Association analysis identifies 65 new breast cancer risk loci

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Abstract
Breast cancer risk is influenced by rare coding variants in susceptibility genes, such as BRCA1 and many common, mostly non-coding variants. However, much of the genetic contribution to breast cancer risk remains unknown. Here we report the results of a genome-wide association study of breast cancer in 152,977 cases and 105,974 controls of European ancestry and 54,683 cases and 43,104 controls of East Asian ancestry. We identified 65 new loci that are associated with overall breast cancer risk at P < 5 × 10⁻⁸. The majority of credible risk single-nucleotide polymorphisms in these loci fall in distal regulatory elements, and by integrating in silico data to predict target genes in breast cells at each locus, we demonstrate a strong overlap between candidate target genes and somatic driver genes in breast tumors. We also find that heritability of breast cancer due to all single-nucleotide polymorphisms in regulatory features was 2.5-fold enriched relative to the genome-wide average, with strong enrichment for particular transcription factor binding sites. These results provide further insight into genetic susceptibility to breast cancer and will improve the use of genomic risk scores for individualized screening and prevention.