Scientists reveal new targets for anti-angiogenesis drugs

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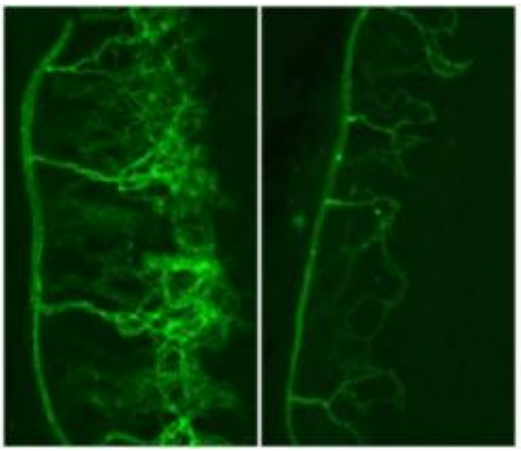

On the left: blood vessel formation that resulted from normal galectin-3 function. On the right: reduced blood vessel formation when galectin-3 was depleted. Credit: Image courtesy of Tufts University.

A new study describes how a carbohydrate-binding protein, galectin-3, promotes angiogenesis, the growth of new blood vessels. Targeting the protein, scientists identified two approaches that significantly reduced angiogenesis in mice. These discoveries, published online August 16 in the *Journal of Experimental Medicine*, may lead to novel treatments for diseases caused by excessive angiogenesis, including age-related macular degeneration, cancer, and diabetes.

When the body needs to expand its network of blood vessels, cells release molecular signals called growth factors that prompt angiogenesis.

While this process is key for normal growth, development, and wound healing, it can be harmful when blood vessels supply tumors or other diseased tissue, or when excessive blood vessel growth encroaches on surrounding tissues.

A growing body of research indicates that a protein called galectin-3 promotes angiogenesis, indicating that it may be a valuable target for drugs that halt harmful blood vessel growth. Until now, though, scientists did not understand how galectin-3 promotes angiogenesis.

Led by Noorjahan Panjwani, PhD, researchers propose a mechanism that explains how galectin-3 brings about angiogenesis. Panjwani is a professor in the department of ophthalmology at Tufts University School of Medicine and a member of the biochemistry and cell, molecular and developmental biology program faculties at the Sackler School of Graduate Biomedical Sciences.

"Our study shows that galectin-3 protein binds to glycans (carbohydrate portions) of specific cell-adhesion proteins, the integrins, to activate the signaling pathways that bring about angiogenesis. This improved understanding may provide a more targeted approach to preventing harmful angiogenesis," said Panjwani.

"We found that application of a galectin-3 inhibitor significantly reduced angiogenesis in mice. We also found that preventing galectin-3 from binding with the integrins reduced angiogenesis," said first author Anna Markowska, a PhD student in the biochemistry program at the Sackler School of Graduate Biomedical Sciences at Tufts.

"By deciphering the mechanism of galectin-3 action, we were able to establish more than one therapeutic target. The more we know about how this pathway works, the more options we have for potential treatments," said Panjwani.

Panjwani's lab is dedicated to understanding the cell biological and biochemical mechanisms of wound healing and angiogenesis, specifically for the purpose of developing improved treatments for blinding eye diseases. Panjwani's research is also focused on Acanthamoeba keratitis, a rare and painful parasitic infection of the cornea that can affect contact lens wearers. She is currently working on strategies to protect against the infection and is developing a test that identifies at-risk individuals by sampling their tears.

More information: Markowska AI, Liu FT, Panjwani N. Journal of Experimental Medicine. 2010. (August 30); 207 (9). "Galectin-3 is an Important Mediator of VEGF- and bFGF-mediated Angiogenic Response." Published online August 16, 2010, doi: 10.1084/jem.20090121

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