Online journal ISSN - 1676-5680
GMR Genetics and Molecular Research
EVOLUTION AND TECHNOLOGY

Mutational analysis of genes p14ARF, p15INK4b, p16INK4a, and PTEN in human nervous system tumors

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Genet. Mol. Res. 7 (2): 451-459 (2008)
Received March 14, 2008
Accepted May 2, 2008
Published May 27, 2008

ABSTRACT. The cancer is one of the most common and severe problems in clinical medicine, and nervous system tumors represent about 2% of the types of cancer. The central role of the nervous system in the maintenance of vital activities and the functional consequences of the loss of neurons can explain how severe brain cancers are. The cell cycle is a highly complex process, with a wide number of regulatory proteins involved, and such proteins can suffer alterations that transform normal cells into malignant ones. The INK4 family members (CDK inhibitors) are the cell cycle regulators that block the progression of the cycle through the R point, causing an arrest in G1 stage. The p14ARF (alternative reading frame) gene is a tumor suppressor that inhibits p53 degradation during the progression of the cell cycle. The PTEN gene is related to the induction of growth suppression through cell cycle arrest, to apoptosis and to the inhibition of cell adhesion and migration. The purpose of the present study was to assess the mutational state of the genes p14ARF, p15INK4b, p16INK4a, and PTEN in 64 human nervous system tumor samples. Homozygous deletions were found

in exon 2 of the p15INK4b gene and exon 3 of the p16INK4a gene in two schwannomas. Three samples showed a guanine deletion (63 codon) which led to a loss of heterozygosity in the p15 gene, and no alterations could be seen in the PTEN gene. Although the group of patients was heterogeneous, our results are in accordance with other different studies that indicate that homozygous deletion and loss of heterozygosity in the INK4 family members are frequently observed in nervous system tumors.

Key words: p14ARF; p15INK4b; p16INK4a; PTEN; Mutations

