Molecular Subtyping of Tumors from Patients with Familial Glioma.


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BACKGROUND: Single-gene mutation syndromes account for some familial glioma (FG); however, they make up only a small fraction of glioma families. Gliomas can be classified into 3 major molecular subtypes based on IDH mutation and 1p/19q co-deletion. We hypothesized that the prevalence of molecular subtypes might differ in familial versus sporadic gliomas, and that tumors in the same family should have the same molecular subtype.

METHODS: Participants in the FG study (Gliogene) provided samples for germline DNA analysis. Formalin-fixed, paraffin-embedded (FFPE) tumor was obtained for a subset of FG cases, and DNA was extracted. We analyzed tissue from 75 families, including 10 families containing a second affected family member. Copy number variation (CNV) data was obtained using a first-generation Affymetrix molecular inversion probe (MIP) array.

RESULTS: Samples from 62 of 75 (83%) FG cases could be classified into the 3 subtypes. The prevalence of the molecular subtypes was: 30 (48%) IDH-wild type, 21 (34%) IDH-mutant non-codeleted, and 11 (19%) IDH-mutant and 1p/19q-codeleted. This distribution of molecular subtypes was not statistically different from that of sporadic gliomas (p=0.54). Of 10 paired FG samples, molecular subtypes were concordant for 7 (κ=0.59): 3 IDH-mutant non-codeleted, 2 IDH-wild type, and 2 IDH-mutant and 1p/19q-codeleted gliomas.

CONCLUSIONS: Our data suggest that within individual families, patients develop gliomas of the same molecular subtype. However, we did not observe differences in the prevalence of the molecular subtypes in FG compared with sporadic gliomas. These observations provide further insight about the distribution of molecular subtypes in FG.

KEYWORDS: Familial glioma (FG); IDH-mutant and 1p/19q-codeleted; IDH-mutant non-codeleted; IDH-wild type; molecular inversion probe (MIP)

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