Angiogenesis, Lymphangiogenesis and Clinical Implications
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Volume Editors

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26 figures, 14 in color and 8 tables, 2014
Chemical Immunology and Allergy
Formerly published as 'Progress in Allergy' (Founded 1939),
continued 1990–2002 as 'Chemical Immunology'

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

XI  Preface
    Marone, G.; Granata, F. (Naples)

1  History of Research on Angiogenesis
    Ribatti, D. (Bari)

   1 Abstract
   2 First Isolation of an Endothelial Cell
   2 Development of in vivo Assays for the Study of Angiogenesis
   4 Isolation of Basic Fibroblast Growth Factor
   4 Isolation of Vascular Permeability Factor/Vascular Endothelial Growth Factor
   5 Isolation of Placental Growth Factor
   5 Early Evidence of Tumor Cells Releasing Specific Growth Factor for Blood Vessels
   6 Absence of Angiogenesis in Tumors in Isolated Perfused Organs and First Evidence of the Existence
      of the Avascular and Vascular Phases in Solid Tumor Growth
   7 First Formulation of the Hypothesis that Tumor Growth Is Angiogenesis Dependent and Isolation
      of the First Tumor Angiogenic Factor
   7 Prognostic Significance of Tumor Vascularity
   8 Antiangiogenesis
   13 References

15  Immune Cells as a Source and Target of Angiogenic and Lymphangiogenic Factors
    Loffredo, S.; Staiano, R.I.; Granata, F.; Genovese, A.; Marone, G. (Naples)

   15 Abstract
   17 Expression of VEGFs and Their VEGFRs in Mast Cells
   19 Expression of VEGFs, Their VEGFRs and NRPs in Human Basophils
   20 Expression of VEGFs and VEGFRs in Monocytes, Macrophages and Dendritic Cells
   20 Monocytes
   20 Macrophages
   21 Angiogenic Activity of Macrophages
   23 Antiangiogenic Activity of Macrophages
   23 Lymphangiogenic Activity of Macrophages
   24 Dendritic Cells
   24 Expression of NRPs in Regulatory T Cells
   25 Expression of Angiopoietins in Immune Cells
   25 Mast Cells and Basophils
   26 Eosinophils
   26 Neutrophils
   26 Macrophages
   27 Direct and Indirect Angiogenic Activity of IL-17
Neuropilins: Role in Signalling, Angiogenesis and Disease
Zachary, I. (London)

37 Abstract
38 Neuropilin Structure
40 Neuropilin Ligands
40 Semaphorins
40 VEGFs
42 NRP Genomic Organisation and Isoforms
45 Neuropilin Function in Development
48 Receptors and Signalling Mechanisms
48 Plexins
49 L1 CAM
50 VEGF Signalling
52 Role of the NRP Cytosolic Domain
54 NRP Regulation of Cell Migration
55 Other Cell Functions
56 Neuropilin Functions in Disease and Adult Tissues
56 Cancer
58 Immune System
59 Wound Healing
60 Liver Cirrhosis
60 Other Functions
60 Conclusions and Perspectives
61 Acknowledgements
62 References

Class 3 Semaphorin in Angiogenesis and Lymphangiogenesis
Bussolino, F. (Candiolo); Giraudo, E. (Candiolo/Torino); Serini, G. (Candiolo)

71 Abstract
72 Semaphorins and Their Receptors
75 Class 3 Semaphorin
76 Semaphorins Control Vascular Development
77 Semaphorins and Lymphatic Development
78 Semaphorins and Tumor Angiogenesis
81 Semaphorins in Revascularization of Ischemic Tissues
82 Conclusion
83 Note Added in Proof
83 Acknowledgements
83 References

Angiogenic and Antiangiogenic Chemokines
Bosisio, D.; Salvi, V.; Gagliostro, V. (Brescia); Sozzani, S. (Brescia/Rozzano)

89 Abstract
89 Chemokine System
92 Cell Activation by Chemokine Receptors
93 Chemokines in Angiogenesis
96 Chemokines in Tumor Angiogenesis
96 Tumor-Associated Leukocytes and Angiogenesis
98 Direct Induction of Angiogenesis by Tumor Cells
207 Miscellaneous Agents
207  JS91
207  TRC105
208  Itraconazole
208  Sodium Selenate
209  Cilengitide
209  TNP-470
209  Conclusion
211 References

216 Therapeutic Perspectives in Vascular Remodeling in Asthma and Chronic Obstructive Pulmonary Disease
Olivieri, D.; Chetta, A. (Parma)

216 Abstract
216 Vascular Remodeling in Asthma
219 Vascular Remodeling in Chronic Obstructive Pulmonary Disease
220 Effects on Vascular Remodeling of the Currently Used Drugs in Asthma and Chronic Obstructive Pulmonary Disease
222 Potential Therapeutic Implications of Bronchial Vascular Remodeling
223 Conclusions
223 References

226 Author Index
227 Subject Index
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 Immunology Research (CISI) of the University of Naples ‘Federico II’.

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