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Scientists identify chemical compound that may stop deadly brain tumors

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Researchers at the University of North Carolina at Chapel Hill School of Medicine have identified a compound that could be modified to treat one of the most deadly types of cancer, and discovered how a particular gene mutation contributes to tumor growth.

The findings and potential treatment apply to a type of brain tumor called secondary glioblastoma multiforme (GBM). GBMs are part of a larger group of brain tumors called malignant gliomas, which is the type of cancer Senator Edward Kennedy suffers from.

A report of the research will appear in the April 10, 2009 issue of the journal *Science*.

In experiments with tumor cells, the researchers reversed the effects of a mutation in a gene called isocitrate dehydrogenase-1 (IDH1) by replenishing a compound called α-ketoglutarate (α-KG).

"When the IDH1 gene is mutated, the level of α-KG is reduced, which in turn contributes to tumor growth by helping to increase the supply of nutrients and oxygen to tumor cells. When we added the α-KG to tumor cells, the effects caused by the IDH1 mutation were reversed," said Yue Xiong, Ph.D., William R. Kenan Jr., Distinguished Professor of Biochemistry and Biophysics and a member of the UNC Lineberger Comprehensive Cancer Center.

"If scientists can develop α-KG into a clinical drug, it could potentially

be used for treating brain tumor patients who have this specific gene mutation. The α-KG compound is already there; it only needs to be modified to be used clinically, so that may save a lot of time," Xiong said.

Xiong is a corresponding author of the study along with Kun-Liang Guan, Ph.D., professor of pharmacology at the University of California, San Diego.

The findings and potential treatment apply mostly to secondary GBM, rather than a different type of tumor called primary GBM. About 75 percent of secondary GBMs have mutations in the IDH1 gene, but only 5 percent of primary GBMs have this mutation, Xiong said. Even though these two types of GBM have a similar end result, the tumor types develop in very different ways, and doctors will need very different treatments to stop them.

The first author of the Science paper is Shimin Zhao, Ph.D., of Fudan University in Shanghai, China. Zhao and students in his lab made key contributions to the research, Xiong said. Those students, also authors on the paper, are Yan Lin, Wei Xu, Wenqing Jiang, Zhengyu Zha, Pu Wang, Wei Yu, Zhiqiang Li, Lingling Gong, Yingjie Peng, Jianping Ding and Qunying Lei.

Xiong and Guan helped develop the lab at Fudan University and supervise graduate student training and project development there.

Xiong and his colleagues are continuing studies of other effects of the IDH1 mutation and are developing a mouse model of secondary GBM that could be used to test the potential treatment.

Source: University of North Carolina School of Medicine (news : web)