Book review

Angiogenesis: from basic science to clinical applications

Edited by Napoleone Ferrara, Taylor & Francis, Oxford
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Thirty-five years ago Judah Folkman put forward the idea that preventing blood vessel growth would stop tumour progression. It has taken the combined efforts of numerous researchers and countless hours spanning three decades, to finally see this come to fruition in the clinic. This book aims to present the latest basic research that both supports and drives the recent clinical advances. Although by its nature this text will date rapidly, it fulfils the important function of putting our knowledge of the basic biology in the context of therapeutic applications. This book also offers a good resource to dip into for specific information about a particular angiogenic pathway, as well as to offer ideas for where the future clinical therapies may be.

Much of the book focuses on VEGF, its receptors and their roles in angiogenesis, which reflects both the pivotal role played by VEGF throughout the angiogenic process and the wealth of biological data that have accumulated. Parts of the book dovetail excellently, describing the biology of VEGF and picking a careful route through the complexities of its signalling pathways. A useful approach taken by Shibuya is to dissect out the signalling pathways utilised by the different angiogenic activities of VEGF, although interestingly those involved in differentiation are not described—perhaps a reflection of our lack of understanding of this particular function.

One drawback of focussing on current research is that the contributions are at times too technical, which together with the often illogical naming of many of the factors and signalling pathways involved, can be off-putting to those outside the immediate field. However, the discussion of factors that play important, but less well known, roles in vascular development is refreshing. These include factors that have been identified and characterised on the basis of their roles in non-angiogenic systems such as neuronal guidance or embryonic development. That these molecules also play a role in angiogenesis serves to highlight the complexity of angiogenic regulation as well as the multiple roles that factors play in outwardly unrelated systems.

While having a central role in angiogenesis, as with other angiogenic factors, VEGF also has a range of non-angiogenic activities. Although not directly relevant to a book pertaining to angiogenesis and its therapeutic potential, this chapter serves to highlight the care that needs to be taken when targeting vascular growth. By blocking the action of VEGF, several other normal activities are also disrupted, which may play a significant part in unwanted side effects or drug intolerance. This leads to further supposition that targeting less potent angiogenic molecules may lead to more effective and better-tolerated treatments.

Many of the contributions in this book are timely. For example, our understanding of lymphangiogenesis has lagged behind that of angiogenesis due mainly to a lack of molecular markers specific for lymphatic vessels. The recent emergence of markers that are suitable for distinguishing lymphatic and vascular endothelial cells will lead to an increased interest in the therapeutic potential of this system. Another example is the contribution of

haematopoietic precursors to neovascularisation. This is a rapidly developing field, again fuelled by the development of better selection markers with which these cells can be isolated and characterised. The therapeutic potential of this system is not described in detail, and as in other areas of the book, more descriptive figures would be beneficial for the less informed reader.

In contrast to anti-angiogenic therapies, the use of pro-angiogenic therapy is also discussed. In the context of coronary heart disease, some of the key pro-angiogenic clinical trials are presented alongside a discussion as to why they may have failed. This highlights an important point: although our increased understanding of the pro-angiogenic process has led to many potential therapies, none have yet progressed to the clinic, suggesting that we do not yet understand all the issues sufficiently to circumvent the problems.

Throughout the book there is a focus that sometimes narrows the perspective too far. While it is difficult to cover the complexity and the wide range of factors that influence angiogenesis, factors such as FGF and PDGF are so fundamental that their omission is surprising. The book loses coherence in places, with repetition between several of the chapters (which is inevitable with the wide range of contributors), inconsistent referencing between the chapters and fuzzy arrangement of topics. However, what this book effectively conveys is the wide range of conditions that are potentially treatable through VEGF-based therapy. Extending this further to encompass other potentially exploitable angiogenic factors, and both pro- and anti-angiogenic strategies could become central to the treatment of numerous diseases.

Avastin™, the single biggest breakthrough in antiangiogenic therapy in the clinic today, is based on an anti-VEGF monoclonal antibody, bevacizumab, developed by Genentech. The description of its route through the preclinical and phase I–III clinical trials is an interesting read for those outside this area and brings an appreciation as to why so many drugs fail at these points. The contribution by Kerbel, describing the chemosensitising effect of antiangiogenic therapy and explaining why the combination of Avastin™ and chemotherapy is more effective in colorectal cancer, is the highlight of the book.

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