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ILLUSTRATED REVIEW

Physical forces regulating hemostasis and thrombosis: Vessels, cells, and molecules in illustrated review

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Abstract

This illustrated review focuses on the physical forces that regulate hemostasis and thrombosis. These phenomena span from the vessel to the cellular to the molecular scales. Blood is a complex fluid with a viscosity that varies with how fast it flows and the size of the vessel through which it flows. Blood flow imposes forces on the vessel wall and blood cells that dictates the kinetics, structure, and stability of thrombi. The mechanical properties of blood cells create a segmented flowing fluid whereby red blood cells concentrate in the vessel core and platelets marginate to the near-wall region. At the vessel wall, shear stresses are highest, which requires a repertoire of receptors with different bond kinetics to roll, tether, adhere, and activate on inflamed endothelium and extracellular matrices. As a thrombus grows and then contracts, forces regulate platelet aggregation as well as von Willebrand factor function and fibrin mechanics. Forces can also originate from platelets as they respond to the external forces and sense the stiffness of their local environment.

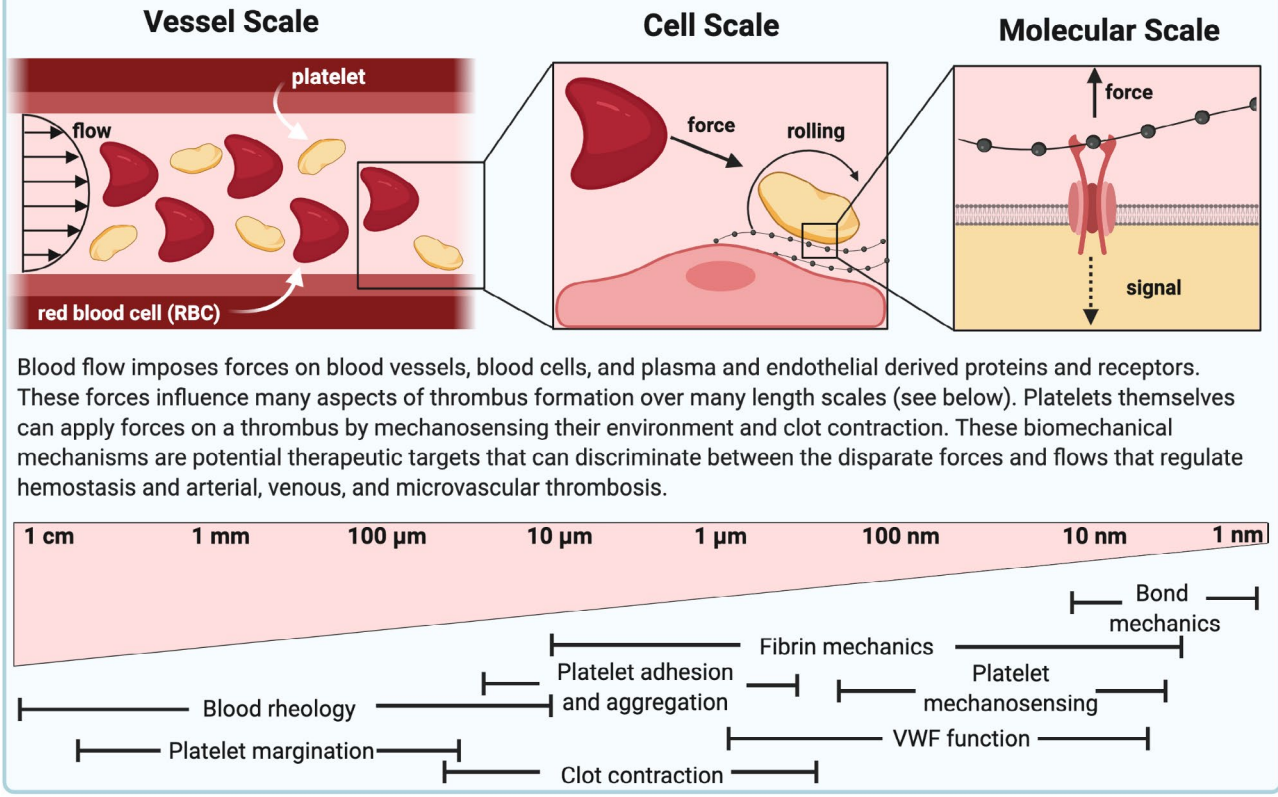
KEYWORDS
biomechanical phenomena, blood platelets, fibrin, hemodynamics, rheology, von Willebrand factor

Essentials

- Physical forces regulate blood clot formation and stability.
- Forces imposed by blood flow regulate platelet adhesion and aggregation at the site of vascular injury.
- Platelets can sense forces and create their own forces during spreading and contraction.
- The structure and function of two biopolymers essential to clot stability—von Willebrand factor and fibrin—are regulated by force.

