Does good cholesterol increase breast cancer risk?

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High levels of high density lipoprotein (HDL), also known as the "good cholesterol," are thought to protect against heart disease. However, what's good for one disease may not be good for another. High levels of HDL have also been linked to increased breast cancer risks and to enhanced cancer aggressiveness in animal experiments. Now, a team of researchers led by Philippe Frank, Ph.D., a cancer biologist in the Department of Biochemistry and Molecular Biology at Thomas Jefferson University, has shown that an HDL receptor found on breast cancer cells may be responsible for this effect, proposing a new molecular target that could help treat the disease.

"If we can block the activity of the HDL receptor in breast cancer, we may be able to limit the harmful effects of HDL, while maintaining levels that are beneficial for blood vessels," says Dr. Frank. The work was published online September 24th in the journal *Breast Cancer Research*.

To study the effect of HDL on cancer cells at the molecular level, Dr. Frank and colleagues exposed breast cancer cell lines to HDL and noticed that signaling pathways involved in cancer progression were activated, and that the cells began to migrate in an experimental model mimicking metastasis.

The researchers then limited the expression of the HDL receptor called SR-BI in the cells using silencing RNA to reduce the receptor's levels. In response, the activities of the signaling pathways that promote tumor

progression were reduced. In addition, cells with fewer SR-BI receptors displayed reduced proliferation rates and migratory abilities than cells with normal SR-BI levels. Most importantly, reduced SR-BI levels were associated with reduced tumor formation in a mouse model of tumorigenesis. The researchers then blocked the SR-BI receptor in a breast cancer cell line with a drug called BLT-1 and noticed reduced proliferation and signaling via proteins linked to tumor formation.

This study supports the idea that HDL plays a role in the development of aggressive breast cancers and that inhibiting its function via SR-BI in breast cancer cells may stall cancer growth.

Additional studies will be needed to develop more specific drugs to inhibit SR-BI. "Also, we need to understand what levels of cholesterol are required by the tumor before trying to reduce or modify lipid levels in cancer patients," says Dr. Frank. "We hope this study will lead to the development of new drugs targeting SR-BI or cholesterol metabolism and eventually preventing tumor progression," he adds.

The authors declare that they have no conflicts of interest.

More information: Christiane Danilo, et al., "Scavenger receptor class B type I regulates cellular cholesterol metabolism and cell signaling associated with breast cancer development," *Breast Cancer Research*, DOI: 10.1186/bcr3483, 2013

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