

Study shines new light on genetic alterations of aggressive breast cancer subtype

August 7 2014



Mammograms showing a normal breast (left) and a cancerous breast (right). Credit: Wikipedia.

Researchers from the Lester and Sue Smith Breast Center at Baylor College of Medicine have uncovered new information about the genetic alterations that may contribute to the development of a subtype breast cancer typically associated with more aggressive forms of the disease and higher recurrence rates.

The study, led by Dr. Xiaosong Wang, assistant professor of medicine – hematology and oncology and of molecular and cellular biology at Baylor, published today in *Nature Communications* and focused on the more aggressive molecular subtype of the <u>estrogen-receptor</u> positive breast cancer known as luminal B breast cancer.



"While expressing the estrogen receptor, the luminal B breast cancers usually have higher tumor grade, larger tumor size, and poor prognosis, with most cases difficult to treat by endocrine therapy," said Wang, the lead and corresponding author on the report. "We wanted to gain a deeper understanding about the <u>genetic alterations</u> underlying this particular form of breast cancer, because we do not know about what malfunctions potentially cause this form to be more aggressive."

In the study, Wang and colleagues identified a particular gene fusion on the estrogen receptor itself (hybrid gene formed from two previously separate genes) that was preferentially present in a subset of samples of tumors that were luminal B and ER-positive.

The fusion was a result of rearrangements in the estrogen receptor gene called ESR1 and another neighboring gene called CCDC170, Wang said.

The findings were based in part from data available through the National Human Genome Research Initiative's <u>Cancer Genome Atlas</u> project.

Rearrangement in the genes causes the disruption of the transfer of information. "In a majority of cases this fusion seems to be generated by a tandem duplication of the genetic material spanning the ESR1 and CCDC170 genes," said Wang.

In 200 tumor samples studied, 8 were found positive for the ESR1-CCDC170 gene fusion. The tumor samples were made available through the Lester and Sue Smith Breast Center's Tumor Bank. In further studies in the lab, the team observed that when ESR1-CCDC170 was introduced into ER-positive breast cancer cells, there was increased cell motility and invasion, as well as enhanced tumor formation, which could explain the increased aggressiveness of ESR1-CCDC170 human tumors.



"The rearrangements between the genes were very cryptic, which makes it very difficult to be detected by conventional cytogenetic approaches," said Wang. "This finding is important because it sheds new light on a much needed better understanding about what may cause these tumors to be more aggressive." The findings also signal a new concept of estrogen receptor pathobiology in breast cancer.

This project is co-advised by Dr. Rachel Schiff, associate professor in the Smith Breast Center at Baylor, and the co-lead authors include Drs. Jamunarani Veeraraghavan, Ying Tan, and Xi-Xi Cao, all of Baylor.

"The aggressive luminal B subtype of <u>breast cancer</u> is a heterogeneous and complex disease. In the era of precision medicine, the current study emphasizes the importance and promise of integrative genomic research methodologies. This approach can identify genetic aberrations that may drive the development and progression of these aggressive tumors and that may guide more personalized effective therapeutic strategies," said Schiff.

Provided by Baylor College of Medicine

Citation: Study shines new light on genetic alterations of aggressive breast cancer subtype (2014, August 7) retrieved 17 May 2024 from <u>https://medicalxpress.com/news/2014-08-genetic-aggressive-breast-cancer-subtype.html</u>

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