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Tissue around tumor holds key to fighting triple negative breast cancer

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A natural substance found in the surrounding tissue of a tumor may be a promising weapon to stop triple negative breast cancer from metastasizing.

A preclinical study published in PLOS ONE September 19 by Thomas Jefferson University researchers found that decorin, a well-studied protein known to help halt tumor growth, induces a series of tumor suppressor genes in the surrounding tissue of triple negative breast cancer tumors that help stop metastasis.

"These findings provide a new paradigm for decorin, with great implications for curbing tumor growth by inducing new tumor suppressor genes within the tumor microenvironment, and for the discovery of novel gene signatures that could eventually help clinical assessment and prognosis," said senior author Renato V. Iozzo, M.D., Professor of Pathology, Anatomy and Cell Biology, at Thomas Jefferson University.

Triple negative breast cancer is the most deadly of breast cancers, with fast-growing tumors, that disproportionately affect younger and African-American women. Today, no such marker is applied in care of triple negative breast cancer, and as a result, patients are all treated the same.

"Originally, we thought that decorin was affecting the tumor, but, surprisingly, decorin affects the so-called tumor microenvironment, where malignant cells grow and invade, igniting genes to stop such

growth," said Dr. Iozzo, who is also a member of Jefferson's Kimmel Cancer Center. "Absence of decorin in the microenvironment could explain metastasis in some patients, where higher levels of the protein may keep cancer from spreading."

In the study, 357 genes were found to be induced by the increased presence of decorin, but more interestingly, the researchers discovered that three of these genes, which were previously unlinked to triple negative breast cancer, were tumor suppressor genes affecting the tumor microenvironment, including Bmp2K, Zc3hav1, and PEG3.

Decorin is a naturally occurring substance in the connective tissue where, among other roles, it helps regulate cell growth by interacting with growth factors and collagen. A decade ago, Dr. Iozzo and his team discovered that decorin, a cell protein, and specifically, a proteoglycan, is increased in the matrix surrounding tumor cells. They also discovered that decorin causes production of a protein, p21, which also can arrest cell growth. However, decorin's role in breast cancer and the mechanism behind its anti-tumor properties remained elusive.

For this study, researchers aimed to investigate the impact of decorin in triple negative breast cancer tumors using human cell lines in mice, as well analyze gene expression activity in the tumor microenvironment.

Tumors treated with decorin were found to have a decreased volume of up to 50 percent after 23 days. Using a sophisticated microarray technique, the researchers then analyzed the mouse tumor microenvironment, finding increased expression of 357 genes, three of which are the tumor suppressor genes of interest.

These results demonstrate a novel role for decorin in reduction or prevention of tumor metastases that could eventually lead to improved therapeutics for metastatic breast cancer.

"Here, we have a molecule that can turn a tumor microenvironment from a bad neighborhood to a clean neighborhood by inducing genes in that neighborhood to stop growth and prevent the tumor from metastasizing," said Dr. Iozzo.

More information: dx.plos.org/10.1371/journal.pone.0045559

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