Tumor Angiogenesis and Microcirculation

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Tumor Angiogenesis and Microcirculation, edited by Emile E. Voest and Patricia A. D'Amore. New York: Marcel Dekker, 2001; 623 pages.

In the last decade, we have made great progress in our understanding of normal and pathological angiogenesis, unveiling the significant role of tumor-induced neovascularization in the growth of various human cancers, including hematologic malignancies. This understanding opens a novel paradigm for anticancer therapy that targets the processes that are essential for the formation and maintenance of tumor-associated blood vessels. Recently, a number of angiogenesis inhibitors became available for clinical trials, and some of these agents are beginning to show their efficacy against tumors that have been highly resistant to conventional therapy. Therefore, the mechanism by which antiangiogenesis therapy prevents tumor progression is of increasing interest to clinicians as well as to basic scientists.

This excellent book, with contributions from more than 60 top-notch investigators, covers most of the latest achievements in vascular biology with special reference to its clinical application to antiangiogenic tumor therapy. Each chapter is independently written in a mini-review style, and there is no doubt that readers will be satisfied with its colorful and harmonious presentation, including a number of informative figures. The book is divided into 6 parts. The first 3 parts are the introductory sections, which include comprehensive cellular and molecular biology of the angiogenic process. Microanatomy of normal and tumor vasculature, angiogenesis-associated extracellular-matrix remodeling by matrixins/plasmins and their inhibitors, and the regulation of endothelial cell migration in the process of neovascular formation are main subjects of the first section. In the second section, technical chapters are carefully written in a manner avoiding overqualified descriptions so that readers can easily grasp the principles and limitations of angiogenesis assays. In the third section, which deals with molecular aspects of angiogenic factors and their receptors, 2 central regulators for blood vessel formation, vascular endothelial growth factor (VEGF)/VEGF receptor and Ang ligands/Tie receptor

systems, are described in detail regarding their roles in physiological and tumor-associated microcirculation. In addition, the putative functions of fibroblast growth factors and other proangiogenic cytokines are discussed.

In the latter half of the book, the authors attempt to depict an integrated perspective for designing and evaluating antiangiogenic tumor therapy. Before proceeding to the clinical section, a general scheme of complex and interdependent events involved in tumor-associated vessel formation is presented from the viewpoints of tumor genetics and surroundings. According to this model, either activation of oncogenes or inactivation of tumor-suppressor genes defines the angiogenic tumor phenotype, and host microenvironment and tumor-associated macrophages contribute to the positive and negative regulations of neovascularization. The next focus is the recent clinical development of endogenous or synthetic angiogenesis inhibitors, with an overview of early clinical trials. The inhibitors listed are matrix-protein fragments, such as endostatin, matrix metalloproteinase inhibitors, integrin antagonists, and inhibitors for angiogenic cytokines and their receptors. In the final section, the future prospects of antiangiogenic therapy are discussed, in the hope of its evolution into "vascular cancer therapy," which includes in vivo modulation of endothelial cell function and the adoptive transfer of endothelial cells engineered to exert specific antitumor effects.

After reading through this omnibus text, readers are assured that an area of vascular oncology has given rise to one of the most crowded crossroads, where clinical researchers and basic scientists closely communicate with each other. Tumor vascularization is indeed becoming a topic of cellular immunotherapy, because recent evidence has suggested that CD4⁺-T-cell-mediated tumor rejection also involves inhibition of angiogenesis. It has been 30 years since Dr. Folkman prophesied that tumor growth is angiogenesis dependent. In an emerging new era of translational medical research, the progress in antitumor therapy may be dependent on the understanding of tumor angiogenesis.