Molecular Profiling Reveals Biologically Discrete Subsets and Pathways of Progression in Diffuse Glioma.


Abstract

Therapy development for adult diffuse glioma is hindered by incomplete knowledge of somatic glioma driving alterations and suboptimal disease classification. We defined the complete set of genes associated with 1,122 diffuse grade II-III-IV gliomas from The Cancer Genome Atlas and used molecular profiles to improve disease classification, identify molecular correlations, and provide insights into the progression from low- to high-grade disease. Whole-genome sequencing data analysis determined that ATRX but not TERT promoter mutations are associated with increased telomere length. Recent advances in glioma classification based on IDH mutation and 1p/19q co-deletion status were recapitulated through analysis of DNA methylation profiles, which identified clinically relevant molecular subsets. A subtype of IDH mutant glioma was associated with DNA demethylation and poor outcome; a group of IDH-wild-type diffuse glioma showed molecular similarity to pilocytic astrocytoma and relatively favorable survival. Understanding of cohesive disease groups may aid improved clinical outcomes.

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