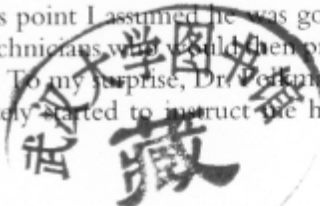


PREFACE: A TRIBUTE TO DR. JUDAH FOLKMAN

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 the field in general. Dr. Folkman inspired a generation of scientists lead an effort to translate basic discovery 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 who are now better off due to anti-angiogenic therapy.

I had a rather interesting initiation to the field of anti-angiogenesis that was completely 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 I come to his lab to learn the chick chorioallantoic member (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. As I took the elevator up to the Folkman lab and 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 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 lead me to a hood, sat down and immediately started to instruct me how to



induce angiogenesis on the CAM. In fact, the next 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 interactive each of these folks were. In fact, I am happy to say that I still maintain close contact with these individuals and have had many opportunities over the years to discuss science and reminisce about the past. In fact, Don, Pat and have all kindly contributed chapters to *Methods in Enzymology* volumes on Angiogenesis.

It was on my airplane ride home that I began to realize my career was about to make 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 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 inhibitors of angiogenesis.

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.

David A. Cheresh