Three new genetic links to breast cancer identified

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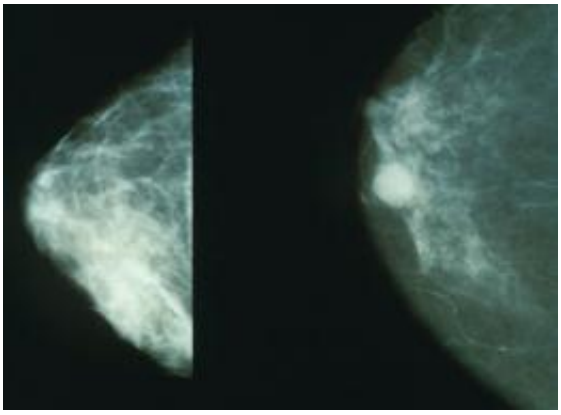

Mammograms showing a normal breast (left) and a cancerous breast (right). Credit: Wikipedia.

(Medical Xpress) -- An international team of researchers has identified three new genetic loci associated with an increased susceptibility to breast cancer. As described in their paper published in *Nature Genetics*, the three new loci will be added to the previous 22 that have been previously found and appear to be associated with mammary gland and bone growth and estrogen receptor signaling.

Breast cancer is the most common form of cancer in women; each year, approximately one million women are diagnosed with it and 400,000 die as a result. Research into its cause spans the globe as scientists continually strive to find out why it occurs so they can prevent it from

happening. The team working on this latest breakthrough has twenty four identifiable members listed and many institutions spanning the globe. All told, people from over twenty two countries contributed.

To find the new genetic links, the research team studied the medical histories of 57,000 breast cancer patients and 58,000 genome profiles from women who had never had the disease. As part of their research, they focused on 72 specific single nucleotide polymorphisms (SNPs), which is where a base in the DNA is different than the base in the average case. Specifically, they looked at three SNPs in just a small group of chromosomes. It was there, on 12p11, that they found the three new links, in this case, variants in the chromosome.

The team's research indicates that one variant that appears in 12p11 is linked to both estrogen receptor-positive and negative breast cancers and that one of the variants appears to be involved in the development of mammary glands and bone growth. This coincides with prior research that has shown that mammary growth in puberty plays a role in the development of breast cancer.

Unfortunately, the newly found genetic links likely play a role in the development of breast cancer in just 0.7 percent of such cases, which when added to the previous 22 links found still brings the total to just nine percent of all cases that have a known genetic link. This means the new results are more of an addition of information to a growing volume that when taken as a whole contribute to the expanding knowledge base.

It also, the authors point out, highlights just how complex cancer is and how difficult it will be to find a way to stop it from occurring in people in the future.

More information: Genome-wide association analysis identifies three new breast cancer susceptibility loci, *Nature Genetics* (2012)

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Abstract

Breast cancer is the most common cancer among women. To date, 22 common breast cancer susceptibility loci have been identified accounting for ~8% of the heritability of the disease. We attempted to replicate 72 promising associations from two independent genome-wide association studies (GWAS) in ~70,000 cases and ~68,000 controls from 41 case-control studies and 9 breast cancer GWAS. We identified three new breast cancer risk loci at 12p11 (rs10771399; $P = 2.7 \times 10^{-35}$), 12q24 (rs1292011; $P = 4.3 \times 10^{-19}$) and 21q21 (rs2823093; $P = 1.1 \times 10^{-12}$). rs10771399 was associated with similar relative risks for both estrogen receptor (ER)-negative and ER-positive breast cancer, whereas the other two loci were associated only with ER-positive disease. Two of the loci lie in regions that contain strong plausible candidate genes: PTHLH (12p11) has a crucial role in mammary gland development and the establishment of bone metastasis in breast cancer, and NRIP1 (21q21) encodes an ER cofactor and has a role in the regulation of breast cancer cell growth.