Regulation of Bacterial Virulence
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EDITED BY

Michael L. Vasil
University of Colorado School of Medicine
Aurora, Colorado

Andrew J. Darwin
New York University School of Medicine
New York, New York

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Michael Vasil dedicates this book to the memory of Martin Stonehouse, Ph.D., who relished science and loved life to the fullest. He left his loving wife, Carly, his sons, Ronan and Morgan, his family, and all of us much too soon, 29 October 2011.

Andrew Darwin dedicates this book to his parents, Frank and Pauline. They have never pushed but always supported.
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CONTRIBUTORS

Meredith A. Benson
Department of Microbiology
New York University School of Medicine
New York, NY 10016

Josephine R. Chandler
Department of Microbiology
University of Washington School of Medicine
1705 NE Pacific Street
Seattle, WA 98195

Sandra Billig
Department of Microbiology
University of Osnabrück
D-49076 Osnabrück, Germany

Yanjie Chao
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany

Alex Böhm
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany

Jackie K. Cheung
Department of Microbiology
Monash University
Clayton, Victoria 3800, Australia

Evan Bradley
Department of Molecular Biology & Microbiology
Tufts University School of Medicine
136 Harrison Avenue
Boston, MA 02111

Peter J. Christie
Department of Microbiology and Molecular Genetics
University of Texas Medical School at Houston
Houston, TX 77030

Daniel J. Bretl
Department of Microbiology and Molecular Genetics
Center for Infectious Disease Research
Medical College of Wisconsin
Milwaukee, WI 53226

Colin P. Corcoran
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany

Andrew Camilli
Department of Molecular Biology & Microbiology
Tufts University School of Medicine
136 Harrison Avenue
Boston, MA 02111

Shipan Dai
Center for Microbial Interface Biology
Department of Microbial Infection and Immunity
The Ohio State University
Columbus, OH 43210

Paul E. Carlson, Jr.
Department of Microbiology and Immunology
University of Michigan Medical School, Box 0620
Ann Arbor, MI 48108

Jennifer L. Dale
Department of Microbiology and Molecular Genetics
University of Texas—Houston Medical School
Houston, TX 77030

Glen P. Carter
Department of Microbiology
Monash University
Clayton, Victoria 3800, Australia

Shandee D. Dixon
Department of Microbiology and Immunology
University of Michigan Medical School, Box 0620
Ann Arbor, MI 48108
Robert K. Ernst  
Department of Microbial Pathogenesis  
University of Maryland, Baltimore  
Baltimore, MD 21201

Allison J. Farrand  
Department of Pathology  
Microbiology and Immunology  
Vanderbilt University Medical Center  
Nashville, TN 37232

Alfonso Felipe-López  
Department of Microbiology  
University of Osnabrück  
D-49076 Osnabrück, Germany

Nancy E. Freitag  
Department of Microbiology and Immunology  
University of Illinois at Chicago College of Medicine  
Chicago, IL 60612

Kathrin S. Fröhlich  
Institute for Molecular Infection Biology  
University of Würzburg  
Würzburg, Germany

Joanna B. Goldberg  
Department of Microbiology, Immunology, and Cancer Biology  
University of Virginia  
Charlottesville, VA 22908

E. Peter Greenberg  
Department of Microbiology  
University of Washington, School of Medicine  
1705 NE Pacific Street  
Seattle, WA 98195-7242

Charley Gruber  
Department of Microbiology  
UT Southwestern Medical Center  
Dallas, TX 75390

John S. Gunn  
Center for Microbial Interface Biology  
Department of Microbial Infection and Immunity  
The Ohio State University  
Columbus, OH 43210

Sanjay K. Gupta  
Institute for Molecular Infection Biology  
University of Würzburg  
Würzburg, Germany

Philip C. Hanna  
Department of Microbiology and Immunology  
University of Michigan Medical School, Box 0620  
Ann Arbor, MI 48108

