TUBERCULOSIS AND THE TUBERCLE BACILLUS
2ND EDITION
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EDITED BY

William R. Jacobs, Jr.
Department of Immunology and Microbiology, Albert Einstein School of Medicine, Bronx, New York

Helen McShane
Cellular Immunology and Vaccine Development Group, Nuffield Department of Medicine, Jenner Institute, University of Oxford, Oxford, United Kingdom

Valerie Mizrahi
Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Faculty of Health Sciences, Rondebosch, South Africa

Ian M. Orme
Department of Microbiology, Immunology, and Pathology, Colorado State University, Fort Collins, Colorado

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Contributors

Else Marie Agger
Department of Infectious Disease Immunology, Statens
Serum Institut, Artillerivej 5, Copenhagen, Denmark

Yossef Av-Gay
Division of Infectious Diseases, Department of Medicine,
University of British Columbia, Vancouver, Canada

Maxime Barbier
Laboratoire Biologie Intégrative des Populations,
Evolution Moléculaire; Institut de Systématique, Evolution,
Biodiversité, UMR-CNRS 7205, Muséum National
d’Histoire Naturelle, Univ. Pierre et Marie Curie, EPHE,
Sorbonne Universités, Paris, France

Randall J. Basaraba
Department of Microbiology, Immunology, and Pathology,
College of Veterinary Medicine and Biomedical Sciences,
Colorado State University, Fort Collins, Colorado

Marcel Behr
McGill International TB Centre & Department of
Epidemiology & Biostatistics, McGill University,
Montreal, Canada

Michael Berney
Albert Einstein College of Medicine, Department of
Microbiology and Immunology, New York, New York

Linda Berney-Meyer
Albert Einstein College of Medicine, Department of
Microbiology and Immunology, New York, New York

Catharina C. Boehme
FIND, Geneva, Switzerland

Eva C. Boritsch
Institut Pasteur, Unit for Integrated Mycobacterial
Pathogenomics, Paris, France

Miriam Braunstein
Department of Microbiology and Immunology, University of
North Carolina – Chapel Hill, Chapel Hill, North Carolina

Susanna Brighenti
Center for Infectious Medicine (CIM), F59, Department
of Medicine, Karolinska Institutet, Karolinska University
Hospital Huddinge, Stockholm, Sweden

Roland Brosch
Institut Pasteur, Unit for Integrated Mycobacterial
Pathogenomics, Paris, France

Bryce M. Buddle
AgResearch, Hopkirk Research Institute, Palmerston North,
New Zealand

Gregory M. Cook
University of Otago, Department of Microbiology and
Immunology, Otago School of Medical Sciences, Dunedin,
New Zealand, and Maurice Wilkins Center for Molecular
Biodiscovery, The University of Auckland, Auckland, New
Zealand

Andrea Cooper
University of Leicester, Infection Immunity and
Inflammation, Leicester, Leicestershire, United Kingdom

Anna K. Coussens
Clinical Infectious Diseases Research Initiative, Division
of Medical Microbiology, Department of Pathology, and
Institute of Infectious Disease and Molecular Medicine,
University of Cape Town, Cape Town, South Africa

Dean C. Crick
Colorado State University, Department of Microbiology,
Immunology, and Pathology, Fort Collins, Colorado

Neeraj Dhar
Global Health Institute, École Polytechnique Fédérale de
Lausanne, Lausanne, Switzerland

Keertan Dheda
Lung Infection and Immunity Unit, Division of Pulmonology
and UCT Lung Institute, Department of Medicine,
University of Cape Town, Cape Town, South Africa
Contributors

Zanele Ditse
MRC/NHLS/UCT Molecular Mycobacteriology Research Unit, DST/NRF Centre of Excellence for Biomedical TB Research, Department of Pathology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

Racquel Domingo-Gonzalez
Department of Molecular Microbiology, Washington University in St. Louis, St. Louis, Missouri

Elsa du Bruyn
Clinical Infectious Diseases Research Initiative, Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Observatory, Republic of South Africa

Elyse Dunn
University of Otago, Department of Microbiology and Immunology, Otago School of Medical Sciences, Dunedin, New Zealand

