
Yuriy A. Knirel • Miguel A. Valvano
Editors

Bacterial Lipopolysaccharides

Structure, Chemical Synthesis,
Biogenesis and Interaction
with Host Cells

SpringerWienNewYork

Yuriy A. Knirel
N.D. Zelinsky Institute of
Organic Chemistry
Russian Academy of Sciences
Leninsky Prospekt 47
119991 Moscow, V-334
Russia
yknirel@gmail.com

Miguel A. Valvano
Centre for Human Immunology and
Department of Microbiology and Immunology
University of Western Ontario
London, ON N6A 5C1
Canada
mvalvano@uwo.ca

This work is subject to copyright.

All rights are reserved, whether the whole or part of the material is concerned, specifically those of translation, reprinting, re-use of illustrations, broadcasting, reproduction by photocopying machines or similar means, and storage in data banks.

Product Liability: The publisher can give no guarantee for all the information contained in this book. The use of registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

© 2011 Springer-Verlag/Wien

SpringerWienNewYork is a part of Springer Science+Business Media
springer.at

Cover design: WMXDesign GmbH, Heidelberg, Germany
Typesetting: SPI, Pondicherry, India

Printed on acid-free and chlorine-free bleached paper
SPIN: 12599509

With 65 Figures

Library of Congress Control Number: 2011932724

ISBN 978-3-7091-0732-4 e-ISBN 978-3-7091-0733-1
DOI 10.1007/978-3-7091-0733-1
SpringerWienNewYork

Preface

The lipopolysaccharide (LPS) is the major component of the outer leaflet of the outer membrane of Gram-negative bacteria. It contributes essentially to the integrity and stability of the outer membrane, represents an effective permeability barrier towards external stress factors, and is thus indispensable for the viability of bacteria in various niches, including animal and plant environment. On the other hand, the presence of the LPS on the cell surface is beneficial for the host as it serves as a pathogen-associated molecular pattern recognized by, and thus activates, the host immune system resulting normally in elimination of the pathogen. Being unable to get rid of the LPS, bacteria evolved various mechanisms for LPS structure modification to make them invisible for the immune system and resistant to defense factors such as complement and antibiotics. This highlights the LPS as the most variable cell wall constituent.

Since its discovery in the late 19th century the LPS, then named endotoxin, has attracted the curiosity of many researchers virtually in all fields of life science such as medicine, microbiology, pharmacology, chemistry, biochemistry, biophysics, immunology, cell biology, and genetics. Attesting this in part, more than 71,000 and 79,000 publications are cited in PubMed at the beginning of 2011 using LPS and endotoxin as queries, respectively. LPS has also attracted interest in biotechnology and the pharmacological industry for the development of diagnostic and therapeutic methods and reagents.

Early in the history of endotoxin, it was appreciated by Peter L. Panum in 1874 that putrid fluids contained a water-soluble, alcohol-insoluble, heat-resistant, non-volatile substance, which was lethal to dogs. Later, Richard Pfeiffer, a disciple of Robert Koch, showed that *Vibrio cholerae*, the cause of cholera, produced a heat-stable toxic substance that was associated with the insoluble part of the bacterial cell, coining the name “endotoxin” (from the Greek ‘endo’ meaning ‘within’). Through pioneer discoveries by Otto Westphal, Otto Lüderitz, Hiroshi Nikaïdo and Mary J. Osborn in the mid 1950s, we learned that the endotoxin corresponds to the LPS. Efficient purification protocols of the LPS were elaborated and principles of its structural organization, genetics and biochemistry were then established. These early studies propelled a long and productive road of chemical and biochemical research to reveal the details of structure and biosynthesis of each of the components of the LPS molecule. In parallel a large body of work resulted in the biological

characterization of the LPS in terms of its function as a potent elicitor of innate immune responses. This work culminated with the discovery by Bruce Beutler of the mouse gene encoding the TLR4 receptor molecule and the subsequent elucidation of the structural basis of the activation of the immune system by the LPS.

The purpose of this book is not to provide a comprehensive examination of all aspects related to the LPS but rather to give an up to date overview of research that applies to its chemistry, biosynthesis, genetics, and activities toward eukaryotic cells from structural and mechanistic perspectives.

Yuriy A. Knirel
Miguel A. Valvano

Contents

1 Lipid A Structure	1
Alba Silipo and Antonio Molinaro	
2 Structure of the Lipopolysaccharide Core Region	21
Otto Holst	
3 Structure of O-Antigens	41
Yuriy A. Knirel	
4 Chemical Synthesis of Lipid A and Analogues	117
Shoichi Kusumoto	
5 Chemical Synthesis of Lipopolysaccharide Core	131
Paul Kosma and Alla Zamyatina	
6 Genetics and Biosynthesis of Lipid A	163
Christopher M. Stead, Aaron C. Pride, and M. Stephen Trent	
7 Pathways for the Biosynthesis of NDP Sugars	195
Youai Hao and Joseph S. Lam	
8 Lipopolysaccharide Core Oligosaccharide Biosynthesis and Assembly	237
Uwe Mamat, Mikael Skurnik, and José Antonio Bengoechea	
9 Genetics, Biosynthesis and Assembly of O-Antigen	275
Miguel A. Valvano, Sarah E. Furlong, and Kinnari B. Patel	
10 Lipopolysaccharide Export to the Outer Membrane	311
Paola Sperandio, Gianni Dehò, and Alessandra Polissi	
11 Evolution of Lipopolysaccharide Biosynthesis Genes	339
Monica M. Cunneen and Peter R. Reeves	
12 The Molecular Basis of Lipid A and Toll-Like Receptor 4 Interactions	371
Georgina L. Hold and Clare E. Bryant	

