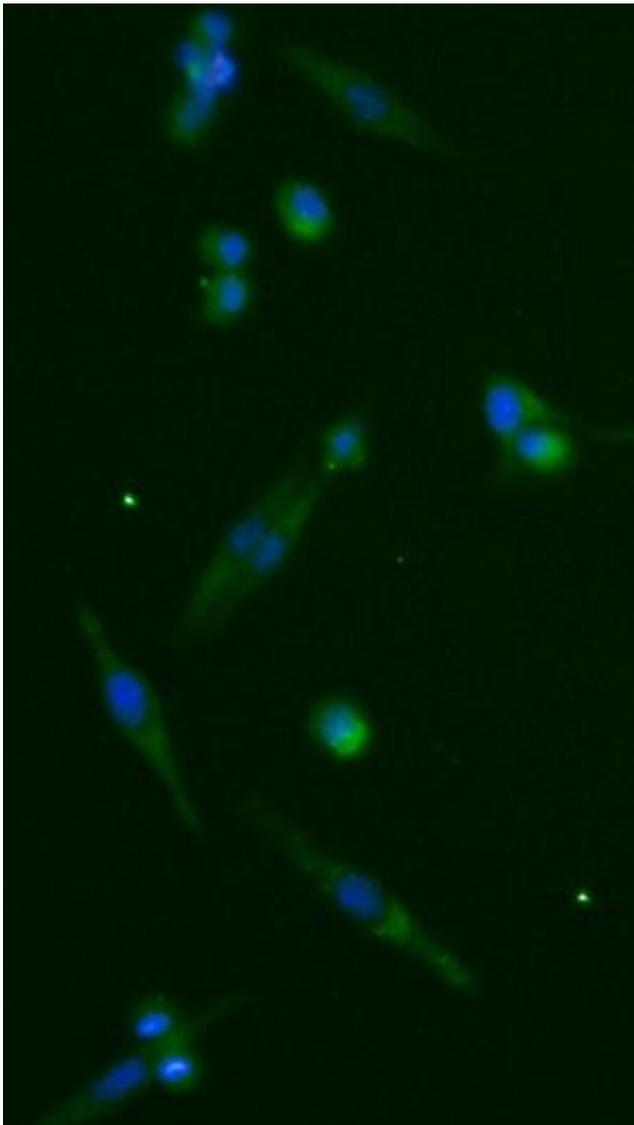


High cholesterol fuels the growth and spread of breast cancer

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These are cells treated with the cholesterol metabolite 27HC. Credit: Duke Medicine

A byproduct of cholesterol functions like the hormone estrogen to fuel the growth and spread of the most common types of breast cancers, researchers at the Duke Cancer Institute report.

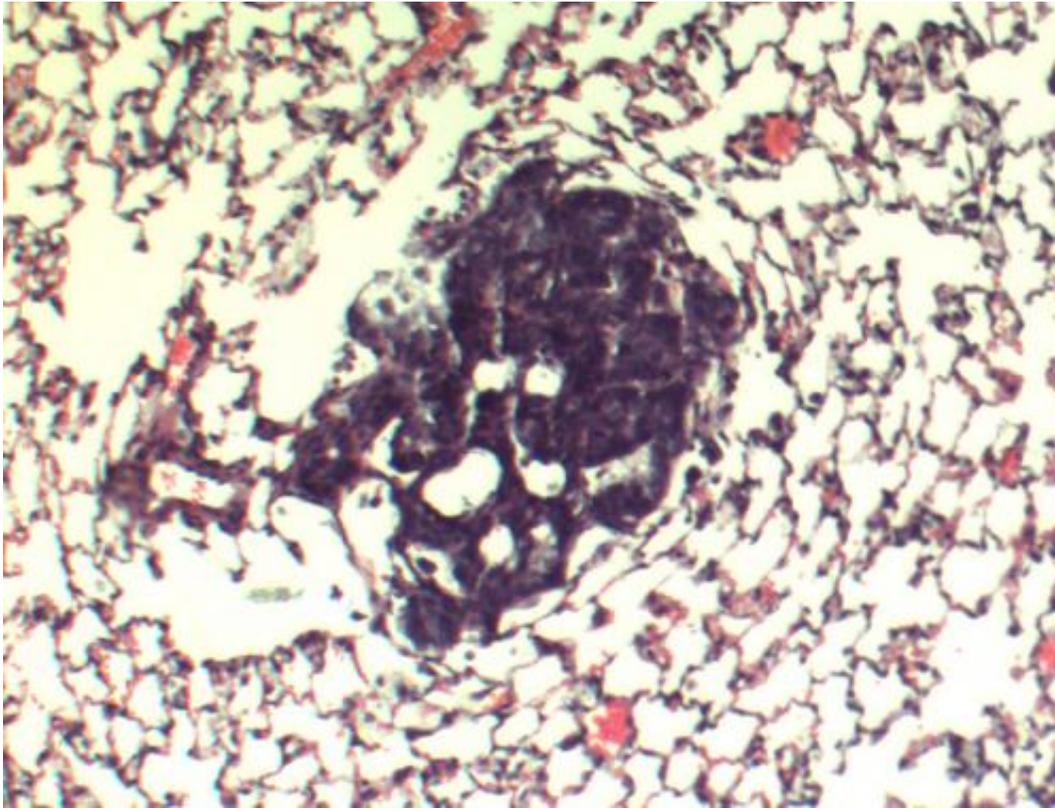
The researchers also found that anti-[cholesterol](#) drugs such as statins appear to diminish the effect of this estrogen-like molecule.

