MedicalXpress

# Researchers unravel important role of Rb tumor suppressor in aggressive form of breast cancer

December 4 2013

The retinoblastoma (Rb) protein plays a critical role in suppressing the multi-step process of cell migration through the bloodstream, lymphovascular invasion and the metastasis of an aggressive type of breast cancer to the lung, researchers at the University of Cincinnati (UC) Cancer Institute, the Cincinnati Cancer Center (CCC) and the UC Brain Tumor Center have found.

The findings of Rb's role at multiple points in the disease process point to a potential new therapeutic target in patients with the most aggressive subset of breast cancer, known as basal-like breast carcinomas. This type of cancer has no estrogen receptor expression, and to date there is no efficient therapy for patients who suffer from it, leaving them with a generally poor prognosis. Basal-like breast carcinomas spread to the lungs in about 25 percent of cases and to the brain in about 30 percent of cases.

The findings are published online in the journal *PLOS ONE*. The investigator-initiated research was funded by the UC Department of Cancer Biology's Startup Fund, the UC Dean's Fund and the Mayfield Education and Research Foundation.

"Our research suggests that Rb inhibits collective cell migration, which in turn inhibits the lymphovascular invasion, the release of cancer cells into the blood circulation and the growth of metastasis," says Samuel

Godar, PhD, who led the study while an assistant professor in the Department of Cancer Biology. Godar is now visiting assistant professor of cancer biology at UC and president of BioTest4U, a biotech startup based in Loveland, Ohio, and Covington, Ky.

The deadly progression begins when decreased levels of Rb are coupled with an increase in the expression of an oncoprotein (a gene that has the potential to cause cancer) called CD44. Basal-like breast carcinomas are known to have an elevated expression of CD44 and relatively low levels of Rb. Expression of the oncoprotein CD44 is required for the breast cancer cells to move actively through the bloodstream.

The researchers studied Rb in two different ways. They studied its ability to suppress collective cell migration in cultures at the Vontz Center for Molecular Studies. They also studied Rb in an animal model, examining its ability to suppress the release of single cancer cells and cancer cell clusters into the bloodstream.

"Our results suggest that Rb suppression stimulates an array of pathological consequences," says co-investigator James Driscoll, MD, PhD, assistant professor in the UC Department of Internal Medicine's Division of Hematology Oncology and member of the CCC. "It stimulates collective rather than single cell-based invasion and migration; it leads to lymphovascular invasion; and it orchestrates metastasis to remote organs through the bloodstream."

The research illuminates the crucial role of the Rb/CD44 pathway in the metastatic progression of basal-like breast carcinomas, Godar says.

"It points to the Rb/CD44 pathway as a promising target for therapy to combat the propensity for these aggressive breast cancers to metastasize to the lung and brain. About 90 percent of cancer patients die primarily because of metastatic disease. We believe that the complex analysis of

metastatic progression in a preclinical model, such as the analysis we used, will become essential for predicting the true powers of novel anti-cancer drugs."

**More information:** dx.plos.org/10.1371/journal.pone.0080590

Provided by University of Cincinnati Academic Health Center