

Specific gene increases susceptibility to breast cancer

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Much work has been done to identify genetic variations that predispose women to breast cancer. Previous work showed that variants in the gene called fibroblast growth factor receptor 2 (FGFR2) were associated with increased risk of the disease, but how these variants translated into increased risk was unknown.

A new paper by Kerstin Meyer and colleagues, published this week in the open-access journal PLoS Biology, shows how specific changes in the FGFR2 gene alter the way regulatory molecules bind to it, leading to increased gene expression, which, in turn, increases the risk of developing breast cancer.

By comparing all of the tiny differences in the genomes of people with breast cancer to those in a control population, FGFR2 had been flagged up as a region of the genome that is consistently different between the two groups. FGFR2 encodes a protein that sits in the membrane of cells and works in a signalling pathway important for cell growth.

This study, conducted in the Cancer Research UK Cambridge Research Institute, has identified just what these slight genetic changes mean at the molecular level. FGFR2 genes altered at two specific points have a greater affinity for binding certain transcription factors—regulatory proteins that influence gene expression patterns. Because of this additional binding, more FGFR2 protein is produced in cells carrying the mutation and this seems to be enough to increase the risk of cancer a small but significant amount.

Interestingly, the mutation occurs not in the coding regions of the genes (the bits translated into protein by cellular machinery), but rather, in an intron (a region of DNA found amongst the coding bits). The two alterations therefore affect the regulation of the gene, but the proteins produced are normal; there is too much of it for the cells to develop as normal, instead becoming cancerous.

Citation: Meyer KB, Maia A-T, O'Reilly M, Teschendorff AE, Chin S-F, et al. (2008) Allele-specific up-regulation of FGFR2 increases susceptibility to breast cancer. PLoS Biol 6(5):e108.
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