Medulloblastoma targeted therapy: From signaling pathways heterogeneity and current treatment dilemma to the recent advances in development of therapeutic strategies

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Abstract

Medulloblastoma (MB) is a major pediatric malignant brain tumor that arises in the cerebellum. MB tumors exhibit highly heterogeneous driven by diverse genetic alterations and could be divided into four major subgroups based on their different biological drivers and molecular features (Wnt, Sonic hedgehog (Shh), group 3, and group 4 MB). Even though the therapeutic strategies for each MB subtype integrate their pathogenesis and were developed to focus on their specific target sites, the unexpected drug non-selective cytotoxicity, low drug accumulation in the brain, and complexed MB tumor microenvironment still be huge obstacles to achieving satisfied MB therapeutic efficiency. This review discussed the current advances in modern MB therapeutic strategy development. Through the recent advances in knowledge of the origin, molecular pathogenesis of MB subtypes and their current therapeutic barriers, we particularly reviewed the current development in advanced MB therapeutic strategy committed to overcome MB treatment obstacles, focusing on novel signaling pathway targeted therapeutic agents and their combination discovery, advanced drug delivery systems design, and MB immunotherapy strategy development.

Keywords: Blood-brain barrier; Drug delivery platforms; Immunotherapy; Medulloblastoma; Targeting therapy strategies.