Novel technique switches triple-negative breast cancer cells to hormone-receptor positive cells

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Within many hormone-receptor positive breast cancers lives a subpopulation of receptor-negative cells – knock down the hormone-receptor positive cells with anti-estrogen drugs and you may inadvertently promote tumor takeover by more dangerous, receptor-negative cells. A study recently published in the *Proceedings of the National Academy of Sciences* describes how to switch these receptor-negative cells back to a state that can be targeted by existing hormone therapies.

"We found that these estrogen-receptor negative cells express high levels of a Notch receptor protein," says James Haughian, PhD, investigator at the University of Colorado Cancer Center and instructor at the University of Colorado School of Medicine. "And when you blockade this Notch activity, you end up with a pure population of hormone-receptor positive cells."

Very basically, within a breast cancer, you frequently have different kinds of cells living together – some that have estrogen receptors and so need to "grab" estrogen in order to survive, grow and replicate. And, Haughian finds, some with similar Notch receptors that need to "grab" Notch proteins in order to survive, grow and replicate. On these cells without estrogen receptors but with Notch receptors, blockade this Notch pathway and the cell again becomes dependent on estrogen – and thus likely treatable with anti-estrogen therapies.

"It's rare to get something that works so fantastically well as this," Haughian says.

Whether this switch from hormone-insensitive to hormone-sensitive is due to basic evolution – killing the triple-negative cells leaves more resources for the growth of hormone-receptor positive cells – or whether inhibiting Notch signaling, in fact, causes triple-negative cells to grow hormone receptors is still under investigation.

Whatever the precise mechanism, drugs that inhibit this Notch activity are already in clinical trials for breast cancer. However, Kathryn Horwitz, PhD, investigator at the CU Cancer Center and Distinguished Professor of Endocrinology at the University of Colorado School of Medicine theorizes that, "monotherapy with a Notch inhibitor might not be enough on its own, but may convert the cancer into a hormone-therapy treatable state."

This finding that Notch inhibition converts a triple-negative cancer subpopulation to a hormone-receptor positive population implies the potential usefulness of combination therapy – perhaps a Notch inhibitor to make all the cancer's cells hormone-sensitive, followed by an anti-estrogen to treat them.

"Theorizing that and proving it is another matter," Horwitz says. "But if a clinician came knocking on our door, we'd say hey, let's try it."

Provided by University of Colorado Denver