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Researchers find new, noninvasive way to identify lymph node metastasis

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Using two cell surface markers found to be highly expressed in breast cancer lymph node metastases, researchers at Moffitt Cancer Center, working with colleagues at other institutions, have developed targeted, fluorescent molecular imaging probes that can non-invasively detect breast cancer lymph node metastases. The new procedure could spare breast cancer patients invasive and unreliable sentinel lymph node (SLN) biopsies and surgery-associated negative side effects.

Their study was published in a recent issue of Clinical Cancer Research (18:1), a publication of the American Association for Cancer Research.

"The majority of breast cancer patients, up to 74 percent, who undergo SLN biopsy are found to be negative for axillary nodal, or ALN, metastases," said corresponding author David L. Morse, Ph.D., an associate member at Moffitt whose research areas include experimental therapeutics and diagnostic imaging. "Determining the presence or absence of ALN metastasis is critical to breast cancer staging and prognosis. Because of the unreliability of the SLN biopsy and its potential for adverse effects, a noninvasive, more accurate method to assess lymph node involvement is needed."

The authors note that the postoperative complications to the SLN biopsy can include lymphedema, seroma formation, sensory nerve injury and limitations in patient range of motion. In addition, biopsies fail to identify disease in axillary lymph nodes in five to 10 percent of patients.

In developing targeted molecular probes to identify breast cancer in axillary lymph nodes, the research team from Moffitt, the University of Arizona and University of Florida used two surface cell markers – CAIX and CAXII. CAIX is a cell surface marker known to be "highly and broadly expressed in breast cancer lymph node metastases" and absent in normal tissues.

CAIX and CAXII are both integral plasma membrane proteins with large extracellular components that are accessible for binding of targeted imaging probes, explained Morse. In addition, several studies have shown that CAIX expression is associated with negative prognosis and resistance to chemo and radiation therapy for breast cancer. CAXII is a protein expressed in over 75 percent of axillary lymph node metastases.

The researchers subsequently developed their targeting agents by using monoclonal antibodies specific for binding CAIX and CAXII, both of which are known to promote tumor growth.

According to the researchers, a number of noninvasive optical imaging procedures for SLN evaluation have been investigated, but the approaches have lacked the ability to target tumor metastasis biomarkers.

"These methods provide only anatomic maps and do not detect tumor cells present in lymph nodes," explained Morse. "Using mouse models of breast cancer metastasis and a novel, monoclonal anti-body-based molecular imaging agents, we developed a targeted, noninvasive method to detect ALN metastasis using fluorescence imaging."

In addition to the imaging study with mice, the researchers also reported that the combination of CAIX and CAXII covered 100 percent of patient-donated samples used in their tissue microarray (TMA) study.

"The imaging probes detected tumor cells in ALNs with high sensitivity," explained Morse. "Either CAIX or CAXII were expressed in 100 percent of the breast cancer lymph node metasatsis samples we surveyed in this study. These imaging probes have potential for providing a noninvasive way to stage breast cancer in the clinic without unneeded and costly surgery."

Provided by H. Lee Moffitt Cancer Center & Research Institute

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