

Theme Issue Editorial

From Molecules to Medicine: New Horizons in Vascular Biology and Thrombosis (Part II)

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We continue in this issue of *Thrombosis and Haemostasis* with the publication of the second part of state-of-the-art reviews, based on invited lectures that were presented at the 52nd annual meeting of the “Society of Thrombosis and Haemostasis Research” (GTH) in Wiesbaden, Germany. The six contributions in this issue particularly concentrate on clinical and therapeutic aspects of atherothrombosis, cardiovascular, metabolic syndrome as well as interstitial lung diseases.

For the prevention of unwanted platelet adhesion and aggregation in association with pathological thrombus formation, specific inhibition of receptor-mediated signaling as well as blockade of platelet adhesion receptor function can serve as major targets of antithrombotic drugs. Christian Gachet (Strasbourg) and Ken Clemetson (Bern) present new mechanistic aspects of the G-protein coupled P2-receptors for ADP/ATP (1) as well as of the glycoprotein (GP) Ib-complex (the von-Willebrand-factor receptor) (2) and recent insights from knock-out studies and intervention studies. The optimal inhibition of these receptor systems should reach clinical efficacy whilst preventing patients from unacceptable bleeding. Against this background, P2Y₁- and P2X₁-receptors have been demonstrated to be attractive targets for new antithrombotic compounds to be discussed. Likewise, the multiple ligand interactions mediated via the GPIb-complex would make this receptor a good candidate for antithrombotic drug development including different classes of compounds to present specific effects.

Platelets are not only of central importance during wound healing, but platelet adhesion to the endothelium is also critical for the initiation of atherosclerotic lesion formation *in vivo*. Harald Langer and Meinrad Gawaz (Tübingen) focus in their review on the pathogenetic role of platelets in the early stages (platelet adhesion governed by disturbed flow at predilection sites and induction of proinflammatory mediators) and late stages (plaque rupture, microembolism) of atherogenesis (3). Platelets may me-

diate recruitment of circulating progenitor cells to sites of vascular injury as well. By deciphering this diverse range of platelet cellular activities on a molecular level, potential therapeutic targets in cardiovascular disease may arise.

Although the dual antiplatelet therapy with aspirin and clopidogrel is currently the standard therapy after coronary stent implantation to prevent a life threatening stent thrombosis, a variety of procedural and individual factors contribute to the individual patient risk. Andreas May et al. (Tübingen) will present stratification procedures to define patient collectives who may benefit from more individualized antithrombotic regimens (4).

Acute inflammatory and chronic interstitial lung diseases are characterized by excessive and persistent fibrin deposition in the lung. In the article by Wygrecka et al. (Giessen) various intraalveolar fibrin-related pathological mechanisms related to disturbed vascular permeability, alterations in cell migration, proliferation and impairment of surfactant function will be discussed (5). While the application of coagulation inhibitors turned out to be beneficial in experimental models of acute and chronic lung injury, the ability of such natural and synthetic anticoagulants to improve clinical outcome remains to be elucidated.

In the final contribution of this series (to be published in the April 2008 issue of *Thrombosis and Haemostasis*), Marie-Christine Alessi and Irène Juhan-Vague (Marseille) review the mechanistic connections between the pathological situation of metabolic syndrome (as it relates to the development of type 2 diabetes) and atherothrombosis (6). Besides the complex pathophysiological aspects observed with the occurrence of a hypercoagulant and hypofibrinolytic state in patients, dysfunction of the endothelium is a central feature as well. New mechanistic insights into the role of fat tissue as an endocrine organ may lead to a better understanding of the vascular consequences of metabolic syndrome, as they relate to atherosclerosis and venous thromboembolism.

References

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