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Genetic variants may affect the risk of breast cancer in women with BRCA2 mutations

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An international study led by researchers at Memorial Sloan-Kettering Cancer Center has identified genetic variants in women with BRCA2 mutations that may increase or decrease their risk of developing breast cancer. The study was published today online in the open-access journal *PLoS Genetics*.

The findings of the study suggest that genetic variants on chromosomes 10 and 20 may modify risk for breast cancer among women with a BRCA2 mutation.

Researchers analyzed DNA samples from 6,272 women with BRCA2 mutations in a two-stage genome-wide association study. The chromosome 10 variant identified in the study, near the gene ZNF365, decreased the risk of breast cancer by approximately 25 percent in women also carrying a mutation of the BRCA2 gene. The current study and a recent report published in Nature Genetics found that variants near the same gene, ZNF365, affect breast cancer risk in the general population. While BRCA2 mutations are rare, the ZNF365 variant is more common, seen in one in ten individuals. In addition, researchers found that other variants, including FGFR2, recognized to increase breast cancer risk in the general population, also served as risk modifiers for women with BRCA2 mutations.

"The risk of breast cancer associated with BRCA2 mutations varies widely. Our goal in this study was to test the hypothesis that common genetic variants may modify cancer risk in those already carrying 'high

risk' mutations," said the study's senior author, Kenneth Offit, MD, MPH, Chief of the Clinical Genetics Service at Memorial Sloan-Kettering. "It's interesting that our study of BRCA2 and a companion study of BRCA1 both found that women with BRCA mutations likely have the same risk modifiers for breast cancer as women in the general population."

While the authors state that these findings do not have any immediate clinical implications, the discovery of these risk modifiers for women with BRCA2 mutations is important for further research into the role of genetic causes of breast cancer.

Provided by Memorial Sloan-Kettering Cancer Center