Nadja Heidrich  
Institute for Molecular Infection Biology  
University of Würzburg  
Würzburg, Germany

Calvin A. Henard  
Department of Microbiology  
University of Colorado Denver  
School of Medicine  
Aurora, CO 80045

Michael Hensel  
Department of Microbiology  
University of Osnabrück  
D-49076 Osnabrück, Germany

Thomas J. Hiscox  
Department of Microbiology  
Monash University  
Clayton, Victoria 3800, Australia

Lauren E. Hittle  
Department of Microbial Pathogenesis  
University of Maryland, Baltimore  
Baltimore, MD 21201

Ansel Hsiao  
Center for Genome Sciences & Systems Biology  
Washington University  
School of Medicine  
St. Louis, MO 63110

Scott J. Hultgren  
Department of Molecular Microbiology  
Washington University School of Medicine  
St. Louis, MO 63110

Michael P. Jennings  
The Institute for Glycomics  
Griffith University  
Gold Coast Campus  
Parklands Drive  
Southport, QLD 4222, Australia

Barbara I. Kazmierczak  
Department of Medicine  
Yale University School of Medicine  
333 Cedar Street, Box 208022  
New Haven, CT 06520-8022
Erica N. Kintz
Department of Microbiology, Immunology, and Cancer Biology
University of Virginia
Charlottesville, VA 22908

Theresa M. Koehler
Department of Microbiology and Molecular Genetics
University of Texas—Houston Medical School
Houston, TX 77030

Jenny A. Laverde-Gomez
Department of Microbiology and Molecular Genetics
University of Texas Medical School at Houston
Houston, TX 77030

Audrey Le Gouellec
TheREx, TIMC-IMAG Laboratory
UMR 5525 CNRS
Université Joseph Fourier
Grenoble, France

Lee-Yean Low
Department of Microbiology
Monash University
Clayton, Victoria 3800, Australia

Dena Lyras
Department of Microbiology
Monash University
Clayton, Victoria 3800, Australia

Kate E. Mackin
Department of Microbiology
Monash University
Clayton, Victoria 3800, Australia

Charlotte D. Majerczyk
Department of Microbiology
University of Washington School of Medicine
1705 NE Pacific Street
Seattle, WA 98195

EmilyKate McDonough
Department of Molecular Biology & Microbiology
Tufts University School of Medicine
136 Harrison Avenue
Boston, MA 02111

Kathleen A. McDonough
Wadsworth Center
New York State Department of Health
Albany, NY 12201-2002

Masatoshi Miyakoshi
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany

Nrusingh P. Mohapatra
Center for Microbial Interface Biology
Department of Microbial Infection and Immunity
The Ohio State University
Columbus, OH 43210

Thomas S. Murray
Department of Basic Medical Sciences
Quinnipiac University School of Medicine
275 Mt. Carmel Avenue, N1-HSC
Hamden, CT 06518-1908

Abiodun D. Ogunniyi
Research Centre for Infectious Diseases
School of Molecular and Biomedical Science
University of Adelaide
Adelaide, SA 5005, Australia

Yuta Okkotsu
Department of Microbiology
University of Colorado School of Medicine
Aurora, CO 80045

Gregory C. Palmer
Institute for Cellular and Molecular Biology
The University of Texas at Austin
Austin, TX 78712

Kai Papenfort
Department of Molecular Biology
Princeton University
Princeton, NJ 08544

Matthew R. Parsek
Department of Microbiology
University of Washington
Seattle, WA 98195

James C. Paton
Research Centre for Infectious Diseases
School of Molecular and Biomedical Science,
University of Adelaide
Adelaide, SA 5005, Australia

Ian R. Peak
The Institute for Glycomics
Griffith University
Gold Coast Campus
Parklands Drive
Southport, QLD 4222, Australia
Robert D. Perry  
Department of Microbiology, Immunology, and Molecular Genetics  
University of Kentucky  
Lexington, KY 40536-0298

