Blocking nuclear receptor may cut off tumor blood supply

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A new method of blocking the genesis of blood vessels that feed tumors may start with the nuclear receptor COUP-TFII (chicken ovalbumin upstream promoter-transcription factor II), said a pair of Baylor College of Medicine researchers who have studied the factor for more than 20 years.

In a report that went online today in the Proceedings of the National Academy of Sciences, a team led by Dr. Ming-Jer Tsai and Dr. Sophia Y. Tsai, both professors of molecular and cellular biology at BCM, described experiments in which the growth of new blood vessels and tumors themselves were suppressed when COUP-TFII was not present. Their work demonstrates that the receptor directly regulates an angiogenic factor called Angiopoietin-1, which enhances the development of new blood vessels. (Angiogenesis means encouraging the formation of new blood vessels.) Without COUP-TFII, Angiopoietin-1 does not carry out its job efficiently meaning that neither the blood vessels nor the tumors grow, probably because there is limited vasculature to provide nourishment.

"This is important because it means we may be able to find an antagonist that can intervene to halt tumor growth and metastasis," said Dr. Ming-Jer Tsai. "Metastasis is the reason most cancer patients die."

At present, studies of vascular endothelial growth factor (VEGF) inhibitors are underway, he said. This factor also plays an important role in the growth of new blood vessels, and the drugs work against the tumors only for a short while.

"They only work on one pathway of angiogenesis," he said. This finding identifies another important pathway and another way to fight the tumors.

"We studied breast cancer tumors in this model," said Dr. Sophia Tsai. She said the team plans to look at other kinds of solid tumors in which they believe COUP-TFII plays a role in angiogenesis.

Another benefit of knocking out COUP-TFII is that it is not needed in adult animals, she said. COUP-TFII is important in blood vessel formation in the developing fetus but plays no important role in maintaining the vasculature afterward, except in situations such as pregnancy or wound healing. The blood vessels of adult animals that lacked the factor remained normal.

She, Dr. Ming-Jer Tsai and their colleagues are also looking at ways to screen known biological chemicals for the ability to inhibit COUP-TFII.

Provided by Baylor College of Medicine