ATVB in Focus
Novel Mediators and Mechanisms in Angiogenesis and Vasculogenesis

Stefanie Dimmeler

This issue of Arteriosclerosis, Thrombosis, and Vascular Biology marks the beginning of a series of review articles addressing recent advances in our understanding of new blood vessel formation. The goal of this review series is to highlight novel mechanisms involved in blood vessel growth. Blood vessel growth is mediated by angiogenesis, which is defined as the new blood vessel growth out of existing vessels, as well as by vasculogenesis. In contrast to angiogenesis, vasculogenesis refers to the contribution of circulating blood–derived cells to adult neovascularization and is also implicated in embryonic vessel development. Angiogenesis and vasculogenesis are regulated by a complex network of mediators and cellular interactions. Although intensively investigated during the last decades, various novel findings have emerged.

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In the area of angiogenesis, leaders in the field will summarize the novel transcriptional integrators modulating endothelial cell responses as well as vessel maturation (Figure). Particularly, vessel maturation is critical to gain functionally intact vessels to recover blood supply after ischemia. Of equal importance is the communication of vascular cells with each other and with the extracellular matrix. Particularly, cadherins play a major role to mediate cell-to-cell communication. Proteases have initially been viewed as matrix-degrading enzymes responsible for migration and invasion activity of vascular cells. However, protease-mediated degradation of extracellular matrix proteins or surface receptors is also of major importance for the generation of angiogenesis-regulating molecules and signaling.

Finally, a review article will summarize the molecular basis for oxygen-sensing and the mechanisms regulating the response of vascular cells to hypoxia.

In addition to regulation of classic angiogenesis, further articles will provide novel information regarding the role and effect of circulating progenitor cells for new blood vessel growth. The discovery of circulating bone marrow–derived endothelial progenitor cells by Asahara and Isner in 1997 and Rafii in 1998 offered promising options to therapeutically improve blood flow. Although it is meanwhile established that the infusion of progenitor cells can enhance therapeutic neovascularization in experimental models and in several clinical pilot trials, multiple questions remain unanswered in this new field of research. The regulatory mechanisms by which progenitor cells are mobilized from their niches, the characterization of vascular progenitor cells, and the mechanisms by which the cells improve neovascularization are under intensive investigations. The basic findings and the clinical implications will be critically reviewed in articles of this series. Finally, the series is complemented by a summary of the principal mechanism by which embryonic development of blood vessels is regulated. The comparison of adult versus embryonic blood vessel growth may give us important hints not only for the better understanding but also for the implementation of novel therapeutic strategies.
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