Helen A. Fletcher
Immunology and Infection Department, London School of Hygiene & Tropical Medicine, London, United Kingdom

Fabio L. Fontes
Colorado State University, Department of Microbiology, Immunology, and Pathology, Fort Collins, Colorado

Susana Gardete
Department of Medicine, Division of Infectious Diseases, Weill Cornell Medical College, New York, New York

Ben Gold
Department of Microbiology and Immunology, Weill Cornell Medical College, New York, New York

Natasha Gous
Department of Molecular Medicine and Haematology, Faculty of Health Sciences, University of the Witwatersrand, National Health Laboratory Service and National Priority Program of the National Health Laboratory Service, Johannesburg, South Africa

Chris Greening
The Commonwealth Scientific and Industrial Research Organization, Land and Water Flagship, Acton, Australia, and Monash University, School of Biological Sciences, Clayton, Victoria, Australia

Kiel Hards
University of Otago, Department of Microbiology and Immunology, Otago School of Medical Sciences, Dunedin, New Zealand

Travis E. Hartman
Department of Medicine, Division of Infectious Diseases, Weill Cornell Medical College, New York, New York

Erik Hasenoehrle
Albert Einstein College of Medicine, Department of Microbiology and Immunology, Bronx, New York

Mark Hatherill
South African Tuberculosis Vaccine Initiative (SATVI) and Institute of Infectious Disease & Molecular Medicine (IDM), University of Cape Town, Wernher & Beit South Building, Anzio Road, Observatory, Cape Town, South Africa

Adam Heikal
University of Otago, Department of Microbiology and Immunology, Otago School of Medical Sciences, Dunedin, New Zealand, and Maurice Wilkins Center for Molecular Biodiscovery, The University of Auckland, Auckland, New Zealand

Marcela I. Henao-Tamayo
Department of Microbiology, Immunology and Pathology, Mycobacteria Research Laboratory, Colorado State University, Fort Collins, Colorado

R. Glyn Hewinson
Animal and Plant Health Agency – Weybridge, Addlestone, Surrey, United Kingdom

Wen-Zhe Ho
Animal Biosafety Level III Laboratory, Center for Animal Experiment, State Key Laboratory of Virology, Wuhan University, Wuhan, China; Department of Pathology and Laboratory Medicine, Temple University Lewis Katz School of Medicine, Philadelphia, Pennsylvania

Lu Huang
Microbiology and Immunology, College of Veterinary Medicine, Cornell University, Ithaca, New York

Robert L. Hunter
Department of Pathology and Laboratory Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, Texas

Robert S. Jansen
Department of Medicine, Division of Infectious Diseases, Weill Cornell Medical College, New York, New York

Tracy L. Keiser
Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York

Shabaana Khader
Department of Molecular Microbiology, Washington University in St. Louis, St. Louis, Missouri

Joanna R. Kirman
Department of Microbiology and Immunology, University of Otago, Dunedin, New Zealand

Thomas Kohl
Molecular Mycobacteriology, Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Biowissenschaften, Borstel, Germany

Laurent Kremer
IRIM (ex-CPBS) UMR 9004, Infectious Disease Research Institute of Montpellier (IDRIM), Université de Montpellier, CNRS, Montpellier, France

Giulia Manina
Microbial Individuality and Infection Group, Institut Pasteur, 25 rue du Docteur Roux, Paris, France
Contributors

John McKinney
Global Health Institute, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Helen McShane
The Jenner Institute, University of Oxford, Old Road Campus Research Building, Roosevelt Drive, Oxford, United Kingdom

Matthias Merker
Molecular Mycobacteriology, Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Biowissenschaften, Borstel, Germany

Brittany K. Miller
Department of Microbiology and Immunology, University of North Carolina – Chapel Hill, Chapel Hill, North Carolina

Yoshio Nakatani
University of Otago, Department of Microbiology and Immunology, Otago School of Medical Sciences, Dunedin, New Zealand, and Maurice Wilkins Center for Molecular Biodiscovery, The University of Auckland, Auckland, New Zealand

