KDM2B

- Non-canonical PRC1.1 licenses transcriptional response to enable Treg plasticity in immune adaptation
- Cervical myelopathy and extensive body destruction caused by primary Gli1 fusion sarcoma
- KDM2B regulates hippocampal morphogenesis by transcriptionally silencing Wnt signaling in neural progenitors
- Histone demethylase KDM2A is a selective vulnerability of cancers relying on alternative telomere maintenance
- CpG island reconfiguration for the establishment and synchronization of polycomb functions upon exit from naive pluripotency
- HOXA-AS2 contributes to regulatory T cell proliferation and immune tolerance in glioma through the miR-302a/KDM2A/JAG1 axis
- CNS tumors with YWHAE:NUTM2 and KDM2B-fusions present molecular similarities to extra-CNS tumors having BCOR internal tandem duplication or alternative fusions
- Up-regulation of miR-663a inhibits the cancer stem cell-like properties of glioma via repressing the KDM2A-mediated TGF-β/SMAD signaling pathway

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KDM2B, also known as Lysine (K)-specific demethylase 2B, is a protein-coding gene found in humans. This gene encodes an enzyme known as a histone demethylase. Histone demethylases plays a crucial role in the regulation of gene expression by removing specific methyl groups from histone proteins. These modifications to histones can influence the accessibility of DNA and, subsequently, gene transcription.

KDM2B specifically demethylates di- and trimethylated lysine 36 on histone H3 (H3K36me2/3). By doing so, it regulates the chromatin structure and gene expression patterns associated with these specific histone marks. KDM2B has been implicated in various cellular processes, including cell cycle regulation, DNA repair, and development.

Alterations or dysregulation of histone demethylases like KDM2B can have implications for gene expression and may be associated with various diseases, including cancer. Research into the role of KDM2B and other histone demethylases continues to shed light on their significance in health and disease.

Zhang et al. removed the chromatin-association capability of KDM2B in the progenitors of developing dorsal telencephalon (Kdm2bΔCxxC) to discover that Kdm2bΔCxxC hippocampus, particularly the dentate gyrus, became drastically smaller with disorganized cellular components and structure. Kdm2bΔCxxC mice display prominent defects in spatial memory, motor learning, and fear conditioning, resembling patients with KDM2B mutations. The migration and differentiation of neural progenitor cells are greatly impeded in the developing Kdm2bΔCxxC hippocampus. Mechanism studies reveal that Wnt signaling genes in developing Kdm2bΔCxxC hippocampi are de-repressed due to reduced enrichment of repressive histone marks by polycomb repressive complexes. Activating the Wnt signaling disturbs hippocampal neurogenesis, recapitulating the effect of KDM2B loss. Together, they unveil a previously unappreciated gene repressive program mediated by KDM2B that controls progressive fate specifications and cell migration, hence morphogenesis of the hippocampus [1)].

Huo et al. showed that the expression of the long KDM2B isoform (KDM2BLF), which contains the demethylase domain, is specifically induced at peri-implantation and that its H3K36me2 demethylase activity is required for PcG enrichment at CGIs. Moreover, KDM2BLF interacts with BRG1/BRM-associated factor (BAF) and stabilizes BAF occupancy at CGIs for subsequent gain of accessibility, which precedes PcG enrichment. Consistently, KDM2BLF inactivation results in significantly delayed post-implantation development. In summary, our data unveil the dynamic chromatin configuration of CGIs during exit from naive pluripotency and provide a conceptual framework for the spatiotemporal establishment of PcG functions [2].

Staberg et al. found that the chromatin regulator, JmjC domain histone H3K36me2/me1 demethylase KDM2B, is highly expressed in glioblastoma surgical specimens compared to normal brains. Targeting KDM2B function genetically or pharmacologically impaired the survival of patient-derived primary glioblastoma cells through the induction of DNA damage and apoptosis, sensitizing them to chemotherapy. KDM2B loss decreased the GSC pool, which was potentiated by the coadministration of chemotherapy. Collectively, our results demonstrate that KDM2B is crucial for glioblastoma maintenance, with inhibition causing loss of GSC survival, genomic stability, and chemoresistance [3]

Wang et al. revealed that KDM2B might influence glioma growth and act as a novel therapeutic target for glioma patients [4].

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