Benoit Polack  
TheREx, TIMC-IMAG Laboratory  
UMR 5525 CNRS  
Université Joseph Fourier  
Grenoble, France

Daniel A. Powell  
Department of Microbial Pathogenesis  
University of Maryland, Baltimore  
Baltimore, MD 21201

Christopher L. Pritchett  
East Tennessee State University  
Department of Health Sciences  
Johnson City, TN 37614

Julian I. Rood  
Department of Microbiology  
Monash University  
Clayton, Victoria 3800, Australia

Mayukh Sarkar  
Department of Microbiology and Molecular Genetics  
University of Texas Medical School at Houston  
Houston, TX 77030

Michael J. Schurr  
Department of Microbiology  
University of Colorado School of Medicine  
Aurora, CO 80045

Drew J. Schwartz  
Department of Molecular Microbiology  
Washington University School of Medicine  
St. Louis, MO 63110

Cynthia M. Sharma  
Research Centre of Infectious Diseases  
University of Würzburg  
Würzburg, Germany

Dakang Shen  
School of Cellular and Molecular Medicine  
University of Bristol  
University Walk  
Bristol BS8 1TD, United Kingdom

Eric P. Skaar  
Department of Pathology, Microbiology and Immunology  
Vanderbilt University Medical Center  
Nashville, TN 37232

Karen Skorupski  
Department of Microbiology and Immunology  
Dartmouth Medical School  
Hanover, NH 03755

Vanessa Sperandio  
Department of Microbiology  
UT Southwestern Medical Center  
Dallas, TX 75390

Yogitha N. Srikhanta  
Department of Microbiology and Immunology  
The University of Melbourne  
Royal Parade, Parkville  
Melbourne, VIC 3010, Australia

Andrew M. Stern  
Department of Microbiology  
Perelman School of Medicine  
University of Pennsylvania  
Philadelphia, PA 19104

Ronald K. Taylor  
Department of Microbiology and Immunology  
Dartmouth Medical School  
Hanover, NH 03755

Victor J. Torres  
Department of Microbiology  
New York University School of Medicine  
New York, NY 10016

Bertrand Toussaint  
TheREx, TIMC-IMAG Laboratory  
UMR 5525 CNRS  
Université Joseph Fourier  
Grenoble, France

Boo Shan Tseng  
Department of Microbiology  
University of Washington  
Seattle, WA 98195

Andrés Vázquez-Torres  
Department of Microbiology  
University of Colorado Denver School of Medicine  
Aurora, CO 80045
Jörg Vogel
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany

Jovanka M. Voyich
Department of Immunology and Infectious Diseases
Montana State University
Bozeman, MT 59718

Aimee K. Wessel
Section of Molecular Genetics and Microbiology
The University of Texas at Austin
Austin, TX 78712

Marvin Whiteley
Institute for Cellular and Molecular Biology and Section of Molecular Genetics and Microbiology
The University of Texas at Austin
Austin, TX 78712

Bobbi Xayarath
Department of Microbiology and Immunology
University of Illinois at Chicago College of Medicine
Chicago, IL 60612

Thomas C. Zahrt
Department of Microbiology and Molecular Genetics Center for Infectious Disease Research
Medical College of Wisconsin
Milwaukee, WI 53226

Jun Zhu
Department of Microbiology
Perelman School of Medicine
University of Pennsylvania
Philadelphia, PA 19104