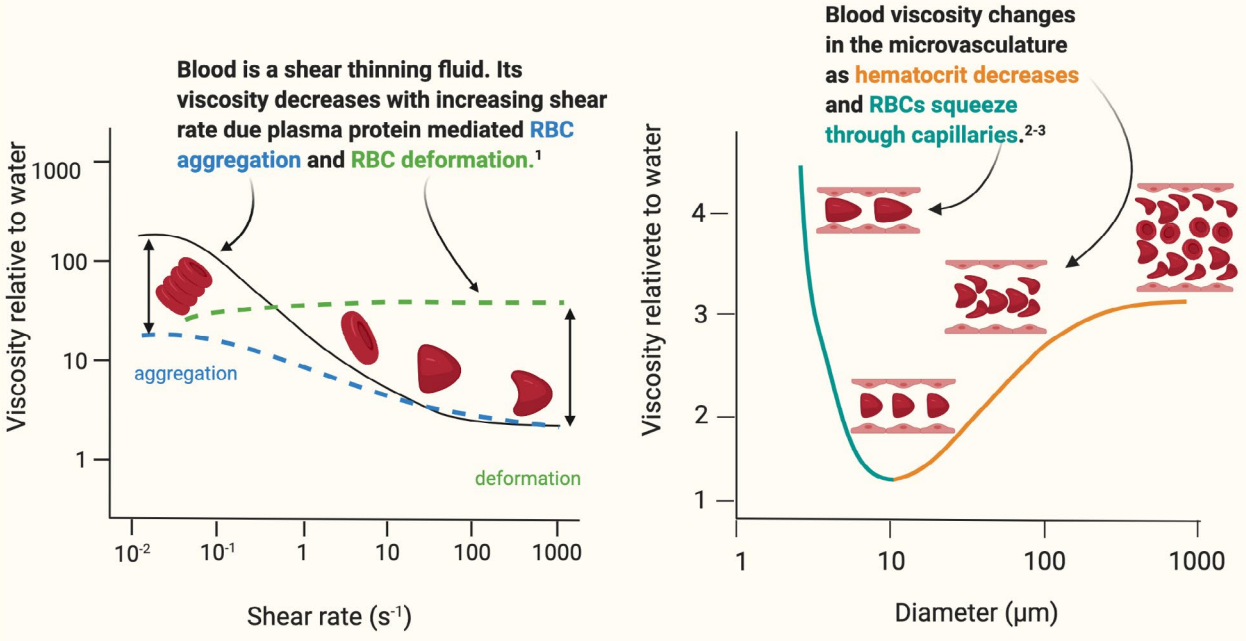
Reference citations[1-3]

Biomechanical phenomena across length scales



Blood flow imposes forces on blood vessels, blood cells, and plasma and endothelial derived proteins and receptors. These forces influence many aspects of thrombus formation over many length scales (see below). Platelets themselves can apply forces on a thrombus by mechanosensing their environment and clot contraction. These biomechanical mechanisms are potential therapeutic targets that can discriminate between the disparate forces and flows that regulate hemostasis and arterial, venous, and microvascular thrombosis.

Blood rheology: Viscosity is a function of shear rate and vessel size



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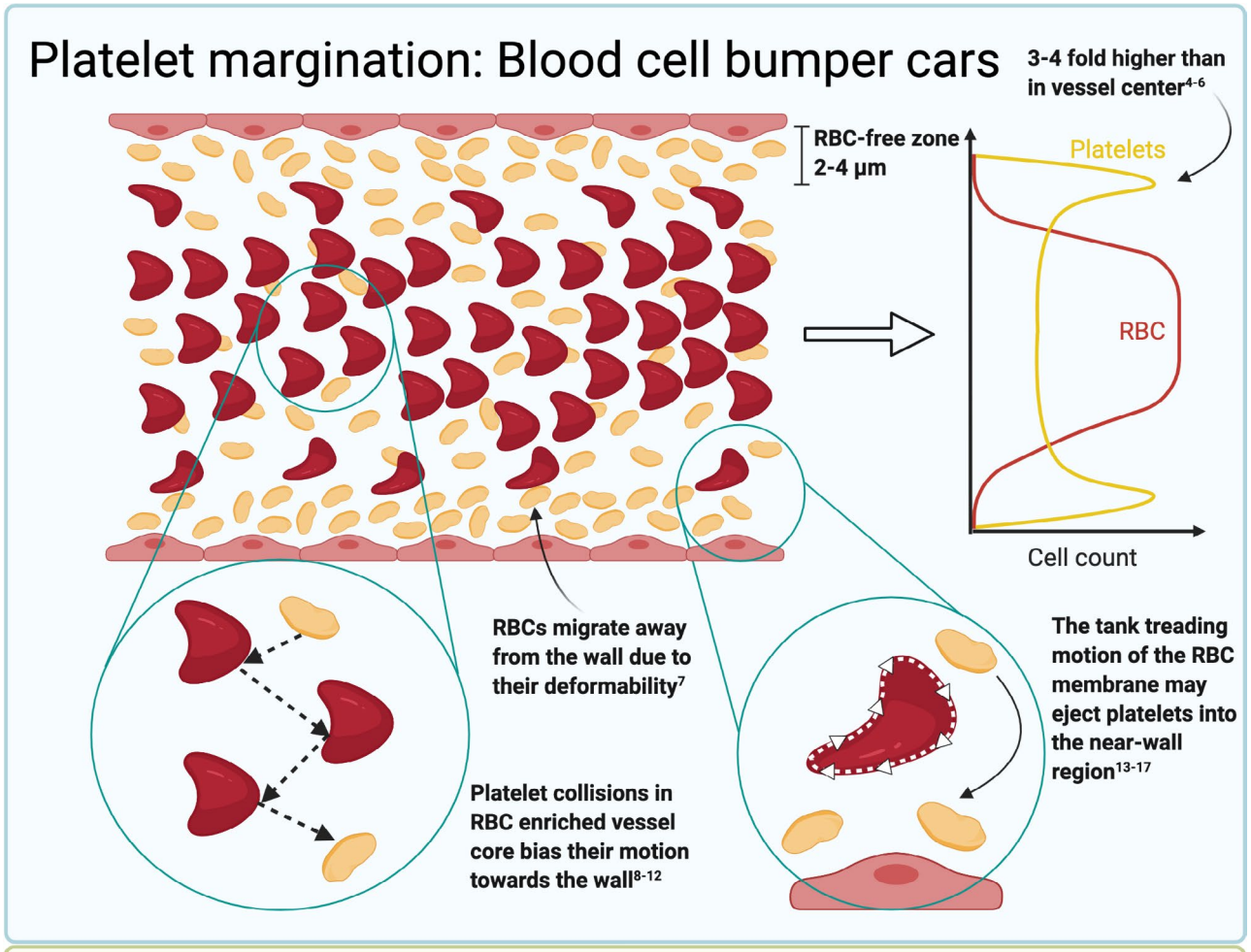

