Breast Milk Protein Linked to Poorer Breast Cancer Survival in Younger Women

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(PhysOrg.com) -- In a study that sheds light on why breast cancer may be deadlier for premenopausal women, a Yale School of Medicine team has linked breast cancer survival with levels of a transport protein that regulates milk production in mammary glands. The paper is published in the online early edition of the *Proceedings of the National Academy of Sciences*.

During breastfeeding, a great deal of calcium must be transported from the circulation into milk. This is accomplished through mammary cells that express the plasma membrane calcium-ATPase 2 (PMCA2). Working with mice, the Yale researchers demonstrated how, when lactation stops, the rapid loss of PMCA2 expression triggers apoptosis - the death of mammary epithelial cells - a natural step that returns breast function and shape to normal.

Lead author John Wysolmerski, M.D., professor of endocrinology at Yale School of Medicine and a member of the Yale Medical Group and Yale Cancer Center, says this is one of the body's most elegant regulatory mechanisms. "The shrinking of the mammary glands when lactation stops is one of the most striking examples of coordinated cell death that exists in nature," he said.

But Wysolmerski's team also showed that persistent PMCA2 expression in breast cancers lowers calcium levels inside malignant cells, allowing them to avoid cell death. Further, the researchers associated these excessively high PMCA2 levels with poorer outcomes in breast cancer -

larger tumors, more lymph node involvement, worse survival and more HER2-positive status. HER2 is a protein that indicates greater aggressiveness in breast cancer. HER2-positive tumors are more common among younger women.

“Our results suggest that PMCA2 may be especially important in the biology of premenopausal breast cancer and/or HER2-positive tumors,” said Wysolmerski.

The Yale team believes that PMCA2 may present a potential target for breast cancer therapy in humans. Ongoing studies are examining the role of PMCA2 in resistance to common chemotherapy agents, and efforts are underway to develop new drugs to block PMCA2's function.

Provided by Yale University