Study identifies potential therapy for disease affecting preemies

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One in five very low-birth-weight, premature infants suffers a life-threatening brain hemorrhage, often originating in a vital region known as the germinal matrix. In a recently published study in the journal *Developmental Cell*, Yale researchers identified a protein that lessens the hemorrhaging in embryonic mice, and they say could potentially serve as

a therapy in affected humans.

To better understand the hemorrhage disorder, the Yale team studied embryonic mice models lacking a key gene (Alk5) in pericytes—cells that contribute to the walls of small blood vessels in the brain. They first observed that mutant embryonic mice lacking this gene in pericytes develop the condition known as germinal matrix hemorrhage. Interestingly, said the researchers, the deleterious effects of gene deletion were primarily on endothelial cells, which form the inner lining of blood vessels. In the mutant mice, communication between pericytes and endothelial cells failed, leading to abnormal vessel dilation and hemorrhage.

Through their experiments, the researchers also identified a protein (TIMP3) that is regulated by Alk5. By injecting this protein into the mutant mice, they were able to compensate for the missing gene and dramatically lessen bleeding.

More research is needed to confirm the benefits of the protein as therapy. If it bears out, the discovery could also have implications for other conditions involving damage to brain vessels, such as hemorrhagic stroke in adults, the researchers said.

More information: Jui M. Dave et al. Pericyte ALK5/TIMP3 Axis Contributes to Endothelial Morphogenesis in the Developing Brain, *Developmental Cell* (2018). DOI: 10.1016/j.devcel.2018.01.018

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