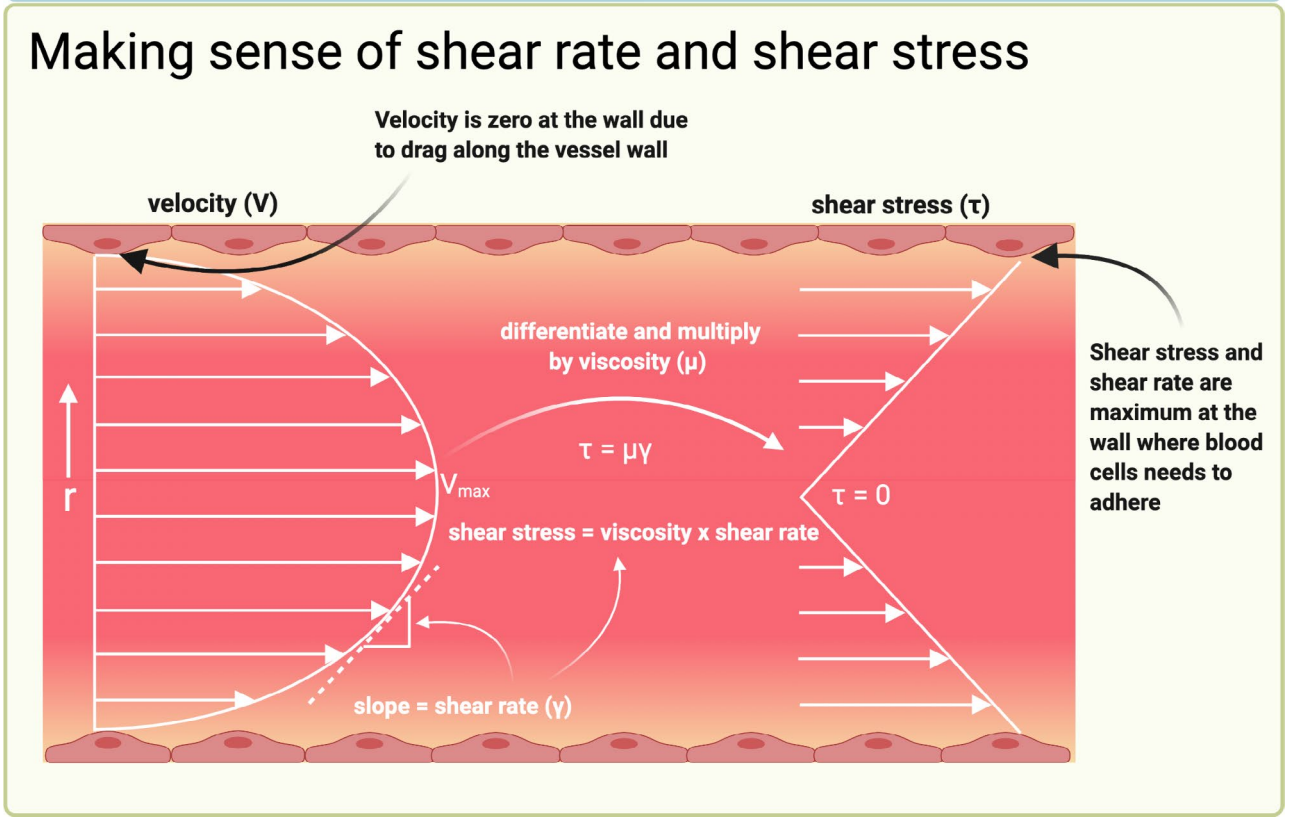

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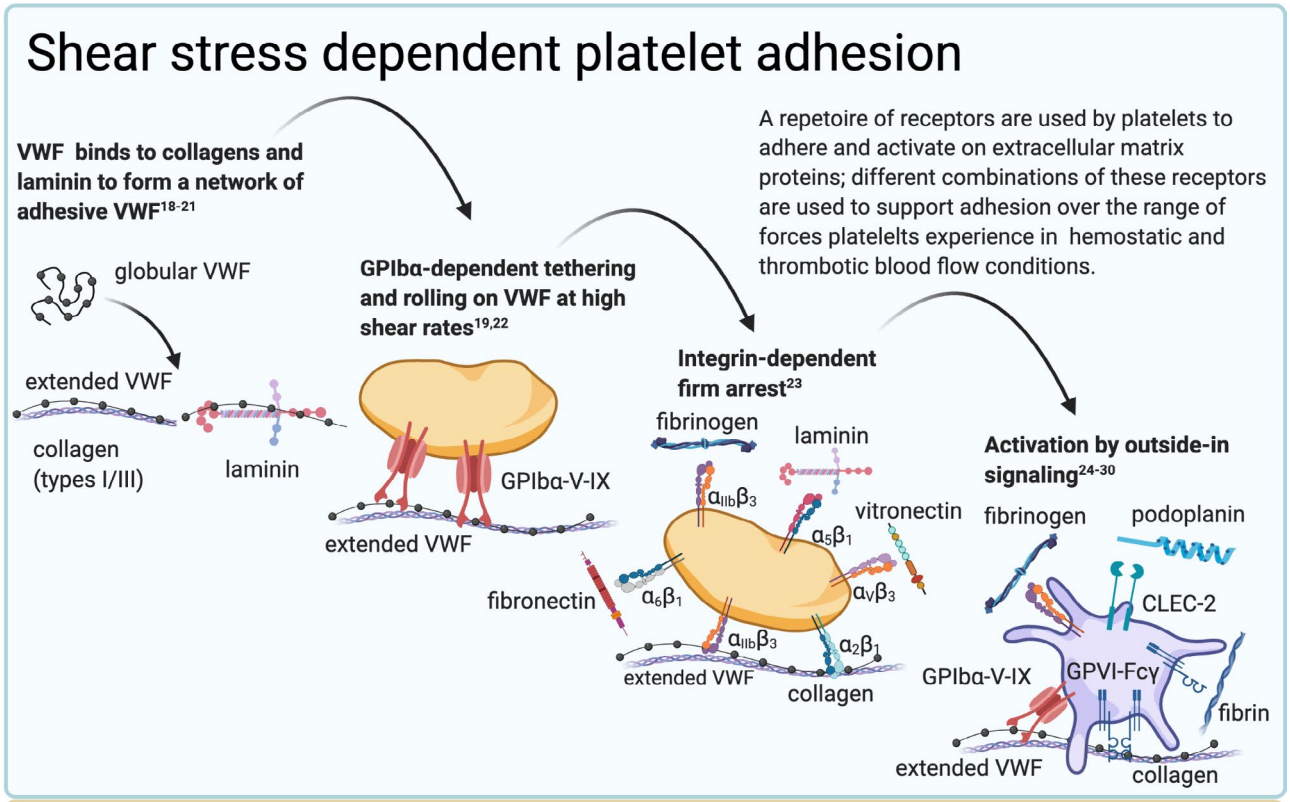

