Coordination of TP53 Abnormalities in Breast Cancer: Data from Analysis of TP53 Polymorphisms, Loss of Heterozygosity, Methylation, and Mutations.

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Abstract: Aims: We have studied whether TP53 rs1042522, rs17878362, and rs1625895 alleles having a protective effect against breast cancer (BC) will be lost in tumors, whereas those allowing disease development will be retained. Methods: Analysis of TP53 polymorphisms was performed in blood leukocytes and tumors from 80 Caucasian BC patients. In addition, TP53 loss of heterozygosity (LOH), methylation, and mutations were studied in tumor DNA of BC individuals with loss of alleles of TP53 polymorphisms. Results: In breast tumors of patients heterozygous for TP53 polymorphisms, we detected loss of rs1042522 C and G and rs17878362 A2 alleles; however, the loss of the C allele was preferential. We found that loss of TP53 alleles, namely rs1042522 C, has been caused by an LOH mechanism, namely TP53 deletions, whereas TP53 point mutations frequently occurred in the retained G allele (p=0.03). In addition, we showed that BC patients with rs1042522 CC genotype were characterized by only unifocal tumors and decreased frequency of lymph node metastases (p=0.03). Conclusions: Taken together, we showed the preferential loss of the rs1042522 C allele, which is protective against BC progression, in breast tumors. Also, the loss of the C allele, which encodes p53 protein with the best DNA repair cupability according to literature data, may create prerequisites for mutations, but not for methylation in a retained G variant, as we found here. However, these results need to be confirmed because of the limited statistical power of the present study and the small sampling.

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