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An enlightening year in vascular biology

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This has been an exceptional year for advances in the vascular biology area. Progress in our understanding of angiogenesis, inflammation and endothelial cell responses and signaling have all been realized. We are fortunate that many of the leaders of these discoveries have contributed manuscripts for the Vascular Biology section of *Current Opinion in Hematology*. These thought-leaders provide unique perspective on developments that have and may continue to shape the future of vascular biology. The topics covered by the seven articles in this edition range from very basic considerations of gene regulation, metabolism and signaling pathways in endothelial cells, to lymphocyte adhesion to endothelium, to the mechanisms of vascular diseases and to up-to-date strategies to treat vascular diseases. The contributions in this issue touch upon a variety of human diseases, including atherosclerosis in its various stages of development, deep vein thrombosis, hemorrhage, cancer and tumor growth, cerebral vascular disease and hypertension. This partial listing represents a truly broad swath of pathologies and hence this issue has a very clinically relevant orientation. At the same time, the basic and translational research described in these articles not only provide insights into the underlying mechanisms but also identify specific targets to treat vascular diseases.

I briefly highlight one or two key take-away points from each article in this issue, but, at the same time, I emphasize that the articles should be read directly. They are all very readable and will be informative to both the seasoned vascular biologist and to the neophyte entering the area.

Chang *et al.* (pp. 224–229) provide an article on the role of Krüppel-like factors (KLFs) in endothelial cell biology. Four members of the KLF family are present in endothelial cell, and their expression is influenced by shear stress and certain miRNAs. Changes in expression of KLFs influence susceptibility to atherogenesis and the prothrombotic and antithrombotic status of the endothelium.

Badimon and Borrell-Pages (pp. 230–239) update us on the role of Wnt signaling in the vessel wall. Wnt signaling, both canonical involving β -catenin and noncanonical pathways, participates in the early, intermediate and late stages of atherosclerosis. Different coreceptors influence downstream signaling and thereby also control transcription of Wnt-regulated genes.

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In their article, Teuwen *et al.* (pp. 240–247) consider how endothelial cell metabolism impacts angiogenesis. Glycolysis and fatty acid oxidation control vessel sprouting, endothelial cell migration and blood vessel maturation. As these pathways are upregulated in tumors undergoing active angiogenesis and lymphangiogenesis, inhibitors targeting key steps in these metabolic pathways become potential suppressors of pathological angiogenesis.

Chrzanowska-Wodnicka's (pp. 248–255) contribution focuses on the small GTPase, Rap1. Rap1 regulates integrins and cadherins and promotes angiogenesis and endothelial cell barrier function. Rap 1 is not essential for vessel formation but is critical for vessel stabilization. Knockout of both Rap1a and Rap1b leads to hemorrhage and embryonic lethality. After birth, Rap1 regulates NO production and other endothelial cell functions.

Lampugnani *et al.* (pp. 256–264) consider the endothelial defects associated with cerebral cavernous malformations (CCM). Loss of function mutation in any one of three *CCM* genes affects the venous microvasculature of the central nervous system. Changes in endothelial cell barrier function are associated with CCM, linking the three *CCM* genes to the organization of endothelial cell junctions. Drugs are in various stages of development to treat CCM.

Abadier and Ley (pp. 265–273) describe the role of P-selectin glycoprotein ligand-1 (PSGL-1) in T-cell regulation. PSGL-1, a ligand for the selectins, binds lymphoid chemokines, can modulate T-cell function during viral infections. Deficiency of PSGL promotes the effector functions of CD4 and CD8 T-cell differentiation and prevents T-cell exhaustion. Tumor growth is reduced in PSGL-1 deficient mice that can be attributed to its regulation of T-cell function.

In the contribution by Schaefer *et al.* (pp. 274–281), they discuss the current state-of-the-art technology in the diagnosis of deep venous thrombosis (DVT). A modified Wells score is the most widely regarded evaluation for risk stratification of patients, and a D-dimer assay may also be useful in clinical decision making. Soluble P-selectin assay is a promising biomarker for DVT diagnosis. For imaging, ultrasound remains the primary approach in use but computed tomography, MRI or nuclear medicine approaches can be justified in certain circumstances.

Vascular biology is a diverse area. The topics covered in this collection address a few selected topics in the vascular biology arena. They have in common that the messages are delivered by world experts. I hope readers find the articles informative and interesting.

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