Vivek Naranbhai
Wellcome Trust Centre for Human Genetics, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, and Centre for the AIDS Programme of Research in South Africa, University of KwaZulu Natal, Durban, South Africa

Carl Nathan
Department of Microbiology and Immunology, Weill Cornell Medical College, New York, New York

Mark P. Nicol
University of Cape Town, Cape Town, South Africa

Stefan Niemann
Molecular Mycobacteriology, Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Biowissenschaften, and German Center for Infection Research (DZIF), partner site Borstel, Borstel, Germany

Lara Noble
Department of Molecular Medicine and Haematology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, Gauteng, South Africa

Eric L. Nuermberger
Center for Tuberculosis Research, Department of Medicine, Johns Hopkins University School of Medicine, and Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Anil K. Ojha
Wadsworth Center, NY State Department of Health and University at Albany, Albany, New York

Diane J. Ordway
Mycobacteria Research Laboratories, Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, Colorado

Ian M. Orme
Colorado State University, Fort Collins, Colorado

Madhukar Pai
McGill International TB Centre & Department of Epidemiology & Biostatistics, McGill University, Montreal, Canada

Juliet C. Peña
Department of Pathology and Laboratory Medicine, Temple University Lewis Katz School of Medicine, 3500 N. Broad St., MERB 843, Philadelphia, Pennsylvania

Kevin Pethe
Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

Oliver Prince
Department of Molecular Microbiology, Washington University in St. Louis, St. Louis, Missouri

Georgiana E. Purdy
Department of Microbiology and Immunology, Oregon Health Sciences University, Portland, Oregon

Kyu Y. Rhee
Department of Medicine and Department of Microbiology & Immunology, Division of Infectious Diseases, Weill Cornell Medical College, New York, New York

Melissa Richard-Greenblatt
Division of Infectious Diseases, Department of Medicine, University of British Columbia, Vancouver, Canada

Kyle H. Rohde
Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, Florida

David G. Russell
Microbiology and Immunology, College of Veterinary Medicine, Cornell University, Ithaca, New York

Larry S. Schlesinger
Department of Microbial Infection and Immunity, Center for Microbial Interface Biology, The Ohio State University, Columbus, Ohio

Jeffrey S. Schorey
Department of Biological Sciences, Eck Institute for Global Health, Center for Rare and Neglected Diseases, University of Notre Dame, Notre Dame, Indiana

Lesley Scott
Department of Molecular Medicine and Haematology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, Gauteng, South Africa
Contributors

Thomas J. Scriba
South African Tuberculosis Vaccine Initiative, Division of Immunology, Department of Pathology, and Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa

Wendy Susan Stevens
Department of Molecular Medicine and Haematology, Faculty of Health Sciences, University of the Witwatersrand, National Health Laboratory Service, and National Priority Program of the National Health Laboratory Service, Johannesburg, South Africa

Philip Supply
INSERM U1019; CNRS UMR 8204; Institut Pasteur de Lille, Center for Infection and Immunity of Lille; and Université Lille Nord de France, Lille, France

Dereck Tait
Aeras, Blackriver Park, First Floor, Observatory, Cape Town, South Africa

Brian C. VanderVen
Microbiology and Immunology, College of Veterinary Medicine, Cornell University, Ithaca, New York

Catherine Vilchèze
Howard Hughes Medical Institute, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York

H. Martin Vordermeier
Animal and Plant Health Agency – Weybridge, Addlestone, Surrey, United Kingdom

Zhe Wang
Department of Medicine, Division of Infectious Diseases, Weill Cornell Medical College, New York, New York

Digby F. Warner
MRC/NHLS/UCT Molecular Mycobacteriology Research Unit, Department of Pathology, and Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Rondebosch, South Africa

Robert John Wilkinson
Department of Medicine, Imperial College London, and The Francis Crick Institute Mill Hill Laboratory, London, United Kingdom

Ann Williams
Health UK, Porton Down, Salisbury, United Kingdom

Thierry Wirth
Laboratoire Biologie Intégrative des Populations, Evolution Moléculaire; Institut de Systématique, Evolution, Biodiversité, UMR-CNRS 7205, Muséum National d'Histoire Naturelle, Univ. Pierre et Marie Curie, EPHE, Sorbonne Universités, Paris, France

