Marker identifies breast cancer patients likely to respond to tamoxifen

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Cancer researchers at the Kimmel Cancer Center at Jefferson and an international team of collaborators have discovered a biomarker in breast cancer that may help identify which women will respond to anti-estrogen therapy.

The research appears in the May 16 online issue of the *Journal of Clinical* Oncology.

Anti-estrogen drugs, most notably tamoxifen, are widely used in patients diagnosed with estrogen receptor-positive breast cancer. However, as many as a third of the women given tamoxifen fail to respond.

In this new study, the investigators found that women whose tumors retain the active form of the protein biomarker Stat5 have an increased likelihood of responding to tamoxifen. In contrast, women treated with tamoxifen whose tumors lacked active Stat5 had up to a 20-fold increased risk of dying from breast cancer after adjustment for effects of standard hormone receptor markers and other pathology data.

"Identification of predictive biomarkers present in breast cancer will lead to improved individualized therapies tailored specifically towards each woman's cancer," said Hallgeir Rui, M.D., Ph.D., professor of oncology, Kimmel Cancer Center at Thomas Jefferson University, and principal investigator of the study. "Absence of the active form of Stat5 could help identify a group of patients unlikely to respond to tamoxifen so they may be offered alternative and more aggressive treatments."

Stat5 protein is a DNA-binding factor that regulates expression of certain genes, many of which remain unknown. During pregnancy, Stat5 is activated by the hormone prolactin, and stimulates milk production in the breast. Active Stat5 is also detectable at lower levels in healthy breast tissue of non-pregnant women. This study further showed that active Stat5 was lost in the majority of more aggressive tumors and when those tumors metastasized to lymph nodes.

In 2004, Rui and colleagues reported that women with early stage breast cancer had higher survival rates when their tumors expressed active Stat5. Therefore, in two independent groups of breast cancer patients that were not treated with chemotherapy or anti-estrogen therapy, they further investigated the relationship between active Stat5 in the tumor and whether the patient had breast cancer recurrence or died of breast cancer over periods as long as 30 years. The team found consistent favorable breast cancer outcomes when tumors retained active Stat5.

The studies presented in this publication utilized a retrospective analysis of five large, independent breast cancer patient materials that included 1,000 patients, giving the studies a solid statistical basis. A benefit of optimizing a marker like Stat5 is that the assay for Stat5 is simple, inexpensive, and can be rapidly adapted to routine analysis in pathology laboratories using standard procedures.

"More work remains to be done, but we are optimistic about the utility of Stat5 as a biomarker," said Amy Peck, PhD, and lead author of the study. "The team is moving forward with plans for a randomized, prospective study with larger patient numbers to further evaluate the utility of Stat5 in managing and treating breast cancer."

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