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

Neurosurgery. POST COPYEDIT, 28 September 2006
Simon, Matthias M.D.; Ludwig, Michael Ph.D.; Fimmers, Rolf Ph.D.; Mahlberg, Ralph; Muller-Erkwoh, Angelika M.D.; Koster, Gertraud Ph.D.; Schramm, Johannes M.D.

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.

Copyright (C) 2006 by the Congress of Neurological Surgeons