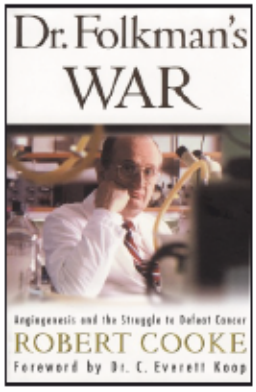
Dr. Folkman's War: Angiogenesis and the Struggle to Defeat Cancer

By Robert Cooke

Random House, 365 pp, $25.95
ISBN: 0375502440, 2001

REVIEWED BY ROBERT BUCKMAN
University of Toronto
Toronto, Ontario, Canada

The life and work of Judah Folkman make a fascinating story. There is an old saying to the effect that truth is like daylight shining behind a curtain which has many pinholes—how much you see doesn't depend on which hole you decide to look through, but on how close to the curtain you get your eye. Judah Folkman, in a research career spanning the last three decades, has clearly got very close to the curtain indeed. Extraordinarily, he arrived in cancer research after starting in a totally different area. The research that eventually moved towards angiogenesis actually began as a project investigating the damage sustained by erythrocytes as they circulated through a prototype heart-lung machine. This was perhaps a rather unpromising pinhole to start peering through, but this book meticulously chronicles and clearly explains every step from that project, to his current research which has far-reaching implications for the way cancers are treated. Folkman wanted to find out why natural blood vessels caused less damage than metal tubes, and to do that he needed a way of looking at blood vessels. That got him interested in what makes blood vessels grow and what stops them from growing, and by that time—from what we learn of his personality—his attention was fully engaged.



At times the story reads almost like science fiction, being somewhat reminiscent of Kurt Vonnegut's creation Felix Hoenikker: the physicist who invents "ice-9" (a form of ice that is solid at room temperature) because he wants to help soldiers walk through mud, and freezing the mud seems a good solution. Folkman was clearly capable of that type of thinking and he showed, even early in his career, a rare ability to back up his thoughts and ideas with the dogged persistence to put in the hours, months and years to get a reliable answer.

Folkman's research into the mechanisms involved in tumor-induced angiogenesis has changed many fundamental aspects of the way we think about tumor growth, and ways in which that growth might be controlled. Perhaps it was inevitable that his ideas, running counter to orthodox thinking, should at first have been dismissed. But history has changed prevailing attitudes. Folkman's work has in many respects now filled the breach created by the failure of high-dose chemotherapy (with autologous marrow or stem-cell support) to cure most common solid tumors. During the 1980s and most of the 1990s when eradication of every last tumor stem-cell seemed the only way to prolong patient survival, it was not surprising that so few people were genuinely interested in tumor vasculature. Now that 'more-is-better' is no longer inviolable dogma, the world is turning its attention to Folkman's suggestion that tumor vasculature might be a far more suitable target for therapy, which might need to be administered virtually continuously rather than as periodic and sometimes highly toxic doses.

What makes this book even more interesting for researchers and clinicians alike is the degree of detail, including the naming of names. Robert Cooke, a well-known science journalist, gives the reader a blow-by-blow account of the research projects themselves and of the accompanying difficulties in grant funding, publication and partnerships with pharmaceutical and biological manufacturers. Two things will impress any researcher who reads this. First, even a major figure like Folkman had years of rejection—when his grants were turned down and some of his colleagues treated him as a pariah. Second, partnerships between academia and industry are fraught with traps, ambushes and reverses. I found myself astounded at how Folkman was able to survive and function despite so many projects that didn't turn out as hoped, rejections from funding agencies for some that had, and tussles with the various hierarchies of academic institutions and major companies.

On top of all that, there is the small matter of public relations. The world at large first heard of Judah Folkman's work in 1998 when the *New York Times* ran a front-page headline that was only a hairsbreadth away from the 'major breakthrough' cliché. It was based on a conversation with Nobel laureate James D. Watson who had said, informally, that Folkman would cure cancer in two years. Folkman has always had a reputation—completely justified in the view of all those who have heard him lecture—for enthusiasm and clarity. But, unlike a few cancer researchers, he has always resisted far-fetched speculations and any 'all-we-need-to-do-is' proclamations, and he has been careful and thoughtful in describing the implications of his work. To someone who always put so much care and thought into his statements, the *New York Times* headline must have been like a bomb. The whole story of that episode, clearly and neatly explained in this book, is a valuable manual for any scientist trying to handle the media—and it shows that things can get out of hand even when you stick to all the rules yourself.

Regarding the future and the import of Folkman's work, it is only rarely that one can agree with blurbs on the back jacket—especially if they are headed 'advance praise'. But when MIT's Robert Weinberg says that Folkman's ideas will "one day dramatically change cancer therapy," my guess is that he is right.

Virus Dynamics: Mathematical Principles of Immunology and Virology

by Martin A. Nowak & Robert M. May

Oxford Press, 237 pp, $70.00 hardcover/$34.95 paperback
ISBN: 0198504179, 2000

REVIEWED BY SIMON WAIN-HOBSON
Unité de Rétrovirologie Moléculaire
Institut Pasteur, Paris, France

When disciplines clash there are bound to be upheavals. Speaking of discipline, it's pretty obvious that biology is in need of a bit. Our blackboards full of circles and arrows are rather too easy metaphors. Genomics and proteomics have increased the number of variables