Genomic Insights into Diffuse Intrinsic Pontine Glioma.

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Abstract
Diffuse intrinsic pontine glioma (DIPG) is a highly aggressive pediatric brainstem tumor with a peak incidence in middle childhood and a median survival of less than 1 year. The dismal prognosis associated with DIPG has been exacerbated by the failure of over 250 clinical trials to meaningfully improve survival compared with radiotherapy, the current standard of care. The traditional practice to not biopsy DIPG led to a scarcity in available tissue samples for laboratory analysis that till recently hindered therapeutic advances. Over the past few years, the acquisition of patient derived tumor samples through biopsy and autopsy protocols has led to distinct breakthroughs in the identification of key oncogenic drivers implicated in DIPG development. Aberrations have been discovered in critical genetic drivers including histone H3, ACVR1, TP53, PDGFRA, and Myc. Mutations, previously not identified in other malignancies, highlight DIPG as a distinct biological entity. Identification of novel markers has already greatly influenced the direction of preclinical investigations and offers the exciting possibility of establishing biologically targeted therapies. This review will outline the current knowledge of the genomic landscape related to DIPG, overview preclinical investigations, and reflect how biological advances have influenced the focus of clinical trials toward targeted therapies.

KEYWORDS: ACVR1; PDGFR; diffuse intrinsic pontine glioma; histone H3K27M; pediatric brainstem gliomas; preclinical studies; targeted therapies

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