Spotlight

By Caroline Seydel

Predicting Drug Resistance in Breast Cancer

Yamauchi *et al.*
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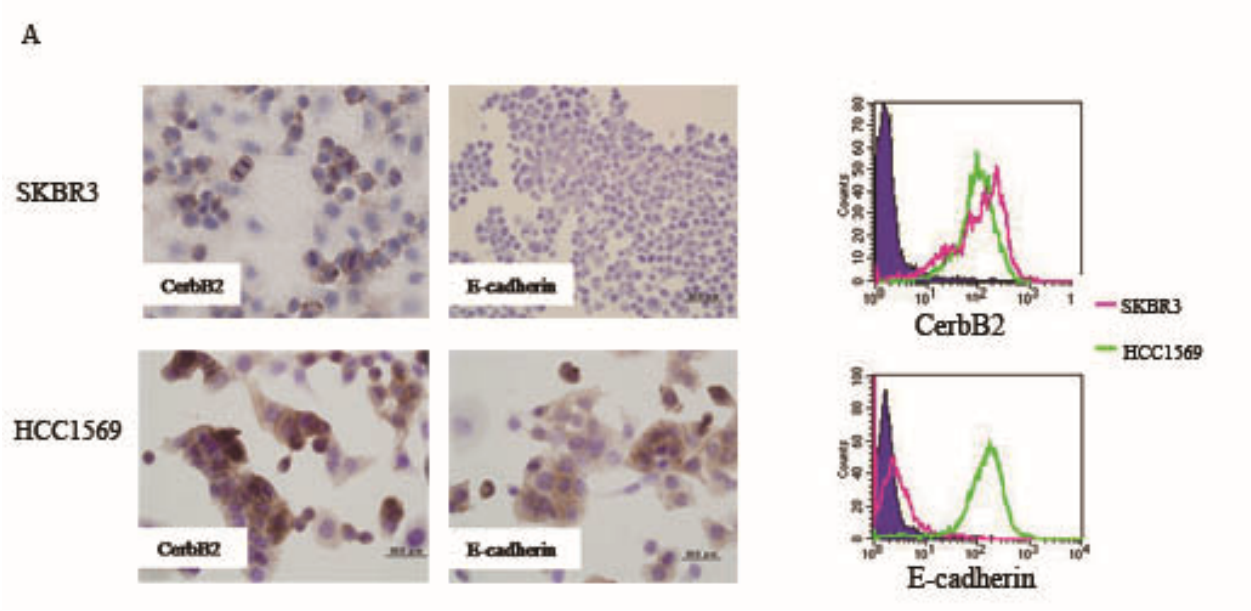
One of the big obstacles in treating cancer is drug resistance. The recombinant antibody drug trastuzumab, which is widely used to treat breast cancer, runs smack into this problem: even when used in combination with other therapies, many patients fail to respond. Yamauchi *et al*. set out to find a way to improve the drug's effectiveness, and they found that getting breast cancer cells to express the transmembrane protein E-cadherin improves trastuzumab's ability to kill those cells.

Breast cancers that overexpress the HER2 receptor tyrosine kinase are among the most aggressive and deadly types of breast cancer. Trastuzumab specifically fights these HER2-overexpressing tumors, but for some, the drug has no effect. Though it's not known precisely how trastuzumab affects the cancer, one hypothesis is that it recruits immune effector cells that kill the tumor by antibody-dependent cellular cytotoxicity. The researchers investigated whether the protein E-cadherin, which acts as a ligand for the KLRG1 receptor on killer T cells, affected trastuzumab's ability to spur the immune response that takes out the tumor cells. They showed that lessening the amount of E-cadherin on the surface of breast cancer cells increased their sensitivity to trastuzumab.

The team also scrutinized the tumors of patients who had responded to trastuzumab and those who had failed to respond; E-cadherin was found in about a third of those whom trastuzumab had helped, and in 81% of those with resistant tumors. Expression of E-cadherin, then, would appear to predict whether a patient's disease will defy treatment with trastuzumab.



E-cadherin expression is low in a cell line, SKBR3, which is susceptible to trastuzumab, but higher in a resistant line, HCC1569