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Developmental Origins and Oncogenesis in Medulloblastoma

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Abstract

Medulloblastoma is the most common pediatric brain cancer and is broadly categorized into four molecular subgroups. Understanding the cell origins of medulloblastoma is crucial for preventing tumor formation and relapse. Recent single-cell transcriptomics studies have identified the potential cell lineage vulnerabilities and mechanisms underpinning malignant transformation in medulloblastoma. Emerging evidence suggests that genetic-epigenetic alterations specific to each subgroup lead to a lineage-specific stall in the neural developmental program and subsequent tumorigenesis. We discuss the putative cells of origin, plasticity, and heterogeneity within medulloblastoma subgroups and delve into the genetic and epigenetic changes that predispose cells to transformation. Additionally, we review the current insights into how cerebellar stem/progenitor cells and lineage plasticity impact medulloblastoma pathogenesis and highlight recent therapeutic advances targeting specific oncogenic vulnerabilities in this malignancy.