

From Molecules to Medicine: New Horizons in Vascular Biology and Thrombosis

Klaus T. Preissner*

Institute for Biochemistry, Medical School, Justus-Liebig-University, Giessen, Germany

The theme issue articles published in the 2008 February and March issues of *Thrombosis and Haemostasis* are based upon invited lectures to be presented at the upcoming 52nd annual meeting of the “Society of Thrombosis and Haemostasis Research” (GTH), the second largest thrombosis congress outside the International Society on Thrombosis and Haemostasis (ISTH) meeting. Previously founded in 1956 as a “German Working Party on Blood Coagulation” by specialists in haemostasis, this study group was replaced and extended in 1982 by the GTH, the largest and most active multinational thrombosis society in Europe, predominantly for German speaking countries. Yet, this year’s meeting, organized by a dedicated group of researchers from Giessen (Germany), is held in conjunction with the French “Groupe d’Etude sur l’Hémostase et la Thrombose” (GEHT). More than 500 presentations (invited lectures, oral and poster presentations as well as workshops, study groups and satellite symposia) are expected to attract many experts in the field from basic science, applied medicine and pharmaceutical industry to provide a multinational platform for the discussion of new horizons in vascular biology and thrombosis.

In the first review, Paquita and Alan Nurden (Bordeaux), who are both well-known experts in platelet pathophysiology, discuss mechanisms of congenital platelet disorders (1). Based on genetic defects of the megakaryocyte lineage, platelets are associated with adhesion and signaling receptor deficiencies resulting in defective haemostasis as well as in abnormalities of signaling pathways leading to trauma-related bleeding. The authors also discuss inherited defects of platelet organelle secretion as well as familial thrombocytopenias, and provide an outlook on challenging therapies including thrombopoietin administration or possible stem cell transplantation. A complementary article by Wolfgang Bergmeier (Philadelphia) (2), previously associated with Denisa Wagner’s laboratory in Boston, deals with new insights gained from experiments in mutant mice on the major von-Willebrand-factor (vWF) receptor complex, the glycoproteins (GP)Ib-V-IX. As elegantly demonstrated in a series of experimental animal models, both, ligand and receptor complex, play important roles in the development of arterial and venous throm-

bosis. With a specific look at the life cycle of vWF, Cécile Denis (Paris) summarizes the various steps of vWF clearance (3), whereby defects in vWF clearance (due to e.g. mutations or glycosylation profile) are relatively common components in the pathogenesis of type 1 vWF disease. Improving the survival of vWF by e.g. chemical modification is now considered as a viable therapeutic strategy to prolong the half-life of factor VIII in order to optimise treatment of haemophilia A in patients.

A signaling kinase family of growing interest are the phosphoinositide-3-kinases (PI3-kinases), whereby the unique PI3-kinase γ is activated by G protein-coupled receptors and plays a pivotal role in inflammation and vascular diseases, as demonstrated in the review by Emilio Hirsch (Turin) (4). PI3-kinase γ is mainly expressed in leukocytes where it plays a significant role in chemotaxis (5), but is also important in endothelial cells. Based on genetic and pharmacological approaches, specific inhibition of PI3-kinase γ has gained increasing attention in the treatment of allergic, autoimmune and inflammatory diseases. A recently described haemostasis protease is “Factor VII activating protease” (FSAP) which activates/proteolyzes various protein substrates including factor VII, pro-urokinase or platelet-derived growth factor. Consequently, the multiple activities of FSAP relate to its putative functions in haemostasis, to cell invasion and as an inhibitor of smooth muscle cell proliferation. In his review, Sandip Kanse (Giessen) (6) summarizes our knowledge about the role of FSAP and its natural variants in the cardiovascular system. It remains to be analysed by e.g. gene knock-out technology in which way and by which type of mechanism FSAP may influence vascular fibroproliferative and inflammatory processes.

The relation between haemostatic / fibrinolytic factors and adipose tissue as an endocrine organ was recognized more than a decade ago (7), and Roger Lijnen (Leuven) provides a detailed insight into respective molecular mechanisms (8). Since obesity is a common disorder in the Western population and also related to cardiovascular disease as well as diabetes, atherosclerosis, hypertension and cancer, the understanding of the role of fibrinolytic and matrix metallo-proteases in the development of obesity

Correspondence to:
Klaus T. Preissner, PhD
Institute for Biochemistry
Justus Liebig University
Friedrichstrasse 24
Giessen, D-35392 Germany
Tel.: +49 641 994 7500, Fax: +49 641 994 7509
E-mail: klaus.t.preissner@biochemie.med.uni-giessen.de

*The author is president of the 52nd GTH-Congress in Wiesbaden, Germany, February 20–23, 2008.

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is of pivotal interest. Nutritionally induced obesity models in transgenic mice have been used extensively to study the pathophysiological role of these enzymes, indicating that they may affect development and alteration of adipose tissue.

In the final theme issue contribution, Gregory Lip (Birmingham) systematically reviews the risk factors and risk stratification related to stroke and thromboembolism in atrial fibrillation (9). These aspects are important to determine the clinical and cost-effectiveness of thromboprophylaxis in each patient. As such, a history of stroke or transient ischemic attack, increasing

age, hypertension and structural heart disease were found to be good predictors of stroke risk in patients affected by atrial fibrillation.

In addition to these contributions, another set of reviews from invited speakers of the 52nd GTH-Congress will appear in the March 2008 issue of *Thrombosis and Haemostasis*. We hope that interested readers enjoy studying these diverse topics of vascular biology and thrombosis; further details about this interdisciplinary meeting can be found at www.gth2008.de.

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Topics: Thrombus formation *in vivo*, structure of cellular kallikreins, circulating endothelial cells, progenitors and microparticles, chemokines and their receptors, platelet functions, thrombus formation, diagnosis, therapy, cardiac remodelling, bleeding disorders, haemostasis and vascular

biology: basic concepts, congenital disorders associated with platelet dysfunctions, RNA aptamers as antithrombotic agents, VKORC1: genes, molecules and mechanisms, infection and haemostasis, platelets in vascular disease, pulmonary system, anticoagulation, cardiovascular medicine, diagnostics and thrombin generation, preventive medicine, ITP, heparins/HIT

Contact: CPO Hanser Service, P. O. Box 12 21, 22882 Barsbüttel, Germany; Tel.: +49 40 670 88 20, Fax: +49 40 670 32 83; E-mail: gth@cpo-hanser.de; <http://www.gth2008.de>