

Polymorphisms and DNA methylation of gene TP53 associated with extra-axial brain tumors

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ABSTRACT. The p53 tumor suppressor gene is the most frequently mutated gene in human cancer; this gene is mutated in up to 50% of human tumors. It has a critical role in the cell cycle, apoptosis and cell senescence, and it participates in many crucial physiological and pathological processes. Polymorphisms of p53 have been suggested to be associated with genetically determined susceptibility in various types of cancer. Another process involved with the

development and progression of tumors is DNA hypermethylation. Aberrant methylation of the promoter is an alternative epigenetic change in genetic mechanisms, leading to tumor suppressor gene inactivation. In the present study, we examined the TP53 Arg72Pro and Pro47Ser polymorphisms using PCR-RFLP and the pattern of methylation of the p53 gene by methylation-specific PCR in 90 extra-axial brain tumor samples. Patients who had the allele Pro of the TP53 Arg72Pro polymorphism had an increased risk of tumor development (odds ratio, OR = 3.23; confidence interval at 95%, 95%CI = 1.71-6.08; P = 0.003), as did the allele Ser of TP53 Pro47Ser polymorphism (OR = 1.28; 95%CI = 0.03-2.10; P = 0.01). Comparison of overall survival of patients did not show significant differences. In the analysis of DNA methylation, we observed that 37.5% of meningiomas, 30% of schwannomas and 52.6% of metastases were hypermethylated, suggesting that methylation is important for tumor progression. We suggest that TP53 Pro47Ser and Arg72Pro polymorphisms and DNA hypermethylation are involved in susceptibility for developing extra-axial brain tumors.

Key words: Polymorphism; Methylation; TP53; Metastases; Meningiomas; Schwannomas