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CONTRIBUTORS

Stephen B. Beres
Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030

A. Casadevall
Departments of Microbiology and Immunology and of Medicine, Albert Einstein College of Medicine, Bronx, NY 10461

Vaughn S. Cooper
Department of Microbiology, 212 Rudman Hall, University of New Hampshire, Durham, NH 03824

William A. Day
Bacteriology Division, U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, MD 21702

Rob DeSalle
Molecular Biology Laboratory, American Museum of Natural History, Molecular Laboratories, Central Park West at 79th St., New York, NY 10024

Ulrich Dobrindt
Institut für Molekulare Infektionsbiologie, Universität Würzburg, D-97070 Würzburg, Germany

David H. Figurski
Department of Microbiology, College of Physicians and Surgeons, Columbia University, 701 West 168th St., New York, NY 10032

J. Ross Fitzgerald
Centre for Infectious Diseases, Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, Scotland, United Kingdom

Jeffrey I. Gordon
Center for Genome Sciences, Washington University School of Medicine, St. Louis, MO 63108

Nicole M. Green
Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030
CONTRIBUTORS

Jörg Hacker
Institut für Molekulare Infektionsbiologie, Universität Würzburg, D-97070 Würzburg, Germany

Bianca Hochhut
Institut für Molekulare Infektionsbiologie, Universität Würzburg, D-97070 Würzburg, Germany

Deborah A. Hogan
Department of Microbiology and Immunology, Dartmouth Medical School, Hanover, NH 03755

James B. Kaper
Center for Vaccine Development, Department of Microbiology and Immunology, University of Maryland School of Medicine, Baltimore, MD 21201

Roberto Kolter
Department of Microbiology and Molecular Genetics, Harvard Medical School, Boston, MA 02115

Ruiting Lan
School of Biotechnology and Biomolecular Sciences, University of New South Wales, Sydney, New South Wales 2052, Australia

Jeffrey G. Lawrence
Pittsburgh Bacteriophage Institute and Department of Biological Sciences, University of Pittsburgh, Pittsburgh, PA 15260

Martin C. J. Maiden
The Peter Medawar Building for Pathogen Research and Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3SY, United Kingdom

Anthony T. Maurelli
Department of Microbiology and Immunology, F. Edward Hébert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD 20814-4799

Didier Mazel
Unité Plasticité du Génome Bactérien, Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris cedex 15, France

Margaret J. McFall-Ngai
Department of Medical Microbiology and Immunology, University of Wisconsin, Madison, WI 53706

John J. Mekalanos
Department of Microbiology and Molecular Genetics, Harvard Medical School, Building D1, Room 421, 200 Longwood Ave., Boston, MA 02115

Rachel Muir
Departments of Genetics and of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA 94305

James M. Musser
Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030

James P. Nataro
Department of Pediatrics, Department of Medicine, Department of Microbiology and Immunology, and Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, MD 21201

Paul J. Planet
Molecular Biology Laboratory, American Museum of Natural History, Molecular Laboratories, Central Park West at 79th St., New York, NY 10024
CONTRIBUTORS

Alexander S. Pym
Medical Research Council of South Africa, 491 Ridge Road, P.O. Box 70380, Overport 4067, Durban, South Africa

Sean D. Reid
Department of Microbiology and Immunology, Wake Forest University School of Medicine, Winston-Salem, NC 27157

Peter R. Reeves
School of Molecular and Microbial Biosciences, University of Sydney, Sydney, New South Wales 2006, Australia

Dean Rowe-Magnus
Department of Microbiology, Clinical Integrative Biology Division, Sunnybrook & Women’s College Health Sciences Centre, 2075 Bayview Ave., S1–26A, Toronto, Ontario, Canada M4N 3N5

Peter M. Small
Global Health Program, P.O. Box 23350, Seattle, WA 98102

Judith N. Steenbergen
Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461

O. Colin Stine
Department of Epidemiology and Preventive Medicine and Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD 21201

Man-Wah Tan
Departments of Genetics and of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA 94305

Rachel Urwin
The Peter Medawar Building for Pathogen Research and Department of Zoology, University of Oxford, South Parks Road, Oxford OX1 3SY, United Kingdom
INTRODUCTION

The 1976 edition of the classic textbook *The Microbial World* by Stanier, Adelberg, and Ingraham (3) relegated the topics “Microbial Pathogenicity” and “Microbial Diseases of Man” to chapters 29 and 30 of a 31-chapter book. Such was the appreciation of microbial pathogenesis in the field of microbiology in the 1970s. More detailed coverage of microbial pathogens is found in the 1978 edition of *Bailey and Scott’s Diagnostic Microbiology* (1), but that book is also a time capsule of the breadth and depth of knowledge in pathogenic microbiology at that time—before the genetics and genomics revolutions of the last 30 years. The sole reference to Legionnaires’ disease makes no mention of *Legionella pneumophila*, which had yet to be discovered. Likewise, although enteropathogenic and enteroxigenic *Escherichia coli* are covered, enterohemorrhagic *E. coli* was not mentioned at all. And of course in 1978 there was no appreciation at all that a microbe, *Helicobacter pylori*, causes human ulcers.

