Genetic variants linked to increased risk of common gynecological disease

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Research published today identifies two genetic variants that increase the risk of developing endometriosis, a common gynaecological disease. The study provides clues to the origin of this often very painful condition, which has a significant impact on the quality of life of sufferers.

Details of the research, carried out at the Wellcome Trust Centre for Human Genetics and the Nuffield Department of Obstetrics & Gynaecology, University of Oxford; the Queensland Institute of Medical Research, Australia, and Brigham; and Women's Hospital and Harvard Medical School, Boston, USA, are published in the journal Nature Genetics.

Endometriosis is a common gynaecological disease affecting an estimated 6 to 10 per cent of all women in their reproductive years – an estimated 170 million women worldwide. It is characterised by the growth of cells similar to those lining the womb on organs in the pelvis, such as the ovaries and bowel. These deposits can cause inflammation and adhesions, and result in pelvic pain as well as infertility in some women. Why the deposits arise in the first place, and thrive outside the womb, is as yet largely unknown.

In some cases, endometriosis will only cause minor symptoms and go undiagnosed, but in more severe cases, debilitating symptoms can have a profound effect on the woman's life. The diagnosis can only be made reliably by looking into the pelvis with a laparoscope, which explains why it is common for years to pass before the diagnosis is made. Current

treatments are limited to surgery and hormonal drugs that have numerous side-effects.

Now, researchers from the International Endogene Consortium have compared the genomes of over 5,500 women surgically diagnosed with the disease from the UK, Australia and the US, and compared them with almost 10,000 healthy volunteers. They have identified two new genetic variants that increase the risk of developing the disease, particularly moderate-severe stages.

"Endometriosis can be a painful and distressing condition that affects a significant number of women in their reproductive years," explains Dr Krina Zondervan, a Wellcome Trust Research Career Development Fellow at the University of Oxford and the study's Principal Investigator. "We've known for some time that endometriosis is heritable, but until now we have been unable to find any robust genetic variants that influence a woman's risk of developing the disease."

The first is a variant on chromosome 7 believed to be involved in regulating nearby genes, probably those involved in the development of the womb and its lining. The second variant was found on chromosome 1, close to the gene WNT4. This is important for hormone metabolism and the development of the female reproductive tract, especially the ovaries, making it an important biological candidate for involvement in endometriosis.

"Our study is a breakthrough because it provides the first strong evidence that variations in DNA make some women more likely to develop endometriosis," says Dr Zondervan. "We now need to understand the effect of these variations on cells and molecules in the body."

Dr Stephen Kennedy, Head of the Nuffield Department of Obstetrics &

Gynaecology and joint senior author on the paper, adds: "We have great confidence that the results of this study will help towards developing less invasive methods of diagnosis and more effective treatments for endometriosis."

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