MedicalXpress

Research describes how glucose regulation enables malignant tumor growth

November 9 2015

A new study led by researchers at The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James) identifies a key pathway used by cancer cells to make the lipids by integrating oncogenic signaling, fuel availability and lipid synthesis to support cell division and rapid tumor growth.

The researchers identified a critical molecule in that pathway that, if blocked, might cripple lipid production by cancer cells and slow tumor growth. This approach would be a new strategy for treating a lethal type of brain cancer called glioblastoma multiforme, as well as other malignancies. This discovery also has significant therapeutic implications on other metabolic disorders with deregulated lipid metabolism, such as atherosclerosis, obesity and diabetes.

The study discovered that activation of the epidermal growth factor receptor (EGFR), which triggers enhanced uptake of glucose, leads to a chemical change in a molecule called SCAP. This enables SCAP to transport a second molecule called SREBP, and this leads to the activation of genes that regulate the production and uptake of lipids. SREBPs are key proteins for regulating lipid metabolism.

The researchers published their findings in the journal *Cancer Cell* Nov. 9, 2015.

"Our findings reveal the previously unrecognized, critical role of glucose

in controlling lipid synthesis during tumor development," says principal investigator Deliang Guo, PhD, assistant professor of radiation oncology at the OSUCCC - James.

"We unraveled the mechanisms behind how glucose drives tumor growth through the specific SREBP pathway. This is an important discovery for future anti-cancer drug development activities." "For this study, Guo and his colleagues used various human cancer cell lines and a glioblastoma animal model. Technical findings include:

- EGFR activation increases glucose uptake and promotes a posttranslational change in SCAP called N-glycosylation;
- That N-glycosylation triggers SCAP/SREBP moving from ER to the Golgi and the subsequent activation of SREBP [and activation of genes involved in lipid production].
- Blocking the glycosylation of SCAP suppressed the growth of glioblastoma tumors in an animal model.

"Our data explains the underlying molecular mechanism of how cancer cells respond and survive the harsh nutritional variability of the tumor microenvironment," Guo says.

Provided by Ohio State University Medical Center