Coactivator stokes continuing fire of endometriosis

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(Medical Xpress) -- Endometriosis, which can cause severe pain and even infertility in the estimated 8.5 million U.S. women it affects, is driven by one of the cell's master regulators steroid receptor coactivator 1 or SRC-1, said researchers at Baylor College of Medicine in a report that appears online today in the journal *Nature Medicine*.

"This finding could lead to new therapies for this age-old condition," said Dr. Bert O'Malley, chair of molecular and cellular biology at BCM and the report's corresponding author.

The causes of endometriosis are unclear, because the molecular pathways involved have not been elucidated previously. The disorder involves the abnormal growth of cells similar to those of the lining of the uterus (the endometrium) outside that organ on the ovaries, fallopian tubes, pelvic cavity lining or other structures.

No one knows for sure how the endometrial tissue travels from the uterus to other structures but most believe that the tissue could back up into the abdomen through the fallopian tubes during a woman's monthly period. Estrogen can promote the growth of endometriosis.

Immortalized cells

Although the cells of endometriosis are not cancerous, they can become "immortalized," growing and reproducing and invading normal tissues.

In studies in mice and human tissue, O'Malley and his colleagues identified a truncated form of SRC-1 in endometrial cells.

This coactivator fragment cooperates with two other proteins known to play a role in endometriosis TNF-alpha (tumor necrosis factor alpha) and MMP9 (matrix metallopeptidase 9) to keep the endometrial cells alive and growing.

"Although the full SRC-1 molecule will actually increase the death of endometriosis cells, the full coactivator gets processed by the inflammatory process into a smaller piece (an isoform) that stops the cells from dying," said O'Malley. "We now know the mechanism that causes this to happen."

SRC-1 isoform

Understanding the role of the isoform of SRC-1 in maintaining the endometriosis is an important step toward developing new ways to treat it, said O'Malley.

Others who took part in this work include a lead coauthor, Dr. Sang Jun Han, and Drs. Shannon M. Hawkins, Khurshida Begum, Sung Yun Jung, Ertug Kovanci, Jun Qin, John P. Lydon, Francesco J. DeMayo, all of BCM.

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