The link between cholesterol and breast cancer

If you don't want to develop breast cancer, make an appointment to get your cholesterol levels checked - research has found a link!

A by-product of cholesterol functions like the hormone oestrogen to fuel the growth and spread of the most common types of breast cancers, according to the recent Duke Cancer Institute report.

High cholesterol levels linked to breast cancer

The findings, using mouse models and tumour cells, are early but for the first time it explains the link between high cholesterol and breast cancer, especially in post-menopausal women.

"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 oestrogen and can independently drive the growth of breast cancer."

27-hydroxycholesterol (27HC) fuels breast cancer

The hormone oestrogen 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 oestrogen in animals.

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

Using mouse models that are highly predictive of what occurs in humans, McDonnell and colleagues demonstrated the direct involvement of 27HC in breast tumour 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 anti-oestrogens 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 tumour 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 tumour.

"The worse the tumours, 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 anti-oestrogen 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 tumours, because they express this enzyme to make 27HC, are making an oestrogen-like molecule that can promote the growth of the tumour. In essence, the tumours have developed a mechanism to use a different source of fuel."

Is there any good news?

There is some good news as McDonnell said the findings suggest that one can reduce the risk of breast cancer by simply keeping cholesterol in check, either with statins or a healthy diet.

Researchers found that anti-cholesterol drugs such as statins appear to diminish the effect of this oestrogen-like molecule. 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.

Source: Duke University Medical Center via EurekAlert