13 Modulation of Lipopolysaccharide Signalling Through TLR4 Agonists and Antagonists	389
Francesco Peri, Matteo Piazza, Valentina Calabrese, and Roberto Cighetti	
14 Lipopolysaccharide and Its Interactions with Plants	417
Gitte Erbs and Mari-Anne Newman	
Index	435

Contributors

José Antonio Bengoechea Laboratory Microbial Pathogenesis, Consejo Superior Investigaciones Científicas, Fundación de Investigación Sanitaria Illes Balears, Recinto Hospital Joan March, Carretera Sóller Km12; 07110, Bunyola, Spain, bengoechea@caubet-cimera.es

Clare E. Bryant Department of Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge, UK CB3 0ES, ceb27@cam.ac.uk

Valentina Calabrese Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, valentina.calabrese@unimib.it

Roberto Cighetti Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, cighetti.roberto@hotmail.it

Monica M. Cunneen Division of Microbiology, School of Molecular and Microbial Biosciences, University of Sydney, Sydney, NSW 2006, Australia, monica.cunneen@sydney.edu.au

Gianni Dehò Dipartimento di Scienze biomolecolari e Biotecnologie, Università di Milano, Via Celoria 26, 20133 Milan, Italy, gianni.deho@unimi.it

Gitte Erbs Department of Plant Biology and Biotechnology, University of Copenhagen, Thorvaldsensvej 40, 1871 Frederiksberg, Denmark, ger@life.ku.dk

Sarah E. Furlong Centre for Human Immunology and Department of Microbiology and Immunology, University of Western Ontario, London, Ontario, Canada, N6A 5C1, sfurlon@uwo.ca

Youai Hao Department of Molecular and Cellular Biology, University of Guelph, 50 Stone Road E., Guelph, Canada, ON, N1G 2W1, haoy@uoguelph.ca

Georgina L. Hold Division of Applied Medicine, University of Aberdeen, Institute of Medical Sciences, Foresterhill, Aberdeen, UK AB25 2ZD, g.l.hold@abdn.ac.uk

Otto Holst Division of Structural Biochemistry, Research Center Borstel, Leibniz-Center for Medicine and Biosciences, Parkallee 4a/c, D-23845 Borstel, Germany, oholst@fz-borstel.de

Yuriy A. Knirel N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospekt 47, 119991 Moscow, V-334, Russia, yknirel@gmail.com

Paul Kosma Department of Chemistry, University of Natural Resources and Life Sciences, Muthgasse 18, A-1190 Vienna, Austria, paul.kosma@boku.ac.at

Shoichi Kusumoto Suntory Institute for Bioorganic Research, Wakayamadai 1-1-1, Shimamoto-cho, Mishima-gun, Osaka 618-8503, Japan, skus@sunbor.or.jp

Joseph S. Lam Department of Molecular and Cellular Biology, University of Guelph, 50 Stone Road E., Guelph, Canada ON, N1G 2W1, jlam@uoguelph.ca

Uwe Mamat Division of Structural Biochemistry, Research Center Borstel, Leibniz-Center for Medicine and Biosciences, Parkallee 4a/4c, D-23845 Borstel, Germany, umamat@fz-borstel.de

Antonio Molinaro Dipartimento di Chimica Organica e Biochimica, Università di Napoli Federico II, Via Cintia 4, 80126 Napoli, Italy, molinaro@unina.it

Mari-Anne Newman Department of Plant Biology and Biotechnology, University of Copenhagen, Thorvaldsensvej 40, 1871 Frederiksberg, Denmark, mari@life.ku.dk

Kinnari B. Patel Centre for Human Immunology and Department of Microbiology and Immunology, University of Western Ontario, London, Ontario, Canada, N6A 5C1, kpatel59@uwo.ca

Francesco Peri Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, francesco.peri@unimib.it

Matteo Piazza Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, matteo.piazza1@unimib.it

Alessandra Polissi Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, alessandra.polissi@unimib.it

Aaron C. Pride Institute of Cellular and Molecular Biology, University of Texas at Austin, Austin, TX 78712, USA, acpride@mail.utexas.edu

Peter R. Reeves Department of Microbiology, School of Molecular and Microbial Biosciences, University of Sydney, Sydney, New South Wales 2006, Australia, peter.reeves@sydney.edu.au

Alba Silipo Dipartimento di Chimica Organica e Biochimica, Università di Napoli Federico II, Via Cintia 4, 80126 Napoli, Italy, silipo@unina.it

Mikael Skurnik Department of Bacteriology and Immunology, Haartman Institute, University of Helsinki, P.O. Box 21, Haartmaninkatu 3, FIN-00014 Helsinki, Finland, mikael.skurnik@helsinki.fi

Paola Sperandeo Dipartimento di Biotecnologie e Bioscienze, Università di Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy, paola.sperandeo@unimib.it

Christopher M. Stead Georgia Health Sciences University, Department of Biochemistry and Molecular Biology, Augusta, GA 30912, USA, cstead@georgiahealth.edu

M. Stephen Trent Section of Molecular Genetics and Microbiology and Institute of Cellular and Molecular Biology, University of Texas at Austin, Austin, TX 78712, USA, strent@mail.utexas.edu

Miguel A. Valvano Centre for Human Immunology and Department of Microbiology and Immunology, University of Western Ontario, London, Canada ON N6A 5C1, mvalvano@uwo.ca

Alla Zamyatina Department of Chemistry, University of Natural Resources and Life Sciences, Muthgasse 18, A-1190 Vienna, Austria, alla.zamyatina@boku.ac.at

