Estrogen replacement therapy speeds ovarian cancer growth, new study reports

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Estrogen therapy used by menopausal women causes a type of ovarian cancer to grow five times faster, according to a new study by researchers at the University of Colorado Cancer Center.

Menopausal estrogen replacement therapy (ERT) also significantly increases the likelihood of the cancer metastasizing to the lymph nodes, according to the study, which will be published in the Nov. 1 issue of *Cancer Research*. The study was released online Oct. 19, 2010. *Cancer Research,* published by the American Association for Cancer Research, is the world's largest circulation medical journal devoted specifically to cancer research.

The effect of ERT was shown in mouse models of estrogen receptor positive(ER+) ovarian cancer, which accounts for about 60 percent of all human ovarian cancer cases. Ovarian cancer is one of the deadliest cancers affecting women. This year alone, nearly 22,000 women will be newly diagnosed with ovarian cancer and an estimated 13,850 women will die from the disease, according to the National Cancer Institute.

"We showed that estrogen replacement substantially increases proliferation and risk of distant lymph node metastasis in ER+ tumors," says Monique Spillman, MD, PhD, the study's lead researcher, a gynecologic oncologist at University of Colorado Hospital and assistant professor at of obstetrics and gynecology at the University of Colorado School of Medicine.

For the first time, Spillman and her team measured ovarian cancer growth in the abdomen of mice using novel techniques for visualizing the cancer. In mice with ER+ ovarian cancer cells, which were tagged with a firefly-like fluorescent protein that allowed them to be tracked, the introduction of estrogen therapy made the tumors grow five times faster than in mice that did not receive the ERT. The risk of the cancer moving to the lymph nodes increased to 26 percent in these mice compared with 6 percent in mice that did not receive ERT.

The team also found that the estrogen-regulated genes in ovarian cancer reacted differently than ER+ genes found in breast cancer, helping to explain why current anti-estrogen therapies used with breast cancer, such as Tamoxifen, are largely ineffective against ovarian cancer.

"Breast cancer and ovarian cancer are often linked when talking about hormone replacement therapy, but we found that only 10 percent of the ER+ genes overlapped," Spillman says. "We were able to identify estrogen-regulated genes specific to ER+ ovarian cancer that are not shared with ER+ breast cancers. We believe these genes can be specifically targeted with new anti-estrogen therapies that could more effectively treat ER+ ovarian cancers."

Spillman and her team now will begin to screen current antiestrogen therapies against the newly identified ovarian cancer genes to identify the pathways and compounds that are more likely to effectively treat ER+ ovarian cancer.

This study looked at the effect of estrogen replacement therapy in mice that already possessed ER+ ovarian cancer cells. It did not test whether the estrogen replacement actually could cause the development of these cancer cells. The study also dealt only with estrogen replacement, which is linked to higher risks of ovarian cancer, not combined estrogen/progesterone therapy that is used with women who retain their

uteruses.

This research is too early to draw implications for use of estrogen replacement therapy in women, Spillman cautions. "We cannot make clinical recommendations based on what is happening in mice," says Spillman, one of just eight gynecological oncologists in Colorado. "Every woman is different and needs to talk to her doctor about the decision to use hormone replacement therapy."

Provided by University of Colorado Denver