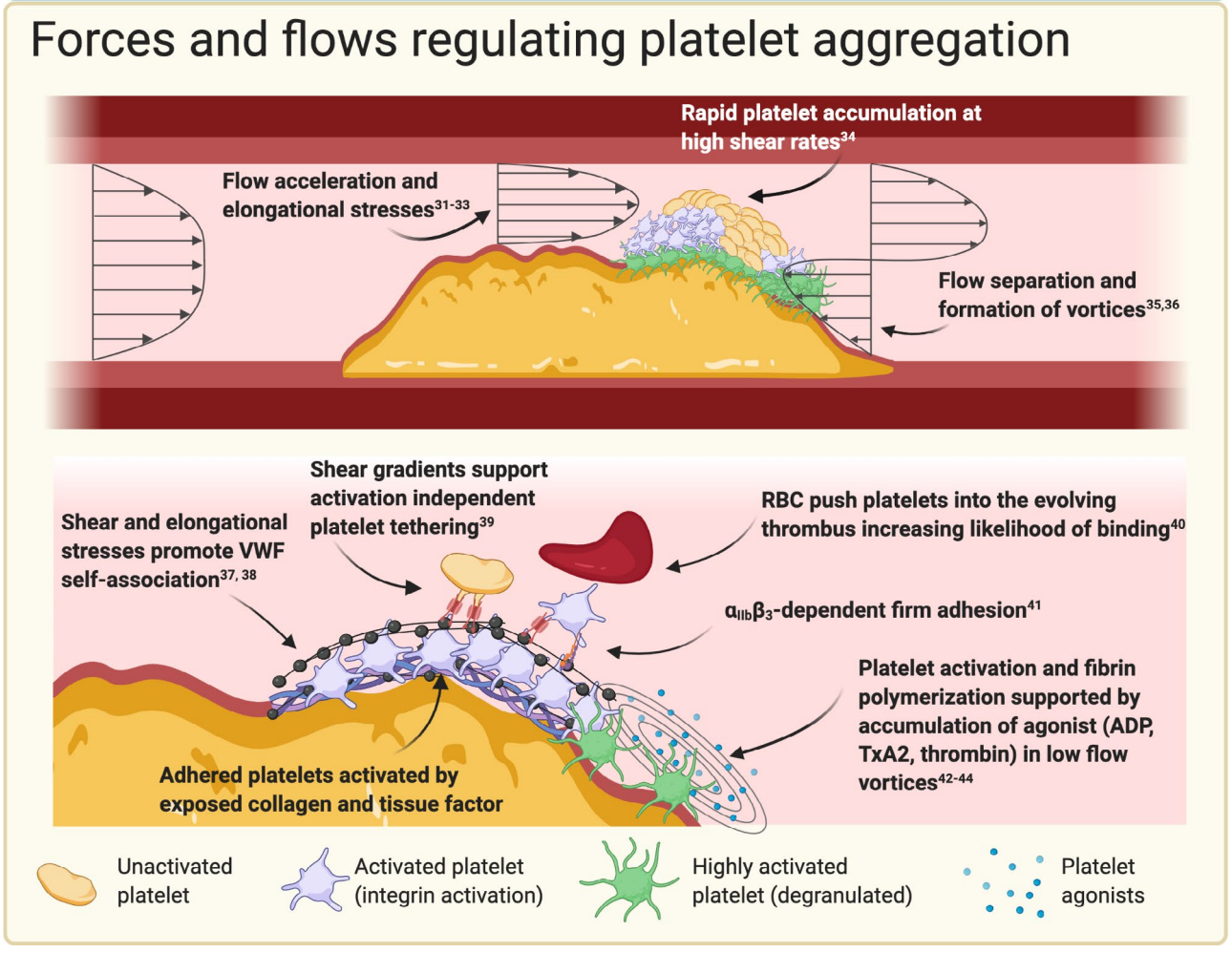

