Recent Advances on the Molecular Pathology of Glial Neoplasms in Children and Adults.

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Abstract

Gliomas represent the most common primary intraparenchymal tumors of the central nervous system in adults and children and are a genetic and phenotypic heterogeneous group. Large multi-institutional studies and The Cancer Genome Atlas have provided firm insights into the basic genetic drivers in gliomas. The main molecular biomarkers routinely applied to evaluate diffuse gliomas include MGMT promoter methylation, EGFR alterations (eg, EGFRvIII), IDH1 or IDH2 mutations, and 1p19q co-deletion. Many of these markers have become standard of care for molecular testing and prerequisites for clinical trial enrollment. Other recent biomarkers include TERT promoter and ATRX mutations, alterations that identify specific molecular subgroups of diffuse gliomas with biological and clinical relevance. It has also become apparent that distinctive patterns of molecular genetic evolution develop in the context of current therapeutic regimens. Important insights have also been uncovered in the field of pediatric glioma, including the identification of recurrent mutation, fusion, and/or duplication events of the BRAF, FGFR1, MYB, and MYBL1 genes in pediatric low-grade gliomas, mutations affecting histone components (H3F3A p.K27M or p.G34) in pediatric high-grade gliomas, and aggressive subsets developing in midline central nervous system structures. Here, we summarize current concepts in molecular testing for glial tumors, including recent findings by large-scale discovery efforts and technologic advances that are affecting routine diagnostic work.