KDM1 may represent a new therapeutic target for glioma

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Researchers have generated preclinical data demonstrating that the protein KDM1, which functions as a lysine demethylase, is a potential target for glioma treatment, according to Gangadhara R. Sareddy, Ph.D., a postdoctoral fellow in the Vadlamudi Laboratory at The University of Texas Health Science Center in San Antonio, who presented the results at the AACR Annual Meeting 2013, held in Washington, D.C., April 6-10.

"We found that KDM1 expression is upregulated in gliomas and have preclinical evidence that suggests pharmaceutical inhibition of the KDM1 axis could have therapeutic implications for the treatment of gliomas," said Sareddy.

Gliomas, the deadliest form of primary central nervous system neoplasms, represent about 70 percent of brain tumors, according to Sareddy. Roughly 20,000 patients are diagnosed with gliomas each year in the United States.

"Patients with malignant gliomas have a survival time of approximately 14 months," Sareddy said. "Novel therapies are urgently needed. Evolving evidence suggests that glioma development is a multistep process that results from changes both in genetic and epigenetic mechanisms. Unlike genetic alterations, epigenetic changes are reversible; therefore, targeting epigenetic changes represents a promising therapeutic approach."

He and his colleagues set out to assess the importance of KDM1 in gliomas. Through immunohistochemical analysis, they found that KDM1 expression was elevated in gliomas. They silenced KDM1 expression with siRNA or inhibited it with pargyline or NCL-1 and found that reducing its expression or inhibiting it pharmacologically reduced glioma cell line growth in vitro. In addition, inhibiting KDM1 pharmacologically reduced the growth of patient-derived primary glioblastoma multiforme cells in vitro and the growth of a human glioma cell line in mice.

Results of mechanistic studies demonstrated that inhibiting KDM1 increased the expression of tumor suppressor p53 target genes through epigenetic modifications, according to Sareddy.

"Because KDM1 plays a critical role in glioma biology and because epigenetic modifications are reversible, pharmacological inhibition of KDM1 could be a potential therapy for gliomas," Sareddy said. "Identification of KDM1 as a therapeutic agent can be readily extended to clinical use with current chemotherapies, providing an additional tool for enhancing survival in patients with glioma."

Provided by American Association for Cancer Research

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