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KDM1 is a novel therapeutic target for the treatment of gliomas

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Glioma development is a multistep process, involving alterations in genetic and epigenetic mechanisms. Understanding the mechanisms and enzymes that promote epigenetic changes in gliomas are urgently needed to identify novel therapeutic targets. We examined the role of histone demethylase KDM1 in glioma progression. KDM1 was overexpressed in gliomas and its expression positively correlated with histological malignancy. Knockdown of KDM1 expression or its pharmacological inhibition using pargyline or NCL-1 significantly reduced the proliferation of glioma cells. Inhibition of KDM1 promoted up regulation of the p53 target genes p21 and PUMA. Patient-derived primary GBM cells expressed high levels of KDM1 and pharmacological inhibition of KDM1 decreased their proliferation. Further, KDM1 inhibition reduced the expression of stemness markers CD133 and nestin in GBM cells. Accordingly, KDM1 expression decreased in differentiated primary GBM cells. Mouse xenograft assays revealed that inhibition of KDM1 significantly reduced glioma xenograft tumor growth. KDM1 inhibition increased levels of H3K4-me2 and H3K9-Ac histone modifications and reduced the levels of H3K9-me2 modifications and promoted expression of p53 target genes (p21 and PUMA), leading to apoptosis. Further, KDM1 inhibition increased the H3K4-me2 and reduced the H3K9-me2 recruitment on p21 promoter regions. Our results suggest that KDM1 is overexpressed in gliomas and could be a potential therapeutic target for the treatment of gliomas

Biography

Gangadhara Reddy Sareddy is currently employed at The University of Texas Health Science Center at San Antonio, in the Department of Obstetrics and Gynecology as a senior post-doctoral researcher. He received his Ph.D in Animal Sciences from the University of Hyderabad (India). Dr. Sareddy has extensively worked in the field of Neuro-oncology for now more than 8 years. His area of expertise includes Glioblastoma, Cerebral Ischemia, Neuroprotection, Endocrinology, Molecular Therapeutics, and Identification of novel molecular targets, Tumor markers of diagnostic/prognostic significance, Pre-clinical drug testing and *in vivo* mice models

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