

Variant Of The Chek2 Gene As A Prognostic Marker In Glioblastoma Multiforme. Clinicopathological Study

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Abstract:

OBJECTIVE: Germline mutations of the CHEK2 tumor suppressor gene have been found in families with the Li-Fraumeni syndrome (LFS). Patients with LFS experience a variety of cancers, including malignant astrocytomas. We investigated a potential role for a CHEK2 gene polymorphism in glioblastomas.

METHODS: A genetic polymorphism of the CHEK2 gene (CHEK2 SNP rs2017309 A/T) was genotyped in a series of glioblastoma patients (n = 213) and population controls (n = 192). Subsets of tumors were analyzed for loss of heterozygosity 22q (n = 66), loss of heterozygosity CHEK2 (n = 53), CHEK2 expression (n = 21), and CHEK2 coding sequence alterations (n = 18). CHEK2 SNP rs2017309 genotyping findings and traditional clinicopathological parameters were correlated with the patients' prognoses.

RESULTS: No association between the CHEK2 SNP and glioblastoma formation was observed. No CHEK2 coding sequence aberrations or tumors completely lacking CHEK2 protein were identified. However, the presence of the CHEK2 rs2017309 A allele was significantly associated with an adverse prognosis (P = 0.034), particularly among patients undergoing postoperative chemotherapy and radiotherapy (n = 28, median survival 10.5 versus 15.5 mo, P = 0.008). We could confirm the patients' age, Karnofsky Performance Scale score, and postoperative radiotherapy and chemotherapy (all P < 0.0001, log-rank test) as decisive prognostic factors.

CONCLUSION: Our data suggest that a CHEK2 gene polymorphism might correlate with the prognosis of glioblastoma patients. These findings may point to an as yet unrecognized role for the CHEK2 gene in glioblastomas.

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