MedicalXpress

Study identifies possible new target for future brain cancer drugs

February 27 2014

A molecule in cells that shuts down the expression of genes might be a promising target for new drugs designed to treat the most frequent and lethal form of brain cancer, according to a new study by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

The findings, published in the journal *Cancer Research*, show that high levels of the enzyme PRMT5 are associated with aggressive growth of the brain cancer glioblastoma multiforme (GBM). The malignancy strikes nearly 14,000 Americans annually. It is a highly invasive form of cancer that is difficult to remove entirely by surgery. Following surgery, chemotherapy and radiation, average survival is still only 15 months, pointing to a critical need for new treatments.

This study shows that inhibiting PRMT5 can significantly improve survival in an animal model of GBM. Blocking the enzyme inhibited the growth, proliferation and migration of GBM cells in laboratory studies, and it increased the number of GBM cells that died by apoptosis.

"Our findings suggest that PRMT5 is a possible prognostic factor and therapeutic target for glioblastoma, and they provide a rationale for developing agents that target PRMT5 in this deadly disease," says co-corresponding author Robert A. Baiocchi, MD, PhD, associate professor of medicine and a hematologist at the OSUCCC – James who is also collaborating on an Ohio State effort to develop a PMRT5 inhibitor.

"Our analyses also helped us identify PRMT5 as a master transcriptional repressor (gene silencer) in this disease, says co-corresponding author Balveen Kaur, PhD, professor of Neurological Surgery at the OSUCCC – James.

"We also learned that PRMT5 inhibition induced the death of glioblastoma cells whether the P53 gene was mutated or not. This has important treatment implications because loss of P53 is associated with a poor prognosis in these patients, so a PRMT5 inhibitor might be particularly important for these patients," says Kaur, who is specializes in glioblastoma research and is chief of Ohio State's Dardinger Laboratory of Neurosciences.

PRMT5 (protein arginine methyltransferase 5) is an enzyme that alters the structure of chromatin to suppress the transcription of genes and the production of proteins. To conduct their study, Kaur, Baiocchi and their colleagues used tumor tissue from patients, cell lines and an animal model. Key findings included:

- PRMT5 is selectively over-expressed in glioblastoma and the degree of PRMT5 expression correlates with cell growth and patient survival.
- In GBM patients, PRMT5 expression levels in tumor were significantly associated with lower overall survival;
- Patients with high PRMT5 tumor expression had shorter overall survival (108 days) compared to patients with medium expression (277 days) and low expression (726 days).

Provided by Ohio State University Medical Center