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# Angiogenesis and Vascularisation



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Józef Dulak • Alicja Józkowicz • Agnieszka Łoboda  
Editors

# Angiogenesis and Vascularisation

Cellular and Molecular Mechanisms  
in Health and Diseases

 Springer

*Editors*

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## Preface

There is no vertebrate life without blood vessels and blood circulation. Therefore, formation of blood vessels is strictly connected with the continuous well-being of human during development and adult life, and finally, disturbed—impaired or exaggerated—angiogenesis leads to development or aggravation of disease.

Understanding the mechanisms of physiological and pathological vascularization is thus really a matter of life and death. The discoveries of the last 25 years have identified plethora of angiogenic mediators including transcription factors, growth factors, cytokines, or extracellular matrix components. Recently, numerous studies have highlighted the role of specific microRNAs in modulating angiogenic signaling. Finally, the conditions in which cells are growing, like oxidative stress, pro-inflammatory state, or hypoxic microenvironment, affect vessel formation and may influence the effectiveness of therapies used for the treatment of angiogenesis-dependent diseases.

Due to such a large area of research we, the editors and authors, are aware that the chapters presented offer only the view on some limited aspects of vascular biology. However, we do believe that this volume can fulfill its aim of presentation of the field from a little bit different perspective than some other books on similar subjects. We hope our wishes will meet the expectations of the readers.

The book is organized in three sections. Part I describes the major components of the angiogenic process with the special emphasis on understanding the significance of different populations of endothelial progenitor cells and the role of specific mediators. A discussion on the mechanisms of lymphangiogenesis is also presented in this part, together with the chapters devoted to endothelial cells and their precursors. Part II continues by discussing the molecular mechanisms of the angiogenic process, concentrating on the role of hypoxia, antioxidant genes, and microRNAs. The significance of gaseous mediators, like carbon monoxide and nitric oxide, is also discussed, presented with some broader perspectives of involvement of Nrf2/heme oxygenase-1 pathway, nitric oxide synthases, and the modulators of their activities. Accordingly, besides stimulators, like ETS transcription factors or immediate early genes, the role of some novel angiogenic inhibitors is also highlighted. Part III concentrates on the pathological aspects of vascularization process in diabetes, rheumatoid arthritis, and cancer, discussing

also some new modalities for potential therapies and presenting novel models for investigation of angiogenesis.

There is no reason to describe in detail each chapter and its content which, we hope, in total will be of interest for every reader of this book. In this preface only some aspects of the book will be highlighted. No doubt, the reader can recognize that this volume content reflects the scientific interests of book editors. The significant part is devoted to the nature and role of potential endothelial cell precursors as well as the involvement of hypoxia and gaseous mediators, like carbon monoxide and nitric oxide, in angiogenesis. The obvious links to inflammatory processes underlying the angiogenesis-related diseases, such as cancer, diabetes, and rheumatoid arthritis, are indicated. The molecular mechanisms are discussed with special emphasis on the role of microRNAs, as well as the new emerging models of angiogenesis are presented.

The authors of the chapters did not avoid to address the controversies in vascular biology. Among them are so-called endothelial progenitor cells (EPCs). Described for the first time by Asahara and coworkers in 1997, EPCs have quite dominated the field of angiogenesis translational research for several years. It appears, however, that the nature of those putative progenitors was not clearly specified and their blood-forming properties were exaggerated. Those issues are discussed in several chapters in this book, and although not claiming to be comprehensive, the presented views may help to clarify this continuous controversy. The initial hypothesis on the plasticity, heterogeneity, or both of the bone marrow cells, claimed to be able to differentiate into the endothelial cells, or even heart or brain cells, appears to be misleading. Although still of course requiring the independent confirmation, a hypothesis on the local stem or progenitor precursors in organs appears to be attractive and may be more biologically valid than widely acclaimed, but not really confirmed, presumptions on the miracle nature of bone marrow cells.

Another issue we want to highlight in this preface are microRNAs. Their involvement in regulation of gene expression in angiogenesis is broadly discussed in this book. Beside the separate chapter, Chap. 9, devoted solely to those regulatory molecules, microRNAs are also described in Chap. 8 on hypoxic regulation of gene expression, in Chap. 14 presenting the zebrafish model of angiogenesis, as well as in Chap. 17, in which the correlation between microRNAs and tumor development is shortly discussed. Also, hypoxic regulation of angiogenesis is described in Chaps. 3, 8, and 9 and is addressed from different points in many others. The significance of the lowered oxygen level for regulation of angiogenesis is being recognized both in physiological and particularly pathological conditions. It links also to the role being played by nitric oxide synthase and nitric oxide itself, as well as to antioxidant systems, such as that dependent on Nrf2 and heme oxygenase-1. The role of those obviously cytoprotective pathways is being now considered also in the context of blood vessel formation, adding more noncanonical functions to these interesting, widely interconnected systems.

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We do hope that this book can be of some help for all who would like with one volume to get a broader perspective on various aspects of blood vessel formation. The book may be, as we believe, of help for graduate and PhD students and scientists starting their research in vascular biology. We are grateful to our colleagues, coauthors of all the chapters, for their willingness and efforts to contribute to the work we present now to the scientific community.

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