

Myeloid Cells to the Rescue: Improving Thrombus Resolution

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Venous thromboembolism (VTE) comprising deep vein thrombosis and pulmonary embolism is one of the leading causes of morbidity and mortality in the world.¹ Therapy today means anticoagulation, which also puts the patient at significant bleeding risk. The number of patients afflicted by VTE indicates that pathophysiology of this disease is not yet fully understood and must be further investigated to provide better strategies for prevention and treatment and to avoid recurrence. In this issue, Kimball et al contribute to a better understanding of the role of monocytes/macrophages (Mo/M Φ) in thrombus formation and resolution.² They were able to show that toxin-mediated depletion of 80 to 90% of the CD11b⁺ Mo/M Φ had no effects on neutrophil recruitment, formation of neutrophil extracellular traps, and venous thrombus formation in a VTE mouse model of vena cava ligation. While thrombogenesis was unaltered, depletion of circulating CD11b⁺ Mo/M Φ resulted in larger thrombi and impaired intrathrombotic fibrinolysis at day 8 post ligation. This phenomenon seemed to be based on removing one of the main cellular components of a dissolving thrombus, the “reparative” Ly6C^{lo} monocytes. To test their hypothesis, CD11b⁺ Ly6C^{lo} monocytes were adoptively transferred into Mo/M Φ depleted mice, resulting in thrombus size comparable to nondepleted controls. In their model, the authors did not provide us with longitudinal data on thrombus resolution over time. Nevertheless, they corroborate earlier reports which showed that skewing the monocyte phenotype away from a Ly6C^{hi}/IL-12⁺/T-bet⁺ subset with ensuing reduction of interferon gamma formation improves thrombus resolution.^{3–5} Individuals suffering from inflammatory bowel disease or active autoimmune disease, in particular when complicated by antiphospholipid antibody syndrome, are at risk to experience VTE recurrence.¹ Rosuvastatin admin-

istered to individuals with increased high-sensitive C-reactive protein reduced first occurrence of symptomatic VTE,⁶ suggesting that modification of the inflammatory burden might represent a valid drug therapy to prevent thrombosis. Further research will be needed to affirm that immunomodulatory strategies based on enhancing the reparative functions of myeloid cells will not only improve healing but also prevent recurrence of VTE.

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Conflict of Interest

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