ABSTRACT

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Understanding the epigenetic landscape and cellular architecture of childhood brain tumors.

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Pediatric brain tumors are the leading cancer-related cause of death in children

and adolescents in the United States, affecting on average 1 in 2000 children per year. Recent advances in cancer genomics have led to profound discoveries about the underlying molecular biology and ontogeny of these tumors. In particular, these studies have revealed epigenetic dysregulation to be one of the main hallmarks of pediatric brain tumorigenesis. In this review, we will highlight a number of important recent findings about the nature of this dysregulation in different types of pediatric brain tumors as well as examine their implications for preclinical research and clinical practice. Specifically,

we discuss the emergence of methylation signatures as tools for tumor stratification/classification while also highlighting the importance of mutations that directly affect the epigenome and clarifying their impact on risk

stratification and pediatric brain tumor biology. We then incorporate recent advances in our understanding of pediatric brain tumor cellular architecture and

emphasize the link between epigenetic dysregulation and the "stalled" development seen in many of these malignant neoplasms. Lastly, we explore recentwork investigating the use of these mutated epigenomic regulators as therapeutic targets and extrapolate their utility in overcoming this "stalling" to halt tumor growth.

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