Medulloblastoma Pathogenesis

A study revealed that Notch pathway activation played a key role in the formation of stem-like cells in MB and had valuable meaning for further investigation of targeted therapies [1)].

Medulloblastoma, occurs with increased frequency in individuals with Fanconi anemia who have biallelic germline mutations in BRCA2.

Tumor necrosis-initiated complement activation stimulates proliferation of medulloblastoma cells [2)].

Combined activation of the Shh/Ptc and IGF signaling pathways is an important mechanism in MB pathogenesis [3)].

Both pathways are essential regulators of granule neuron precursors (GNP) proliferation during cerebellar development. In cultured GNPs, IGF signaling stabilizes the oncogenic transcription factor N-myc by inhibiting glycogen synthase kinase 3beta-dependent phosphorylation and consequent degradation of N-myc. However, determinants of Shh and IGF tumorigenicity in vivo remain unknown

Activation of the Sonic hedgehog (Shh)/Patched signaling pathway in the postnatal cerebellum is sufficient to induce medulloblastoma in mice. Activation of the phosphatidylinositol 3-kinase (PI3K) signaling pathway by insulin-like growth factor-II, inactivation of the p53 tumor suppressor protein, loss of DNA damage repair mechanisms, and ectopic expression of Myc oncoproteins cooperate with Shh/Patched signaling to enhance tumor formation in mice. Ectopic expression of alpha and beta interferons in the developing brain also induces Shh-mediated medulloblastoma formation, suggesting a possible role for antiviral response in the genesis of medulloblastoma [4)].

BMI1 in medulloblastoma

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1)
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