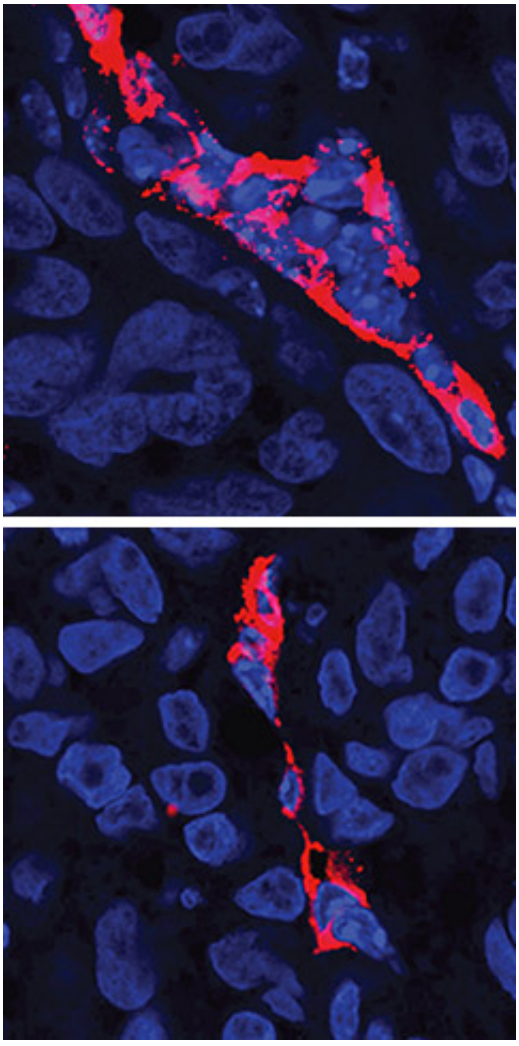
Drug is identified that could block the spread of melanoma

April 3 2014, by Zach Veilleux



By treating melanoma tumors with a compound called GW3965, researchers found they could reduce the tumor's recruitment of blood vessels (red areas, bottom) when compared to a conventional anti-tumor drug (top). Because blood vessels are necessary for metastasis, the results suggest the compound could slow or halt the cancer's spread.

(Medical Xpress)—Cancer is at its most curable when it's caught before it spreads. That's especially true in the case of melanoma, where survival rates can be as high as 97 percent when caught early—and as low as 15 percent if it's not. New research at Rockefeller has now identified a promising route to slowing or even preventing the metastasis of melanoma cells—something no current therapy can effectively accomplish.

"In order to cure melanoma, you need to prevent metastasis. We have identified a molecular target and a drug that shows promise in accomplishing just that—suppressing the spread of this deadly cancer within the body" says co-first author Nora Pencheva, a researcher in Sohail Tavazoie's laboratory and a 2014 recipient of the prestigious Harold M. Weintraub Graduate Student Award.

That newly identified molecular target is a protein called the liver-X-beta receptor. Although it is named for the organ in which it was first discovered, liver-X-beta is found in the nucleus of cells throughout the body. It belongs to a class of receptors that respond to chemical signals called hormones. Treatments for some reproductive cancers, such as those of the breast and prostate, have homed in on similar nuclear hormone receptors, but liver-X-beta is the first such receptor researchers have targeted in the fight against skin cancer.

Like other nuclear hormone receptors, liver-X receptors can control the expression of genes. In this case, the relevant gene codes for a protein known as ApoE, which Tavazoie's group had previously discovered to have a potent ability to both suppress cancer cells' ability to invade new tissue and the tumors' ability to recruit blood vessels, cellular processes necessary for metastasis. This protein has already received scrutiny from scientists, including Rockefeller's Jan Breslow, who studied its role in

cardiovascular disease, and compounds have been developed targeting the liver-X pathway to lower cholesterol, although they never made it to human efficacy testing.

In research recently described Cell, the researchers treated mice bearing human and mouse melanoma cells with one such drug, called GW3965, which is known to increase levels of ApoE. They found this drug greatly reduced the progression of metastasis in the lungs and brain, but also suppressed the growth of tumors. The findings could have a significant impact on survival because the metastatic spread of cancer is the primary determinant of mortality in patients.

If further testing bears it out, this discovery may help fill a deadly gap in the arsenal against melanoma. Current therapies either target defects caused by a genetic mutation often linked with melanoma or they seek to stimulate the patient's own immune system against the tumor. However, neither is approved for use in the clinic for reducing the likelihood that a tumor will metastasize.

"We are moving forward with testing the safety of a more potent version of this drug to make certain patients could tolerate this new anti-cancer agent at doses that are effective against melanoma. Our ultimate goal is to develop a treatment to reduce the risk of melanoma metastasis" says Tavazoie, who is Leon Hess Assistant Professor and Head of the Elizabeth and Vincent Meyer Laboratory of Systems Cancer Biology.

More information: "Broad-spectrum therapeutic suppression of metastatic melanoma through nuclear hormone receptor activation." Nora Pencheva, Colin G. Buss, Jessica Posada, Taha Merghoub, Sohail F. Tavazoie. *Cell* 156: 986-1001 (February 27, 2014)

Medical Xpress

Provided by Rockefeller University

Citation: Drug is identified that could block the spread of melanoma (2014, April 3) retrieved 23 April 2024 from https://medicalxpress.com/news/2014-04-drug-block-melanoma.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.