Genetic polymorphisms in DPF3 associated with risk of breast cancer and lymph node metastases.

BACKGROUND: Several studies have identified rare genetic variations responsible for many cases of familial breast cancer but their contribution to total breast cancer incidence is relatively small. More common genetic variations with low penetrance have been postulated to account for a higher proportion of the population risk of breast cancer. METHODS AND RESULTS: In an effort to identify genes that influence non-familial breast cancer risk, we tested over 25,000 single nucleotide polymorphisms (SNPs) located within approximately 14,000 genes in a large-scale case-control study in 254 German women with breast cancer and 268 age-matched women without malignant disease. We identified a marker on chromosome 14q24.3-q31.1 that was marginally associated with breast cancer status (OR = 1.5, P = 0.07). Genotypes for this SNP were also significantly associated with indicators of breast cancer severity, including presence of lymph node metastases (P = 0.006) and earlier age of onset (P = 0.01). The association with breast cancer status was replicated in two independent samples (OR = 1.35, P = 0.05). High-density association fine mapping showed that the association spanned about 80 kb of the zinc-finger gene DPF3 (also known as CERD4). One SNP in intron 1 was found to be more strongly associated with breast...
cancer status in all three sample collections (OR = 1.6, P = 0.003) as well as with increased lymph node metastases (P = 0.01) and tumor size (P = 0.01). CONCLUSION: Polymorphisms in the 5’ region of DPF3 were associated with increased risk of breast cancer development, lymph node metastases, age of onset, and tumor size in women of European ancestry. This large-scale association study suggests that genetic variation in DPF3 contributes to breast cancer susceptibility and severity.

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