infertility issues.

[Endometriosis](#) has a negative impact on eggs' quality; 30 percent of women with this disease require fertility treatments in order to conceive, say the researchers. Women who develop OHSS have a lower chance of conception and a higher chance of miscarriage during their IVF

treatment cycles. If these diseases could be eradicated, it would ease the sometimes difficult road towards conception, they suggest.

Provided by Tel Aviv University

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