Any active field of study will accumulate new information after nearly 30 years, but in the area of pathogenic microbiology the fruits of research since the 1970s have been quite extraordinary. Not only have new microbial diseases been uncovered, but appreciation about the diversity of mechanisms underlying the way that microbes and hosts interact has also grown. Microbes that have historically been challenging to study in the laboratory have yielded to the ingenuity of researchers who have brought an impressive toolbox of techniques and experimental models to bear on questions of microbial pathogenicity. The 1980s saw the development and application of genetic approaches for uncovering new virulence factors. The 1990s were a time of incredible advances in the study of how microbes exploit or disrupt host cell functions, and the field of “cellular microbiology” was born. Currently we are in the genomic era, with dozens of genomes from pathogenic microbes being mined for new virulence factors and therapeutic targets using bioinformatics and high-throughput approaches and new genome sequences appearing weekly. The quantum leap in knowledge from the field of genomics has also reinvigorated the study of...
microbial physiology, microbial metabolism, and microbial communities in a diverse range of environments. It is the amazing amount of data available from prokaryotic genome sequences which has fueled a renewed interest in the study of the evolution of microbes, and in parallel the study of the evolution of microbial pathogens. It is at this point that we considered the suggestion of assembling a book that could provide central concepts about evolution to the microbiological community in the context of pathogenesis. Given our interest in the subject, as well as the fact that sufficient knowledge to allow a thoughtful approach to it is now available, we decided to take on the project.

Most biologists like to speculate about the evolution of their particular area of focus, but to discuss evolution intelligently requires familiarity with the basic concepts about the subject. Evolutionary biologists have much to teach general physiologists, biochemists, geneticists, and infectious disease specialists, but the concepts and language of this area of study have become sufficiently specialized that there are barriers to a microbiologist who wants to learn more about evolution. This leads to a scenario where microbiologists sometimes make evolutionary arguments that are not well supported by the accepted theories of evolution.

It is often assumed that traits associated with pathogenicity were acquired as a way to improve the fitness of those microbes living in an otherwise hostile host environment. This is a simplistic view of a complicated relationship between microbes and the many environments they encounter. We undoubtedly place too much emphasis on the host and disease in trying to understand selection forces operating on microbes that live in a wide range of environments. Environmental reservoirs, where pathogens spend so much more time relative to that spent in a susceptible host who then becomes sick, may be better places to look for answers to questions of how pathogenicity traits have become fixed in microbial populations.

In this context, disease may simply be a consequence of specific microbial mechanism acting on a host that does not have a long natural history of coevolution with the microbe. A theme that has emerged from recent work on pathogenic microbes challenges even the basic notion of what a pathogen is. Microbes that cause disease in some hosts may be perfectly harmless in others. In turn, mechanisms that have evolved to enable microbes to disrupt the host in a way that causes symptoms and disease can be used by other microbes or in other hosts to establish asymptomatic, long-term associations.

The genomic era has provided new knowledge regarding the evolution of specific pathogenic species, in which some of the common themes, such as pathogenicity islands, are seen in action. Valuable information can be obtained by determining the genome sequence of pathogenic microbes as well as closely related non-pathogenic strains. This has enabled investigators to focus on unique sequences in the pathogenic strains both as a way to design new control strategies, and as a way to better understand the forces that govern evolution of pathogenicity. Why, for example, are some serogroups of a particular species pathogenic whereas others are not? What traits have evolved along with serogroup specificity that contribute to this segregation of specific antigenic types with virulence traits?
As we assembled this book, the topic of bacterial genetics kept cropping up in the majority of the chapters. To understand the process of evolution in bacteria without thinking about the horizontal transmission of genetic material within and between species is like trying to understand a baseball box score without thinking about hits, runs or errors. Rather than offer a basic primer for bacterial genetics (or baseball), we refer readers who are not familiar with the details of genetic processes to the textbook *Molecular Genetics of Bacteria* by Snyder and Champness (2) or any of the wonderful texts that also describe the mechanisms of gene exchange such as transformation, transduction, and conjugation.

Our goal with this book is to offer a current understanding of virulence evolution with the microbiologist in mind. The content is offered from three different perspectives. In the first section, our emphasis is on broad themes and the business of how evolution is studied. Principles that relate not only to pathogenesis, but to evolution in general, are covered in some detail by looking at specific cases. The second section offers examples of how problems common to a number of pathogens have been solved in evolutionary terms. This section also discusses the question of how microbial ecology has played a role in the evolution of pathogenicity. These first two sections discuss model systems that have provided new knowledge relevant to study of many other microbes. In the third section, we focus on a few well-studied classes of pathogens to learn how they may have evolved their disease-causing mechanisms. In this section we see some more specific examples of the themes developed in the first two sections, but the points are more finely drawn. In all chapters we are fortunate to have as collaborators outstanding authors who have made important contributions to the literature regarding their topics. Each section is also introduced and put into broader perspective by an eminent investigator whose own work relates to that section. We have learned a lot about both evolution in general, the evolution of pathogenic systems, and examples from specific microbial pathogens while assembling this book. We hope it will be useful to many who are learning about or studying pathogenic microbes and set the stage for further research into this important area of biology.

HANK S. SEIFERT
VICTOR J. DIRITA

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