For many decades, hemostatic and immune defense mechanisms were thought to act independently. More recently, this concept has been revised largely. Thus, it is becoming apparent that platelets, like leukocytes, have multiple functions in innate and adaptive immunity, changing their role from “innocent bystanders” to integral players in inflammatory or infectious processes and immunity (1, 2). For example, platelets express and secrete a variety of pro-inflammatory molecules that can trigger or modulate immune responses (3). Apart from that, up-regulation of plasma components such as distinct adhesive proteins and several coagulation factors in response to inflammatory processes (commonly designated “acute phase reaction”) is a frequent and well-known but less well-understood phenomenon. The multiple functions of tissue factor also illustrate the extensive cross talk between inflammation and coagulation. For example, apart from its crucial role in initiating coagulation by activating FVII (4), membrane-bound tissue factor is also capable of signal transduction, thus mediating inflammatory pathways (5).

A brief look at the evolution reveals that hemostasis and immune defense have emerged from a “common trunk”. Thus, invertebrates possess circulating cells termed hemocytes that have a dual role: hemocytes protect the host from invading microbes, prevent loss of hemolymph by initiating coagulation upon injury, and mediate wound healing (1, 6). Only at the level of lower vertebrates, immune defense and hemostatic mechanisms are carried out through distinct cell populations, i.e. leukocytes and nucleated thrombocytes, while anucleated platelets are only found in mammals. Recently proposed concepts and designations such as “immuno-thrombosis” (7) or “thrombo-inflammation” (8) are reflecting both the evolutionary nexus and the up-to-date contention of a multifunctional link between hemostasis and the immune system.

This theme issue of Hämostaseologie presents several highlights of the GTH Congress 2015 (9, 10) and offers the opportunity to reflect and strengthen a central topic, which was covered in various state-of-the-art lectures at the Düsseldorf conference.

Ruggeri and Mendolicchio provide a comprehensive review on the key role of plasma von Willebrand factor (VWF) and its interaction with platelet and endothelial cell receptors or extracellular matrix components during physiological hemostasis and abnormal thrombus formation (11). Specifically, the impact of flow dynamic conditions on the action of VWF after traumatic injury or atherosclerotic plaque rupture is discussed in detail. Complementary to this contribution, Reininger reports on the function of ultra-large VWF multimers that are being formed under abnormally high shear stress and modulated by ADAMTS13-induced proteolytic cleavage. This interaction appears to provide an effective regulatory mechanism to control highly reactive ultra-large VWF multimers (12). Vögtle et al. summarize recent insights into platelet receptors, including the C-type lectin-like (CLEC) receptor 2, and their role as potential pharmacological tar-
gets in the development of novel, more effective and safer strategies to prevent and treat arterial thrombotic and thrombo-inflammatory disorders (13). Neurovascular inflammation affecting larger vessels and the neuronal microcirculation, is discussed by Mezger et al. (14). The authors provide an innovative approach to the pathology of multiple sclerosis, experimental autoimmune encephalomyelitis, and stroke. Von zur Muhlen and Bode review current concepts of molecular imaging techniques both in vascular inflammation and thrombosis (15). Specifically, magnetic resonance imaging and its limitations are discussed. Platelets can either initiate or accelerate immune responses in a variety of inflammatory disorders. Cattaneo addresses the role of adenine nucleotides and platelet P2 receptors, including P2Y12 variants, through their direct or indirect interactions with pro-inflammatory cysteinyl leukotrienes in allergic bronchial asthma (16). Diabetes mellitus represents another clinical setting of inflammatory responses, promoting atherogenesis and plaque destabilization. Current concepts and mechanisms leading to increased vascular vulnerability in hyperglycemia, are summarized by Gleißner (17). Metabolic dysfunction in obesity can also result in inflammation associated with increased atherogenesis and thrombogenesis. Zirlik and Lutgens focus on co-stimulatory molecules of the B7 and tumor necrosis factor receptor families, including CD40-CD40L, providing an inflammatory link between obesity and atherosclerosis (18). Interestingly, up-regulation of tissue factor (TF) expression is frequently found in adipocytes and macrophages obtained from obese patients. As discussed by Ruf and Samad, recent genetic and pharmacological evidence indicates that TF contributes to the development of metabolic syndrome-related disorders by signaling through G protein-coupled protease-activated receptors (PAR) (19). Preclinical studies suggest that targeting the inflammatory and prothrombotic TF-PAR2 signaling may improve metabolic complications of obesity.

Collectively, the up-to-date reviews compiled here cover a broad spectrum and provide distinct perspectives on the nexus between hemostasis and inflammation. As Editor-in-Chief, I am grateful to all contributors and hope that this issue will be received with the warmth and candor that the authors deserve.

References