

Monoclonal Antibodies against Bacteria

Volume III

Edited by

Alberto J. L. Macario

Everly Conway de Macario



Monoclonal Antibodies against Bacteria

Volume III

Edited by

Alberto J. L. Macario

Everly Conway de Macario

*Wadsworth Center for Laboratories and Research
New York State Department of Health
Albany, New York*

1986



ACADEMIC PRESS, INC.

Harcourt Brace Jovanovich, Publishers

Orlando San Diego New York Austin

Boston London Sydney Tokyo Toronto

141
B
1

COPYRIGHT © 1986 BY ACADEMIC PRESS, INC.
ALL RIGHTS RESERVED.
NO PART OF THIS PUBLICATION MAY BE REPRODUCED OR
TRANSMITTED IN ANY FORM OR BY ANY MEANS, ELECTRONIC
OR MECHANICAL, INCLUDING PHOTOCOPY, RECORDING, OR
ANY INFORMATION STORAGE AND RETRIEVAL SYSTEM, WITHOUT
PERMISSION IN WRITING FROM THE PUBLISHER.

ACADEMIC PRESS, INC.
Orlando, Florida 32887

United Kingdom Edition published by
ACADEMIC PRESS INC. (LONDON) LTD.
24-28 Oval Road, London NW1 7DX

Library of Congress Cataloging in Publication Data
(Revised for vol. 3)

Monoclonal antibodies against bacteria.

Includes bibliographies and indexes.

1. Bacterial antigens—Analysis—Collected works.
2. Antibodies, Monoclonal—Collected works. I. Macario,
Alberto J. L. II. Conway de Macario, Everly. [DNLM:
1. Antibodies, Monoclonal. 2. Bacteria. QW 575 M7472]
QR186.6.B33M66 1985 616.9'20793 84-24455
ISBN 0-12-463003-0 (v. 3 : alk. paper)

PRINTED IN THE UNITED STATES OF AMERICA

86 87 88 89

9 8 7 6 5 4 3 2 1

Contributors

Numbers in parentheses indicate the pages on which the authors' contributions begin.

Pertti Arstila (119), Department of Virology, University of Turku, SF-20520 Turku, Finland

David E. Briles (143), The Cellular Immunobiology Unit of the Tumor Institute, Departments of Microbiology and Pediatrics, and The Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama 35294

Everly Conway de Macario (181), Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, New York 12201

Joseph M. DiRienzo (249), Department of Microbiology, School of Dental Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104

Jan Holmgren (77), Department of Medical Microbiology, University of Göteborg, S-413 46 Göteborg, Sweden

Mikko Hurme (99), Department of Bacteriology and Immunology, University of Helsinki, 00290 Helsinki, Finland

Timo U. Kosunen (99), Department of Bacteriology and Immunology, University of Helsinki, 00290 Helsinki, Finland

Olli-Pekka Lehtonen (119), Department of Medical Microbiology, University of Turku, SF-20520 Turku, Finland

Pak Leong Lim (29), Department of Microbiology, University of Hong Kong, Hong Kong

Leif Lindholm (77), Department of Medical Microbiology, University of Göteborg, S-413 46 Göteborg, Sweden

Linnéa Linko (119), Department of Medical Microbiology, University of Turku, SF-20520 Turku, Finland

- Sheila A. Lukehart** (1), Department of Medicine, University of Washington School of Medicine, Seattle, Washington 98195
- Alberto J. L. Macario** (181), Wadsworth Center for Laboratories and Research, New York State Department of Health, Albany, New York 12201
- R. J. F. Markham**¹ (295), Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, Minnesota 55108
- Larry S. McDaniel** (143), The Cellular Immunobiology Unit of the Tumor Institute, Departments of Microbiology and Pediatrics, and The Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama 35294
- Charlotte D. Parker** (165), Department of Microbiology, School of Medicine, University of Missouri, Columbia, Missouri 65212
- Hiroko Sato** (203), Department of Applied Immunology, National Institute of Health, Shinagawa-ku, Kaniosaki, Tokyo 141, Japan
- David M. Sherman** (295), Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, Minnesota 55108
- Ann-Mari Svennerholm** (77), Department of Medical Microbiology, University of Göteborg, S-413 46 Göteborg, Sweden
- T. Uchida** (229), Institute for Molecular and Cellular Biology, Osaka University, Suita, Osaka 565, Japan
- Matti K. Viljanen** (119), Department of Medical Microbiology, University of Turku, SF-20520 Turku, Finland
- Andrej Weintraub** (119), Karolinska Institute, Department of Clinical Bacteriology, Huddinge University Hospital, Huddinge, Sweden
- Marianne Wikström** (77), Department of Medical Microbiology, University of Göteborg, S-413 46 Göteborg, Sweden
- T. Yoshimori** (229), Department of Physiology, Kansai Medical University, Moriguchi-shi, Osaka 570, Japan

¹Present address: Department of Pathology and Microbiology, Faculty of Veterinary Medicine, University of Prince Edward Island, Charlottetown, Prince Edward Island, Canada C1A 4P3.

