Platelets are normally responsible for the arrest of bleeding but this function, for example, their ability to aggregate can contribute to pathological states, such as atherosclerosis and heart disease. In addition to their obvious role in hemostasis/thrombosis, platelets also seem to be firmly rooted with a great deal of other tasks primarily related to inflammatory/immune mechanisms. In particular, platelets express many important immune molecules such as T- and B-lymphocyte costimulatory CD154/CD40 molecules, bactericidal proteins, and most of the members of the Toll-like receptor family. It is becoming increasingly recognized that these types of molecules empower platelets with the ability to play critical proinflammatory immune-like roles in infectious states such as sepsis. Toll-like receptors are germ-line pattern recognition receptors and probably the most important immune sentinels of infectious attack, and all 13 members contain a common structural motif in the form of leucine-rich repeat units. Similarly, the GPIb-IX complex on the platelet also contains leucine-rich repeat; however, whether this shared sequence with Toll-like receptors confers anti-inflammatory properties to GPIb-IX is not clear. In this issue, Corken et al have attempted to define some of the physiological (Figure) functions of platelet GPIb-IX in a murine model of sepsis.

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The authors used von Willebrand factor (vWF) knockout mice and mice devoid of GPIb-IX and exposed them to a well-characterized cecal ligation and puncture (CLP) procedure to assess the role of the GPIb-IX/vWF axis during sepsis. The murine GPIb-IX–deficient mice (hIL-4R/Ibα4) have attempted to define some of the physiological (Figure) functions of platelet GPIb-IX in a murine model of sepsis. The authors show us yet another unidentified piece of the platelet/immune axis, but their results also raise several questions related to how the lack of GPIb-IX reduces platelet–leukocyte aggregate formation and dampens chemokine/cytokine responses. For example, as the authors discuss, does this reflect the activation status of the platelets in the CLP mice? However, is it possible that like Toll-like receptor, GPIb-IX interacts with and binds infectious agents and does this affect the physiological (Figure) functions of platelet GPIb-IX in a murine model of sepsis.

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monocytes and neutrophils? And from an immunologist’s perspective, the only cytokine that seemed to be dependent on intact GPIb-IX was interleukin-15, a predominantly monocyte-derived cytokine that essentially supports the generation of T-lymphocyte responses; do GPIb-IX–dependent lymphocyte responses, for example, T-regulatory cells aid in the observed anti-inflammatory effect? It is only a matter of time before the fine details of how GPIb-IX dampens proinflammatory responses in sepsis are revealed.

**Disclosures**
The author declares no financial conflicts.

**References**