Addressing high false-positive rates for mammograms

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We've heard it repeatedly: early detection is key to surviving breast cancer. But even with recent advances in mammography, finding indications of breast cancer before it can metastasize remains a problem. Scientists at Pacific Northwest National Laboratory and Duke University Medical Center have increased the ability to determine if a positive result on a breast cancer screen is true or false.

They found that different breast cancer subtypes produce distinct profiles of protein biomarkers in blood and that these biomarkers have the potential to differentiate between true and false positive screens. These subtype-specific biomarker panels may also be useful as an additional way to detect breast cancer.

High false-positive rates for mammograms have become a controversial issue in the last 2 years, and have been reported by the popular press. Existing screening methods for breast cancer are commonly incorrect in that the majority of times a suspicious lump is found, it is not cancer. Therefore, alternative tests are needed to either assist in early detection of this common form of cancer, which kills more than 40,000 women each year in the United States, or improve the existing methods' accuracy.

One potential alternative is the use of circulating biomarkers for early detection, when the disease is more readily cured, and typically the cure does requires less harsh interventions. However, established breast cancer biomarkers are not useful for detecting the disease. Gene

expression information suggests that breast cancer is composed of five major subtypes. The PNNL/Duke team determined whether breast cancer subtypes influence circulating protein biomarkers. Their results suggest that patterns of circulating biomarkers are not only influenced by breast-cancer subtype, but that it may be essential to consider breast cancer subtypes when using biomarkers in blood.

The researchers used a sandwich-ELISA microarray platform to evaluate 23 candidate biomarkers in plasma samples from people having either benign breast disease or invasive breast cancer. The platform can analyze multiple biomarkers quickly and efficiently. An important aspect of this study is that the plasma samples were collected when the patients had biopsies, which were done based on a suspicious screening test, such as a mammogram. Thus, both the patients and persons collecting the blood were ignorant of the presence or absence of cancer. Based on the results of the biopsy analysis, breast cancer subtypes were defined based on the HER2 and estrogen receptor statuses.

The researchers found that ten proteins were altered in at least one breast cancer subtype. But only one protein, the cytokine RANTES, was significantly increased in all four subtypes. Even so, the best discrimination was obtained with analyses that combined data from multiple biomarkers, and were dependent upon cancer subtype.

Although the results for RANTES are consistent with previous publications, the multi-assay results need to be validated in independent sample sets.

More information: Gonzalez RM, et al. 2011. "Plasma Biomarker Profiles Differ Depending on Breast Cancer Subtype but RANTES is Consistently Increased." Cancer Epidemiology, Biomarkers & Prevention Published Online First May 17, 2011. doi: 10.1158/1055-9965.EPI-10-1248

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