Two new breast cancer genes emerge from Lynch syndrome gene study

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Researchers at Columbia University Irving Medical Center and NewYork-Presbyterian have identified two new breast cancer genes. Having one of the genes—MSH6 and PMS2—approximately doubles a woman's risk of developing breast cancer by age 60.

The study, in collaboration with GeneDx, a genetic testing company, was published online today in *Genetics in Medicine*.

The two genes were previously known to cause Lynch syndrome, an inherited condition that raises the risk of colorectal, ovarian, stomach, and endometrial cancer. Lynch syndrome is the most common inherited cause of colorectal cancer, accounting for about 3 percent of newly diagnosed cases. One in 440 Americans has a gene variant that causes Lynch syndrome.

Researchers had suspected that Lynch syndrome genes may also cause breast cancer. Some studies had found a link, whereas others had not.

"People with Lynch syndrome aren't thinking they may also be at risk for breast cancer," said Wendy Chung, MD, PhD, the Kennedy Family professor of pediatrics (in medicine) at Columbia University Irving Medical Center, clinical geneticist at NewYork-Presbyterian/Columbia, and the study's senior author. "Given the fact that genomic analysis is becoming more common in patients with a personal or family history of cancer, we have an opportunity to do more targeted breast cancer screening in women who carry any of the genes associated with risk for this disease."

The researchers analyzed a database of more than 50,000 women who had undergone multi-gene hereditary cancer testing between 2013 and 2015. Of these, 423 women had a mutation in one of the four genes that cause Lynch syndrome: MLH1, MSH2, MSH6, and PMS2.

Additional analyses revealed that women with a mutation in two specific Lynch syndrome genes—MSH6 and PMS2—had a two-fold higher risk of breast cancer compared to women in the general population.

Based on the incidence of cancer in the study population, the researchers calculated that about 31 to 38 percent of women with cancer-causing MSH6 and PMS2 variants will develop breast cancer, compared to around 15 percent of women in the general population.

"The new study suggests MSH6 and PMS2 should be added to the list of genes to screen for when there is a history of breast cancer," said Dr. Chung, who is also director of the clinical genetics program at NewYork-Presbyterian/Columbia. "Screening for these genes also would give these families potentially life-saving information to prevent colon cancer by encouraging individuals with the genes to increase the frequency of their colonoscopies."

Currently, testing for Lynch syndrome genes is generally only done when someone has a personal or family history of colon or uterine cancer.

Dr. Chung added, "Given that Lynch syndrome is

not rare in the general population, this finding has the potential to impact tens of thousands of people in the U.S. and could change standard practice related to one of the most common cancer predisposition syndromes."

More information: Maegan E Roberts et al, MSH6 and PMS2 germ-line pathogenic variants implicated in Lynch syndrome are associated with breast cancer, *GENETICS in MEDICINE* (2018). DOI: 10.1038/gim.2017.254

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