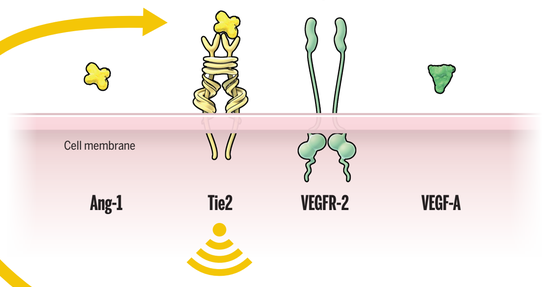
Angiopoietins: Key Regulators of Vascular Stability

Ang-1 Promotes Vascular Stability to Maintain Healthy Vessels

1 Ang-1 Binds to and Activates Tie2...

Ang-1 is made by platelets and pericytes and activates Tie2 receptors on endothelial cells to maintain vascular stability.

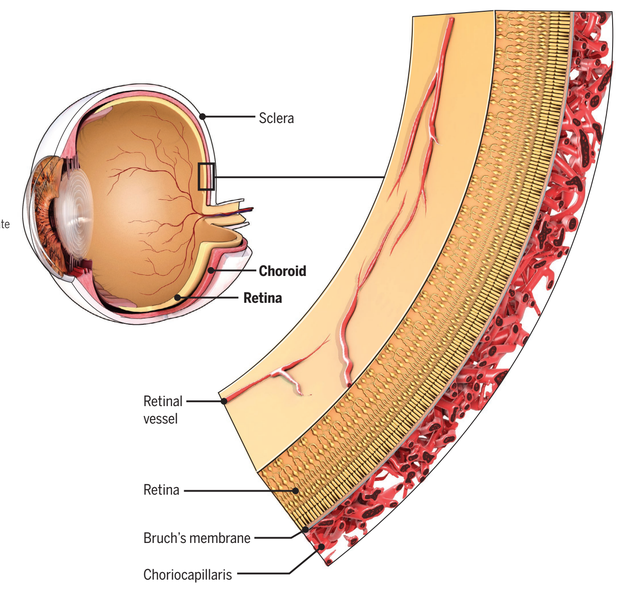


3 Pericytes are Recruited for Vascular Stability and Maturation

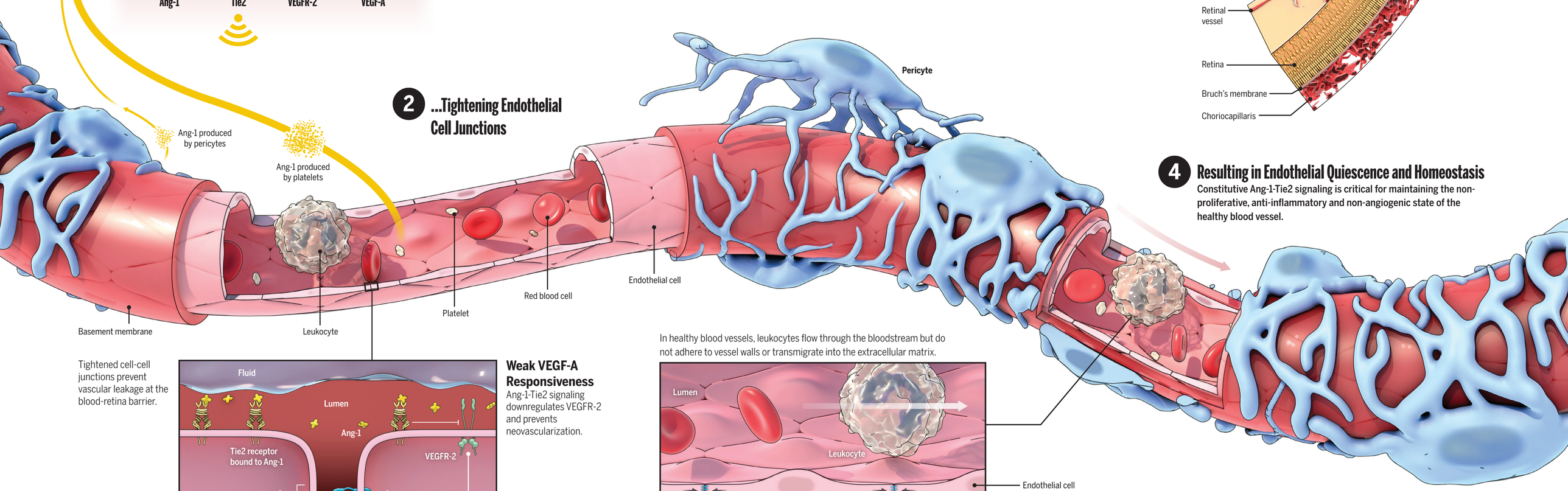
As perivascular cells wrap around vessels, they inhibit endothelial proliferation and further reduce vascular leakage.

