



Reviews and Resources

BOOKS

Molecular Paradigms of Infectious Disease: a Bacterial Perspective

Cheryl A. Nickerson and Michael J. Schurr (ed.). Springer Science & Business Media, LLC., New York, 2006, 645 p., \$199.00 (hardcover).

A paradigm can be defined as a collection or set of logically related assumptions, concepts, propositions, or practices that orient thinking and research. *Molecular Paradigms of Infectious Disease: a Bacterial Perspective* is about the molecular paradigms of infectious disease that have emerged over the last 10 years. More specifically, a group of 29 scientists discuss in 15 chapters their viewpoints on the rather complex cellular and molecular mechanisms that underlie bacterial virulence and the infectious disease process. This book is part of a series entitled *Emerging Infectious Diseases of the 21st Century*.

The chapters of this book contain four basic parts: a description and discussion of the most important techniques that have been used for recent discoveries in bacterial pathogenesis; the major structures and mechanisms for virulence; the regulators of virulence determinants; and selected bacterial biowarfare agents.

The first chapter deals with the genetic analysis of bacterial pathogenesis. The author describes fusion-based and transposon-based methodologies, as well as infection experiments in animals that led to the identification of virulence genes pathogens use for the adaptation to host environments. Chapter 2 outlines the mechanisms of genetic exchange in bacteria. The emphasis is on four major horizontal gene transfer paradigms (transformation, conjugation, transduction, and transposition) that give bacteria an advantage in the fight for survival. The following chapter discusses recent advances in the

use of genomic tools to study pathogenic bacteria, such as genome sequencing, genome annotation, microarray technology, comparative genomics, and genomic rearrangements. The fourth chapter is devoted to the discussion of pathogenicity islands (PAIs) that harbor virulence genes. The author describes the characteristics of PAIs of important pathogens, including their base composition, genetic instability, evolution, and transfer.

Bacterial capsules are the focus of Chapter 5. The genetics and classification of capsules of various bacteria, their function in pathogenesis, and the mechanisms of their synthesis are described. Chapter 6 highlights the role of the bacterial cell wall in pathogenesis. More specifically, the authors take a closer look at the structure of gram-positive and gram-negative bacteria, and also discuss exceptions such as acid-fast bacteria and mycoplasmas. Other topics discussed in this chapter include cytoplasmic membrane components, surface-exposed structures, antibiotics and antibiotic resistance, as well as innate immune responses to cell wall components. The mechanisms of bacterial adhesion and the consequences of attachment are the topic of the next chapter. The authors discuss different adhesive strategies used by bacteria and describe vaccines that work against those adhesive structures. Chapter 8 is about the specific mechanisms of invasion of two selected bacteria (*Salmonella* and *Listeria*) in nonphagocytic cells. The following chapter deals with the various bacterial protein secretion mechanisms that are essential for the interaction of bacteria with host cells.

Chapter 10 discusses the important topic of bacterial toxins as host cell modulators. The authors give an overview of major toxin classes and names, their origin and production, as well as their effects on host cells. The next chapter is about quorum sensing (or intercellular signaling), a

form of cell-to-cell communication that coordinates gene expression among groups of cells. Chapter 12 discusses sigma factors (a family of proteins) that play a role in regulating bacterial stress responses and pathogenesis. Chapter 13 describes two-component regulatory systems that are used by bacteria for transmembrane signal transduction. The following chapter discusses the oxidative stress systems in four bacteria: *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, and *Mycobacterium tuberculosis*. The final chapter is about bacterial biowarfare agents. The authors of this chapter provide a historical overview about these agents and then discuss three specific examples: *Bacillus anthracis*, *Yersinia pestis*, and *Francisella tularensis*. For each of these organisms, information about the biology, pathogenesis, virulence, treatment and prevention, vaccines, and immunity is provided.

I like that every chapter of this book starts with a brief historical overview of important discoveries in the specifically discussed areas of bacterial pathogenesis, and ends with a section of well-selected questions and answers. I would highly recommend this book to students, scientists, and researchers of the biological, medical, and veterinary sciences who have an interest in bacterial pathogenesis.

