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Killing Kindlin-3 to cure breast cancer: 'Blood' protein implicated

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A protein believed to be limited to the hematopoietic system, called Kindlin-3, has been identified as a major player in both the formation and spread of breast cancer to other organs. This discovery, published in the May 2014 issue of *The FASEB Journal*, could open the door to an entirely new class of breast cancer drugs that targets this protein's newly found activity.

"Kill Kindlin-3 to cure cancer," said Elzbieta Pluskota, Ph.D., a researcher involved in the work from the Department of Molecular Cardiology at the Cleveland Clinic Lerner Research Institute in Cleveland, Ohio. "Let our moms, wives, sisters and daughters live long and healthy lives."

To make this discovery, Pluskota and colleagues searched gene expression databases to identify gene products that are elevated in breast cancer, and therefore, likely candidates to be involved in the disease progression. They found that Kindlin-3 expression levels are significantly elevated in breast cancer tumors when compared to the adjacent normal mammary tissue. In fact, Kindlin-3 was in the top 3 percent of gene products elevated in breast cancer cells. Then the scientists studied two groups of animal models. The first group (control group) was implanted with cancer cells that did not express Kindlin-3, while the second group (experimental group) received cancer cells that were engineered to express high levels of Kindlin-3.

The experimental group developed bigger tumors that grew significantly

faster, metastasized more, and were more angiogenic than the control group. Further biochemical analyses showed that Kindlin-3 enhanced the production and secretion of VEGF, a molecule that is required for the formation of new blood vessels. This study also identified a previously unknown function of Kindlin-3; the regulation of epithelial-mesenchymal transition, a process required for cancer cells to become mobile and invasive.

"Just when scientists thought they knew all there was to know about Kindlin-3, we now learn that this protein has mostly been flying under the radar in breast cancer research all along," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "This discovery puts us on a path toward developing treatments, which slow, stop or reverse the progression of some of the most aggressive breast cancers."

More information: Khalid Sossey-Alaoui, Elzbieta Pluskota, Gangarao Davuluri, Katarzyna Bialkowska, Mitali Das, Dorota Szpak, Daniel J. Lindner, Erinn Downs-Kelly, Cheryl L. Thompson, and Edward F. Plow. Kindlin-3 enhances breast cancer progression and metastasis by activating Twist-mediated angiogenesis. *FASEB J* May 2014 28:2260-2271; DOI: 10.1096/fj.13-244004

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