Researchers find pathway that drives spread of pediatric bone cancer in preclinical studies

October 25 2010

Researchers have identified an important signaling pathway that, when blocked, significantly decreases the spread of pediatric bone cancer.

In their study, researchers at The University of Texas MD Anderson Children's Cancer Hospital in Houston found that blocking the Notch pathway in mice decreased metastases in the lungs 15-fold. The results of a series of pre-clinical studies were reported Sunday in an oral presentation at the 42nd Congress of the International Society of Pediatric Oncology.

Their research showed that the Notch pathway and Hes1 gene play a key role in promoting the metastasis of osteosarcoma, the most common form of bone cancer in children.

Approximately 400 children and teens under the age of 20 are diagnosed with osteosarcoma annually, and the majority present with cancer that has already metastasized. The primary destination for the cancer to spread is to the lungs, which accounts for more than 35 percent of pediatric patients dying from osteosarcoma.

"Knowing the initial results from blocking Notch in mice, we are encouraged to keep investigating the entire metastasis process, so we can find additional therapies and targets to prevent cancer from spreading and growing," said Dennis Hughes, M.D., Ph.D., lead investigator and assistant professor at MD Anderson Children's Cancer Hospital.

In addition to Notch and Hes1's role in metastasis, Hughes believes that their expression can be correlated with a patient's prognosis. Hughes conducted a small retrospective study looking at patient samples, and 39 percent of patients with high expression levels of Hes1 survived 10 years versus the 60 percent survival rate for patients who had lower levels.

Ongoing research is studying the impact of various therapies, such as Gamma-secretase inhibitors and histone deacetylase (HDAC) inhibitors, that regulate the Notch pathway and have the potential to affect cancer cell survival. Hughes found that HDAC inhibitors actually increased the Notch pathway in osteosarcoma cells that had low Hes1 expression, which was an unfavorable response in that sample group. However, for cells that presented with high Hes1 expression, where Notch was already maximized, the HDAC inhibitors led to osteosarcoma cell death.

"By defining vital signaling pathways in bone sarcomas, we hope small molecule inhibitors can be applied, leading to longer survival and reducing morbidity and late effects from intensive chemotherapy," said Hughes.

"We also hope these new findings may apply to other solid tumors such as breast, prostate, colon and more, but we'll need additional research to determine whether or not that is the case," he added.

Provided by University of Texas M. D. Anderson Cancer Center