Preface

This volume was conceived following the same principles that guided the production of the earlier ones. A variety of topics is encompassed by the twelve chapters. They are linked by the basic principles of hybridoma technology, which are similar, if not identical, no matter which bacterial species is studied. While these basic principles ensure unity, the special features of each chapter endow this volume with a wealth of knowledge. A broad range of biologic, medical, and biotechnologic themes is covered. A representative cross-section of contemporary developments involving monoclonal antibodies against bacteria is presented.

The format of the chapters is the same as that of those in Volumes I and II. Introductory material helps to explain the novel data presented in the Results and Discussion sections. Anticipated developments are included near the end of each contribution. (These extrapolations are as inspiring as the data presented.) Each chapter closes with a comprehensive bibliography.

A call has recently been made to "revive systematics" [E. O. Wilson (1985). *Science* 230, 1227]. Systematics is much more than classification of organisms. It is a source of knowledge, a springboard for launching research aimed at understanding biologic diversity at all levels. From this vantage point, monoclonal antibodies emerge as essential instruments, particularly in bacteriology, as illustrated by the contents of this treatise. For example, discovering better ways to extract energy from biomass depends to a significant extent on taxonomic exploration (see E. O. Wilson, cited above). Paradigmatic in this respect are monoclonal antibodies against bacteria that produce methane gas from organic wastes.

Another important field of biotechnology in which monoclonal antibodies against bacteria are playing a momentous role is vaccine design and production.

The antibodies are useful for identifying antigens which elicit protective immunity and which should be part of a vaccine. The same antibodies aid in preparing the vaccine, in the quality control of its production, and in monitoring the response it elicits in vaccinated individuals.

What next? Research aimed at improving hybridoma technology and monoclonal antibody generation goes on. Major efforts are devoted toward optimizing *in vitro* procedures to immunize lymphocytes before fusion and toward producing large amounts of antibodies (thus avoiding the use of animals for this purpose). Techniques to obtain human monoclonal antibodies are also being actively tested. Especially interesting is work concerned with designing antibody molecules, in the laboratory, according to specifications. This work draws on hybridoma and recombinant DNA technologies and on genetic and chemical strategies. Manipulations of the components of the antibody molecule (fragments, chains) and of their DNA and RNA counterparts are employed. The ideal of constructing antibody molecules with all the necessary attributes to meet certain demands, but lacking unwanted properties, is approaching its realization. Undoubtedly these advances will greatly benefit bacterial immunology.

Recent work with bacteria found in plants [S. H. DeBoer and A. Wieczorek (1984). *Phytopathology* **74**, 1431] adds still another facet to the theme of monoclonal antibodies against bacteria. The same could be said about studies using monoclonal antibodies for the investigation of cell differentiation and the formation of supracellular structures in fruiting bacteria [J. Gill, E. Stellwag, and M. Dworkin (1985). *Ann. Inst. Pasteur/Microbiol.* **136A**, 11]. These two examples from very different disciplines, with the variety of topics dealt with in this treatise, demonstrate that monoclonal antibodies against bacteria have become an essential component of bacteriology in various areas of scientific endeavor. Consequently, Volume III aims to provide, as does the treatise as a whole, a forum in which medicine, dentistry, and veterinary science cross-fertilize with one another and with other disciplines such as engineering. Interaction of scientists across traditional borders that divide science into compartments may quicken the progress of research toward achievements of practical interest. This is, at least, our hope.

The chapters in this volume are concerned with important topics: treponemal antigens of significance for understanding syphilis, yaws, and pinta (Chapter 1); salmonellosis (Chapter 2) and other gastroenteropathies (Chapters 3–5); pediatric infections (Chapters 6 and 7); strategies for molecular analyses of bacterial antigens, focusing on cell walls, S layers, and sheaths (Chapter 8); bacterial toxins involved in gaseous gangrene (Chapter 9) and other forms of cell damage, as in diphtheria (Chapter 10); caries and periodontal disease (Chapter 11); and bacteria relevant to animal sciences (Chapter 12).

