

Angiogenesis, Lymphangiogenesis and Clinical Implications

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Angiogenesis, Lymphangiogenesis and Clinical Implications

Volume Editors

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*To Graziella Persico
whose life and science continue to inspire us*



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Preface

Angiogenesis, namely the formation of blood vessels, plays a fundamental role in such diverse physiological processes as embryonic and postnatal development, reproductive functions, and wound repair. It was Judah Folkman who, in 1971, first suggested that angiogenesis is a major factor also in tumor growth, and proposed that blockade of angiogenesis might represent a novel therapy for solid tumors. Since then, we have witnessed explosive progress in our understanding of the molecular mechanisms governing the growth and differentiation of new blood vessels.

A major breakthrough in this field came when Harold Dvorak and collaborators purified and named the vascular permeability factor that was later cloned and designated 'vascular endothelial growth factor' (VEGF), which is the most potent proangiogenic mediator known so far. The VEGF family is constituted by five members (VEGF-A, VEGF-B, VEGF-C and VEGF-D) and placental growth factor. Placental growth factor was identified and named by the late Graziella Persico, an extraordinary and brilliant investigator to whom this volume is dedicated. Evidence obtained in recent years indicates that the lymphatic vascular system is crucial not only in tumor growth and the formation of metastases, but also for the modulation of immune functions and fat metabolism. Although VEGF-C and VEGF-D are the key growth factors that can directly stimulate lymphatic endothelial cells, the other growth factors have also been implicated in lymphangiogenesis.

Notwithstanding the concept that both angiogenesis and lymphangiogenesis are essential for tumor growth, there is increasing evidence that the two aspects play an important role in an increasing number of immune disorders and metabolic diseases. Another important issue is the observation that although tumors are a major source of angiogenic/lymphangiogenic factors, several cells of the innate and adaptive immune system can produce a distinct set of these factors. Moreover, it has been shown that several angiogenic/lymphangiogenic factors can exert a variety of proinflammatory effects by engaging VEGF receptors and angiopoietin receptors (Tie1 and Tie2) present on immune cells.

Given the rapid advances made in this field, it is difficult to produce a timely reference text and a comprehensive overview of the field. Despite these difficulties, I accepted the invitation of the editors of the *Chemical Immunology* series to produce a

volume entitled 'Angiogenesis, Lymphangiogenesis and Clinical Implications'. This work was designed to highlight some of the results obtained mainly with human immune cells as a source and target of angiogenic and lymphangiogenic factors. The clinical part of the volume deals with some of the disorders in which treatment with antiangiogenic molecules appears to be promising.

It is already obvious that several issues remain to be solved in this area. The spectrum of angiogenic and lymphangiogenic factors produced by the different components of the human innate and adaptive immune system is still largely unknown. Similarly, the specific and selective distribution of receptors and coreceptors for the different angiogenic and lymphangiogenic molecules on immune cells is incomplete. Moreover, it is becoming evident that there are striking differences in the mediators and their receptors between human and rodent immune cells. Although angiogenesis and lymphangiogenesis are important in tissue remodeling in certain chronic inflammatory disorders (e.g. bronchial asthma, rheumatoid arthritis, psoriasis), it is still unknown whether alterations of angiogenesis and lymphangiogenesis could be a target in these disorders.

Many contributors to this volume are working or have worked in Italian research centers. This probably reflects the fact that thanks to Graziella Persico, many of her friends and pupils found the various aspects of angiogenesis and lymphangiogenesis a fertile field of study.

I would like to thank Karger Publishers and their staff for their assistance throughout the production of this volume. This volume owes much to the stimulating intellectual environment provided by our collaborators at the Division of Clinical Immunology and the Center for Basic and Clinical and Immunology Research (CISI) of the University of Naples 'Federico II'.

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