New study identifies molecular features tied to breast cancer tumor spread

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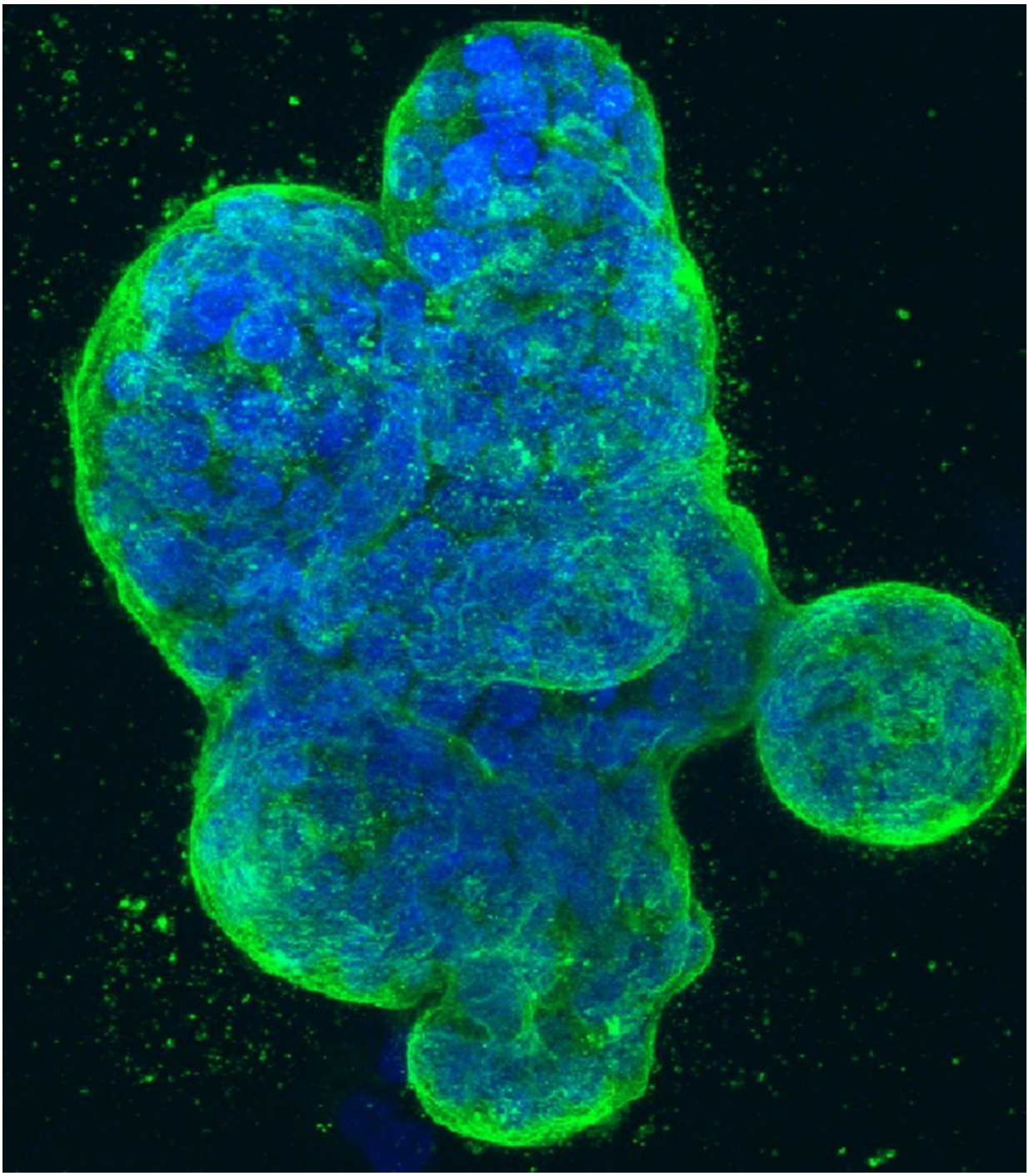

Three-dimensional culture of human breast cancer cells, with DNA stained blue and a protein in the cell surface membrane stained green. Image created in 2014 by Tom Misteli, Ph.D., and Karen Meaburn, Ph.D. at the NIH IRP.

Susana Garcia-Recio, Ph.D., a research associate in the lab of Charles M. Perou, Ph.D., at UNC Lineberger Comprehensive Cancer Center, will present findings that identified molecular features responsible for the development and progression of metastatic breast cancer at the 2022 American Association for Cancer Research annual meeting.

Focused on understanding the difference in the microenvironments that surround cancer cells in original—or primary—tumors versus sites where the tumor metastasizes, the investigators studied tumor tissue from 55 metastatic breast cancer patients, representing 51 primary cancers and 102 metastases. The investigators used advanced genetic tools to identify significant differences in tumor cells and immune features, or markers of change in the immune response, between primary tumors and their metastatic progeny.

They discovered genetic changes that led to lower levels of immune cells being able to infiltrate and attack tumor cells, which were more common at metastatic sites. The lower levels were notable in the two central components of any immune response, namely T cells and B cells, that largely direct the anti-tumor immune response. The researchers also looked at differences between various sites of metastasis; liver and brain metastasis showed lower levels of an immune cell response compared to levels of immune cells found in lung metastases.

"We had two pressing questions we wanted to answer: Starting at the genetic level, does the way genes are expressed in a cancer vary in primary tumors compared to its metastases and do these gene expression features vary according to the site of metastasis?" Garcia-Recio said. "We found that around 17% of metastatic tumors had reduced expression of a gene that affects cellular immunity, had specific changes to their DNA and reduced ability of immune cells to infiltrate their environment and fight off cancer cells."

Knowledge gained from this research could have important clinical implications: One in eight women will be diagnosed with breast cancer and one-third of those diagnosed will develop metastatic breast cancer, pointing to the need for a diversity of treatment options. "We will probably need to take immune response differences into account when we treat individual patients based upon their biopsies as well as their immune system biomarkers," Garcia-Recio noted.

These and other tumor research efforts in the Perou lab were made possible, in large part, by tissue samples gathered by the multi-institutional national AURORA US Project, which has a major component at UNC. This project provided investigators with a unique ability to look at hundreds of primary tumor and metastatic specimens, including metastases to the liver, lung, brain, and lymph nodes. AURORA also utilized three different genetic technologies on each tumor or metastasis specimen, using facilities at three institutions that give the consortium of researchers a leg up in helping to elucidate key differences between primary and metastatic tumors.

The resources made available by AURORA point out the importance of getting biopsies from the metastases as many current treatments are based on just the profile of a primary tumor, and the AURORA project learned that often the metastases are different. "This is where patients play such a key role," said Garcia-Recio. "We used tissue samples from the AURORA tumor bank, but we need a higher number of biopsy samples to be able to carry out more expansive future research efforts. We owe our patients a tremendous round of thanks for helping us advance our research efforts to this point and for any contributions they make in the future."

More information: Read the abstract here.

Provided by UNC Lineberger Comprehensive Cancer Center