

## Distribution of coding apoptotic gene polymorphisms in women with extreme phenotypes of breast cancer predisposition and tolerance

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### ABSTRACT

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**Aims and background.** Comparison of subjects with extreme phenotypes of cancer susceptibility and tolerance allows to detect low-penetrance gene-disease interactions with a relatively small study size.

**Methods and study design.** We analyzed the distribution of 19 coding apoptotic gene polymorphisms (Bid Gly10Ser; Casp2 Leu141Val; Casp5 Ala90Thr and Val318Leu; Casp7 Glu255Asp; Casp8 His302Asp; Casp9 Val28Ala, His173Arg and Arg221Gln; Casp10 Ile479Leu; Faim Thr117Ala and Ser127Leu; DR4 Arg141His, Thr209Arg, Ala228Glu and Lys441Arg; Survivin Lys129Glu; TNFR1 Gln121Arg; XIAP Pro423Gln) in 121 breast cancer patients with clinical features of a hereditary predisposition (family history and/or early onset and/or bilaterality) and 142 elderly tumor-free women.

**Results.** None of the individual single nucleotide polymorphisms (SNPs) demonstrated an association with breast cancer risk. The analysis of gene interactions revealed that the combination of XIAP Pro423Gln (rs5956583) AA genotype with Casp7 Glu255Asp (rs2227310) CG genotype appeared to prevail in "supercases" relative to "supercontrols" (25/121 [21%] vs 11/142 [8%],  $P = 0.002$ ). We attempted to validate this association in the second round of case-control analysis, which involved 519 randomly selected breast cancer patients and 509 age-matched healthy women, but no difference was detected upon this comparison.

**Conclusions.** Coding apoptotic gene polymorphisms do not play a major role in BC predisposition. The results of this investigation may be considered while designing future studies on breast cancer-associated candidate SNPs.

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**Key words:** breast cancer, gene polymorphisms, apoptosis, case-control study.

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