Bugs as Drugs

THERAPEUTIC MICROBES
FOR THE PREVENTION AND TREATMENT OF DISEASE

EDITED BY
Robert A. Britton
Baylor College of Medicine, Molecular Virology and Microbiology, Houston, Texas

Patrice D. Cani
Université catholique de Louvain, Louvain Drug Research Institute, WELBIO-Walloon Excellence in Life Sciences, Brussels, Belgium

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Contributors

Stephen T. Abedon
Department of Microbiology, The Ohio State University, Mansfield, Ohio

Emma Allen-Vercoe
Molecular and Cellular Biology, University of Guelph, 50 Stone Road East, Guelph, Ontario, Canada

Anissa M. Armet
Department of Agricultural, Nutritional and Food Science, University of Alberta, Edmonton, Alberta, Canada

Jennifer M. Auchtung
Alkek Center for Metagenomics and Microbiome Research and Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas

Guido J. Bakker
Department of Internal and Vascular Medicine, Academic Medical Center, Amsterdam, The Netherlands

Rodolphe Barrangou
Department of Food, Bioprocessing and Nutrition Sciences, North Carolina State University, Raleigh, North Carolina

Luis G. Bermúdez-Humarán
Micalis Institute, INRA, AgroParisTech, Université Paris-Saclay, Jouy-en-Josas, France

Robert A. Britton
Baylor College of Medicine, Molecular Virology and Microbiology, Houston, Texas

Patrice D. Cani
Université catholique de Louvain, Louvain Drug Research Institute, WELBIO – Walloon Excellence in Life Sciences, Brussels, Belgium

Paul E. Carlson, Jr.
Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines Research and Review, Center for Biologics Evaluations and Research, Food and Drug Administration, Silver Spring, Maryland
Anne-Marie Cassard  
INSERM U996 Inflammation, Chemokines and Immunopathology,  
DHU Hepatinov, Univ Paris-Sud, Université Paris-Saclay,  
Clamart, France

Fraser L. Collins  
Department of Physiology, Michigan State University, East Lansing, Michigan

James Collins  
Alkek Center for Metagenomics and Microbiome Research and Department  
of Molecular Virology and Microbiology, Baylor College of Medicine,  
Houston, Texas

Edward C. Deehan  
Department of Agricultural, Nutritional and Food Science, University of  
Alberta, Edmonton, Alberta, Canada

Susana Delgado  
Department of Microbiology and Biochemistry of Dairy Products,  
Dairy Research Institute of Asturias, Spanish National Research  
Council (IPLA-CSIC), Villaviciosa, Asturias, Spain

Patricia I. Diaz  
Division of Periodontology, Department of Oral Health and Diagnostic Sciences,  
University of Connecticut Health, Farmington, Connecticut

Sheila M. Dreher-Resnick  
Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines  
Research and Review, Center for Biologics Evaluations and Research,  
Food and Drug Administration, Silver Spring, Maryland

Rebecca M. Duar  
Department of Agricultural, Nutritional and Food Science,  
University of Alberta, Edmonton, Alberta, Canada

Krista Dubin  
Immunology Program and Infectious Disease Service, Memorial  
Sloan-Kettering Cancer Center, and Immunology and Microbial  
Pathogenesis Program, Weill Cornell Graduate School of Medical  
Sciences, New York, New York

Melinda A. Engevik  
Department of Pathology and Immunology, Baylor College of Medicine, and  
Department of Pathology, Texas Children’s Hospital, Houston, Texas

Philippe Gérard  
Micalis Institute, INRA, AgroParisTech, Université Paris-Saclay,  
Jouy-en-Josas, France

Claudio Hidalgo-Cantabrana  
Department of Microbiology and Biochemistry of Dairy Products,  
Dairy Research Institute of Asturias, Spanish National Research  
Council (IPLA-CSIC), Villaviciosa, Asturias, Spain
Contributors

Anilei Hoare
Division of Periodontology, Department of Oral Health and Diagnostic Sciences, University of Connecticut Health, Farmington, Connecticut

Mingliang Jin
Department of Microbiology and Immunology, Northwestern Polytechnical University, Xi’an, Shaanxi, China

Brian P. Landry
Department of Bioengineering, Rice University, Houston, Texas

Philippe Langella
Micalis Institute, INRA, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France

Abelardo Margolles
Department of Microbiology and Biochemistry of Dairy Products, Dairy Research Institute of Asturias, Spanish National Research Council (IPLA-CSIC), Villaviciosa, Asturias, Spain

