Methyl-CpG-binding domain protein 2

Methyl CpG binding domain protein 2 in humans is encoded by the MBD2 gene.

DNA methylation is the major modification of eukaryotic genomes and plays an essential role in mammalian development. Human proteins MECP2, MBD1, MBD2, MBD3, and MBD4 comprise a family of nuclear proteins related by the presence in each of a methyl-CpG-binding domain (MBD). Each of these proteins, with the exception of MBD3, is capable of binding specifically to methylated DNA. MECP2, MBD1, and MBD2 can also repress transcription from methylated gene promoters. The protein encoded by this gene may function as a mediator of the biological consequences of the methylation signal. It is also reported that this protein functions as a demethylase to activate transcription, as DNA methylation causes gene silencing if present in promoter regions.

ADGRB1 gene, which encodes Brain-specific angiogenesis inhibitor 1 (BAI1), is epigenetically silenced in medulloblastomas (MBs) through a methyl CpG binding domain protein MBD2-dependent mechanism. Knockout of Adgrb1 in mice augments proliferation of cerebellar granule neuron precursors, and leads to accelerated tumor growth in the Ptch1+/- transgenic MB mouse model. BAI1 prevents Mdm2-mediated p53 polyubiquitination, and its loss substantially reduces p53 levels. Reactivation of BAI1/p53 signaling axis by a brain-permeable MBD2 pathway inhibitor suppresses MB growth in vivo. Altogether, this data define BAI1's physiological role in tumorigenesis and directly couple an ADGR to cancer formation [1)].

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Zhu D, Osuka S, Zhang Z, Reichert ZR, Yang L, Kanemura Y, Jiang Y, You S, Zhang H, Devi NS, Bhattacharya D, Takano S, Gillespie GY, Macdonald T, Tan C, Nishikawa R, Nelson WG, Olson JJ, Van Meir EG. BAI1 Suppresses Medulloblastoma Formation by Protecting p53 from Mdm2-Mediated Degradation. Cancer Cell. 2018 Jun 11;33(6):1004-1016.e5. doi: 10.1016/j.ccell.2018.05.006. PubMed PMID: 29894688.