# Protein Stops Blood-Vessel Growth, Holds Promise as Cancer Therapy

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DENVER — Researchers at National Jewish Medical and Research Center have identified a protein that inhibits the formation of new blood vessels. Combined with previous findings that the protein is depleted or missing in a majority of metastatic human cancers, the findings suggest that fibulin-5 may one day be an effective cancer therapy. William Schiemann, PhD, Assistant Professor in the Program in Cell Biology at National Jewish, and postdoctoral fellow Allan R. Albig reported their findings in the June issue of *DNA and Cell Biology*.

"We believe fibulin-5 shows real promise as a cancer therapy," said Schiemann. "When we slightly altered the naturally occurring protein it was even more effective at inhibiting the sprouting of new blood vessels."

Cancer tumors need nutrients and oxygen supplied by blood vessels in order to grow. They also use blood vessels to spread to other parts of the body. This process, known as metastasis, is the most lethal characteristic of cancer and the leading cause of cancer-related death. The strategy of fighting cancer by preventing the growth of new blood vessels has generated great interest in recent years, with the first antiangiogenic drug being approved earlier this year.

Endothelial cells have been the target of most antiangiogenic strategies. Endothelial cells are specialized cells that develop into blood vessels. Fibulin-5, a member of a family of extracellular matrix proteins that regulate tissue development, remodeling and repair, interacts with endothelial cells.

In cell culture studies, Schiemann and Albig showed fibulin-5 levels drop significantly when endothelial cells begin to form blood vessels, a process known as tubulation. They also show that high levels of fibulin-5 could prevent the sprouting of new blood vessels by inhibiting the proliferation and movement of endothelial cells.

Fibulin-5 interfered with signaling by the proangiogenic factor VEGF, and increased levels of the antiangiogenic factor thrombospondin-1. The researchers believe that fibulin-5 may work by controlling the relative levels of VEGF and thrombospondin-1.

In a previous paper, published in 2002, Schiemann and his colleagues showed the fibulin-5 expression is reduced or lost in a majority of metastatic human malignancies. Schiemann believes that future research on fibulin-5 should focus on patients in whom tumors have not already metastasized. His group is continuing to examine fibulin-5 functions at the molecular level and will soon evaluate its effects in mice.

The protein may also serve as a diagnostic tool, a marker of cancer status. Rapidly dropping levels of fibulin-5 might signal a tumor preparing to grow and/or spread.

"The good thing about this protein is it's extra-cellular, especially as a diagnostic marker," said Emmanuel Hilaire, a technology transfer specialist at National Jewish. "It's very important because it's detectable in serum and urine."

A provisional patent citing the diagnostic merits of fibulin-5 has been filed with additional claims filed after researchers made their most recent observations.

## Media Contacts

Our team is available to arrange interviews, discuss events and story ideas.

**William Allstetter**
303.398.1002
allstetterw@njhealth.org

**Adam Dormuth**
303.398.1082
dormutha@njhealth.org