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Researchers develop model to study, find ways to target rare tumor

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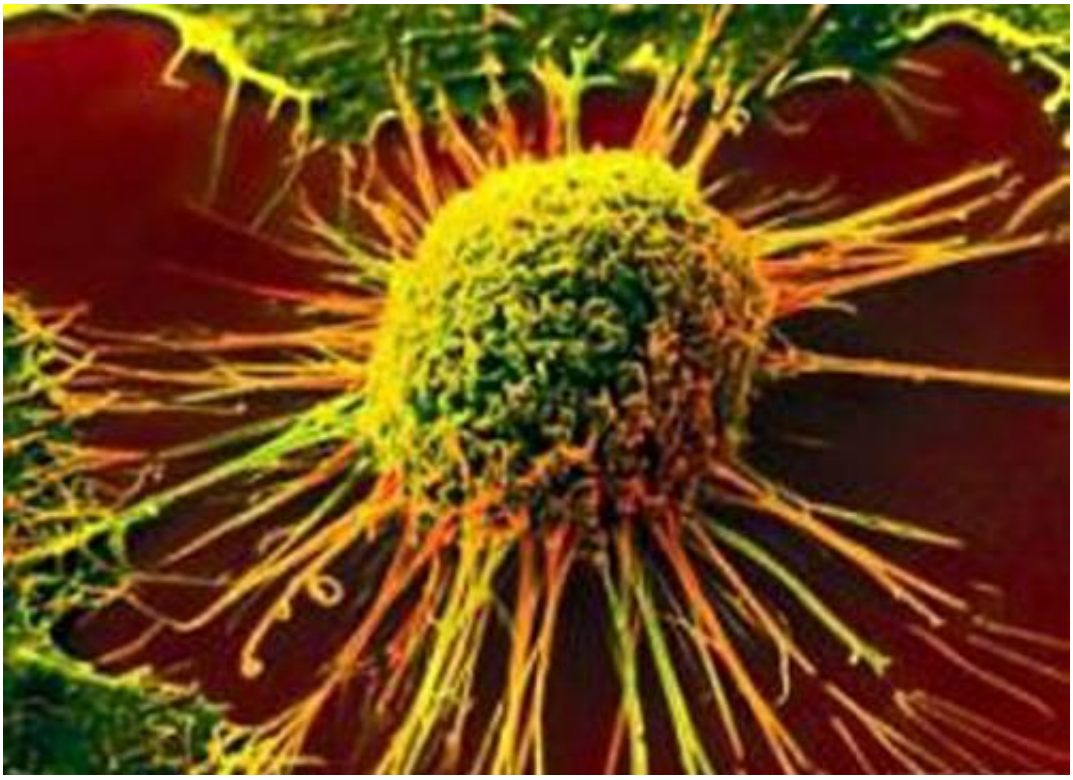

Cancer researchers at the University of Cincinnati (UC) have found a new target that could lead to therapies for a rare type of tumor.

These findings are being reported in the Nov. 9 advance online edition of the journal *Cancer Cell*.

"Angiosarcoma or lymphangiosarcoma, a rare malignant tumor of the blood or lymphatic vessels, has no cure," says principal investigator Jun-Lin Guan, PhD, chair of the Department of Cancer Biology and a member of both the Cincinnati Cancer Center and UC Cancer Institute, adding that a multidisciplinary team including scientists at Cincinnati Children's Hospital Medical Center and the University of Michigan was involved in the study. "In addition to spontaneous cases, angiosarcomas have been reported to develop in breast cancer patients undergoing radiation treatment. The mechanism of angiosarcoma development is largely unknown, and there is no animal model for the disease to help researchers molecularly define its development.

"In this study, we did develop an animal model for the disease by controlling the activity of mTORC1—a multiprotein complex enzyme that coordinates many important cellular processes such as protein formation—which resulted in lymphangiosarcoma development and progression and mimicked features of human tumors including invasion of cells and spread."

Guan says that to stop activities of mTORC1 causing angiosarcoma development and progression in the animal model, scientists found that blocking a number of its key targets, including the vascular endothelial growth factor, a protein that restores the oxygen supply to tissues when blood circulation is inadequate, effectively halted tumor development and growth.

"In addition to the animal model, we prepared tissue collections of multiple human angiosarcoma samples and checked signaling changes; mTORC1 signaling was highly active in human angiosarcomas. The majority of angiosarcoma samples—71 percent—showed strong staining for phosphorylated S6, a protein marker for mTORC1 activity, whereas few inactive blood vessels in normal tissues were positive—around 12 percent. This data shows a correlation between mTORC1 signaling and

the development of human angiosarcomas.

"Results from this study provide significant insight into potential future therapies for a previously poorly characterized but deadly cancer. The spontaneous and varied nature of the vascular tumors in our animal model also provide an opportunity for further investigation into the molecular and genetic mechanisms of vascular tumors as well as a powerful tool for testing therapeutic methods."

Provided by University of Cincinnati Academic Health Center