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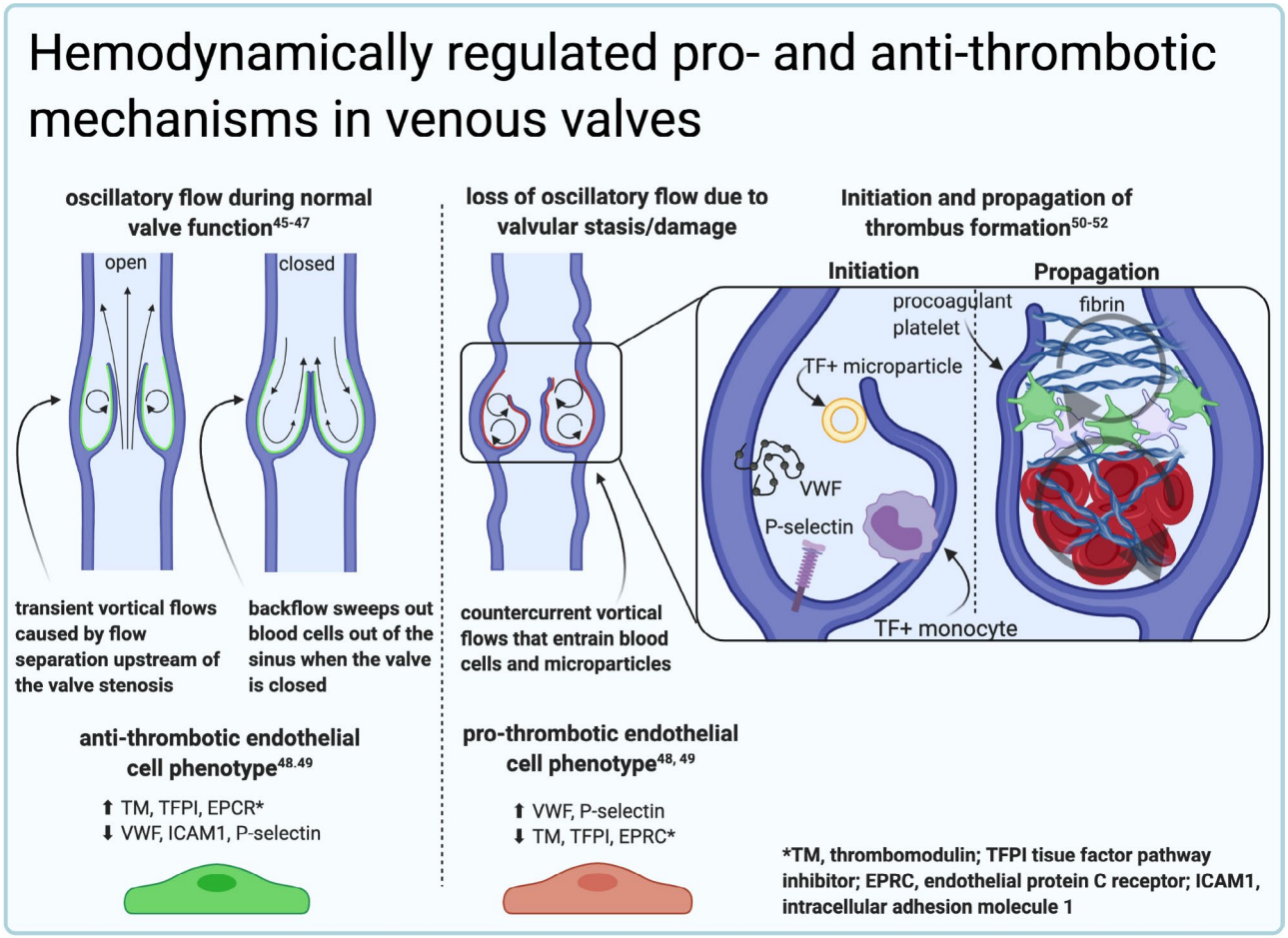

