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**Exploring the Link Between Endometriosis and Ovarian Cancer**

**Grantee**: Michael R. Wilson, PhD (sent headshot but may be too tiny to use)

**Institution**: Michigan State University (North Central)

**Area of Research**: Develop, Differentiation and Cancer

**Grant Term**: 1/1/2018 to 12/31/2020

**The Challenge:** The origin of ovarian cancer has long been the subject of debate. There's evidence that some ovarian cancers may not start in the ovary at all.

Endometriosis is a disorder where cells lining the uterus don't flow out of the body during menstruation but instead travel to and grow in other nearby organs and tissues. It's a risk factor for ovarian cancer, but few experiments have tested whether cells from the uterus can give rise to ovarian cancer.

**The Research:** Both endometriosis and endometriosis-associated ovarian cancers have high rates of mutation in the gene that makes ARID1A protein. This suggests that the two problems may be related. Michael R. Wilson, PhD, and his team are using genetically engineered mice to study whether mutant cells from the inner lining of the uterus can form tumors on the ovary.

They're removing endometrium tissue with faulty ARID1A genes from altered mice and placing it into normal mice to determine:

* How ARID1A prevents tumors in the endometrial cells in the uterus
* What's required to enable tissues outside the uterus to spread these cells to the ovary and later start tumors

They are also comparing mutant ovary cells to mutant endometrial cells, looking for biomarkers —signs that ovarian cancers come from the endometrium.

**The Goal and Long-term Possibilities:** Wilson seeks a better understanding of the origins of endometriosis-associated ovarian cancer and the role endometriosis plays. His work may lead to future research as well as pointing to surgeries that could prevent these cancers.

**ORIGINAL**

An estimated 14,000 women will die this year from ovarian cancer. Despite being a deadly disease, ovarian cancer treatment options are very limited. Even still, there are debates within the oncology community over the origins of ovarian cancer. There is evidence that some ovarian cancers may not originate in the ovary at all, but that ovarian cancer may be the result of cells that have moved to the ovary from other parts within the female reproductive tract. Nearly a century ago, Dr. John Sampson proposed that certain types of ovarian cancer might be caused by endometriosis, a painful disease which reduces fertility and affects 5-10% of all women. Endometriosis occurs when cells lining the uterus do not flow out of the body via menstruation, but instead colonize other tissues within the reproductive tract, such as the ovaries, or in other parts of the body, including the abdomen. Although endometriosis is a risk factor for ovarian cancer, there have been few experiments designed to test the hypothesis that cells from the uterus are capable of traveling to the ovary before giving rise to ovarian cancer.

Here, we present a new model to study endometriosis-associated ovarian cancer. We use genetically engineered mice to target recurrent ovarian cancer mutations to the endometrial epithelium, the cells lining the uterus. We propose to use this model to understand several aspects of endometriosis-associated ovarian cancers and ask the age-old question: Do mutant cells from the endometrium metastasize to the ovary? By removing mutant endometrium from genetically altered mice and placing it into normal mice, we can study whether mutant endometrium is capable of forming tumors on the ovary. Adding precedence to my studies, another subtype of ovarian cancer, serous carcinoma, which originates from cells in the fallopian tubes, can be treated with surgery to remove the fallopian tubes. To identify potential preventative surgeries for endometrium-derived ovarian cancer, we will perform a series of surgeries on mutant mice in which various reproductive organs are removed. By comparing mutant ovary cells to mutant endometrial cells, we can identify biomarkers for ovarian cancers which are derived from the endometrium. An understanding of the origins of endometriosis-associated ovarian cancer will be essential to increase the clinical relevance of endometriosis, and to inform the effort towards developing preventative surgeries for these cancers.