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# A Brief History of Blood and Lymphatic Vessels

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Andreas Bikfalvi

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 Springer

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## Foreword

The vascular tree irrigates all tissues throughout the body, provides oxygenation and nutrient supply, and eliminates waste products. It is a system of considerable size and of paramount importance because, without a vascular connection, tissue dies. In humans, more than 80 diseases are linked to dysfunction of the vascular system. Understanding how the vascular tree is formed is therefore a major issue in medical research.

This book provides a historical view of important discoveries in angiogenesis research, information about current studies, and a discussion of still unresolved issues. It also contains a section of more conceptual and philosophical aspects related to the field. It is important that a recognized scientist actively working in this field write a synthesis on this topic.

In this book, Andreas Bikfalvi faced a triple challenge: To write a book that is interesting and readable for both the specialist and the general public, to describe original and new observations on the subject especially related to the history of different discoveries, and to discuss the more general aspects and conceptual issues of this research field. He has met this challenge admirably.

The book is indeed easy to read, is well illustrated, and deals with fundamental and translational aspects of vascular biology related to vascular development. It should therefore be of interest not only to biologists or medical students, but also to scientists active in this field as well as anyone interested in biology and medicine and in the history of science. It was a great pleasure to read it.

This book was published in 2016 in French, and it is now very timely that Springer Verlag publishes this English version to make it accessible to a wider audience.

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## Preface

This book deals with blood and lymphatic vessels. Blood vessels are made of tubes of different calibers conducting the blood to the tissues and from tissues to the heart. Blood vessels are not inert ducts but are formed during embryonic development and endowed with plasticity during adult life. The formation of new vessels received the scientific term “angiogenesis” derived from ancient Greek angeon (αγγειον) and genesis (γενεσις).

If it was accepted that angiogenesis plays a role in embryonic development, its role in the development of different diseases was controversial. In this regard, the hostility of the scientific establishment toward the concept of tumor angiogenesis is revealing. In the 1980s, research on the cell cycle and oncogenes (tumor transformation-inducing genes) were dominant, and angiogenesis observed in tumors was considered a non-specific inflammatory reaction. At these times, any attempt at research on tumor angiogenesis was denigrated or even ridiculed, and it was difficult to obtain funding. Thanks to the tenacity of a man, Judah Folkman, considered the founding father of angiogenesis, the scientific establishment gradually changed its opinion and people hostile to the field became fervent defenders and even embraced the subject.

The idea of this book came to me in January 2008, when Judah Folkman was meant to attend a Keystone meeting in Denver, Colorado. We learned of his sudden death at Denver airport. This was a considerable shock for all researchers working in the field. For decades, Judah Folkman had given constant input and made angiogenesis emerge from the dark to become one of the flagship areas of biomedical research. I still remember very well the effects the reading of some of his work had on me. In particular, when I read one of his articles in the prestigious journal *Science* in 1984 on the effect of angiogenesis inhibitors, I was soon convinced that I must do angiogenesis research. The call was so strong that I abandoned my residency in hematology-oncology that I was doing in Germany at that time to come to Paris to work on angiogenesis.

The path taken following the initial work of Judah Folkman is considerable. Key factors and inhibitors of angiogenesis have been identified together with their mechanisms of action. Different mechanisms of angiogenesis have been defined and the cellular interactions that are involved in this process have been clarified. Inhibition of angiogenesis has been clearly validated clinically in cancer and in

ocular and inflammatory diseases, and angiogenesis inhibitors have emerged in clinical use.

In Europe, a community of angiogenesis researchers has emerged, competing with laboratories across the Atlantic. Very fruitful collaborations have been established across Europe and conferences such as those we have organized with the European School of Hematology for over 10 years across Europe testify to this.

In France, we have set up a French Network of Angiogenesis, which has since 2008 become a society (the French Angiogenesis Society) and which brings together the main laboratories working in this field in France.

I would like to dedicate this book to my father Andras Bikfalvi Sr, a surgeon at the University of Giessen in Germany, who, apart from his profession as a thoracic surgeon, had a strong interest in research, especially in experimental surgery. He would certainly have liked to read my writings. I also dedicate the book to my children Alexis and Marianne, who are both physician and teacher. This book is a reflection of their respective interests. Finally, I would like to dedicate this book to our friend and colleague Jean Plouet, who died in 2010. Jean was a research director at CNRS and co-discovered with Napoleone Ferrara the growth factor of the vascular endothelium (VEGF, a major factor in angiogenesis) during his stay in the laboratory of Dr. Denis Gospodarowcz in San Francisco [1]. Jean was one of the co-founders of our French Angiogenesis Network. He had a very original and unconventional mind, which did not fit very well with the French academic system.

The story that is told in this book is closely related to my personal history with angiogenesis. Indeed, I have been a witness of and actor in most of the events described in this book alongside my cited colleagues, some of whom are my friends.

If I have not been able to cite all the significant works, it is not for any other reason than to keep a coherent narrative. My colleagues can forgive me surely. I wanted to avoid a too “academic” narrative and to remain comprehensible to a wide audience. I hope that this book, beyond the accessibility that I hope to offer, is of interest both to those who are versed in biology and medicine and to those who have no in-depth knowledge of the subject. For those who would like to go deeper into the subject, references that seemed to me essential are indicated at the end of the book.

This book is also, I think, a good introduction to vascular biology and angiogenesis for all those who want to start and pursue their research in these fields, and it is especially aimed at young students and post-doctoral scientists.

It should be noted that in this book I have focused primarily on blood vessel development and its role in physiology and pathology. I have not dealt with other important aspects, such as atherosclerosis and hypertension. I leave it to the experts in these fields to answer your questions.

