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Breast cancer risk amplified by additional genes in combo with BRCA mutation

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Many women with a faulty breast cancer gene could be at greater risk of the disease due to extra risk-amplifying genes, according to research published this month in the American Journal of Human Genetics.

Researchers at the University of Pennsylvania School of Medicine join an international consortium of research groups that looked at more than 10,000 women carrying a BRCA1 or BRCA2 mutation for breast-cancer risk.

“These results suggest that knowledge of a BRCA1 or BRCA2 mutation is necessary, but not sufficient, to fully understand cancer risk in women who carry these mutations,” says co-author and head of the North American coalition Timothy R. Rebbeck, PhD, Professor of Epidemiology at Penn. “This paper demonstrated that other genes, and possibly exposures, could provide important information that may refine our ability to predict cancer in this high-risk population. Because carriers of BRCA1 or BRCA2 mutations are relatively rare in the population, the only way to undertake studies of this type is by forming large consortia.” Rebbeck is also the Associate Director for Population Science at Penn’s Abramson Cancer Center.

“This is the first time we have found evidence that common changes in other genes can amplify the risk of breast cancer in women known to have faulty BRCA genes,” says lead author Professor Doug Easton, director of Cancer Research UK’s Genetic Epidemiology Unit at the University of Cambridge. “This is the first step in finding a set of genes

that modify the risk in BRCA carriers, and may influence how we monitor women with a family history of the disease."

The international team of scientists have found that common versions of two genes – FGFR2 and TNRC9 – known to increase breast cancer risk in the general population – also increase the risk in women carrying damaged versions of the BRCA2 gene.

Around one in eighteen women will develop breast cancer by the age of 65. On average, half of women carrying a faulty BRCA2 gene will develop the disease by the age of 70.

This study found that particular combinations of the FGFR2 and TNRC9 genes modify breast cancer risk in BRCA2 mutation carriers. One percent of BRCA2 mutation carriers have the highest risk combination of FGFR2 and TNRC9 genes. Seven in every 10 women in this category are predicted to develop breast cancer.

Around twenty percent of the BRCA2 mutation carriers have the lowest risk combination of the FGFR2 and TNRC9 genes. The researchers found that their risk is lowered so four in every 10 women in this category are expected to develop the disease.

These findings are the first step in a series of studies hunting for breast cancer susceptibility genes, which aims to better monitor and treat women with a family history of the disease.

Source: University of Pennsylvania

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