Methods in ENZYMOLOGY

Volume 445

Angiogenesis: *In Vivo* Systems, Part B

Edited by

David A. Cheresh

VOLUME FOUR HUNDRED AND FORTY-FIVE

METHODS IN ENZYMOLOGY

Angiogenesis: *In Vivo* Systems, Part B

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Angiogenesis: *In Vivo* Systems, Part B

EDITED BY

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ISBN-13: 978-0-12-374314-5

PRINTED IN THE UNITED STATES OF AMERICA
08 09 10 11 9 8 7 6 5 4 3 2 1

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Preface

A Tribute to Dr. Judah Folkman

The field of angiogenesis has recently lost its pioneer and leader, Dr. Judah Folkman. This was a tremendous loss to many of us who knew him and to the field in general. Dr. Folkman inspired a generation of scientists in efforts to translate basic discoveries toward new therapeutics for a wide range of diseases including cancer, blinding eye disease, and inflammatory disease. Due in large part to Dr. Folkman's efforts and direction, we now have the first generation of therapeutics that disrupt angiogenesis in patients suffering from cancer and macular degeneration. While Dr. Folkman clearly passed away before his time, he did live long enough to observe that many thousands of patients are now better off due to antiangiogenic therapy.

I had a rather interesting initiation to the field of antiangiogenesis that was wholly inspired by Dr. Folkman. In the mid-1980s as a junior faculty at the Scripps Research Institute, I was studying what many of us in the field were beginning to appreciate were a family of cell adhesion receptors, later termed "integrins." I had developed a monoclonal antibody (LM609) to the vitronectin receptor later referred to as integrin $\alpha v \beta 3$. During the course of my work, LM609 was used to stain a variety of diseased and normal tissues. To my surprise, LM609 reacted strongly with blood vessels in tumors and inflammatory sites, but failed to react with blood vessels in normal tissues. After seeing this result, I began to read up on the emerging field of angiogenesis research. It was clear that most of the literature in the field came from Dr. Folkman or one of his disciples. I immediately contacted Dr. Folkman. By the time I finished describing our results, I realized that he was excited as I was about our studies. In fact, before I could ask him any questions, he suggested that I visit his lab to learn the chick chorioallantoic membrane (CAM) assay to determine whether LM609 might have an impact on angiogenesis in a quantitative animal model.

Naturally I arranged a trip to the Folkman lab within the next couple of weeks. I had never been to Harvard, and was a bit intimidated by the place. I introduced myself to his administrative assistant, who welcomed me and indicated that Dr. Folkman was expecting me. Within minutes, Dr. Folkman, clad in a lab coat greeted me and suggested that we get started. At this point, I assumed he was going to introduce me to one of his students or technicians who would then proceed to show me the CAM assay step by step. To my surprise, Dr. Folkman led me to a hood, sat down,

and immediately started to instruct me in how to induce angiogenesis on the CAM. In fact, the next thing I knew, I was sitting at the hood next to Dr. Folkman going through the procedure in detail. Therefore, I can say I learned the technique from the master. Ultimately, Dr. Folkman introduced me to several members of the Folkman lab, including Drs. Donald Inber, Pat D'Amore, and Mike Klagsburn. I remember how enthusiastic and communicative all of these folks were. In fact, I am happy to say that I still maintain close contact with them and have had many opportunities over the years to discuss science and reminisce about the past. In fact, Don, Pat, and Mike have all kindly contributed chapters to *Methods in Enzymology* volumes on angiogenesis.

While on the airline flight home from the Folkman lab, I began to realize that my career was about to take a change in course. From that point forward, I began to focus on the role of adhesion receptors in angiogenesis and began to realize that blocking angiogenesis with integrin antagonists could have a very impressive impact on the growth of tumors in mice. Importantly, two of the agents we developed, including humanized LM609, have shown clinical activity in patients with late-stage cancer.

Since my initiation to the field, I have since followed Dr. Folkman's work and have attended dozens of his lectures. Listening to a Folkman lecture is like watching one of your favorite movies—you can watch it over and over again and still find something interesting to think about. It was difficult for anyone to attend his lecture and not come away excited about science in general and angiogenesis in particular. The field of angiogenesis has matured over the past 25 years due in large part to Dr. Folkman's drive, enthusiasm, perseverance, and kindness. Dr. Folkman's leadership has helped to recruit many scientists and physicians from the academic and private sectors to focus on new approaches to develop angiogenesis inhibitors.

In the early days, there were a limited number of technological approaches to measure and study angiogenesis. The CAM assay was among the first quantitative approaches to measure the growth of newly forming blood vessels. From this humble beginning, the field has exploded and as a result we now have a wide range of techniques, approaches, and animal models designed to monitor and study the growth of new blood vessels in development, tissue remodeling, and disease. These methods are described in detail in this volume by many of the current leaders of the field.

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