This book was published in 2016 in French and my publisher (EDP Science) allowed me to proceed with an English version that is now published by Springer Verlag. The English version follows the structure of the French version, albeit several parts have been revised and updated. I published an article with regard to the conceptual analysis in the journal *Angiogenesis* (History and conceptual developments in vascular biology and angiogenesis research: a personal view.

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Angiogenesis (2017) Nov 20(4):463–478) in 2017. Elements of this article have been incorporated in the last part (see Chapter 17 “Philosophy of the Vascular Tree”) of this book.

I invite you to take an exciting journey through the history and the most current concepts concerning the research on the blood and lymphatic vessels. It probably did not escape you that the title of my book resembles the famous little book of Stephen Hawkins “A brief history of time”. If I can touch you with my writings in the same way as this book by communicating my enthusiasm and awakening your curiosity, I have reached my goal.

Pessac, France  
December 8, 2017

Andreas Bikfalvi

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# Contents

<b>1</b>	<b>The Vascular System: What Is It?</b> . . . . .	<b>1</b>
<b>2</b>	<b>History of the Vascular System</b> . . . . .	<b>5</b>
<b>3</b>	<b>Evolution of the Vascular System</b> . . . . .	<b>35</b>
<b>4</b>	<b>Where It All Began</b> . . . . .	<b>43</b>
<b>5</b>	<b>Culture of Vascular Cells In Vitro</b> . . . . .	<b>49</b>
<b>6</b>	<b>Discovery of the First Stimulating Factors of Blood Vessels</b> . . . . .	<b>53</b>
<b>7</b>	<b>Vascular Endothelial Growth Factor: The Cornerstone of Vascular Development Factors</b> . . . . .	<b>57</b>
<b>8</b>	<b>Inhibition of Angiogenesis, “Disappointments and Success”</b> . . . . .	<b>61</b>
<b>9</b>	<b>Stimulating Angiogenesis</b> . . . . .	<b>65</b>
<b>10</b>	<b>The Situation Is More Complex Than Anticipated</b> . . . . .	<b>67</b>
10.1	TIP Cells . . . . .	67
10.2	Formation of Vascular Lumen . . . . .	70
10.3	Formation of Lymphatic and Venous Valves . . . . .	72
10.4	Vascular Permeability . . . . .	73
10.5	Other Cellular Factors and Interactions . . . . .	74
10.5.1	VEGF-C . . . . .	74
10.5.2	PLGF . . . . .	75
10.5.3	Angiopoietins . . . . .	75
10.5.4	The Return of the FGFs . . . . .	76
10.5.5	Role of Pericytes and Platelet-Derived Growth Factors (PDGF) . . . . .	77
10.5.6	Microglial Cells . . . . .	79
10.6	Angiogenic Switch . . . . .	80
10.7	Signaling Induced by Angiogenic Factors . . . . .	81



10.8	Metabolism and Angiogenesis . . . . .	84
10.9	Endothelial Cell-Derived Factors Have Perfusion-Independent Effects on Organs . . . . .	85
10.10	Paradigm Revisited . . . . .	86
<b>11</b>	<b>How to Study Angiogenesis?</b> . . . . .	<b>91</b>
<b>12</b>	<b>What About the Clinic?</b> . . . . .	<b>99</b>
<b>13</b>	<b>Lymphangiogenesis Enters the Dance</b> . . . . .	<b>107</b>
<b>14</b>	<b>What About Stem Cells?</b> . . . . .	<b>111</b>
<b>15</b>	<b>The Neuronal Connection</b> . . . . .	<b>115</b>
15.1	Neuronal Factors as Angiogenic Factors . . . . .	116
15.2	Angiogenic Factors as Neuronal Factors . . . . .	117
15.3	Innervation of Blood Vessels . . . . .	117
15.4	Vascularization of Peripheral Nerves . . . . .	117
<b>16</b>	<b>What Future for Angiogenesis?</b> . . . . .	<b>119</b>
16.1	Molecular Characterization of Vascular Heterogeneity for the Identification of New Molecular Markers . . . . .	119
16.2	Inhibition of Angiogenesis . . . . .	120
16.3	Stimulation of Angiogenesis in the Context of Therapeutic Angiogenesis . . . . .	121
16.4	Lymphangiogenesis . . . . .	122
16.5	Biomarkers and Angiogenesis . . . . .	123
16.6	MicroRNAs and Long Non-coding RNAs . . . . .	125
<b>17</b>	<b>Philosophy of the Vascular Tree</b> . . . . .	<b>129</b>
17.1	Changing Paradigms . . . . .	129
17.2	Angiogenic Factors in Question . . . . .	133
17.3	Conceptual Categories Shaping Vascular Development Research . . . . .	134
17.4	Interactions Between Different Scientific Fields ("Cross-Fertilization of Fields") . . . . .	136
17.4.1	Vasculature, the Central Ingredient of the Integrated Ecosystem in Tumors . . . . .	136
17.4.2	Angiogenic Factors Have Extravascular Properties and Vice-Versa . . . . .	137
17.5	Technological Advances and Impact on Vascular Biology . . . . .	138
17.6	Evolutionary Considerations and Principles . . . . .	139
17.7	Model Organisms and Angiogenesis . . . . .	141
17.8	Scientific Methodology in Vascular Biology . . . . .	142
17.9	Summary and Concluding Remarks on Conceptual Issues . . . . .	145
<b>18</b>	<b>General Conclusion</b> . . . . .	<b>149</b>

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<b>Erratum to: Evolution of the Vascular System . . . . .</b>	<b>E1</b>
<b>Acknowledgements . . . . .</b>	<b>151</b>
<b>Appendix: Explanatory Note of Concepts and Technical Terms Used in the Book . . . . .</b>	<b>153</b>
<b>References . . . . .</b>	<b>167</b>
<b>Index . . . . .</b>	<b>187</b>