Diverse genetic alterations found in triple-negative breast cancers after neoadjuvant chemotherapy

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Many different genetic alterations were detected in tumor cells left behind after patients with triple-negative breast cancer were treated with chemotherapy prior to surgery (neoadjuvant chemotherapy), according to data presented at the 2012 CTRC-AACR San Antonio Breast Cancer Symposium. The investigators hope this knowledge will help move toward early personalized treatment to combat this aggressive subtype of breast cancer.

"The standard of care for many patients with triple-negative breast cancer is to administer chemotherapy before surgery to shrink the tumor," said Justin M. Balko, Pharm.D, Ph.D., research faculty who led this study in the laboratory of Carlos Arteaga, M.D., at the Vanderbilt-Ingram Cancer Center in Nashville, Tenn.

"Unfortunately, about 70 percent of patients still have some residual disease at the time of surgery, despite treatment," Balko said. "We speculate this residual disease in the breast should look just like simultaneous micrometastases that are destined to recur in the same patient. Thus, we need to know what is in this tissue that is left behind to conceive targeted therapies to treat and prevent recurrence of metastases down the road."

Balko and colleagues profiled residual tumor tissue from 102 patients with triple-negative breast cancer who had received neoadjuvant

chemotherapy. In DNA from 89 evaluable tumors, the investigators used deep sequencing to examine 182 oncogenes and tumor suppressors that are known to be altered in human cancers. Instead of finding similar genes affected among the patients, they found a diverse set of genes were altered.

"We already knew that triple-negative breast cancer is driven by a diverse group of genetic alterations," said Balko. "So, in one way, we fell further down this rabbit hole, but we also found some things that could be promising therapeutically, such as frequent MYC, MCL1 and JAK2 amplifications as well as mutations in the PI3K pathway."

According to Balko, the next step is to confirm the findings in a larger patient cohort, and if the findings are replicated, broad molecular approaches will be needed to help inform personalized therapies for triple-negative breast cancer. Furthermore, it will be necessary to explore the therapeutic sensitivity of breast cancers harboring these lesions in the laboratory to know how to treat patients with breast cancer who have these alterations.

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