

First confirmed common genetic risk factors for breast cancer

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The most powerful genetic analysis of the DNA codes of over 40,000 women -- including those with breast cancer as well as those without the disease – has uncovered five common genetic variants that increase an individual's risk for breast cancer.

In a paper published online today in the journal Nature, the international team of scientists who conducted the genome-wide association study report that these five genes code for proteins crucial to biological activities that previously had not been implicated as triggers of breast cancer. The genes carry the DNA recipes for proteins important to the growth and duplication of body cells and the signalling, or communications, that must occur between cells in order for the body to function normally.

Previous investigations have identified about a dozen genetic mutations associated with breast cancer susceptibility. Normal versions of these genes help prevent cancer from occurring in the first place, by helping cells to repair DNA breaks and other abnormalities that can result from chance or exposure to an environmental toxin, such as excessive UV sunlight. However, BRCA-1, BRCA-2 and the other previously identified breast cancer susceptibility genes are mutated in a relatively small percentage of women.

"Risk mutations within these genes are so rare that only a very small number of breast cancer incidences are caused by these mutations," said Jianjun Liu, Ph.D., co-author of the Nature paper and Senior Research



Scientist at the Genome Institute of Singapore, one of the over 20 research institutions collaborating in the international study of breast cancer genes.

The five genetic variants identified by Dr. Liu and collaborators occur more frequently among women with breast cancer than do BRCA and the other previously identified breast cancer susceptibility genes.

The five genes are the FGFR2, TNRC9/ LOC643714, MAP3K1, and LSP1.

"This is a truly landmark breakthrough for breast cancer research, because these genes are the first confirmed common genetic risk factors for breast cancer," said Dr. Liu.

As common genetic risk factors, these genes likely have more impact than the previously identified risk genes on disease prevalence across a large population of women. However, Dr. Liu pointed out, breast cancer susceptibility is conferred by a large number of genetic loci, each with a small effect on breast cancer risk.

"Breast cancer likely involves many risk genes, and each gene only confers a moderate risk for disease," Dr. Liu explained.

While the findings of the international research collaboration hopefully will fuel the development of more effective ways of preventing and treating breast cancer, Dr. Liu said that the most immediate benefit of the new results may be in understanding the molecular mechanisms of breast cancer.

The Nature paper is the second major research report published this year by this international team of scientists. In February of this year, the team reported in Nature Genetics that they had identified a gene (Caspase 8)



that could reduce cancer risk by as much as 10 percent.

The international research collaboration, known as the Breast Cancer Association Consortium, was established in 2005 to provide large sample sizes for examining genetic associations. In addition to GIS, participants include the Karolinska Institute with which the GIS has several other collaborations, and scientific institutions in other countries of Europe, as well as the U.S., and Australia.

Source: Agency for Science, Technology and Research (A*STAR), Singapore

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