Five genetic variations increase risk of ovarian cancer

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An international research collaboration has found five new regions of the human genome that are linked to increased risks for developing ovarian cancer. Duke Medicine researchers played a leading role analyzing genetic information from more than 40,000 women.

The findings are published in four studies, two appearing in the journal *Nature Communications* and two in *Nature Genetics* on March 27, 2013. The research is being published as part of a coordinated release of new data from the Collaborative Oncological Gene-environment Study (COGS), an international effort to identify genetic variations that make certain people susceptible to developing breast, prostate and ovarian cancers.

According to the National Cancer Institute, ovarian cancer accounts for 3 percent of all cancers in women and is the leading cause of death among cancers of the female reproductive system. This is due to the lack of early symptoms or effective screening tests.

Inherited mutations in the BRCA1 and BRCA2 genes dramatically increase ovarian cancer risk. Genetic testing for BRCA1 and BRCA2 mutations can identify women who would benefit most from surgery to prevent ovarian cancer, but this is relevant to less than 1 percent of the population. Other genetic variants that are more common may also affect ovarian risk. The Ovarian Cancer Association Consortium previously described six such genetic differences and now the COGS project has found five more.

"Because ovarian cancer is relatively uncommon, it is critically important to identify subsets of women at increased risk," said senior coauthor Andrew Berchuck, MD, director of the division of gynecologic oncology at Duke Cancer Institute. "Although the common genetic risk variants for ovarian cancer discovered thus far are not strong enough to use in practice, this may become a reality as additional variants are discovered. This could facilitate development of ovarian cancer screening and prevention strategies directed towards women most likely to benefit."

"Our hope is that these genetic variants, along with established epidemiologic factors, such as reproductive history, will not only enhance our ability to predict which women are at increased risk for developing this highly fatal disease, but will also provide new insight into the underlying biology and pathogenesis of ovarian cancer," said epidemiologist Joellen Schildkraut, PhD, director of the Cancer Control and Population Sciences program at Duke Cancer Institute. She is a senior coauthor of one of the Nature studies and the principal investigator of the North Carolina Ovarian Cancer Study, one of the studies that contributed data to this discovery.

"Because of the large number of study subjects, we were able to determine that some genetic variants were important to specific subgroups of ovarian cancer, suggesting possible differences in the underlying cause of these subtypes," Schildkraut said.

Additional studies on the biology of these genetic variants could help researchers develop new tests to predict which women are at risk of developing ovarian cancer, and potentially lead to therapies that better treat the disease.

Provided by Duke University Medical Center