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Association of genetic variants at TOX3, 2q35 and 8q24 with the risk of familial and early-onset breast cancer in a South-American population.

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Abstract

Recent Genome-Wide Association Studies have identified several single nucleotide polymorphisms (SNPs) associated with breast cancer (BC) among women of Asian, European, and African-American ancestry. Nevertheless, the contribution of these variants in the South American population is unknown. Furthermore, there is little information about the effect of these risk alleles in women with early BC diagnosis. In the present study, we evaluated the association between rs3803662 (TOX3, also known as TNRC9), rs13387042 (2q35), and rs13281615 (8q24) with BC risk in 344 Chilean BRCA1/2-negative BC cases and in 801 controls. Two SNPs, rs3803662 and rs13387042, were significantly associated with increased BC risk in familial BC and in non-familial early-onset BC. The risk of BC increased in a dose-dependent manner with the number of risk alleles (P-trend < 0.0001 and 0.0091, respectively). The odds ratios for BC in familial BC and in early-onset non-familial BC were 3.76 (95%CI 1.02-13.84, P = 0.046) and 8.0 (95%CI 2.20-29.04, P = 0.002), respectively, for the maximum versus minimum number of risk alleles. These results indicate an additive effect of the TOX3 rs3803662 and 2q35 rs13387042 alleles for BC risk. We also evaluated the interaction between rs3803662 and rs13387042 SNPs. We observed an additive interaction only in non-familial early-onset BC cases (AP = 0.72 (0.28-1.16), P = 0.001). No significant association was observed for rs13281615 (8q24) with BC risk in women from the Chilean population. The strongly increased risk associated with the combination of low-penetrance risk alleles supports the polygenic inheritance model of BC.