Philip D. Marsh
Division of Oral Biology, School of Dentistry, University of Leeds, Leeds, United Kingdom

Laura R. McCabe
Department of Physiology, Department of Radiology, and Biomedical Imaging Research Center, Michigan State University, East Lansing, Michigan

Max Nieuwdorp
Dept. of Internal & Vascular Medicine, Academic Medical Center, and Dept. of Internal Medicine, VU Univ. Medical Center, Amsterdam, The Netherlands; Wallenberg Laboratory, Dept. of Molecular and Clinical Medicine, Univ. of Gothenburg, Gothenburg, Sweden

Laura Ortiz-Velez
Baylor College of Medicine, Molecular Virology and Microbiology, Houston, Texas

Paul W. O'Toole
School of Microbiology and APC Microbiome Institute, University College Cork, Ireland

Eric G. Pamer
Memorial Sloan-Kettering Cancer Center and Weill Cornell Graduate School of Medical Sciences, New York, New York

Narayanan Parameswaran
Department of Physiology, Michigan State University, East Lansing, Michigan

Maria Elisa Perez-Muñoz
Department of Agricultural, Nutritional and Food Science, University of Alberta, Edmonton, Alberta, Canada
Contributors

Gabriel Perlemuter
INSERM U996 Inflammation, Chemokines and Immunopathology, 
DHU Hepatinov, Univ Paris-Sud, Université Paris-Saclay, and AP-HP, 
Hepatogastroenterology and Nutrition, Hôpital Antoine-Béclère, 
Clamart, France

Hubert Plovier
WELBIO-Walloon Excellence in Life Sciences and Biotechnology, and 
Metabolism and Nutrition Research Group, Louvain Drug Research Institute, 
Université Catholique de Louvain, Brussels, Belgium

Gregor Reid
Lawson Health Research Institute, Human Microbiome and Probiotics, 
F3-106, 268 Grosvenor Street, London, Ontario, Canada

Naiomy D. Rios-Arce
Department of Physiology, Michigan State University, East Lansing, Michigan

Patricia Ruas-Madiedo
Department of Microbiology and Biochemistry of Dairy Products, 
Dairy Research Institute of Asturias, Spanish National Research 
Council (IPLA-CSIC), Villaviciosa, Asturias, Spain

Lorena Ruiz
Department of Microbiology and Biochemistry of Dairy Products, 
Dairy Research Institute of Asturias, Spanish National Research 
Council (IPLA-CSIC), Villaviciosa, Asturias, Spain

Elisa Salvetti
School of Microbiology and APC Microbiome Institute, University College 
Cork, Ireland

Borja Sánchez
Department of Microbiology and Biochemistry of Dairy Products, 
Dairy Research Institute of Asturias, Spanish National Research 
Council (IPLA-CSIC), Villaviciosa, Asturias, Spain

Jonathan D. Schepper
Department of Physiology, Michigan State University, East Lansing, Michigan

Leopoldo N. Segal
Department of Medicine, NYU Division of Pulmonary, Critical Care, 
& Sleep Medicine, New York, New York

Scott Stibitz
Division of Bacterial, Parasitic, and Allergenic Products, Office of Vaccines 
Research and Review, Center for Biologics Evaluations and Research, 
Food and Drug Administration, Silver Spring, Maryland

Jeffrey J. Tabor
Department of Bioengineering and Department of Biosciences, Rice University, 
Houston, Texas
Jan-Peter van Pijkeren  
Department of Food Science, University of Wisconsin-Madison, Madison, Wisconsin

Terence Van Raay  
Molecular and Cellular Biology, University of Guelph, 50 Stone Road East, Guelph, Ontario, Canada

James Versalovic  
Department of Pathology and Immunology, Baylor College of Medicine, and Department of Pathology, Texas Children’s Hospital, Houston, Texas

Jens Walter  
Department of Agricultural, Nutritional and Food Science and Department of Biological Sciences, University of Alberta, Edmonton, Alberta, Canada

Benjamin G. Wu  
Department of Medicine, NYU Division of Pulmonary, Critical Care, & Sleep Medicine, New York, New York
About the Editors

Dr. Robert Britton is a Professor in the Department of Molecular Virology and Microbiology and is a Member of the Alkek Center for Metagenomics and Microbiome Research at Baylor College of Medicine. He presently directs a Therapeutic Microbiology laboratory that is focused on the use of microbes to prevent and treat human disease. Currently funded research projects in the laboratory range from the study of how traditional probiotic strains can ameliorate osteoporosis to how intestinal microbial communities resist invasion by the diarrheal pathogen Clostridium difficile. His laboratory has made several advances in the development of genetic and microbial growth platforms to aid in the understanding of how microbes promote health and disease. These include the development of precision genome engineering technologies for lactic acid bacteria and the development of human fecal minibioreactor arrays to study the function of microbial communities in a high-throughput manner.

