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Researchers discover antibody that may help detect ovarian cancer in earliest stages

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Using a new approach to developing biomarkers for the very early detection of ovarian cancer, researchers at Rush University Medical Center have identified a molecule in the bloodstream of infertile women that could one day be used to screen for those at high risk for the disease — or even those with early-stage ovarian cancer.

The molecule, an antibody that the human body manufactures, is an autoimmune response to mesothelin. This well-studied protein is found in abundance on the surface of ovarian cancer cells but present only in limited amounts in normal human tissue.

The study is published in the online version issue of *Cancer Epidemiology, Biomarkers & Prevention*, published by the American Society for Cancer Research.

"The finding is extremely important because at present medical tests are unable to detect ovarian cancer in its early stages, which is why death rates from this disease are so high," said Judith Luborsky, PhD, professor of pharmacology, obstetrics and gynecology and preventive medicine at Rush and lead author of the study.

"Our approach to discovering cancer biomarkers was unique in this study. Instead of investigating molecules specific to ovarian cancer alone, we asked what molecules women with a risk of ovarian cancer and those with ovarian cancer had in common," Luborsky said.

The study enabled the researchers to explain the link between infertility and ovarian cancer that has been established in numerous epidemiological surveys.

"More important, with the discovery of the mesothelin antibody, we now have what appears to be a biomarker that can potentially be used in screening tests to help us conquer ovarian cancer," Luborsky said.

According to the American Cancer Society's most recent estimates, there are expected to be about 21,900 new cases of ovarian cancer in the U.S. in 2011 and about 15,460 deaths from the disease. Ovarian cancer is the ninth most common cancer in women (not counting skin cancer) and ranks fifth as the cause of cancer death in women. The poor prognosis for women with ovarian cancer is due to the lack of both clinical symptoms when the cancer first develops and the absence of laboratory tests specific to the disease.

In the study at Rush, researchers tested for mesothelin antibodies in the bloodstream of 109 women who were infertile, 28 women diagnosed with ovarian cancer, 24 women with benign ovarian tumors or cysts, and 152 healthy women. Infertility was due to endometriosis, ovulatory dysfunction or premature ovarian failure or was unexplained.

Significant levels of mesothelin antibodies were found in women with premature ovarian failure, ovulatory dysfunction and unexplained infertility, as well as in women with ovarian cancer, although not in women with endometriosis and not in healthy women or women with benign disease. Endometriosis is generally associated with a different kind of ovarian carcinoma than other types of infertility, which may explain why mesothelin antibodies were not found in these cases.

Why the presence of mesothelin antibodies in the bloodstream should be linked with ovarian cancer is not clear.

"It has been hypothesized that an autoimmune response precedes or somehow contributes to the development and progression of malignant tumors," Luborsky said. "We think that antibodies may arise in response to very early abnormal changes in ovarian tissue that may or may not progress to malignancy, depending on additional triggering events. Or, alternatively, antibodies may bind to normal cells in the ovary, causing dysfunction and leading to infertility -- and, in a subpopulation of women, to the development of ovarian cancer."

Provided by Rush University Medical Center