# Scientists discover how deadly skin cancer spreads into other parts of the body

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The study's lead author is Paul B. Fisher, M.Ph., Ph.D. Credit: VCU Massey Cancer Center

After recently announcing success in eliminating melanoma metastasis in laboratory experiments, scientists at Virginia Commonwealth University Massey Cancer Center have made another important discovery in understanding the process by which the gene mda-9/syntenin contributes to metastasis in melanoma (the spread of skin cancer) and possibly a

variety of other cancers.

Published in the journal Cancer Research, the study demonstrated that mda-9/syntenin is a key regulator of angiogenesis, the process responsible for the formation of new blood vessels in tumors. Mda-9/syntenin was originally cloned in the laboratory of the study's lead author Paul B. Fisher, M.Ph., Ph.D., Thelma Newmeyer Corman Endowed Chair in Cancer Research and program co-leader of Cancer Molecular Genetics at Virginia Commonwealth University Massey Cancer Center, chairman of VCU's Department of Human and Molecular Genetics and director of the VCU Institute of Molecular Medicine.

"Our research brings us one step closer to understanding precisely how metastatic melanoma, a highly aggressive and therapy-resistant cancer, spreads throughout the body," says Fisher. "Additionally, analysis of the human genome has indicated that mda-9/syntenin is elevated in the majority of cancers, which means novel drugs that target this gene could potentially be applicable to a broad spectrum of other deadly cancers."

Fisher's team discovered that mda-9/syntenin regulates the expression of several proteins responsible for promoting angiogenesis, including insulin growth factor binding protein-2 (IGFBP-2) and interleukin-8 (IL-8). The study is the first to provide proof of the pro-angiogenic functions of IGFBP-2 in human melanoma.

In in vivo and in vitro experiments, the scientists confirmed that mda-9/syntenin binds with the extracellular matrix (ECM) to start a series of biological processes that eventually cause endothelial cells to secrete IGFBP-2. The ECM is the substance that cells secrete and in which they are embedded. Endothelial cells are the cells that line the interior surface of blood vessels throughout the entire circulatory system. The secretion of IGFBP-2, in turn, caused the endothelial cells to

produce and secrete vascular endothelial growth factor-A (VEGF-A), a protein that mediates the development of and formation of new blood vessels.

The researchers also noted that IGFBP-2 could potentially serve as a novel biomarker to monitor for disease progression in melanoma patients.

"This is a major breakthrough in understanding angiogenesis and its impact in melanoma metastasis," says Fisher. "We are now focusing on developing novel small molecules that specifically target mda-9/syntenin and IGFBP-2, which could be used as drugs to treat melanoma and potentially many other cancers."

**More information:** cancerres.aacrjournals.org/con … 472.CAN-12-1681.long

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