Dr. Patrice D. Cani is a Professor at the Université catholique de Louvain (UCL) and investigator for WELBIO (Walloon Excellence in Lifesciences Biotechnology) and the Fund for Scientific Research (FRS-FNRS). He is a member of the Royal Academy of Medicine of Belgium and the recipient of prestigious grants and prizes. He has published more than 200 papers, reviews, and chapter books in the field of gut microbiota, prebiotics/probiotics, and metabolism. In the early 2000s, he started to investigate the interactions between gut microbes and complex biological systems (endocannabinoids, immunity) by using prebiotics. In 2007, he discovered the concept of metabolic endotoxemia and more recently the role of specific bacteria (e.g., Akkermansia). Twitter: @MicrObesity.
Preface

The reinvigoration of research into the human microbiome—the collection of microbes that reside within and on our body—has resulted in novel insights into the role of these microorganisms in health and disease. Associations between the composition of the intestinal microbiome and many human diseases, including inflammatory bowel disease, cardiovascular disease, metabolic disorders, and cancer, have been elegantly described in the past decade. Because of these seminal discoveries and the increased public interest in the use of probiotics and prebiotics to impact health, many researchers and entrepreneurs are working toward translating the human microbiome into novel diagnostics and therapeutics. Thus, one of the main objectives of this volume is to provide insights into how one may capitalize on the enormous amount of knowledge being generated in microbe-human interactions for the translation into products that will benefit humankind.

We note that microbiome research, and the use of microbes as therapeutics, is not of recent origin. Elie Metchnikoff posited over 100 years ago that lactic acid bacteria found in fermented milk were beneficial to health and prevented intestinal “putrefaction.” Ben Eiseman and colleagues began using fecal enema as an adjunct therapy in the treatment of pseudomembranous enterocolitis in 1958, a full 20 years prior to Clostridium difficile being identified as one of the main causative agents of this disease. Indeed, fecal transplantation for the treatment of disease dates back centuries to the 4th century, when Ge Hong, a well-known traditional Chinese medicine doctor, described the use of human fecal material by mouth to treat his patients with severe diarrhea.

Why, then, the increase in developing novel therapeutics and diagnostics using microbes now? Significant improvements in genetic engineering of non-model organisms, next-generation sequencing technology, and metabolic profiling have certainly stimulated much confidence in being able to harness microbes to improve health. In addition, systems biology approaches and synthetic engineering of microbes are now high-throughput and cost-effective enough to explore a much wider range of therapeutic possibilities to be vetted.

Finally, we note there is much hype and enthusiasm over the use of microbes—not only classical probiotics but also future next-generation beneficial microbes and engineered bacteria—to make significant impacts on many human diseases and to restore healthy microbial communities. However, our understanding of how microbial communities function to influence health is still quite shallow, and translation to therapeutics will require patience and basic research. For example, the linking of many diseases to altered microbial communities is only
by association, and in many cases these correlations have only been uncovered in mouse models. We must acknowledge that despite the explosion of science in the gut microbiome in the past decade, much of the work has described associations between the microbiome and disease with few instances of causation. Until microbiome shifts that are associated with disease are shown to be truly driving disease manifestation, it will be difficult to know which diseases can be tackled via microbiome manipulation. It is important to remind the scientific community that just because one or several bacteria are increased or decreased in a specific pathological situation, this does not necessarily mean they play a role in disease. Therefore, a deeper understanding of the mechanisms and functions of microbiome-human interaction will be required to fully realize the potential of developing drugs for the treatment of acute and chronic diseases. Another objective of this book is for readers to identify key gaps that exist in their respective fields that need to be closed in order to assist in moving therapeutic microbes from the bench to the bedside.

We are indebted to the authors for their contributions to this book, which we know took a considerable amount of time to produce. We hope you find the chapters informative and useful in your endeavors.

Robert A. Britton
Patrice D. Cani
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