Editorial

Animal and Cellular Models in Thrombosis and Hemostasis

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Standardized In Vitro and In Vivo Model Systems to Simplify Complexity—That's How We Learn

The discovery of new target molecules and translational progress in the development and refinement of antithrombotic therapies as well as the improved treatment of bleeding disorders strongly relies on standardized ex vivo and in vivo models that closely resemble the respective human pathologies. The standardization of these models requires sound training in specialized hemostasis and thrombosis research laboratories as well as a consistent daily routine. In this theme issue of *Hämostaseologie—Progress in Haemostasis*, four review articles cover key models that have proven instrumental to gain mechanistic insights on thrombogenesis and hemostatic processes. In recent decades, these models have moved our field forward and enabled translation across scales, from cell-based research to isolated flow chamber systems, to mouse thrombosis models reflecting the pathologic situations as observed in patients, to large animal models.

Endothelial colony-forming cells (ECFCs), a subset of endothelial progenitor cells, can be isolated from peripheral blood. Their close resemblance to mature endothelial cells regarding morphology, function, genetic, and even epigenetic features makes them excellent surrogates to study mature endothelial cells. In the first article of this theme issue, **Nadine Schwarz and Hamideh Yadegari**[1] present state-of-the-art methodologies for the isolation and cultivation of ECFCs, followed by an overview of key studies in which ECFCs were utilized to elucidate the pathophysiology of hemostasis and thrombosis disorders, including von Willebrand disease, disorders of the protein C pathway, antiphospholipid syndrome, and sickle cell disease. Furthermore, they explore the potential of ECFCs for future diagnostic and therapeutic applications.

The review article by **Kim Jürgen Krott et al.**[2] highlights how the process of arterial thrombosis can be studied mechanistically using flow chamber models. The authors put focus on the Maastricht flow chamber and explain how this model can complement in vivo mouse thrombosis models.[3] In addition, Krott et al. provide an overview on the relevant platelet signaling pathways engaged in matrix-induced thrombosis (i.e., by collagen), with an emphasis on the regulation of GPIb–GPVI-mediated integrin activation. Importantly, this review explains how defects in the reorganization of the platelet cytoskeleton may impact thrombosis. The authors also touch on a field of growing interest, namely, the interplay of platelets with blood cells and leukocytes. Furthermore, the interaction of platelets with activated endothelial cells influences thrombus formation and stability under defined flow conditions. Krott et al. exemplify cholestatic liver disease and Alzheimer's disease as disease states where GPVI and integrin αIIbβ3-mediated platelet adhesion are involved.

Intravital imaging of thrombosis based on genetic mouse models has significantly improved our understanding of the vessel-specific cellular, spatial, and time-resolved in vivo processes that contribute to thrombus growth and resolution.[4,5] **Klytaimnistra Kiouptsi et al.**[6] provide an overview on various arterial and venous thrombosis models reflecting human pathologies such as carotid artery thrombosis, ischemic stroke, and deep vein thrombosis. They also describe relevant models to study thromboinflammatory processes in the microcirculation: thrombus formation in the mesentery, the mesenteric ischemia–reperfusion injury model, the hepatic ischemia–reperfusion injury model, the cremaster arteriole laser injury model, and infection-mediated liver thrombosis. They detail the ways in which various stimuli could be used to induce thrombotic processes (e.g., flow reduction, ischemia, ferric chloride injury, laser injury, injection of toxins) and describe the different readouts and

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possibilities for image analysis. In vivo mouse thrombosis models remain essential to gain an improved understanding of thrombosis in various settings.

As each of these articles have been thematically presented in increasing scale, we conclude this theme issue with a comprehensive review of large animal models that are being used to study the complex pathophysiology of trauma-induced bleeding and to develop clinical strategies for the treatment of coagulopathies, an especially challenging field of medicine. **Farahnaz Rayatdoost and Oliver Grottke**[7] have performed a systematic literature review including articles on studies in pigs, sheep, dogs, and nonhuman primates. They discuss advantages, disadvantages, and challenges of various hemorrhagic shock models across these species, highlighting their potential to improve the understanding of pathomechanisms, develop novel therapeutic strategies, and evaluate the effectiveness of existing and emerging interventions.

On behalf of the editorial board, we greatly appreciate the work of the contributing authors and are deeply grateful for the time and work spent to prepare articles of outstanding quality. We are confident that the articles in this theme issue will be of use not only for laboratory researchers but also provide new insights for clinically oriented scientists and physicians.

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