A genetic variant in the pre-miR-27a oncogene is associated with a reduced familial breast cancer risk.

MicroRNAs (miRNAs) regulate pathways involved in cell differentiation, proliferation, development, and apoptosis by degradation of target miRNAs and/or repression of their translation. Although the single nucleotide polymorphisms (SNPs) in miRNAs target sites have been studied, the effects of SNPs in miRNAs are largely unknown. In our study, we first systematically sequenced miRNA genes reported to be involved in breast cancer to identify/verify SNPs. We analyzed four SNPs, one located in the pre-miRNA and the other three located in miRNA flanking regions, for a putative association with breast cancer risk. The SNP rs895819, located in the terminal loop of pre-miRNA-27a, showed a protective effect. In a large familial breast cancer study cohort, the rare [G] allele of rs895819 was found to be less frequent in the cases than in the controls, indicating a reduced familial breast cancer risk ([G] vs. [A]: OR = 0.88, 95% CI 0.78-0.99, P = 0.0287). Furthermore, age stratification revealed that the protective effect was mainly observed in the age group of 50 years of age, indicating a possible hormone-related effect. It has been shown that artificial mutations in the terminal loop of miR-27a can block the maturation process of the miRNA. We hypothesize that the G-variant of
rs895819 might impair the maturation of the oncogenic miR-27a and thus, is associated with familial breast cancer risk.