Published in the Nov. 29, 2013, edition of the journal *Science*, the findings are early, using mouse models and tumor cells. But the research for the first time explains the link between [high cholesterol](#) and [breast cancer](#), especially in post-menopausal women, and suggests that dietary changes or therapies to reduce cholesterol may also offer a simple, accessible way to reduce [breast cancer risk](#).

"A lot of studies have shown a connection between obesity and breast cancer, and specifically that elevated cholesterol is associated with breast cancer risk, but no mechanism has been identified," said senior author Donald McDonnell, Ph.D., chair of the Department of Pharmacology and Cancer Biology at Duke. "What we have now found is a molecule – not cholesterol itself, but an abundant metabolite of cholesterol – called 27HC that mimics the [hormone estrogen](#) and can independently drive the growth of breast cancer."

The hormone estrogen feeds an estimated 75 percent of all breast cancers. In a key earlier finding from McDonnell's lab, researchers determined that 27-hydroxycholesterol – or 27HC – behaved similarly to estrogen in animals.

For their current work, the researchers set out to determine whether this estrogen activity was sufficient on its own to promote breast cancer growth and metastasis, and whether controlling it would have a converse effect.



High 27HC lung: a section of lung with a metastatic nodule (large dark blue in center). Credit: Duke Medicine

Using mouse models that are highly predictive of what occurs in humans, McDonnell and colleagues demonstrated the direct involvement of 27HC in [breast tumor](#) growth, as well as the aggressiveness of the cancer to spread to other organs. They also noted that the activity of this cholesterol metabolite was inhibited when the animals were treated with antiestrogens or when supplementation of 27HC was stopped.

The studies were substantiated using human breast cancer tissue. An additional finding in the human tissue showed a direct correlation between the aggressiveness of the tumor and an abundance of the enzyme that makes the 27HC molecule. They also noted that 27HC

could be made in other places in the body and transported to the tumor.

"The worse the tumors, the more they have of the enzyme," said lead author Erik Nelson, Ph.D., a post-doctoral associate at Duke. Nelson said gene expression studies revealed a potential association between 27HC exposure and the development of resistance to the antiestrogen tamoxifen. Their data also highlights how increased 27HC may reduce the effectiveness of aromatase inhibitors, which are among the most commonly used breast cancer therapeutics.

"This is a very significant finding," McDonnell said. "Human breast tumors, because they express this enzyme to make 27HC, are making an estrogen-like molecule that can promote the growth of the tumor. In essence, the tumors have developed a mechanism to use a different source of fuel."

McDonnell said the findings suggest there may be a simple way to reduce the risk of breast cancer by keeping cholesterol in check, either with statins or a healthy diet. Additionally, for women who have breast cancer and high cholesterol, taking statins may delay or prevent resistance to endocrine therapies such as tamoxifen or [aromatase inhibitors](#).

The next steps for research include clinical studies to verify those potential outcomes, as well as studies to determine if 27HC plays a role in other cancers, McDonnell said.

More information: "27-Hydroxycholesterol Links Hypercholesterolemia and Breast Cancer Pathophysiology," by E.R. Nelson et al. *Science*, 2013.

Provided by Duke University Medical Center

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