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Contact: Eileen Scahill
614-293-3737
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# Precancerous stem cells can form tumor blood vessels

COLUMBUS, Ohio ---Tumors require a blood supply to grow, but how they acquire their network of blood vessels is poorly understood. A new study here shows that tumor blood vessels can develop from precancerous stem cells, a recently discovered type of cell that can either remain benign or become malignant.

Researchers say the findings provide new information about how tumors develop blood vessels, and why new drugs designed to block tumor blood-vessel growth are often less effective than expected.

The study by scientists at the Ohio State University Comprehensive Cancer Center and Department of Pathology is to be published Feb. 20 in the journal PLoS ONE.

These findings suggest that tumor blood vessels are derived mainly from tumor cells, with a smaller number coming from normal blood-vessel cells, says principal investigator Jian-Xin Gao, assistant professor of pathology.

This may explain why many anti-angiogenic drugs fail to block tumor growth.

Gao notes that potential anti-angiogenic drugs are usually screened using normal blood-vessel cells, also called endothelial cells, or their progenitors.

The screened drugs may be very good at blocking the formation of blood vessels made by normal endothelial cells, but have little effect on blood-vessel formation by precancerous stem cells or other blood-vessel-forming cancer cells, Gao says. Our findings suggest that screening of these agents should include precancerous stem cells.

Normal stem cells are unspecialized cells that can give rise to other types of cells. Recent evidence suggests that tumors consist of a small number of cancerous stem cells, or cancer-propagating cells with some features of stem cells, and a large number of their malignant progeny.

Precancerous stem cells are thought to be cells that can remain noncancerous or progress to cancer, depending on subsequent environmental influences.

For this study, Gao and his colleagues used mouse precancerous stem cells grown in the laboratory and transplanted into immune-deficient mice. The researchers removed the resulting tumors from the mice and, using tests for various molecular markers, observed that the tumor blood vessels were largely derived from precancerous stem cells.

The tumor blood-vessel cells were abnormal and highly variable in appearance compared with normal cells, Gao says.

The precancerous stem cells also produced similar levels of substances that stimulate blood-vessel growth (i.e., angiogenic factors), but they were much more potent in forming new blood vessels and larger tumor masses compared with tumors grown from typical tumor cells.

The researchers examined new blood vessel formation in human tumors transplanted into mice, and observed changes similar to those previously seen in the mouse tumors.

Lastly, the researchers examined the appearance of blood vessels in human cervical and breast tumors and observed that the blood-vessel cells displayed similar abnormalities and aberrant patterns of molecular markers.

This suggests that the ability of these tumors to form blood vessels is likely linked to precancerous stem cells or other blood-vessel-forming tumor cells, Gao says.

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Other Ohio State researchers involved in this study were Rulong Shen, Yin Ye, Li Chen, Qingtao Yan and Sanford H. Barsky.

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