

Pathogens, Metals, and Handedness

Pathogenomics: Genome Analysis of Pathogenic Microbes

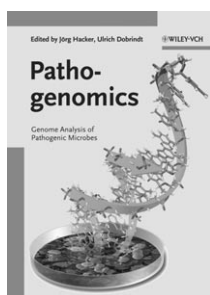
Edited by Jörg Hacker and Ulrich Dobrindt.

Wiley-VCH, Weinheim 2006. XLVIII + 568 pp., hardcover € 169.00.—ISBN 978-3-527-31265-8

An age-long battle has been waged between humans and infecting microbes, with some of the more pathogenic organisms often having the upper hand. Diseases once thought defeated are resurgent, and antibiotic resistance is an increasingly effective and disseminated foe. Emerging pathogens are new adversaries, often with ingenious strategies of evasion, and a global culture ensures that geography can no longer provide an effective means of isolation or time to mobilise defenses.

One of the basic tenets of war is "Know thine enemy as thyself" (Sun Tsu, *The Art of War*, c. 512 BC), and the premise of the emerging field of "pathogenomics" is based on the most intimate possible knowledge of the opponent, that being their complete genomic DNA sequence. This intelligence not only allows prediction of gene products and comparative analysis, but also provides the backdrop for whole system studies. Analysis of global gene expression levels and patterns that link regulation pathways, metabolism, virulence, and resistance reveals ongoing evolution of 'adapt and survive' strategies to overcome host defense mechanisms, either by stealth or brute force attacks.

This book outlines the interdisciplinary use of new technologies to use genome information in the study of microbial



pathogens. The 24 chapters are contributed by different authors, casting expert insight into each specialist area. With over 2100 references in total it may sound like a dry academic tome, but careful editing for style and content makes for a surprisingly easy read. A minor quibble is that the full author list is given for each reference. Although important to acknowledge the foot soldiers that do the hard work, repeating the large number of co-authors on a genome sequence paper (for instance 151 for *Bacillus subtilis*) a number of times does seem excessive. The book is split broadly into three main sections and is amply illustrated. Despite the colour figures being collected together at the front, appropriate reproductions in black and white are at the relevant parts of the text.

The first section deals with the methods and tools used, representing the arsenal available. The information that global analyses at the mRNA (transcriptomic) and protein (proteomic) levels can provide is outlined with representative chapters, and includes a description of microarray analysis. Functional gene analysis is also introduced, and all is prefaced by a description of the bioinformatics involved. The techniques are clearly described, although owing to brevity, their power is only hinted at. In particular, understanding the sophisticated bioinformatics used would require the reader to seek a more specialised text.

The second, and major, section comprises chapters on a number of pathogenic bacteria, including enteric species, *Mycobacteria*, Gram-positive rods and cocci, *Neisseria*, *Bartonella*, *Helicobacter*, and *Legionella*. Each chapter is only long enough to highlight special features of each, in particular the prediction of potential virulence factors from sequence gazing and comparative analysis, but all are richly referenced to the primary liter-

ature. As in any text describing a scientific endeavour, it is impossible to keep up-to-date, and the footnote added 'in proof' to the *Streptococci* chapter indicating that eight new genomes are also available serves as a warning that a bit of research would be required to get a current picture. There are some notable absences. *Yersinia* (bubonic plague) is not covered, maybe explaining why the perfunctory index ends at 'V' in the alphabet; neither are the causative agents of diphtheria or cholera. This is a shame, as future prospects of curing disease can only be assessed in the perspective of past skirmishes.

The final section follows in the same vein, beginning with a description of what is emerging from the genomics of viruses, fungi, and pathogenic protozoa. This leads into the use of model systems to study host-pathogen interactions, which reflect a complex interplay of distinct genomes. Unravelling the patterns is a major challenge, as is the need to integrate data from emerging technologies to the in vivo disease state. The techniques pioneered in oncology are beginning to be extended to genome-wide analysis of clinical samples isolated from pathologically compromised tissues. The ability to monitor changes in human gene expression as well as those in the infectious organism will lead to important insight for diagnostics and vaccine development, and could point to novel antibiotic targets. This section nicely wraps current knowledge onto future promise.

