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New molecular pathway regulating angiogenesis may fight retinal disease, cancers

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Scientists identify in the journal *Nature* a new molecular pathway used to suppress blood vessel branching in the developing retina – a finding with potential therapeutic value for fighting diseases of the retina and a variety of cancers.

Researchers report that myeloid cells, blood cells involved in the immune system, use this molecular pathway to guide blood vessel patterning in the retina. Furthermore, in the same study researchers were able to reverse this pathway to accelerate the growth of branching vessels, which could be important to developing new methods for repairing damaged tissues.

"We show in the setting of retina that myeloid cells use this pathway to direct vascular traffic," explained Richard Lang Ph.D., senior investigator on the study and director of the Visual Systems Group in the Division of Ophthalmology at Cincinnati Children's Hospital Medical Center. "We think modulation of this pathway might become a promising therapeutic option."

The study, to be published online May 29, demonstrates how retinal myeloid cells regulate blood vessel branching in the still-developing retinas of postnatal mice by using the Wnt protein signaling network. The Wnt pathway is known for its role in embryonic and early development as well as in cancer. Although myeloid cells play an

important part in the immune system, these cells are also found in many different tumor types and promote tumor progression.

Through a series of experiments in cell cultures and mouse models, researchers determined the new pathway works by myeloid cells utilizing the Wnt pathway to regulate expression of a gene known as Flt1. Flt1 encodes a protein called vascular endothelial growth factor receptor-1 (VEGFR1), which suppresses vascular growth by binding vascular endothelial growth factor (VEGF). The expression of Flt1 can be adjusted so that when ramped up it inhibits VEGF and vascular branching, or when turned down it allows VEGF to increase branching.

Dr. Lang said the Wnt-Flt1 response is a new pathway for regulating VEGF-stimulated angiogenesis (blood vessel formation). This presents a number of new research opportunities to test its influence on retinal diseases that are often associated with abnormal blood vessel development and in tumor formation, he added.

Provided by Cincinnati Children's Hospital Medical Center

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