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MicroRNA related polymorphisms and breast cancer risk.
Genetic variations, such as single nucleotide polymorphisms (SNPs) in microRNAs (miRNA) or in the miRNA binding sites may affect the miRNA dependent gene expression regulation, which has been implicated in various cancers, including breast cancer, and may alter individual susceptibility to cancer. We investigated associations between miRNA related SNPs and breast cancer risk. First we evaluated 2,196 SNPs in a case-control study combining nine genome wide association studies (GWAS). Second, we further investigated 42 SNPs with suggestive evidence for association using 41,785 cases and 41,880 controls from 41 studies included in the Breast Cancer Association Consortium (BCAC). Combining the GWAS and BCAC data within a meta-analysis, we estimated main effects on breast cancer risk as well as risks for estrogen receptor (ER) and age defined subgroups. Five miRNA binding site SNPs associated significantly with breast cancer risk: rs1045494 (odds ratio (OR) 0.92; 95% confidence interval (CI): 0.88-0.96), rs1052532 (OR 0.97; 95% CI: 0.95-0.99), rs10719 (OR 0.97; 95% CI: 0.94-0.99), rs4687554 (OR 0.97; 95% CI: 0.95-0.99, and rs3134615 (OR 1.03; 95% CI: 1.01-1.05) located in the 3' UTR of CASP8, HDDC3, DROSHA, MUSTN1, and MYCL1, respectively. DROSHA belongs to miRNA machinery genes and has a central role in initial miRNA processing. The remaining genes are involved in different molecular functions, including apoptosis and gene expression regulation. Further studies are warranted to elucidate whether the miRNA binding site SNPs are the causative variants for the observed risk effects.

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