Healthy Eye

The normal ocular vasculature is maintained in a state of homostasis.



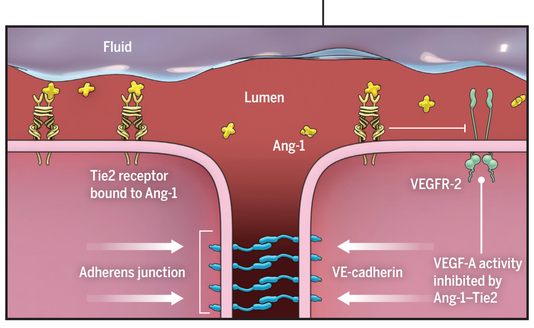
2 ...Tightening Endothelial Cell Junctions



4 Resulting in Endothelial Quiescence and Homeostasis

Constitutive Ang-1-Tie2 signaling is critical for maintaining the non-proliferative, anti-inflammatory and non-angiogenic state of the healthy blood vessel.

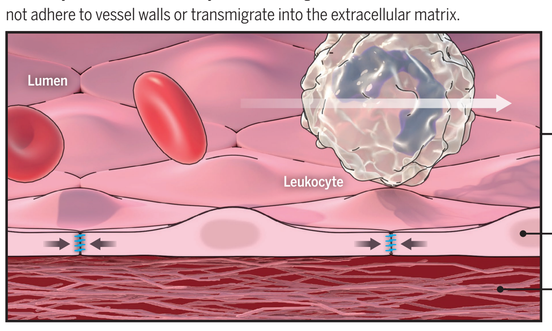
Tightened cell-cell junctions prevent vascular leakage at the blood-retina barrier.

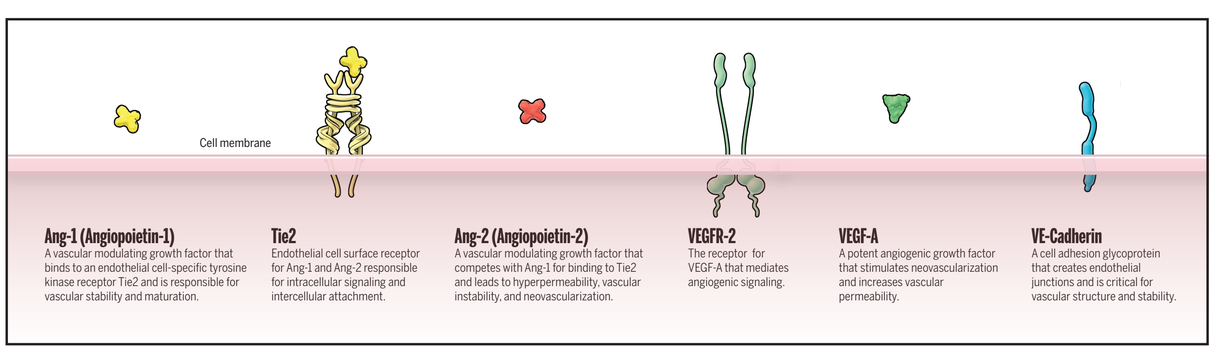


Weak VEGF-A Responsiveness

Ang-1-Tie2 signaling downregulates VEGFR-2 and prevents neovascularization.

