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BAI1 is a brain-specific tumor suppressor

Brain-specific Angiogenesis Inhibitor 1 (BAI1) is a seven transmembrane G protein-coupled receptor (GPCR), and we have previously shown that it has potent anti-angiogenic and anti-tumorigenic properties in gliomas.¹⁻⁶ We now found that BAI1 expression is reduced in human medulloblastoma (MB) by epigenetic mechanisms, involving methylated DNA binding protein MBD2 and histone methylase EZH2. Restoration of BAI1 expression reduced MB cell proliferation and tumor growth in mice xenografts. Targeting MBD2 and EZH2 with small molecules reactivated BAI1 expression, and suppressed tumor growth, supporting the use of epigenetic therapeutics against MB. To more directly examine whether loss of BAI1 expression may favor tumor development during cerebellar development, we generated a *Bai1* knockout (KO) mouse.⁷ We detected a thicker external granular layer (EGL) during early postnatal cerebellum development, which was accompanied by increased proliferation in cGNPs and aberrant activation of Sonic hedgehog signaling. *Bai1* loss was not sufficient to initiate tumorigenesis *per se*, but dramatically accelerated MB tumorigenesis when crossed to mice heterozygous for *patched 1* (*ptc1*^{+/-}), and we will present some of the underlying mechanisms. Altogether, our findings provide insight into the physiological function of BAI1 in the brain, in particular the suppression of medulloblastoma formation in the cerebellum.

Biography

Erwin G. Van Meir has completed his PhD from the University of Lausanne, Switzerland and postdoctoral studies from the Ludwig Institute for Cancer Research, La Jolla, CA. He is the leader of the cancer cell biology program at the Winship Cancer Institute, an NCI-designated Cancer Center. He has published over 150 manuscripts in peer-reviewed International journals and these have been cited over 15,000 times (H-index 63).

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