Partially blocking blood vessels' energy source may stop cancer growth, blindness, other conditions

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Inhibiting the formation of new blood vessels is a common strategy for treating a range of conditions such as cancer, inflammatory diseases, and age-related macular degeneration. Unfortunately, drug inefficiency, resistance, and relapse have limited the success of this approach. Now new research publishing online December 12 in the Cell Press journal *Cell Metabolism* reveals that targeting the metabolism of blood vessels may be a way around these shortcomings.

"Our findings reveal a new strategy to block blood vessel growth in various pathological conditions by depriving them of energy and building blocks necessary for growth," says senior author Dr. Peter Carmeliet of the University of Leuven and the Vesalius Research Center, VIB in Belgium.

While current strategies to thwart pathological blood vessel formation focus primarily on inhibiting vascular endothelial growth factor (VEGF), this latest research centers around blocking glycolysis, the process that endothelial cells rely on for generating most of the energy they need to multiply and migrate. Endothelial cells form the inner lining of a blood vessel and provide a barrier between the vessel wall and blood.

Dr. Carmeliet and his team previously found that the glycolytic activator PFKFB3 promotes blood vessel formation by stimulating glycolysis in endothelial cells. In their new work, the investigators discovered that blocking PFKFB3 with a small molecule called 3PO reduced blood vessel sprouting by inhibiting the proliferation and movement of endothelial cells.

3PO also amplified the effects of VEGF blockade. And although 3PO reduced glycolysis only partially and transiently, this sufficed to decrease pathological blood vessel formation in both ocular and inflammatory laboratory models. "As many cells in the body need glycolysis for growth and survival, the partial and transient reduction of glycolysis might limit the side effects and toxicity of this therapy in the clinic," Dr. Carmeliet notes.

The findings could lead to new treatments that block the excessive blood vessel growth that supports cancer spread, causes blindness, and fuels inflammatory diseases such as psoriasis and inflammatory bowel disease.

More information: *Cell Metabolism*, Schoors et al.: "Partial and Transient Reduction of Glycolysis by PFKFB3 Blockade Reduces Pathological Angiogenesis."
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