In healthy blood vessels, leukocytes flow through the bloodstream but do not adhere to vessel walls or transmigrate into the extracellular matrix.

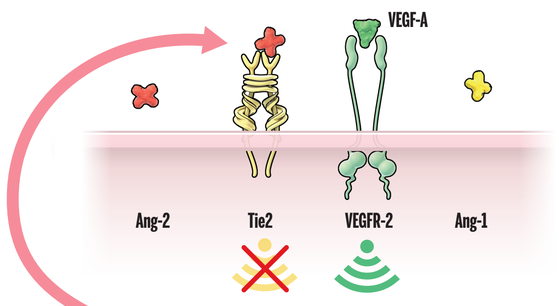




Ang-2 Promotes Vascular Instability in Disease by Blocking Ang-1-Tie2

1 In Diseases, Upregulated Ang-2 Binds to and Blocks Tie2 Signaling ...

Elevated Ang-2 competitively disrupts Ang-1-Tie2 activation.

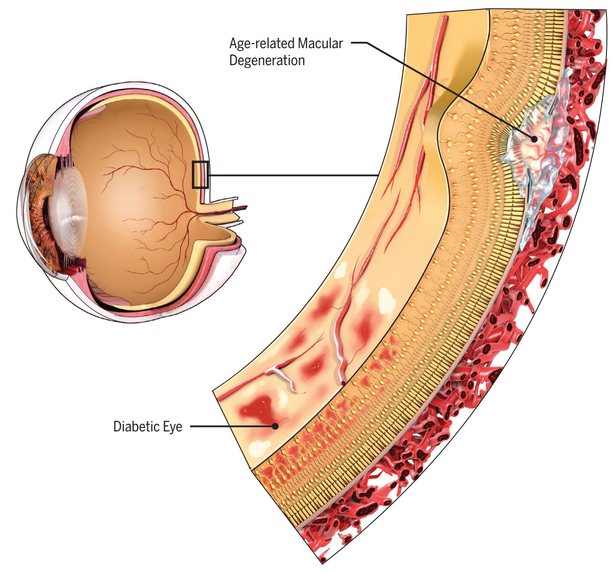


4 Upregulated Ang-2 Leads to Pericyte Drop Out and Loss, Destabilizing Vessels

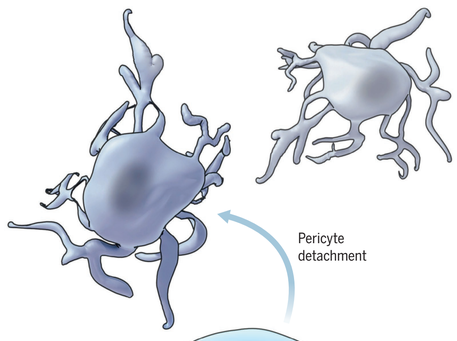
Pericytes detach and further destabilize vessels which prepares them to initiate neovascularization, and exerbates leakage.

Diseased Eye

Elevated Ang-2 levels are associated with choroidal and retinal vascular diseases along with high levels of VEGF-A.



3 ... and Increased Inflammation



5 Vascular Sprouting and Neovascularization Occurs ...

Ang-2 binding to Tie2 results in increased expression of VEGFR-2, leading to greater responsiveness to VEGF-A, potentiating neovascularization.

6 ...Leading to the Progression of Choroidal and Retinal Vascular Diseases

Together VEGF-A and Ang-2 play a critical role in the development of retinal diseases.