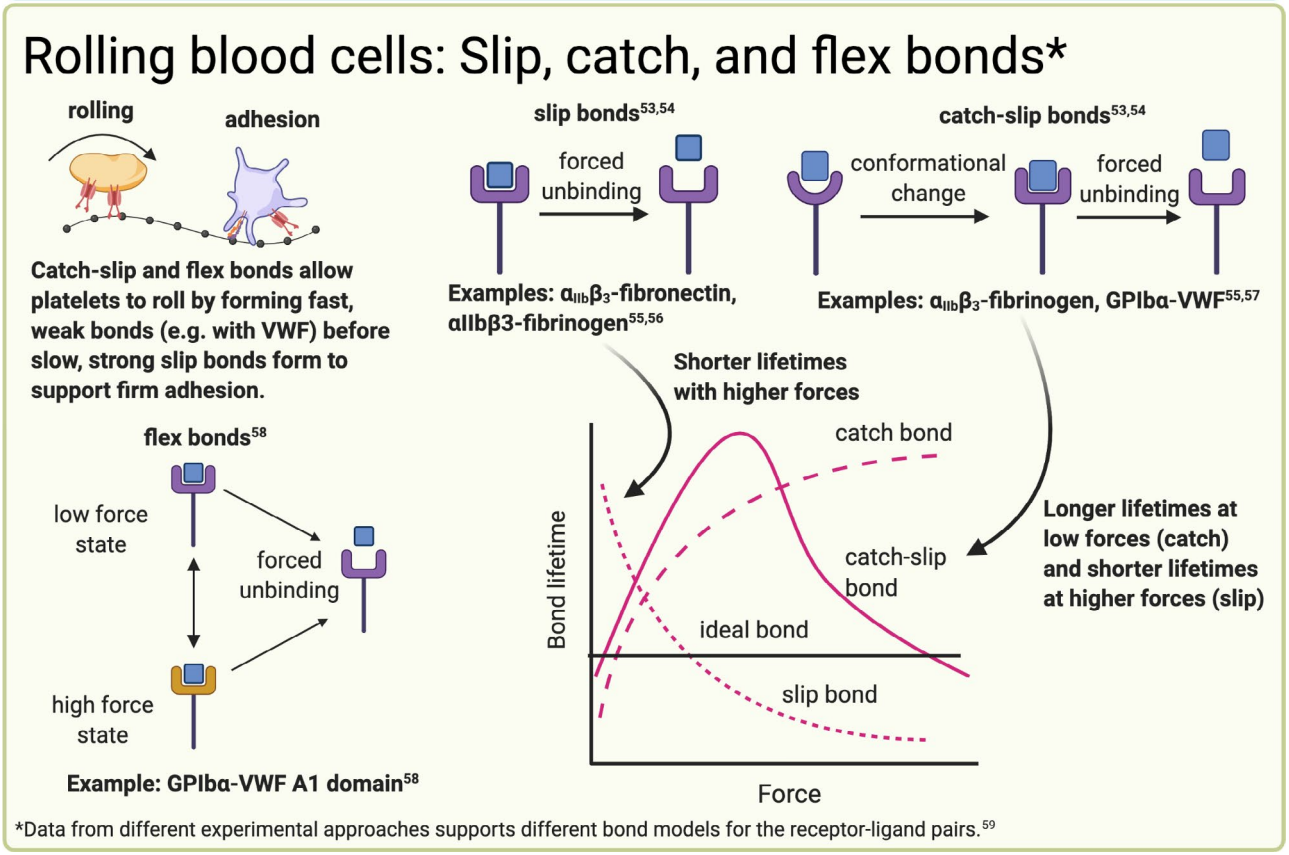

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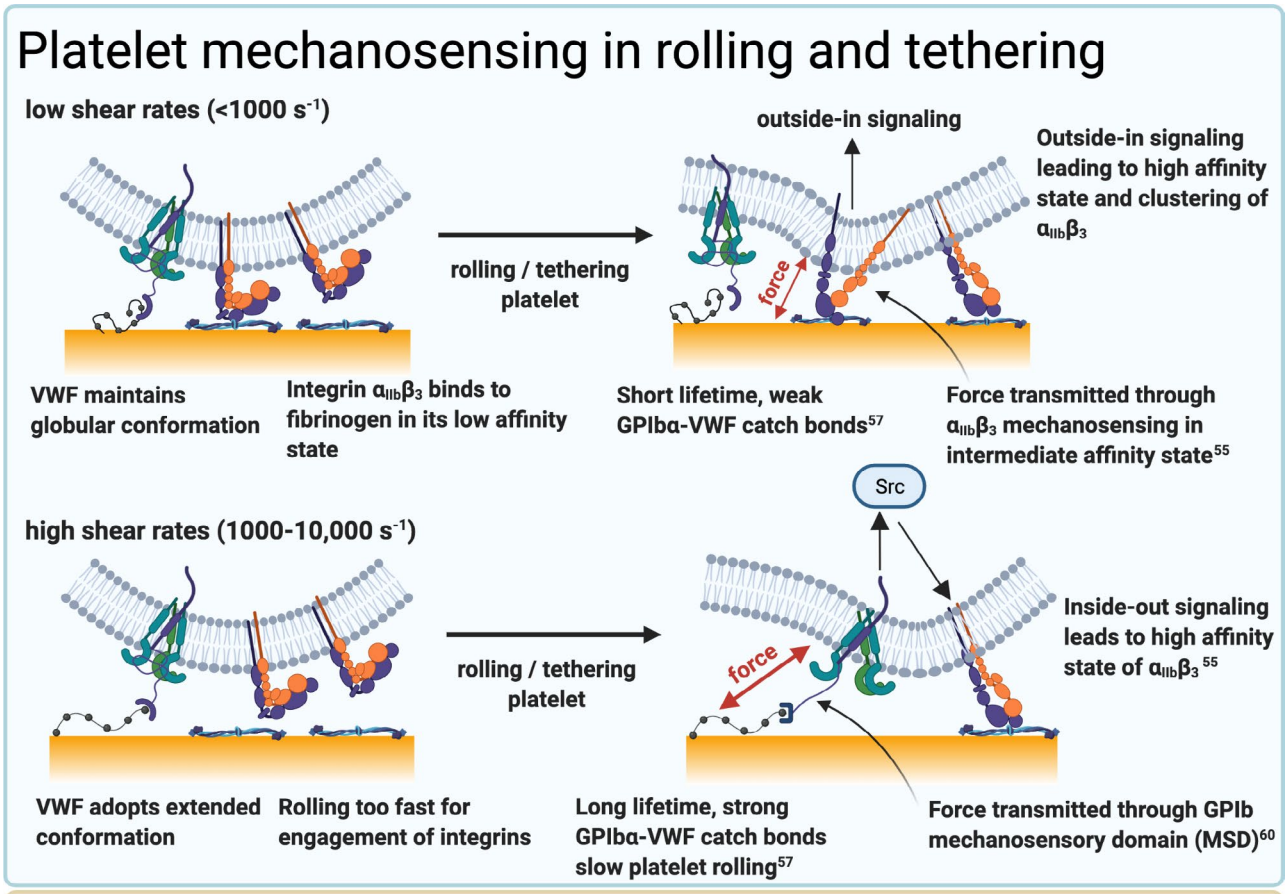

