Proteins Stop Blood-Vessel and Tumor Growth in Mice

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DENVER — Researchers at National Jewish Medical and Research Center report in the March issue of *Cancer Research* that a pair of promising proteins, known as fibulins 3 and 5, slow the growth of cancer tumors in mice by preventing blood vessels from sprouting. The proteins are promising candidates for use in cancer therapy.

"Healthy humans produce fibulin proteins, which regulate cell proliferation, migration and invasion. In the past, we have seen that they are depleted in numerous metastatic cancers, and that they inhibit the formation of new blood vessels in cell culture," said William Schiemann, PhD, Assistant Professor in the Program in Cell Biology at National Jewish. "Our current findings show that fibulins can inhibit both tumor growth and blood-vessel formation in mice."

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 stage of cancer and the leading cause of cancer-related death. Fighting cancer by starving tumors of life-giving blood vessels has generated great interest in recent years.

In their most recent experiments, Dr. Schiemann and his colleagues injected a biological material, called Matrigel, into mice. The Matrigel contained a growth factor that promotes blood-vessel growth and either a control substance or fibulin 3 or fibulin 5. After seven days, researchers found that the Matrigel plugs containing either fibulin had about half as many blood vessels as did the control plugs.

The researchers then injected fibrosarcoma tumor cells into mice. The tumor cells were genetically engineered to produce either fibulin 3 or fibulin 5. Three weeks after the cells were implanted, developing tumors that produced the fibulins were approximately 24 percent to 45 percent smaller than the control tumors.

"We are thrilled that the fibulins continue to show promise as we move into animal models," said Dr. Schiemann. "We also found evidence that the fibulins work through more than one biological pathway, which suggests a very robust effect. We further expect the mice to tolerate quite large doses of the fibulins, which makes us hopeful that toxicity will not be a problem."

The researchers have not yet discovered what receptors the fibulins interact with to produce their anti-angiogenic effect. But in the current paper, they report that the fibulins alter levels of extracellular proteins involved in dissolving and remodeling the extracellular matrix, which can make way for blood-vessel growth.

Moving forward, Dr. Schiemann is working to isolate the portion of the fibulin molecules that actually binds to receptors and causes their biological effect. If they can find a small molecule capable of producing the fibulins' effects, it would hold more promise as a viable therapy.

Media Contacts

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

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