Researchers find protein that might be key to cutting cancer cells' blood supply

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UT Southwestern Medical Center researchers have discovered a protein that guides blood vessel development and eventually might lead to a treatment to keep cancer cells from spreading.

The researchers showed in mice that the Ras interacting protein 1 (Rasip1) is so specific and central to so many cellular processes that without it new blood vessels simply cannot form, said Dr. Ondine Cleaver, assistant professor of molecular biology at UT Southwestern and senior author of the study in the April issue of *Developmental Cell*.

"What we've found is really the first factor that is important in all blood vessels for inner channel formation and tubulogenesis, i.e., the transformation of something that looks like a rope into something that looks like a garden hose," Dr. Cleaver said.

Cancer cells depend on the body's creation of new blood vessels to deliver the nutrients that fuel cancer's rapid growth. Cancerous tumors also use the circulatory system as a superhighway through which they send malignant cells to colonize other parts of the body. A Rasip1-blocking drug conceivably could fight cancer on two fronts: by starving the cancerous cells and by cutting off their transport routes, Dr. Cleaver said.

During fetal development the body creates many tube-shaped organs such as the intestines of the digestive system and the vessels of the cardiovascular system. The mechanisms by which blood vessel

progenitor cells transform into tubes that can carry blood are only beginning to be understood, she said.

Scientists have found many regulatory molecules important in different tissues and even in other aspects of blood vessel formation or maintenance, but all of them are active in multiple body tissues. Rasip1 is the first blood vessel-specific regulator of molecular switches called GTPases, she said. The protein appears to be active only in the endothelium, the layer of cells that line the blood vessels, and is not found in the smooth muscle cells that make up the outside of the vessels.

The UT Southwestern scientists also discovered that Rasip1 and a protein binding partner are both required for blood vessels to form channels through which blood can flow, she said.

Most approaches to therapies aimed at blocking blood vessel formation have focused on growth factors that occur outside the cell rather than intrinsic cellular growth factors like Rasip1, Dr. Cleaver said.

"Although this is still a mouse study, we feel that future studies of Rasip1 and the molecular processes under its control hold great promise to provide tools and models for advancing clinical therapies aimed at blocking vessel formation in tumors," she said.

The researchers now plan to look for drugs that block Rasip1 in order to eventually develop strategies to stop the growth of functional blood vessels and starve cancerous tumors, she said.

Provided by UT Southwestern Medical Center