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Researchers find possible genetic keys to surviving epithelial ovarian cancer

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Researchers at Moffitt Cancer Center and colleagues from 11 other institutions in the United States and the United Kingdom have used two genome-wide association studies (GWAS) – one from the U.S. and one from the U.K. – to detect a novel set of genes found to be associated with epithelial ovarian cancer patient survival. The discovery could open the door to new therapies for treating epithelial ovarian cancer (EOC), the most lethal kind of gynecologic malignancy.

The study appeared in a recent issue of *Cancer Epidemiology, Biomarkers & Prevention* published by the American Association for Cancer Research.

The research team applied gene set analysis (GSA) for the first time to epithelial ovarian cancer gene databases. The gene set analysis mapped 857genes related to EOC that pass signals "downstream" to components in the cell which, in turn, are activated and trigger a change in the state of the cell.

One of the most significant gene sets they analyzed was comprised of a set of eight genes involved in macrolide (a class of drugs) "binding" which interact with immune suppressant FK506 and involve intracellular signaling.

Other studies have indicated that the binding protein (FKBP65) was "highly expressed in ovarian epithelium." FKBP65 has also been found to be inversely associated with the expression of tumor suppressor gene

P53.

Researchers expect that the results of their GSA can be used to focus on the role and function of these specific gene sets and may ultimately help uncover additional genetic causes of complex traits.

"Epithelial ovarian cancer is the fifth leading cause of cancer mortality among women in the U.S.," said study co-author Thomas A. Sellers, Ph.D., M.P.H., Moffitt executive vice president and director of the Moffitt Research Institute. "Because women may vary in their ability to eradicate disease or tolerate treatment, genetic association studies like ours are needed to identify the genetic bases related to outcome. Until this study, GWAS have not uncovered any outcome-associated genetic traits for EOC."

The gene set analysis the researchers used in this study focused specifically on EOC survival data in the genome-wide association studies. According to Sellers, GSA helps to systematically narrow the search for relevant genes.

"Unfortunately, GSA does not allow us to determine the gene set's effect on outcome," explained Sellers. "GSA does, however, contribute to our understanding of the relationship between EOC genetic variation and mortality. Our results using GSA may lead to the discovery of other possible gene sets and novel genes related to EOC that can be followed up in future studies."

Provided by H. Lee Moffitt Cancer Center & Research Institute