Hypoxia

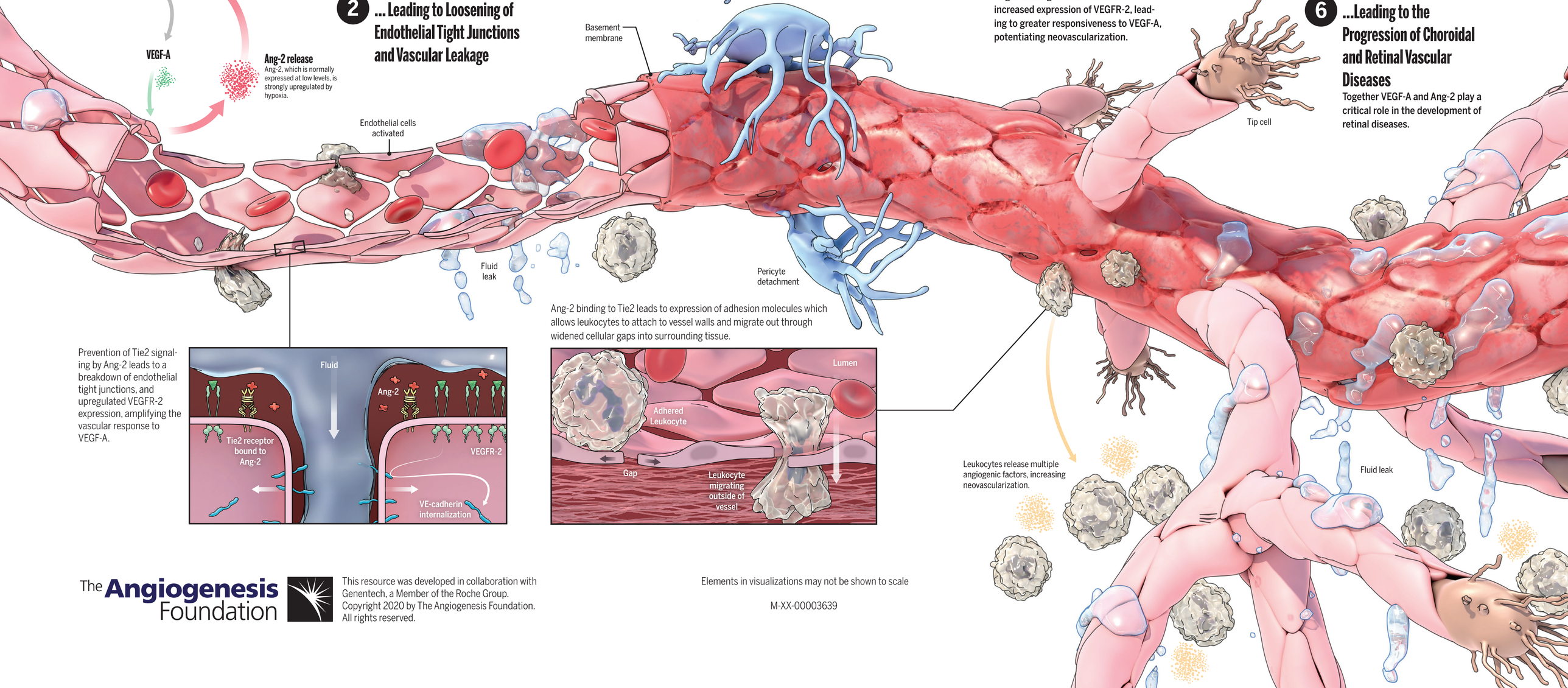
Lowered oxygen levels stimulate VEGF-A production.

VEGF-A

Ang-2 release

Ang-2, which is normally expressed at low levels, is strongly upregulated by hypoxia.

2 ... Leading to Loosening of Endothelial Tight Junctions and Vascular Leakage



Prevention of Tie2 signaling by Ang-2 leads to a breakdown of endothelial tight junctions, and upregulated VEGFR-2 expression, amplifying the vascular response to VEGF-A.

Ang-2 binding to Tie2 leads to expression of adhesion molecules which allows leukocytes to attach to vessel walls and migrate out through widened cellular gaps into surrounding tissue.

Leukocytes release multiple angiogenic factors, increasing neovascularization.

Elements in visualizations may not be shown to scale

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