

processes; for example, genistein inhibits mitochondrial respiratory function, lactate transport and aldehyde dehydrogenase. Another flaw (and there aren't many in this book) is the general statement in the first chapter (dealing with labelling of phosphoproteins in intact cells), that this should be done in phosphate-free medium – this is certainly not applicable to all types of cells.

The molecular genetics referred to above appear in the form of chapters devoted to the cloning of protein kinases

(using homology-based approaches suited to this diverse family of enzymes) and, similarly, the identification of members of the protein phosphatase family. They give valuable accounts of the principles involved and information on how to do it.

A small book like this cannot hope to cover everything and there is plenty of scope for a second volume. This might cover more on the characterization of protein kinases, the study of protein kinase cascades, and up-and-coming

molecular genetic techniques such as interaction cloning of protein kinase substrates. This book should find a home on a wide range of laboratory bookshelves – although it might not spend much of its time actually on the shelf!

CHRIS PROUD

Department of Biochemistry, University of Bristol, Bristol Walk, Bristol, UK BS8 1TD.

Feeling his way into the unknown

Hans Krebs: Architect of Intermediary Metabolism 1933–1937 (Vol. II)

by **Frederic L. Holmes**, Oxford University Press, 1993. \$49.50 (xvi + 481 pages) ISBN 0 19 507657 5

Krebs, the name linked to the citric acid cycle, is the most famous name in biochemistry. The first volume of this biography describes Hans Krebs and his family life in Hildesheim, his medical education, postdoctoral work with Otto Warburg in Berlin, posts in the Department of Medicine in Altona then Freiburg, and his discovery of the ornithine cycle. After being dismissed from his position at the University of Freiburg by German political authorities, Krebs emigrated to England in 1933.

The second volume begins with Krebs' arrival at Victoria Station in London and continues through his formulation of the citric acid cycle in 1937. He obtained a temporary position in the Biochemistry Department in Cambridge, where he continued experiments on the metabolism of glutamate using Warburg's manometric techniques. Krebs was already world-famous for his discovery of the ornithine cycle and, although the position was not commensurate with his accomplishments, Krebs took it without complaint. After the rejection and isolation he had endured in Germany, the atmosphere in England was a welcome change.

Krebs lectured on basic aspects of biochemistry to university students and, for the first time, directed laboratory practical classes. Despite his unfamiliarity with English, his lectures were regarded as lucid and stimulating. He also gave research papers at meetings of the Biochemical Society and other forums soon after arriving in England, a practice that continued throughout his life.

One year later, Krebs moved to the Department of Pharmacology at Sheffield, where he continued his work on glutamate, urea and uric acid metabolism, but worked intermittently on the oxidative metabolism of carbohydrates. Albert Szent-Györgyi had established the role of four-carbon dicarboxylic acids on tissue respiration by 1935 and, in early 1937, Carl Martius and Franz Knoop demonstrated that citrate could form 2-oxoglutarate. They suggested that it could undergo further reaction to form succinate. W. A. Johnson, a research technician with Krebs, showed that citrate was converted to succinate. They also showed that citrate acted catalytically to promote the oxidation of 2-glycerol phosphate. Krebs sketched his ideas on paper as a circle for an enquiring visitor, with the conversion of oxaloacetate and pyruvate to citrate followed by the oxidative conversion of citrate back to oxaloacetate. The idea of a metabolic cycle emerged in May and June of 1937 but, when his idea was submitted to *Nature*, the paper was not accepted for publication. Krebs, who had published more than 50 papers, was distressed by this first rejection.

The citric acid cycle enjoyed a favorable reception from the time of its publication in *Enzymologia*, although several more years passed before it emerged as the centerpiece of intermediary metabolism. Krebs presented the cycle as initiated by the reaction of 'triose' with oxaloacetate to produce citrate. The conversion of pyruvate to acetyl-CoA had to wait for Fritz Lipmann's discovery of coenzyme A ten years later. Severo Ochoa showed that acetyl-CoA and oxaloacetate form citrate. This completed the cycle and resulted in the awarding of the Nobel prize to Krebs and Lipmann jointly in 1953.

Holmes has woven many aspects of Krebs' professional and personal life into the path of discovery. For example, the negotiations about heading a cancer research institute in Palestine dragged on during the entire time covered by this volume, a post that Krebs finally declined.

Krebs' shyness could sometimes come over as unaccommodating. Soon after a chance meeting, Krebs asked his future bride, Margaret Fieldhouse, to a dance to which he cycled and she drove her red MG sports car. At the end of the dance, he cycled away, leaving Margaret alone to seek alternative transportation after finding that her car would not start.

This scientific biography is noteworthy because the author had full access to Krebs' laboratory notebooks and related documents. Moreover, Holmes interviewed Krebs over a five-year period (1976–1980) and obtained recollections of experiments and thoughts that had occurred many years earlier. The contemporary evaluation of these experiments, based on hindsight, can be made at various levels or passed over. Krebs drew heavily from the published literature for ideas to test experimentally. As Warburg has written, it is important to perform numerous experiments with little critical hesitation, and this describes Krebs' approach.

Krebs wrote that he was guided to the idea of metabolic cycles because of his previous demonstration of the urea cycle. Holmes dispels this idea, and this may be the most important conclusion of this volume. The innumerable experiments that are described in the book were not directed at finding a metabolic cycle. The notion of metabolic cycles besides the ornithine cycle also did not occur in Krebs' research papers or reviews at the time, but appeared later. Moreover, the catalytic effect of citrate was almost the last phenomenon that he examined on the route to the citric acid cycle.