Wilma Ziebuhr
Institute for Molecular Infection Biology
University of Würzburg
Würzburg, Germany
Arguably, the theme of virulence regulation within the field of bacterial pathogenesis began as early as the 1930s, with a relatively straightforward observation about the inhibitory effect of iron on the in vitro production of diphtheria toxin by Corynebacterium diphtheriae. Three independent laboratories reported this important discovery (those of Pappenheimer and Johnson, Locke and Main, and Pope). It was then nearly two decades later before the next major leap of insight into the regulation of diphtheria toxin came about. In 1951, Freeman reported in the Journal of Bacteriology that the conversion of a nontoxigenic (i.e., avirulent) strain of C. diphtheriae to one that expresses diphtheria toxin required exposure of the avirulent strain to lysates containing phage B (β) but not phage A. Ultimately, these two discoveries provided an extraordinary amount of stimulating fodder to generations of other investigators. First, they established a solid foundation for the further understanding of the mechanisms of C. diphtheriae toxin regulation. Second, they offered novel and fascinating paradigms that were clearly worthy of further investigation in the context of the regulation of virulence in a plethora of other animal, as well as plant, bacterial pathogens.

In the time following those key discoveries, there have been thousands of publications directly relating to the topic of this book (>8,000 references found in a PubMed search from 1980, with the query “Regulation of Bacterial Virulence”). Clearly, this field is advancing at a remarkable pace. As a consequence, we felt that it would be worthwhile at this time to assemble a compendium of many of the more fascinating and contemporary insights relating to this topic from outstanding authorities in the field, with the wish to stimulate further research efforts.

Therefore, in this book we have attempted to provide a wide range of topics that represent a balance between the newest information along more established lines of investigation (e.g., iron, chapters 5, 6, and 16), as well as information describing refreshing new paradigms that have been investigated within only the past few years (e.g., vesicle formation and host signaling, chapters 23 and 27). It is true that the book devotes significant focus toward some areas, such as the effects of iron on bacterial virulence. Most likely this is a consequence of both its early discovery in relation to the regulation of bacterial virulence (see above) and the increasing realization that the role of environmental iron levels in virulence is magnificently complex, from the standpoint of both the pathogen and the host. That is, iron has an impact that reaches far beyond simply regulating the expression of virulence determinants. Although iron was subsequently discovered to affect the expression of other major bacterial toxins (e.g., Shiga toxin and Pseudomonas aeruginosa exotoxin A), environmental iron levels have also been shown to have an extraordinary impact on increasingly intricate processes relating to bacterial virulence, including biofilm formation, basic physiological processes, resistance to oxidative stress, and basic intermediary metabolism (see chapters 1, 5, 6, 9, 16, and 22).

Another example of how early observations can establish an important paradigm is provided by the requirement of a bacteriophage in the regulation of bacterial virulence, as described above with the β phage of C. diphtheriae. Decades later came the observations about the requirement of a different type of bacteriophage in the production of cholera toxin. In fact, cholera toxin provides an amazingly complex story about virulence gene regulation, as well as the intricate overlapping control mechanisms of different virulence factors (see chapter 12). For this reason, Vibrio cholerae features prominently in more than one chapter. Even so, it is clear that much still needs to be explored about the regulation of cholera toxin expression and how phage-associated genes affect the virulence of V. cholerae.

We have also provided chapters (see chapters 2, 27, and 28) from outstanding authors who are investigating the regulation of extremely complex behaviors of bacterial pathogens. These include descriptions of how some bacteria (e.g., P. aeruginosa) control gene regulation before, during, and after their transition from an acute infection to a more chronic one. Along similar lines, also included is a chapter (chapter 28) that provides new insights about the regulatory transition of V. cholerae from inside a human host to its more natural environments, such as estuaries, where
it exists in planktonic form as well as in biofilms, and then back into a human host.

Last, but not least, we gratefully acknowledge all the other outstanding chapters we were not able to mention above, due to space constraints of this preface. The omission of any chapter in this book would most certainly diminish its value. As the editors, we offer our sincere thanks to all of the authors for their dedication and hard work toward the production of this book.

It is hoped that the exciting discoveries described by all of the wonderful authors of this book will be as inspirational to both young and more seasoned investigators, as the early observations about the regulation of diphtheria toxin were to scores of scientists for decades. We can only hope that this will most certainly be so.

Michael L. Vasil
Andrew J. Darwin
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