

# ANTIANGIOGENIC AGENTS IN CANCER THERAPY

# CANCER DRUG DISCOVERY AND DEVELOPMENT

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# ANTIANGIOGENIC AGENTS IN CANCER THERAPY

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Edited by

**BEVERLY A. TEICHER**

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*For the beautiful ones  
Emily and Joseph*

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Originally published by Humana Press Inc. in 1999

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Cover illustration: From Fig. 1 in Chapter 14, "Discovery of TNP-470 and Other Angiogenesis Inhibitors," by Donald E. Ingber, in *Cancer Therapeutics: Experimental and Clinical Agents*, Edited by Beverly A. Teicher, Humana Press, 1997.

Cover design by Patricia F. Cleary.

This publication is printed on acid-free paper.   
ANSI Z39.48-1984 (American National Standards Institute) Permanence of Paper for Printed Library Materials.

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The fee code for users of the Transactional Reporting Service is: [0-89603-641-3/98 \$8.00 + \$00.25].

Library of Congress Cataloging-in-Publication Data

Antiangiogenic agents in cancer therapy/edited by Beverly A. Teicher.

p. cm.—(Cancer drug discovery and development)

Includes index.

ISBN 978-1-4757-4518-4 ISBN 978-1-59259-453-5 (eBook)

DOI 10.1007/978-1-59259-453-5

1. Neovascularization inhibitors. 2. Cancer—Chemotherapy. I. Teicher, Beverly A., 1952–. II. Series.  
[DNLM: 1. Neoplasms—drug therapy. 2. Neovascularization, Pathologic—drug therapy. 3. Antineoplastic Agents—therapeutic use. QZ 267 A628 1999]

RC271.N46A58 1999

616.99'4061—dc21

DNLM/DLC

for Library of Congress

98-45812  
CIP

# PREFACE

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The importance of normal cells and tissues to support the growth of tumors has been recognized for centuries. The observations of Van der Kolk (1), Jones (2), and Paget (3) more than 100 years ago documented this knowledge in the clinical science literature. Fifty years ago, Algire and Chalkey (4) reported that host vascular reactions could be elicited by growing tumors and described in exquisite detail the extent and tumor-specific nature of the induction of host capillaries by transplanted tumors. The central hypothesis of Algire and Chalkey was that vascular induction by solid tumors may be the major, and possibly, the only distinguishing factor leading to tumor growth beyond normal tissue control levels. By the late 1960s, Folkman and his colleagues (5–7) had begun the search for a tumor angiogenesis factor (TAF) and in 1971 in his landmark report in the *New England Journal of Medicine*, Folkman proposed “antiangiogenesis” as a means of holding tumors in a nonvascularized dormant state (8).

Over the nearly 40 years since publication of that landmark paper, great strides have been made in understanding angiogenesis, blood flow, and tumor growth. Several angiogenic signaling molecules and angiogenic factors have been identified. Antiangiogenic agents from a wide variety of chemical classes, including steroids, polyanionic molecules, antibiotics, small molecule nutrients, synthetic small molecules, proteins, nucleic acid molecules (ribozymes and antisense DNA), and gene therapy agents have been identified. The significance of angiogenic activity as an important prognostic factor in many of the common solid tumors, and even in leukemia, is becoming more widely recognized.

Early clinical trials of antiangiogenic agents in cancer patients have been successful in that the toxicities observed with many of these new drugs have been mild. However, these early clinical trials have also highlighted the need to develop criteria by which to assess the clinical efficacy of these new agents. Finally, preclinical and early clinical studies have begun to incorporate antiangiogenic agents into combined modality regimens that are potentially curative.

*Antiangiogenic Agents in Cancer Therapy* describes our state of understanding of tumor growth and its dependence on vascular development as well as the present status of antiangiogenic agents on preclinical and clinical development and what is known about the mechanisms by which these molecules and treatment agents interfere with tumor vascular growth.

We are entering a potentially very exciting period in anticancer agent discovery where the therapeutic focus is expanding to include not only agents cytotoxic toward malignant cells, but agents that may be growth controlling, growth inhibitory, or activating or deactivating toward stromal cells or malignant cells, as well as agents that may alter signaling cascades from one cell type to another. At this important time in the development of cancer treatment, this volume takes stock

of what has been accomplished in the area of angiogenesis, where the experimental therapeutics of antiangiogenic agents is going, and the continuing evolution of the means and methods of cancer treatment and new drug development.

*Beverly A. Teicher*

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