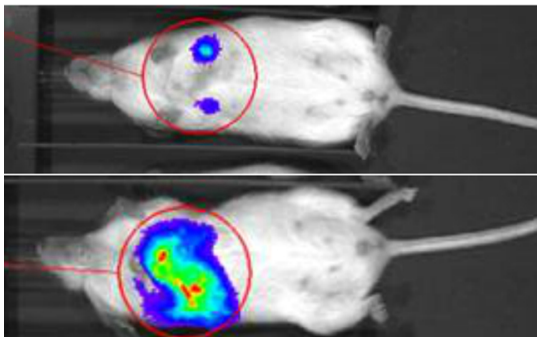
UC San Diego
UC San Diego News Center

September 02, 2014 | By Scott LaFee and Christina Johnson

Enzyme Controlling Metastasis of Breast Cancer Identified

Researchers at the University of California, San Diego School of Medicine have identified an enzyme that controls the spread of breast cancer. The findings, reported in the current issue of *PNAS*, offer hope for the leading cause of breast cancer mortality worldwide. An estimated 40,000 women in America will die of breast cancer in 2014, according to the American Cancer Society.



A tumor with reduced levels of enzyme UBC13 (top) and a control tumor (bottom) that has spread to the lungs.

"The take-home message of the study is that we have found a way to target breast cancer metastasis through a pathway regulated by an enzyme," said lead author Xuefeng Wu, PhD, a postdoctoral researcher at UC San Diego.

The enzyme, called UBC13, was found to be present in breast cancer cells at two to three times the levels of normal healthy cells. Although the enzyme's role in regulating normal cell growth and healthy immune system function is well-documented, the study is among the first to show a link to the spread of breast cancer.

Specifically, Wu and colleagues with the UC San Diego Moores Cancer Center found that the enzyme regulates cancer cells' ability to transmit signals that stimulate cell growth and survival by regulating the activity of a protein called p38 which when "knocked down" prevents metastasis. Of clinical note, the researchers said a compound that inhibits the activation of p38 is already being tested for treatment of rheumatoid arthritis.

In their experiments, scientists took human breast cancer cell lines and used a lentivirus to silence the expression of both the UBC13 and p38 proteins. These altered cancer cells were then injected into the mammary tissues of mice. Although the primary tumors grew in these mice, their cancers did not spread.

“Primary tumors are not normally lethal,” Wu said. “The real danger is cancer cells that have successfully left the primary site, escaped through the blood vessels and invaded new organs. It may be only a few cells that escape, but they are aggressive. Our study shows we may be able to block these cells and save lives.”

Researchers have also defined a metastasis gene signature that can be used to evaluate clinical responses to cancer therapies that target the metastasis pathway.

Co-authors include: Weizhou Zhang, UC San Diego and University of Iowa; Joan Font-Burgada,Trenis Palmer, Alexander S. Hamil, Lesley G. Ellies, Jing Yang, Steven F. Dowdy and Michael Karin, UC San Diego; Subhra K. Biswas, Agency for Science, Technology and Research, Singapore; Michael Poidinger, Agency for Science, Technology and Research, Singapore and National University of Singapore; Nicholas Borcherding and Qing Xie, University of Iowa; Nikki K. Lytle, Raymond G. Fox and Tannishtha Reya, UC San Diego and Sanford Consortium for Regenerative Medicine; Li-Wha Wu, UC San Diego and National Cheng Kung University, Taiwan.

Funding for this study was provided, in part, by Susan G. Komen for the Cure, National Institutes of Health (grants CA163798 and AI043477) and Pedal the Cause San Diego.

MEDIA CONTACT

Scott LaFee, 858-249-0456, slafee@ucsd.edu