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'Obscurins' in breast tissue may help physicians predict and detect breast cancer

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A new discovery published online in *The FASEB Journal* may lead to a new tool to help physicians assess breast cancer risk as well as diagnose the disease. In the report, researchers from Johns Hopkins University and the University of Maryland, explain how proteins, called "obscurins," once believed to only be in muscle cells, act as "tumor suppressor genes" in the breast. When their expression is lost, or their genes mutated in epithelial cells of the breast, cancer develops. It promises to tell physicians how breast cancer develops and/or how likely it is.

"Our studies on the role of obscurins in the development of breast cancer lay the framework for a series of in-depth investigations aiming to understand how these proteins act to prevent tumor formation," said Aikaterini Kontrogianni-Konstantopoulos, Ph.D., a researcher involved in the work from the Department of Biochemistry and Molecular Biology at the University of Maryland School of Medicine in Baltimore, MD. "It is our hope that our research will provide important new insights into breast tumor biology and ultimately yield new targets for the development of innovative therapeutic strategies."

To make this discovery, Kontrogianni-Konstantopoulos and colleagues used a highly specific antibody probe to detect obscurins in normal and cancerous breast, skin, and colon cells. They observed that cancer cells expressed significantly lower amounts of obscurins compared to normal cells, leading to the hypothesis that loss of obscurins allowed normal cells to become cancerous. The researchers then compared two breast

epithelial cell populations: a "normal" one, which expressed obscurins and served as a control, and an "altered" one, which failed to express obscurins through genetic manipulations. Both cell populations were treated with a chemical called "etoposide," which causes massive DNA damage and induces cell death. Scientists detected and quantified cell death with a number of different methodologies, and found that etoposide caused a significantly high percentage of cell death in normal cells, but only a very low percentage of cell death in the altered, obscurin-deficient cells. This suggests that the loss of obscurins makes breast epithelial cells more resistant to the natural cell death necessary to prevent damaged cells from transforming into a run-away cancer.

"This study is important for a number of reasons. First, it shows that there is a lot more to obscurins than previously thought, making future research into this family of proteins important. Second, it reveals a previously unknown group of tumor suppressors in the breast that prevent normal cells from becoming cancerous. Finally, it opens doors to new tools to help doctors assess a person's risk for cancer and possibly to diagnose it in the earliest of stages," said Gerald Weissmann, M.D., Editor-in-Chief of *The* FASEB Journal.

More information: Nicole A. Perry, Marey Shriver, Marie G. Mameza, Bryan Grabias, Eric Balzer, and Aikaterini Kontrogianni-Konstantopoulos. Loss of giant obscurins promotes breast epithelial cell survival through apoptotic resistance. *FASEB J.* doi: 10.1096/fj.12-205419

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