

Recent advances in vascular biology: Selected highlights from IVBM 2008



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The contributions encapsulated in this themed issue of *Thrombosis and Haemostasis* derive from invited lectures at the 15th International Vascular Biology Meeting (IVBM) held in June, 2008 in Sydney, Australia. IVBMs, which are held every two years, have become the most prestigious international biomedical conference in blood vessel biology and disease. The scientific programme featured 130 talks couched in seven plenary sessions (14 keynote speakers), 17 workshops (2–3 invited speakers and 2–3 speakers selected from abstracts), two sponsored symposia, and almost 400 posters. The programme also featured three memorial orations honoring true giants in vascular biology that had passed away since the last IVBM in Amsterdam in 2006, namely Judah Folkman, Tucker Collins and Rudi Busse. The following provides a brief synopsis of six areas covered at IVBM 2008.

Angiogenesis underpins normal physiological processes such as reproduction and wound healing, as well as a wide range of vascular disorders such as atherogenesis, and invasive tumour growth and metastasis. Angiogenesis involves the suppression of adhesion receptors, such as ICAM-1, VCAM-1, E-selectin and CD34 in tumour endothelium (1). Angiogenesis inhibitors are able to normalise endothelial adhesion molecule expression in tumour blood vessels, restoring leukocyte vessel wall interactions and enhancing inflammatory infiltration in the tumours, thus making tumours more vulnerable to attack by the immune system. Arjan Griffioen (VU University Medical Center, Amsterdam, The Netherlands) and Florry Vyth-Dreese (Netherlands Cancer Institute, Amsterdam, The Netherlands) have reviewed (2) the potential of angiostasis therapy to stimulate immune-mediated tumour inhibitory activity and speculate on new therapeutic approaches involving angiostasis in immunotherapy. The various mechanisms with which angiogenesis inhibitors might improve immuno-targeted approaches include tumour cell lysis stimulating tumour antigen presentation, reduced inhibitory molecule load that improves immune reactivity, limited release of immunosuppressive cytokines into the tumour microenvironment, and the creation of a pro-inflammatory microenvironment.

Blood vessels adjust their calibre size in order to adapt to the demands of tissues or organs for nutrients and oxygen. The mechanisms involved in calibre size determination in blood vessels are not well understood. Nobuyuki Takakura and Hiroyasu Kidoya (Osaka University, Osaka, Japan) recently discovered that apelin, a factor secreted from endothelial cells following activation of Tie2 receptor tyrosine kinase, regulates the calibre size of blood vessels through its cognate endothelial G protein-coupled receptor APJ (3). Takakura and Kidoya have reviewed (4) the cooperative effect of apelin and VEGF on endothelial cell proliferation and capillary tube formation, and apelin's regulation of cell-to-cell aggregation and cord hollowing.

Integrins are heterodimeric cell-surface molecules that mediate molecular interactions between cells and their extracellular matrix (ECM) environment (5). These signalling receptors transmit information in both "inside-out" and "outside-in" directions across the cell membrane. A necessary and sufficient final step in integrin activation is the binding of the cytoskeletal protein talin to the integrin β -subunit. Brian Petrich (University of California, San Diego, USA) has reviewed (6) our current understanding of the mechanisms regulating the interaction of talin and that of numerous other proteins (such as filamin and kindlin) with the β -integrin subunit and modulation of integrin activation. Our growing appreciation of the functional significance of integrin signalling in haemostasis and thrombosis has been facilitated by mutational analysis in recombinant cell lines and very recently by the use of genetically modified mice. These and other advances focusing mainly on integrin α IIB β 3 (GPIIb-IIIa) are reviewed.

Antibodies represent the fastest growing class of human therapeutics and the second largest class of drugs after vaccines, and these molecules are widely used as therapeutic agents in a diverse range of clinical settings, including cancer, inflammatory disease and cardiovascular disease. Single-chain antibodies (7) are one of the smallest possible formats for a recombinant antibody. Karlheinz Peter and colleagues (Baker IDI Heart and Diabetes Institute, Melbourne, Australia) have described (8) the

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structure, selection and production of single-chain antibodies, and review the use of fibrin- and platelet-specific single-chain antibodies coupled with anticoagulants and thrombolytic agents as antithrombotic drugs. Single-chain antibodies are also being used as immunosensing, magnetic resonance and near-infrared imaging tools in non-invasive imaging applications for the diagnosis of thrombosis and inflammation.

Atherosclerotic plaque rupture is the principal cause of myocardial infarction and stroke. Matrix metalloproteinases (MMPs) have long been implicated in both intimal thickening and plaque instability (9). MMPs generated by invading monocytes/macrophages degrade collagen and other ECM proteins in the plaque that provide tensile strength, thereby weakening the plaque cap and promoting rupture. Smooth muscle cells produce collagen and other ECM proteins, yet these cells also produce MMPs capable of digesting ECM proteins. Thus, certain MMPs are thought to promote plaque instability, whilst others stimulate plaque inflammation and rupture. Andrew Newby et al. (Bristol Heart Institute, Bristol, UK) have reviewed (10) recent evidence suggesting that distinct macrophage phenotypes express characteristically different patterns of MMPs and tissue inhibitors of metalloproteinases (TIMPs), which modify functions including migration, proliferation and apoptosis.

The development of therapeutic approaches that stabilise plaques and prevent rupture remains an ongoing challenge because of the lack of surrogate endpoints to demonstrate efficacy. Traditional risk factors do not allow hierarchical arrangement of risk at an individual level. Athero-Express is a prospective longitudinal vascular biobank study, initiated in 2002, that has enabled investigation of the etiological value of plaque characteristics for long-term outcome (11). Hurks and colleagues (University Medical Center, Utrecht, The Netherlands) have reviewed (12) recent findings from this biobank study, which indicate that the composition of the atherosclerotic plaque is an independent predictor of restenosis after carotid endarterectomy. Low macrophage infiltration and small lipid core is associated with risk of restenosis after an intervention. In the future, studies such as these may predict risk for the individual patient and pave the way for personalised treatment based on a multifactorial approach including vulnerable plaque characteristics, classic risk factors, systemic biomarkers and genetic profiling.

This summary provides a small vignette of the diverse range of topics covered at the conference. The IVBM spirit will continue in Los Angeles in 2010, where the 16th meeting will be held from June 20–24.

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