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Inherited predisposition to glioma.

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In gliomas, germline gene alterations play a significant role during malignant transformation of progenitor glial cells, at least for families with occurrence of multiple cancers or with specific hereditary cancer syndromes. Scientific evidence during the last few years has revealed several constitutive genetic abnormalities that may influence glioma formation. These germline abnormalities are manifested as either gene polymorphisms or hemizygous mutations of key regulatory genes that are involved either in DNA repair or in apoptosis. Such changes, among others, include hemizygous alterations of the neurofibromatosis 1 (NF1) and p53 genes that are involved in apoptotic pathways, and alterations in multiple DNA repair genes such as mismatch repair (MMR) genes, x-ray cross-complementary genes (XRCC), and O6-methylguanine-DNA methyltransferase (MGMT) genes. Subsequent cellular changes include somatic mutations in cell cycle regulatory genes and genes involved in angiogenesis and invasion, leading eventually to tumor formation in various stages. Future molecular diagnosis may identify new genomic regions that could harbor genes important for glioma predisposition and aid in the early diagnosis of these patients and genetic counseling of their families.

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