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Bacterial Genomes and Infectious Diseases

V. L. Chan, P. M. Sherman, and B. Bourke (ed.). Humana Press, Totowa, N.J., 2006, 288 p., \$135.00.

The focus of *Bacterial Genomes and Infectious Diseases* is the rapidly expanding field of bacterial genomics, which is driven

by the recent increase in the number of genomes sequenced from representatives of different species of bacterial pathogens, as well as the same or closely related species. The book demonstrates how a comparative approach in bacterial genomics can contribute to our understanding of the basic biology of important human pathogens; thus, furthering the exploration of infectious pathogenesis. The book consists of 14 chapters, the first four of which provide a brief summary of the major concepts and paradigms established in bacterial genomics relevant to infectious diseases. The nine subsequent chapters cover individually selected human pathogens, and describe the biological and medical relevance of the genomic data. The final chapter is devoted to the future directions of infectious disease research, particularly research on gastrointestinal tract diseases. All chapters are well written and organized, each with short summaries and insightful concluding remarks.

The first four introductory chapters of the book serve as a good basic text for both students and researchers new to the field of bacterial genomics. The first chapter describes in a condensed, yet comprehensive, manner the number and origin of bacterial genomes that are available, or in the process of being sequenced, at the time of this edition of the book. It also describes the general structure of microbial genomes, including chromosome structure, codon usage, gene organization, and mobile elements. The second chapter provides a brief discussion of microbial evolution, putting special emphasis on the role of horizontal gene transfer in the genesis of bacterial virulence. However, while the role of mutations in virulence evolution is well acknowledged, no specific examples are given. The third chapter describes the use of genomic DNA microarrays and of whole-genome PCR scanning (a relatively little-known technique) for comparative analyses of genomes of closely related strains, in the search for putative virulence factor genes. Overall, these chapters provide a good (though at times, overly brief) outline of some general topics in pathogen genomics, followed by insightful discussions of the recent literature. The fourth chapter pro-

vides a very good overview of the mechanisms of innate immunity; unfortunately, it says almost nothing about the role genomics can play in understanding these types of pathogen-host interactions.

The following chapters are devoted to illustrating how a comparative genomics approach can be used to understand the biology of individual pathogens. Most of the chapters succeed in this endeavor, with excellent reviews of the genomics of *Helicobacter* (chapter 6), *Listeria* (chapter 7), *Mycoplasma* (chapter 10), *Staphylococcus* (chapter 11), and *Vibrio* (chapter 13) species. These chapters provide a really stellar, comprehensive analysis of how genomics are employed to dissect the molecular mechanisms of the pathogenesis and virulence evolution of the corresponding pathogens. Chapter 12 is well written, but focuses rather narrowly on the comparative genetic analysis of *Yersinia* type III secretion systems. The overview of genomic information on *Leptospira* (chapter 7) is well done; however, too much time is devoted to the attempt (though admittedly necessary) to resolve gene annotation discrepancies between different genomes. Chapter 5, on *Campylobacter*, is rather disappointing in that it is barely relevant to the general theme of the book, namely, bacterial genomics and pathogenesis. Instead it focuses on analyses of the entire pool of glycan structures of the bacteria (glycome) belonging to the *Campylobacter* species, with an excessively detailed description of the mass spectrometry techniques employed therein. The concluding chapter is also disappointing. It is very brief, and concentrates on what the editors of the book believe (with some justification) will be the future focus of infectious disease research (e.g., the identification of nonculturable organisms and the use of probiotics). Unfortunately, it gives very little insight into the future of the field of bacterial pathogen genomics itself.

Despite a few minor shortcomings, the book provides a good introduction to the field of bacterial genomics, and a useful overview of the genomic data for the selected bacterial pathogens. It may also be of interest to clinicians desiring a better understanding of the ways in which bacterial genome plasticity can affect pathogenesis. Readers should find

this book a valuable addition to their working reference library.

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Guide to Effective Grant Writing: How to Write an Effective NIH Grant Application

Otto O. Yang (ed.) Kluwer Academic/Plenum Publishers, New York, 2005, 93 p., \$24.95 (softcover).