Holmes gives a lucid analysis of Krebs' research style, its strengths and weaknesses. Krebs' strategy was to establish the reactions of metabolism and to study the enzymes later. Others, including Warburg, took the opposite approach. Krebs switched easily from experiment to experiment; his hit-or-miss approach and his preference for moving on to another problem when he felt that he was getting bogged down were probably the most effective strategies

that he could have devised. He worked on small sets of subproblems in the context of larger problems.

Although a careful worker, Krebs published several ideas that turned out to be wrong. He asserted that amino acids are deaminated primarily in kidney, that carbamino ornithine completed the urea cycle, and he formulated an erroneous pathway for ketone body synthesis.

However, an impressive group of hits were also established by 1937, including the ornithine cycle, the identification of two intermediates in the synthesis of uric acid, the synthesis of glutamine and the citric acid cycle. Although Krebs did not invent the metabolic pathway, he is its most celebrated architect. This biography provides insights of both Krebs and Holmes that will prove invaluable to

individuals with an interest in biochemistry and to historians of science. Both volumes are highly recommended.

ROBERT ROSKOSKI, JR

Department of Biochemistry and Molecular Biology, Louisiana State University Medical Center, New Orleans, LA 70119, USA.

Immunology for all

Principles of Cellular and Molecular Immunology

by **Jonathan M. Austyn and Kathryn J. Wood**, Oxford University Press, 1993.
£25.00 (xii + 735 pages)
ISBN 0 19 854195 3

Teaching can be a great stimulus to write a book. So, Jonathan Austyn and Kathryn Wood, two immunologists widely known for their research, have written a large textbook seeded by a series of lectures that they gave in Oxford. In the nature of things, their audience for the lectures included students and active scientists, and they tell us in their disarmingly candid preface that the book is similarly directed at a diverse audience. This is a bold aim, so let's examine how they meet their own intention.

How to teach immunology? Lecture courses and textbooks must be able to stand alone, so there will be limits to the content of both. Here we are concerned with cellular and molecular issues, but who is to say that these do not involve all of immunology, including protective immunity which, here, is subordinated to cell mechanisms? The first line of text tells us 'immunology is the study of the immune system'. This is sufficient to warn readers of what is to follow. This is definitely not a book for the novice undergraduate, but there is a concise introduction to define the language of immunology. As much as lecturers want their students to learn, rather than the lecturer to teach, there is a vital teaching element given through speech that cannot be matched by the written word. However, good textbooks both teach and enable the reader to learn. Here, we find good ideas that allow the book to achieve this. For example, there are pieces of boxed text to be tackled on second reading or when in search of deeper enlightenment than given by the standard text. Personally, I have always appreciated this approach in textbooks and it is good to see it used here. The reading lists in each chapter include

reviews and primary papers, clearly intended for different audiences, but in reality both are useful to readers at every level. This is a valuable feature and one that will benefit from being kept up-to-date through new editions.

How to learn immunology? Well, you could read this book through and learn a great deal about the cells of the immune system. Its approach reflects very much the way in which immunological research operates today: cells dealt with at the molecular level, the context of which encompasses their surface receptors for antigen, cytokines, other cells and so on; how their genes are regulated; and how they communicate with each other. Pursuing the contemporary style, the book starts with the major histocompatibility complex and moves through antigen presentation, T-cell responses and repertoires, to B cells and antibodies. A measure of how the traditional approach to immunology is eschewed is that it is not until half way through the book that a section on antibodies appears, and then they are described as receptors for antigens. Good! This way, the real and central importance of T cells in immunity and the genetic control of their actions is strongly emphasized.

The second half of the book – my division, not the authors' – deals with the immunoglobulin superfamily, B-cell responses, inflammation, cytotoxicity and regulation by idiotypes and suppressor cells. The last chapter will test the new-found faith of non-immunologists who read this far. Each chapter is written and presented in a self-sufficient way, with more complicated or contentious issues boxed so that difficult topics, such as regulation of immune responses, can be approached at two levels by the reader. In their desire to make the book accessible to readers with different backgrounds, the authors give us a good learning tool. Of course, one could argue over details, but I find the book to be of an admirably uniform level and style throughout; authoritative and thoughtful in places (to be expected from senior research scientists), clear in explanation and not overly didactic.

There are numerous illustrations, not only providing the expected cartoons of

molecules, genes and cells going about their immunologic business, but also flow diagrams to explain experiments of particular historical or contemporary significance. There are tables too that give very useful compilations of data: three examples taken at random deal respectively with the characteristics of the CD8 molecule, which bits of the T-cell receptor different superantigens interact with, and polyreactive antibodies made by CD5⁺ B cells. Two colours, black and red (and tints thereof), are used throughout, producing a visual range that will not satisfy all. In places, such as in densely painted cell masses, the colour rather dominates the message of the picture. In general, however, the illustrations are clear and used sensibly to complement the text.

What this book does deliver is very good in itself, and the authors deserve our admiration for their efforts in writing such a valuable book. It contains much topical information and many contemporary views, which means that parts of it will undoubtedly age rapidly, necessitating frequent revisions if the book is to maintain its deserved position. My personal preference would be for more integration of the mechanisms and agents, so well handled here, with functional protective immunity and immune pathology. There is a whiff of scientific abstraction that may not help all readers to appreciate the full scope of immunology. On the other hand, its scholarly approach makes this a book to be recommended to the intermediate or advanced student of immunology. We teach undergraduate courses with names close to the title of the book and we like it; it is also equally valuable to postgraduate research students and those on taught masters' courses. Anyone who teaches the subject will find this book a very useful and accessible source of information. Highly recommended; keep a copy in your laboratory for your research students and fellows, too.

NORMAN A. STAINES

Infection and Immunity Research Group, King's College London, Campden Hill Road, London, UK W8 7AH.