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Researchers find two biomarkers with potential to predict breast cancer spread

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Expression of two different proteins taken from primary tumor biopsies is highly associated with spread of breast cancer to nearby lymph nodes, according to researchers who say this protein profile could help identify at an early stage those patients whose disease is likely to metastasize.

In the December 15 issue of Cancer Research, the researchers say over-expression of one unidentified protein and under-expression of another is 88 percent accurate in identifying breast cancer that has spread in a group of 65 patients, compared to an analysis of lymph nodes and outcomes.

If the predictive and diagnostic power of these proteins is validated, they could be analyzed in primary tumor biopsies that are routinely collected at the time of diagnosis, saving some women from extensive and possibly unnecessary treatment as well as from undergoing a second surgery to collect lymph nodes for analysis, the researchers say.

"We want to be able to predict, at the earliest stages, if a tumor has spread and how dangerous it will be," said the study's lead author, Dave S. B. Hoon, Ph.D., director of Molecular Oncology at the John Wayne Cancer Institute, Saint Johns Health Center, in Santa Monica, California. "These two proteins may allow us to target aggressive tumors with more extensive therapy management to some women, while sparing others from needless treatment."

"Our approach is not to rely on hunting for lymph nodes during surgery,

which will then only tell you whether the nodes are positive or negative, but to look at the primary tumor to predict how aggressive the cancer is at early stages," Hoon said.

The lymph system collects the fluid that surrounds tissue cells, which is then processed by nearby draining lymph nodes, so checking these nodes for the presence of cancer is currently one of the most important prognostic factors predicting breast cancer survival, he said. "One of the best predictors of systemic cancer spread is whether the draining lymph node has any signs of metastasis," he said.

Biopsy of this "sentinel" node occurs after the tumor has been removed in an initial surgery, and if metastasis is found there, surgeons continue to sample "downstream" nodes to check for degree of spread. While this procedure, called "sentinel node biopsy" is now practiced routinely in the U.S. and in many other countries, there remains controversy in the accurate assessment of micrometastasis in sentinel lymph nodes, according to Hoon. He said recent studies have found that it can produce both false positive and false negative results.

Furthermore, microdisease seen in the sentinel lymph node doesn’t always predict that a patient will go on to develop metastatic breast cancer, said Hoon. "If the primary tumor and nodes are removed in some women, they will not develop recurrent disease, but in other women, removal of the nodes may have no impact on the spread of the metastatic disease that has already occurred prior to surgery."

In this study, 65 patients with invasive cancer who underwent surgery and biopsy of the sentinel lymph node and/or other lymph nodes were enrolled, and investigators were blinded as to the findings of these lymph node biopsies.

In all, 24 patients (37 percent) were found to have cancer in their nodes

and 41 patients (63 percent) were node negative. To predict lymph node metastasis, the investigators used a ProteinChip™ to identify biomarkers that distinguished between the tumor profile with paired positive and negative nodes.

Two protein peaks associated with lymph node metastasis were identified. Specifically, over-expression of protein peaks at 4,871 Da (which represents the molecular weight of the protein) and under-expression of a protein peak at 8,596 Da were highly predictive of lymph node metastasis.

Patients with two or more positive lymph nodes were significantly more likely to show over-production of 4,871 Da, compared to patients with no lymph node spread. The peak at 4,871 could also predict patients with four or more metastatic nodes who have significantly worse outcomes.

Although they don't know what these proteins are, by searching a protein database Hoon suggests that 4,871 Da may represent thymosin beta-10, a peptide that has already been associated with out-of-control growth and cell differentiation, and that 8,596 Da could represent an ubiquitin protein associated with a good prognosis in node-negative breast cancer.

"Protein peaks found in our study may be useful as prognostic biomarkers, but we must be cautious until the identities of these proteins are known and validated in a larger study," Hoon said.

Source: American Association for Cancer Research