To quote again from the earliest military treatise, the idiom "It is a matter of life and death, a road either to safety or to ruin. Hence it is a subject of inquiry which can on no account be neglected" may be an appropriate description of this self-styled discipline of pathogenomics. Whether this book is remembered as a new landmark in the fight against infectious diseases will depend on the abil-

ity of functional studies to understand the large percentage of genes currently annotated as 'unknown function' and the delivery of new therapies based on the genomic studies. In any case, as a snapshot of current knowledge, it is a comprehensive treatment of the field, and would prove useful in any research environment with an interest in infectious diseases.

Jim Brannigan

University of York (UK)

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Bioorganometallics: Biomolecules, Labeling, Medicine

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Why should a journal for medicinal chemistry such as *Chem-MedChem* contain a book review on bioorganometallic chemistry? Perhaps this is a question you are asking as you remember from your lectures as an undergraduate that organometallic compounds are synonymous with toxicity. Wasn't one of the classic, prototypical organometallic compounds discovered by Mond, viz. Ni(CO)_4 , even believed to be responsible for the discoverer's death? It is certainly true that most of us are aware of the indispensable qualities of organometallic compounds in organic synthesis and catalysis, and that the pharmaceutical industry goes to great lengths to make sure that no organometallic residues are left in their organic (drug) products, but perhaps the medicinal and biological properties of organometallic compounds are less well known. The word *bioorganometallic* has been around since 1985 when it was introduced, quite ap-



propriately, by the editor of this book published some 20 years later. And although nature may have arrived there first, with living systems harnessing the utility of metal-carbon bonds in a plethora of different processes, this book is an excellent place to learn about what has been going on in the last 20 years or so with respect to human efforts to integrate organometallic compounds into the realm of the biosciences.

The book is devoted to transition-metal compounds and does not cover (with the exception of a few prominent examples in the introductory chapter) main-group compounds of biological relevance. This is a huge field in its own right, and is concerned more with speciation of such compounds in the environment and their associated toxicity, although we also learn that some have been in clinical use for many years.

Anybody with even a passing interest in the subject should at least read the first chapter of this book. It not only defines the field and indicates where organometallic compounds play a role in the life sciences, but it also gives an excellent overview. The chapter has not only been written from a chemist's perspective, but it has been researched and structured in the way that a historian would compose a thesis. However, it is in the ensuing 11 chapters that we learn the detailed chemistry that is *bioorganometallic*. These chapters were contributed by the pioneers and leading practitioners of the field, and while it is impossible to give a detailed description of the topics covered in this text, a brief summary of the main topics can be made. Following the introductory chapter the next three chapters are concerned with the pharmaceutical applications of organometallic compounds, describing the state of the art and setting out strategies for future drug design. Whereas cancer is the main disease of interest, other diseases are included. For example, a ferrocene derivative of quinine that overcomes quinine-resistant malaria is in phase II clinical trials. The next two chapters focus on the use of organometallic reagents to label various biomolecules, notably peptides and proteins. Organometallic bioprobes, tracers, sensors, and receptors constitute the following four

chapters. Thus far, all of these chapters are of direct relevance to medicinal chemistry. The final two chapters take a somewhat different direction, describing the structure, function, and synthetic modelling of bioorganometallic reaction centres in enzymes. The chapters contain not only the detailed chemistry involved, but also manage to place the research in context with sufficient information on the medicinal or other applications or potential applications of the compounds described. Remarkably for an edited text, there is very little overlap between the chapters, and one does not suffer from the sense of déjà vu often encountered when browsing or reading edited texts.

It is worth emphasising that this is the first book devoted to the subject of bioorganometallic chemistry. It is also noteworthy that this book is not just a bioorganometallic version of a bioinorganic textbook; in fact, the emphasis of this book is quite different. It is directed much more towards the medicinal applications of bioorganometallic compounds (although not exclusively), from the cisplatin-like compounds that are remarkably effective without containing an obvious biological ligand to determine activity, through those which are closer to organic drugs, with an organometallic appendage providing unique and beneficial properties, to those where the metal imparts a unique property as in radiopharmaceuticals. As such, I believe that this book is not only indispensable to all those working in the field of bioorganometallic chemistry, which has grown tremendously since the term was first introduced in 1985, but also for those involved in research and as a source of useful information for teaching material. The book will also be of interest to medicinal chemists, who will discover the unique properties that organometallic compounds possess in addition to being useful intermediates in the preparation of purely organic drugs.

Paul J. Dyson

Ecole Polytechnique Fédérale de
Lausanne (Switzerland)