

## **A locus on 19p13 modifies risk of breast cancer in BRCA1 mutation carriers and is associated with hormone receptor-negative breast cancer in the general population.**

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### **Source**

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### **Abstract**

Germline BRCA1 mutations predispose to breast cancer. To identify genetic modifiers of this risk, we performed a genome-wide association study in 1,193 individuals with BRCA1 mutations who were diagnosed with invasive breast cancer under age 40 and 1,190 BRCA1 carriers without breast cancer diagnosis over age 35. We took forward 96 SNPs for replication in another 5,986 BRCA1 carriers (2,974 individuals with breast cancer and 3,012 unaffected individuals). Five SNPs on 19p13 were associated with breast cancer risk ( $P(\text{trend}) = 2.3 \times 10^{-8}$  to  $P(\text{trend}) = 3.9 \times 10^{-8}$ ), two of which showed independent associations (rs8170, hazard ratio (HR) = 1.26, 95% CI 1.17-1.35; rs2363956 HR = 0.84, 95% CI 0.80-0.89). Genotyping these SNPs in 6,800 population-based breast cancer cases and 6,613 controls identified a similar association with estrogen receptor-negative breast cancer (rs2363956 per-allele odds ratio (OR) = 0.83, 95% CI 0.75-0.92,  $P(\text{trend}) = 0.0003$ ) and an association with estrogen receptor-positive disease in the opposite direction (OR = 1.07, 95% CI 1.01-1.14,  $P(\text{trend}) = 0.016$ ). The five SNPs were also associated with triple-negative breast cancer in a separate study of 2,301 triple-negative cases and 3,949 controls ( $P(\text{trend}) = 1 \times 10^{-8}$  to  $P(\text{trend}) = 8 \times 10^{-8}$ ; rs2363956 per-allele OR = 0.80, 95% CI 0.74-0.87,  $P(\text{trend}) = 1.1 \times 10^{-8}$ ).

### **Comment in**

- [Nat Rev Cancer. 2010 Nov;10\(11\):743.](#)
- [Nat Genet. 2010 Oct;42\(10\):819-20.](#)