

Breast cancer classified into 12 unique biological groups

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Researchers at UNC Lineberger Comprehensive Cancer Center have taken a major step forward in melding two key methods for studying breast cancer: one by genetic analysis and the second by looking at the architecture of cells, or their pathology. The investigators were able to link the two thanks to a decade-long effort made possible by the federally funded resource of The Cancer Genome Atlas (TCGA) Breast Cancer Data set. The scientists found much agreement between genetic and pathologic classifications but developed a novel way to use data from both systems to arrive at a classification method that divides breast cancers into 12 distinct biological groups.

The findings appeared December 8, 2021, in *Cell Genomics*.

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The World Health Organization has long classified breast tumors into multiple types based on a tumor cell's unique shape, structure and size. The most common type of breast cancer has been defined as invasive ductal breast carcinoma; it accounts for 70 percent to 80 percent of all breast cancers. While this predominant type of breast cancer was of interest to the researchers, it was the rarer types that held the most opportunity for new discoveries in this finding.

TCGA's 10,000-plus tissue repository of 33 different types of cancer

types allowed the investigators to explore the previously known, but rarer breast pathologies. However, obtaining a sufficient number of samples to adequately study rarer types and subtypes of cancer was a challenge. But the TCGA Breast Cancer team, led by Perou, was able to obtain enough samples for at least six rare breast cancer subtypes, each of which yielded interesting and unique molecular features.

Of particular note were rare metaplastic carcinomas, a [breast cancer](#) subtype with a poor clinical prognosis. Through comparison to the entire TCGA set of 10,000 tumors, the researchers found that some metaplastic cancers were related closely to melanomas, which are aggressive skin cancers, and to sarcomas, which are typically found in bone and connective tissue.

"Our effort finishes all planned analyses on TCGA, which has been a major undertaking," said Aatish Thennavan, a Ph.D. graduate student in Perou's lab and first author of the article. "In our study, we validated our findings with other datasets that also had rarer subtypes. We would urge future studies to incorporate rarer subtypes so we can build on this foundational analysis."

For their next efforts, the researchers plan to delve deeper into the molecular features and cellular origins of metaplastic breast cancers. They are also interested in why some of the 12 biological groups show evidence of immune cells that are capable of infiltrating tumor cells, and why others tend not to have these immune infiltrates. This line of research has therapeutic implications as there are treatments that have been developed that target immune cells in breast cancers.

In addition to Perou and Thennavan, other authors at UNC include Youli Xia, Ph.D., Susana Garcia Recio, Ph.D., and Katherine A. Hoadley, Ph.D. Other authors include Francisco Beca, MD, Ph.D. (previously of Stanford University), Seattle Genetics, Seattle; Kimberly Allison, MD,

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