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Protein in blood exerts natural anti-cancer protection

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Researchers from Thomas Jefferson University's Kimmel Cancer Center have discovered that decorin, a naturally occurring protein that circulates in the blood, acts as a potent inhibitor of tumor growth modulating the tumor microenvironment.

The study, published June 24 online in the *Proceedings of the National Academy of Sciences*, suggests it may be possible to harness the power of this naturally occurring anticancer agent as a way to treat cancer, including metastases.

In several different publications it has been described the ability of decorin to affect a number of biological processes including inflammatory responses, wound healing, and angiogenesis.

In this new article, the study's senior investigator, Renato Iozzo, M.D., Ph.D., has labeled decorin a "soluble tumor repressor"—the first to be found that specifically targets new blood vessels, which are pushed to grow by the cancer, and forces the vessel cells to "eat" their internal components. This reduces their potential to feed the cancer overall causing an inhibition of tumor progression.

"The tumor suppressors we all know are genes inside tumors that a cancer deletes or silences in order to continue growing. I call decorin a tumor repressor because its anti-tumor activity comes from the body, outside the cancer," says Dr. Iozzo, Professor of Pathology & Cell Biology, Biochemistry & Molecular Biology at Kimmel Cancer Center.

"Decorin is a soluble compound that we found has a powerful, natural protective effect against cancer—an exciting finding that we believe will open up a new avenue for both basic research and clinical application," Dr. Iozzo says. "Acting from the outside of the cells, decorin is able to modify the behavior of the cancer cells and of the normal cells in order to slow down the progression of the tumor. For this reason, decorin acts as a guardian of the matrix, the complicated structure built around the cells in our body."

Absence of decorin promotes tumor growth

Decorin has long been known to be involved in human development. It is so named because deposits of decorin "decorate" collagen fibrils after the human body forms.

A second pool of decorin has been found circulating in blood after production by connective tissue throughout the body. This connective tissue is part of the extracellular matrix, which provides both structural support and biological regulation of tissue cells.

But no one has understood the biological function of this second pool of decorin, according to Dr. Iozzo.

The research team, including the two co-first authors, Simone Buraschi, Ph.D., and Thomas Neill, a graduate student, who work in the laboratory of Dr. Iozzo, decoded the function of soluble decorin. They found that addition of exogenous decorin to the tumor microenvironment induces autophagy, a mechanism by which cells discard unnecessary or damaged intracellular structures. "This process regulates a lot of cellular activities," says Dr. Iozzo.

The researchers specifically found that decorin evoked autophagy in both microvascular and macrovascular endothelial cells—cells that line

the interior surface of blood vessels.

"This matters because autophagy can exert a potential oncosupressive function by acting to discard critical cell components that would otherwise be involved in promotion of tumor growth through angiogenesis, the production of new blood vessels that can provide nutrition to the tumor," Dr. Iozzo says. "In contrast, absence of decorin permits tumor growth."

Therefore, the presence of decorin in the surroundings of the tumor is essential to control tumorigenesis and formation of new blood vessels, he says. Moreover, Dr. Iozzo's laboratory has characterized for the first time Peg3, a known tumor-suppressor gene, as a master player in the autophagy process induced by decorin. "This discovery is important as it opens up to the study of new unexplored genes and signaling pathways in the field of autophagy," he says.

"Circulating decorin represents a fundamental cellular process that acts to combat tumor angiogenesis," Dr. Iozzo says. "Treatment based on systemic delivery of decorin may represent a genuine advance in our ongoing war against cancer."

More information: www.pnas.org/content/early/201 … /1305732110.abstract

Provided by Thomas Jefferson University