MedicalXpress

Researchers discover patterns of genes associated with timing of breast cancer recurrences

December 7 2011

An international research team led by Georgetown Lombardi Comprehensive Cancer Center has found biological differences in hormone-receptor positive breast cancer that are linked to the timing of recurrence despite endocrine therapy.

They say their findings, presented at the 2011 CTRC-AACR San Antonio Breast Cancer Symposium, may help oncologists find ways to individualize systemic therapy to delay or prevent recurrences, and to avoid excessive treatment of patients who will never recur.

"We found that, at the time of diagnosis, there are clear biological differences within the supposedly uniform group of hormone receptor positive breast cancers, and these differences distinguish subtypes relative to the time at which they recur," says Minetta Liu, M.D., director of translational breast cancer research at Georgetown Lombardi Comprehensive Cancer Center.

"We need to exploit these differences and use our data to figure out what drives a tumor to never metastasize. Then we will try to manipulate the cancers that are programmed to recur to act like that of the non-recurrences," she says.

Tamoxifen is credited with saving the lives of thousands of women with estrogen receptor-positive (ER+) breast cancer, which accounts for two-

thirds of all diagnoses of invasive breast cancer in the United States. As the world's leading breast cancer treatment and prevention drug, tamoxifen can stave off cancer recurrences for more than 10 years in some patients, but for others, the cancer returns much earlier.

To determine why some ER+ cancers treated with tamoxifen recur earlier rather than later, if at all, Liu and her Georgetown team collaborated with researchers at the University of Edinburgh and with engineers at Virginia Tech.

The Scottish collaborators shared high quality tumor biopsies collected from patients with different stages of breast cancer before they had started tamoxifen therapy. Critical clinical information was available to determine whether or not patients developed metastatic disease, and when the recurrence (if any) was found. The samples were processed and analyzed at Georgetown. Then scientists at Virginia Tech examined the gene expression patterns generated from the tumor biopsies relative to the known clinical outcomes to develop a predictive model of early, late or no disease recurrence.

The final analysis revealed distinct patterns in cancers that recurred early (up to three years from diagnosis) or late (more than ten years from diagnosis). Liu says that some of the genes that were identified were "expected and reassuring," but others were "unexpected and novel." Work is ongoing to validate selected genes as biological drivers of metastasis.

"Endocrine therapy and chemotherapy are not without toxicity," Liu says. "The ability to predict which patients will recur early in their treatment course can lead to more appropriate recommendations for adjuvant chemotherapy. It might also identify those women who would benefit most from studies using investigational agents to enhance the effects of tamoxifen or aromatase inhibitors."