Ka-Wing Wong
Shanghai Public Health Clinical Center, Key Laboratory of Medical Molecular Virology, School of Basic Medical Sciences, Shanghai Medical College of Fudan University, Shanghai, People’s Republic of China

Katelyn E. Zulauf
Department of Microbiology and Immunology, University of North Carolina – Chapel Hill, Chapel Hill, North Carolina
It is the height of irony that the man who discovered the smallpox vaccine, Edward Jenner, lost both his wife and son to tuberculosis (TB). By the time smallpox was essentially eradicated, it is estimated that over 300 million people had died from this disease over the preceding century. Its eventual prevention—by a simple vaccine—clearly illustrates the power of scientific discovery and how its application can affect human health. Hundreds of millions of people have been spared death and suffering from infectious diseases because of the development of vaccines and chemotherapeutic agents in the last 100 years. Millions of lives have been saved with the use of the TB vaccine, BCG, and the development of chemotherapeutic regimens for TB. Depressingly, despite these effective interventions, TB remains one of the most challenging problems of global health, with over 9 million new cases and 1.6 million deaths each year. This crisis has been further compounded by the emergence of the HIV epidemic, as this explosive and deadly combination has dramatically increased the global spread of TB, including increasing numbers of cases of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Historically, mycobacterial disease has long been at the forefront of scientific discovery for infectious diseases. The leprosy bacillus, Mycobacterium leprae, the first bacterium to be associated with human disease, was initially visualized by Gerhard Armauer Hansen in 1873. Earlier, Jean Antoine Villemin was the first person to realize that lung tubercles were infectious and not cancerous. By the 1880s, Robert Koch, aware of both of these discoveries, not only observed the tubercle bacilli in tubercles, but developed a growth medium of heated serum to cultivate the tubercle bacillus outside of humans. He went on to repeat the transfer experiment of Villemin and transferred the disease of TB to numerous animal species, establishing the experimental paradigm (“the postulates”) of how to prove that an infectious agent is a cause of a disease. Koch’s findings led Albert Calmette and Camille Guérin to follow Jenner’s approach of developing an attenuated pathogen for use as a vaccine, using the bovine tubercle bacillus to develop the bacille Calmette-Guérin (BCG) vaccine that bears their names and is still used to this day.

It is noteworthy that Paul Ehrlich was sitting in the lecture hall when Robert Koch presented his work in 1882; he later went on to help Koch improve his staining techniques. By observing the selective staining of various cell types, including human cells and different bacteria, Ehrlich also developed the idea of chemotherapy—“magic bullets” that could kill microbial pathogens. He tried for years to develop a chemical that could kill the tubercle bacillus, with little success, though at the same time was far more successful in developing a treatment for syphilis. In the 1930s, his protégé Gerhard Domagk discovered the first sulfonamide to treat bacterial infections such as streptococcus, and as this fledging field expanded, para-amino salicylic acid and isoniazid were discovered to be active against the TB bacillus. Parallel studies by Salaman Waksman and Albert Schatz in the 1950s led to the discovery of streptomycin, the first bactericidal drug for the tubercle bacilli.

Despite these many historical advances, the TB bacillus—Mycobacterium tuberculosis—has proven to be a formidable adversary against numerous interventions. Nevertheless, despite the arduous challenges of
working with this dangerous pathogen, the field continues to persevere, and our continued success in the pursuit of knowledge would, we suspect, be applauded by Koch, Ehrlich, Calmette, and many others, as we strive to find and apply more effective cures for this dreadful disease. In this spirit, this textbook is a collection of state-of-the-art research aimed at understanding the TB bacillus, the way it infects its host, the mechanisms by which it persists in the face of host immunity, and current intervention and therapeutic methods. The contributors of this book believe that such continued and dedicated research efforts will eventually lead to better vaccines, better chemotherapies, and ultimately the eradication of TB—Edward Jenner’s revenge.

William R. Jacobs, Jr.
Helen McShane
Valerie Mizrahi
Ian M. Orme
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