Successfully writing a grant application is a crucial skill for faculty members at academic research institutions. Grant funding allows for hiring laboratory personnel, purchasing laboratory equipment and reagents, and conducting laboratory experiments. Successful research leads to publications which, in turn, play a significant role for faculty promotions. Thus, effective grant writing helps academic researchers survive in the competitive field of biomedical research.

Preparing a grant application is not easy. It requires a comprehensive, yet specific knowledge of the research literature, good writing skills, attention to detail, a broad knowledge of applicable research methodologies, and an understanding of the financial aspects of the proposed study. Taken all together, the writing of a grant application is a difficult and time-consuming task that should not be left to trial and error but rather should be addressed by formal guidance and training.

Otto O. Yang's book *Guide to Effective Grant Writing* provides valuable information and advice on all aspects of the grant writing process. Yang points out that although his advice is specifically directed at grant applications to the National Institutes of Health (NIH), he believes that the principles he describes may also be applicable to many other types of grant applications.

The book is divided into 19 carefully developed chapters. The first four chapters provide an overview about grant writing and grant applications. More specifically, chapter 1 discusses the importance of getting and keeping the attention of reviewers, of balancing between clarity and depth, and of the art of telling an interesting story. In the second chapter, Yang



provides a guide on how to use his book most effectively. Chapter 3 outlines issues that should be considered before a grant application can be submitted, such as the type of grant, deadlines, institutional approvals, application strategy, budget estimation, decisions on collaborators and consultants, familiarization with the NIH format, and information on how to obtain NIH forms for the application. Chapter 4 introduces the reader to the different types of NIH grants, including “F (Individual Fellowship) awards,” “K (Career Development) awards,” and “R (Research Project) awards.”

The fifth chapter describes the anatomy of an NIH grant application and the connection between the different sections of a research proposal. Chapter 6 deals with the organization and aesthetics of the application. The reader learns about the importance of clear organization and neatness of the proposal and the rules set by the NIH, the text and figure organization, the

writing styles, the importance of detail, the layout, the difficult-to-understand sections, and common errors. Chapters 7 through 11 describe individual sections of the application, such as “Specific Aims” (Chapter 7), “Background and Significance” (Chapter 8), “Preliminary Results” (Chapter 9), “Research Design and Methods” (Chapter 10), and “Literature Cited” (Chapter 11). These chapters include examples and the discussion of commonly made errors.

In the 12th chapter, Yang talks about the proper use of appendices, such as the documentation of technical capabilities or additional details relevant to the proposed study. In the following chapter, the administrative sections of an NIH application are reviewed, including the face page, description, biosketch, personnel, resources and environment, consortium agreement, budget and budget justification, human subjects, vertebrate animals, checklist, and cover letter. Chapter 14 is devoted to the

role of collaborators and consultants on grant applications. Yang gives an overview about the NIH scoring process in the next chapter. Chapter 16 describes the process of resubmitting an application after initial rejection, while Chapter 17 is about the case of submitting a competing renewal application. Chapter 18 discusses non-NIH grants. In the final chapter, Yang emphasizes that clarity, brevity, and proper documentation are the key aspects of a successful grant application.

This book is unique in that it describes the views of the grant writer and that of the grant reviewer. I highly recommend it to scientists and faculty members at academic research institutions. Furthermore, I suggest that every student who plans a research career in the health and life sciences should read this book.

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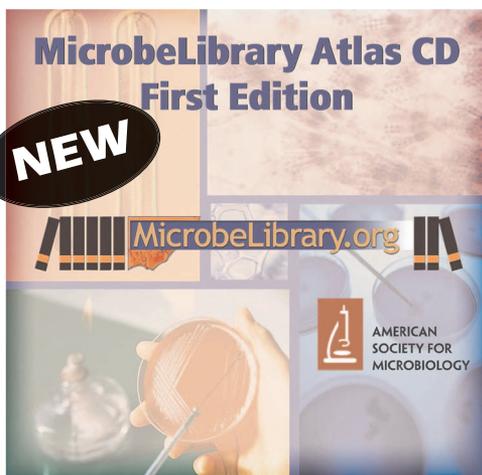
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