Protein targeted to stop melanoma tumor growth

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Halting the growth of melanoma tumors by targeting the MIC-1 protein that promotes blood vessel development in tumors may lead to better treatment of this invasive and deadly cancer, according to Penn State College of Medicine researchers in The Foreman Foundation Research Laboratory.

"Preventing vessels from developing in tumors is one way to stop them from growing," said lead author Gavin Robertson, Ph.D., professor of pharmacology, pathology, dermatology and surgery. "However, the identity of the proteins secreted by tumors cells enabling the angiogenesis process to occur remains to be determined." Angiogenesis is the growth of new blood vessels from existing ones surrounding the growing tumor mass.

Tumors start as clusters of cells that transport nutrition and waste through cell walls as well as into and out of gaps between cells. This process is inefficient and provides poor nutrition to the cells in the interior of a growing tumor. As a result, the tumor mass cannot grow.

Tumor cells overcome this obstacle by secreting proteins that interact with blood vessels surrounding the tumor, causing formation of new vessels from these existing ones. The new vessels grow into the tumor to provide nutrition and remove waste. Angiogenesis leads to the formation of a fully functioning vascular structure that supplies the needed nutrition and removes cell waste, allowing tumors to grow.

By targeting the proteins that lead to angiogenesis, tumor growth can be halted. In the past, the protein VEGF was identified as a major factor in this process. However, targeting VEGF alone does not prevent tumor development in melanoma patients. The researchers looked for other proteins involved in angiogenesis and ultimately discovered MIC-1 as a regulator of this process.

The researchers reported in the American Journal of Pathology that MIC-1 is present in levels five to six times higher in 67 percent of melanoma patients compared to people without cancer.

"This suggests that the MIC-1 protein produced and secreted by these tumors might be performing an important role in the development of melanoma by controlling a key process outside of the tumor," Robertson said.

MIC-1 stands for macrophage inhibitory cytokine-1, a member of a group of proteins that regulate cellular proliferation, migration, adhesion and immune surveillance. It was originally discovered to be associated with regulating inflammation.

By targeting MIC-1, protein levels dropped 300 to 400 percent in animal and human tissue samples, preventing blood vessel formation and decreasing tumor development by about 300 percent.

"Therapies removing MIC-1 from the blood of patients could be used to prevent tumor vessel development," says Robertson "and as a result, the tumors would not be able to get bigger because of a lack of needed nutrition and removal of toxic cell waste products. Thus, a drug performing the job of MIC-1 removal would be an important part of a therapeutic arsenal of agents to more effectively treat melanoma."

Working with Robertson are graduate students Sung Jin Huh and Chin-

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