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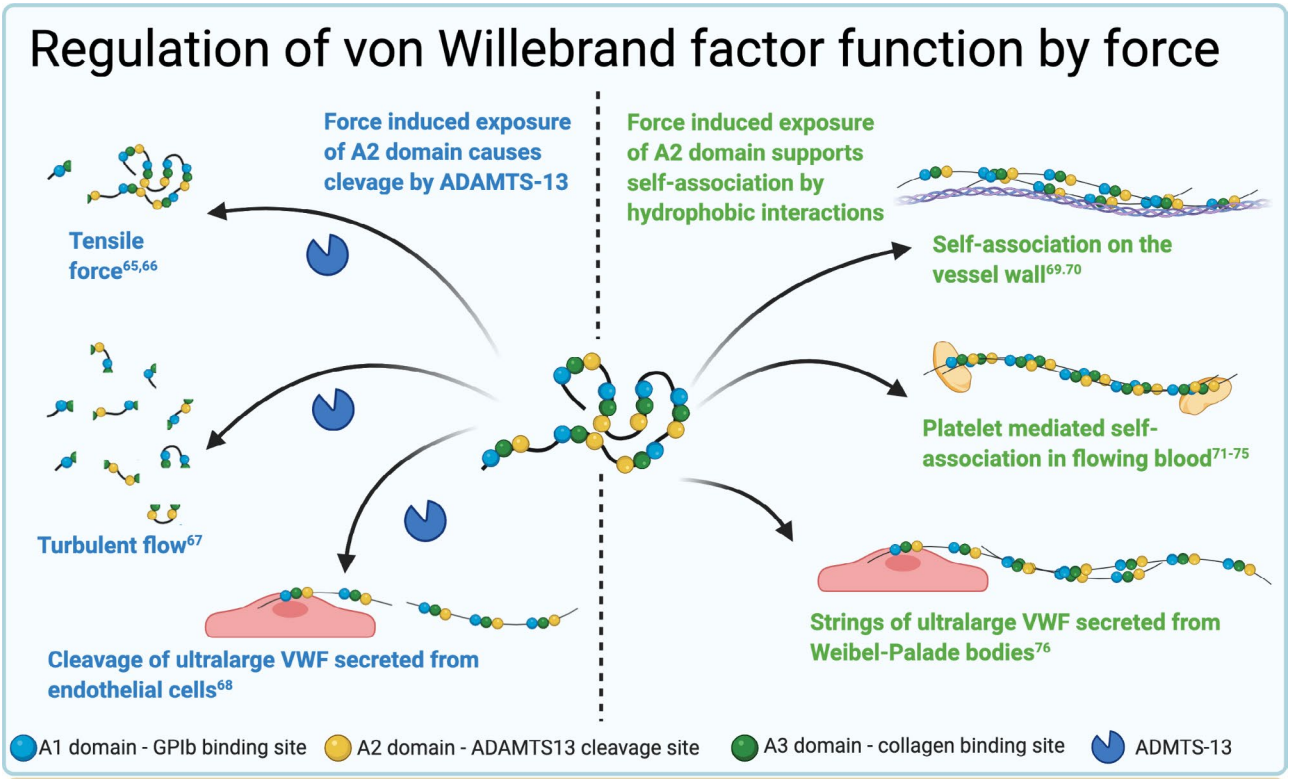

