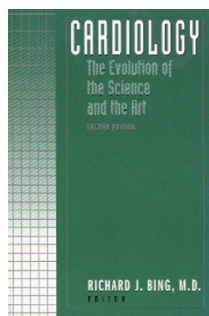


## BOOK REVIEW

to the text, Richard Bing's input into each of the chapters allowed him to accomplish a major goal stated in the preface: "to dwell on the mind and emotions, on the lives of the scientists and physicians, their successes and failures, their struggles and disappointments." We learn that Helen Taussig gained many of her insights on congenital heart disease from the fluoroscope, because her hearing impairment prevented effective auscultation. Rene Favaloro moved from general surgery practice in a small Argentinian farming village to the Cleveland Clinic because he "could no longer watch the



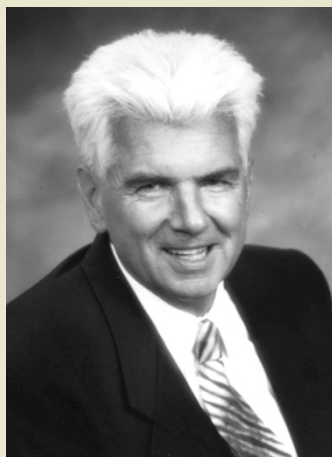
revolution in cardiac surgery" from a distance." William Rashkind was a "brilliant human being" who "loved good food and wine" so much that "he traveled widely in the disguise of medical education."

Another very nice feature of this book is the inclusion of photographs of the key individuals. These put faces with the human descriptions, serving to place the history of the scientific accomplishments in a personal perspective.

This book also gives equal attention to the physician's art and the scientist's science, often for the same individual. For example, Levine and Lown substituted

chair rest for bed rest following myocardial infarction because "it appeared to have beneficial psychological effect on the patient." The Paul Dudley White philosophy had three components: "an attitude of optimism, regular physical activity, and avoidance of premature invalidism and retirement from useful living." Taussig noticed that "babies who had continuous murmurs were less blue than others."

*Cardiology: the Evolution of the Science and the Art* is a gift to today's medical community from a physician who has lived through three phases of cardiology: from "purely clinical" to "stressing the dynamics of the circulation" to "invasive procedures and molecular biology."



## A Nobel for Blobel

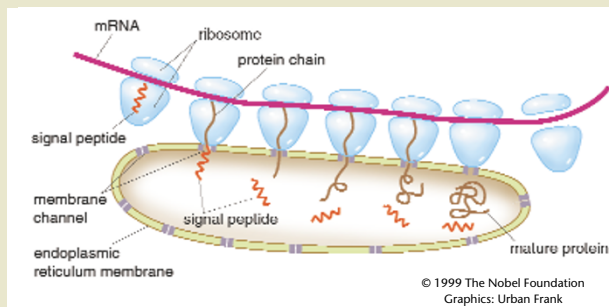
The 1971 hypothesis, validated experimentally in 1975, that proteins find their way around the cell thanks to a molecular luggage label—the so called 'signal hypothesis'—has earned Rockefeller University professor and Howard Hughes Investigator Günter Blobel the 1999 Nobel Prize for physiology or medicine. Blobel won the Albert Lasker Basic

Medical Research Award for this theory in 1993.

It is estimated that a typical cell contains around one billion proteins, which need constant replenishment. Thus, after being manufactured by ribosomes, proteins must be distributed to the appropriate location within the cell—that is, the relevant organelle. Blobel's early work focused on transport through the endoplasmic reticulum. He proposed that the amino-terminal portion of a protein—the first 20 or so amino acids to be assembled—acts as a signal sequence, permitting that protein to attach to a receptor in the membrane of the endoplasmic reticulum, where it opens a channel through which the protein can travel.

This hypothesis has been extended by Blobel and others to protein trafficking to all organelles. It has also been used to explain the molecular basis of some diseases, such as the hereditary condition hyperoxaluria, which causes kidney stones in the young, and a form of hypercholesterolemia. The phenomenon of directing proteins to organelles could also be exploited in the development of drugs that target specific components of the cell known to be faulty. Or it could be used in the production of human therapeutic proteins within complex cell models, such as yeast-biological 'protein factories'.

Blobel moved to Rockefeller University in 1967 to work as a postdoctoral fellow in George Palade's laboratory. Blobel has described Palade, who shared a Nobel Prize in 1974 with Albert Claude and Christian de Duve, as a great mentor and has said, "My work was a direct extension of the work Dr. Palade had started at Rockefeller." Blobel now works on identifying signal sequence channels in other organelles, and on elucidating the movement of large proteins, such as protein-bound RNA or DNA, into the nucleus through nuclear pore complexes.



The signal hypothesis

As with all scientists who reach the top of their field, stories about Blobel's character within the laboratory abound. Many wonder why his signal hypothesis colleague, David Sabatini, did not share the prize, and some mention Cesar Milstein's 1972 paper showing that immunoglobulin expresses a transient signal sequence. However, Blobel supporters outweigh detractors, and in addition to winning the last Nobel Prize in physiology or medicine of this millenium, Blobel is credited with having nurtured generations of scientists who will become leading cell biologists in the next millenium.

KAREN BIRMINGHAM