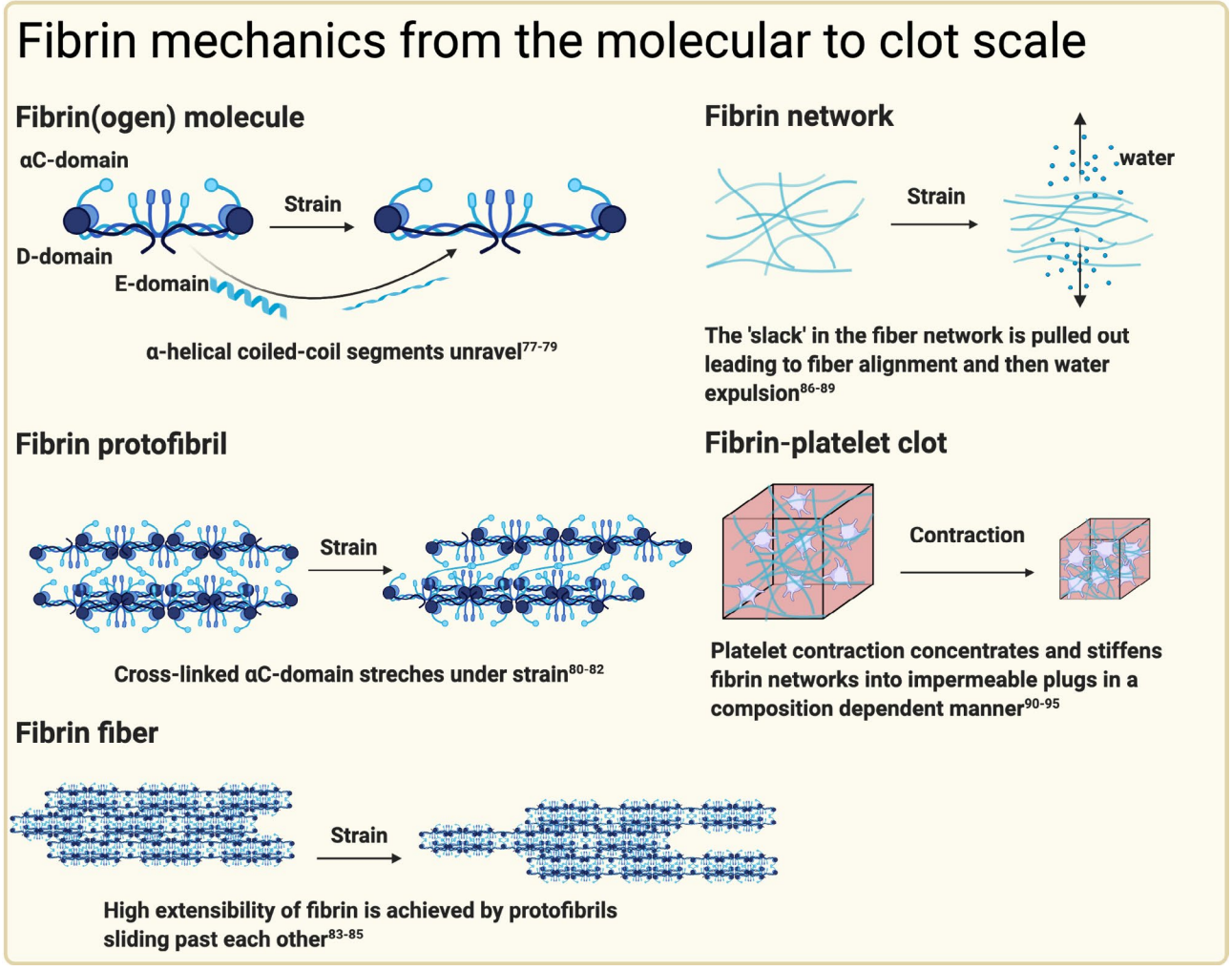

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AUTHOR CONTRIBUTIONS

JL, MGS, WAL, and KBN wrote the manuscript.

RELATIONSHIP DISCLOSURE

The authors declare no conflicts of interest.

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