Alberto J. L. Macario
Everly Conway de Macario

Contents of Previous Volumes

Volume I*

- 1 Monoclonal Antibodies against *Gonococcal* Pili:
Uses in the Analysis of Gonococcal
Immunochemistry and Virulence
J. E. Heckels and M. Virji
- 2 Monoclonal Antibodies against Group B
Streptococcus
Richard A. Polin and Mary Catherine Harris
- 3 Studies with Monoclonal Antibodies to *Mycobacteria*
J. Ivanyi, J. A. Morris, and M. Keen
- 4 Monoclonal Antibodies to Characterize the Antigenic
Heterogeneity of *Bacteroides intermedius*
Rudolf Gmür and Christoph Wyss
- 5 Monoclonal Antibodies against *Legionella*
pneumophila Serogroup 1 Antigens: Characterization
and Their Potential Applications
K. K. Sethi
- 6 Monoclonal Antibodies Specific for the O-Antigen of
Shigella flexneri and *Shigella sonnei*:
Immunochemical Characterization and Clinical
Usefulness
Nils I. A. Carlin and Alf A. Lindberg

7 Monoclonal Antibodies against Group- and Type-Specific Antigens of *Vibrio cholerae* O:1

Tord Holme and Björn Gustafsson

8 Monoclonal Antibodies against Tetanus Toxin and Tetanus Toxoid

Ernst Habermann and Karin Goretzki

9 Human Monoclonal Antibodies for Prophylaxis and Therapy of Bacterial Infections

Kenneth W. Hunter, Jr.

10 Monoclonal T Cells and T-Cell Hybridomas with Antibacterial Activity

Stefan H. E. Kaufmann

11 A Preview of the Uses of Monoclonal Antibodies against Methanogens in Fermentation Biotechnology: Significance for Public Health

Alberto J. L. Macario and Everly Conway de Macario

12 An International Hybridoma Data Bank: Aims, Structure, Function

Alain Bussard, Micah I. Krichevsky, and Lois D. Blaine

Volume II

1 Structure-Function Analysis of Group A Streptococcal M Proteins with Hybridoma Antibodies

James B. Dale, David L. Hasty, and Edwin H. Beachy

2 Monoclonal Antibodies to the Enterotoxins and to the Toxic Shock Syndrome Toxin Produced by *Staphylococcus aureus*

*Nancy E. Thompson, Merlin S. Bergdoll, Richard F. Meyer,
Donald W. Rennett, Llonas Miller, and James D. Macmillan*

- 3 The Use of Monoclonal Antibodies for Detecting and Serotyping *Neisseria meningitidis*
Renee J. Sugawara

- 4 Development of Monoclonal Antibodies to *Brucella* Cell Surface Antigens
Patricia J. Holman, Gerhardt Schurig, and James T. Douglas

- 5 Monoclonal Antibodies to *Legionella pneumophila*: Possible Applications in Clinical Diagnostic Tests and Epidemiologic Investigations
Jean R. Joly, Roger M. McKinney, and Ian D. Watkins

- 6 Use of Monoclonal Antibodies in the Study of Common Antigens of Gram-Negative Bacteria
Lucy M. Mutharia, Joseph S. Lam, and Robert E. W. Hancock

- 7 Application of Monoclonal Antibodies to the Study of the Surface Antigens in *Pseudomonas aeruginosa*
Joseph S. Lam, Lucy M. Mutharia, and Robert E. W. Hancock

- 8 Analysis of Antigenicity and Structure of *Clostridium botulinum* Type C₁ and D Toxins by Monoclonal Antibodies
Keiji Oguma, Bunei Shuto, Shuichiro Kubo, and Hiroo Iida

- 9 *Escherichia coli* Capsules and Pili: Serological, Functional, Protective, and Immunoregulatory Studies with Monoclonal Antibodies
Tommy Söderström

- 10 Monoclonal Antibodies of Predefined Molecular Specificity for Identification and Classification of Methanogens and for Probing Their Ecologic Niches
Alberto J. L. Macario and Evelyn Conway de Macario

11 Monoclonal Antibodies and the Structure of Bacterial Membrane Proteins

Joëlle Gabay, Sergio Schenkman, Catherine Desaymard, and Maxime Schwartz

12 Industrial Applications of Monoclonal Antibodies against Bacteria

Daniel H. Zimmerman, Francis K. Mondon, and Sean P. O'Neill

Contents

Contributors	xi
Preface	xiii
Contents of Previous Volumes	xv

1 Identification and Characterization of *Treponema pallidum* Antigens by Monoclonal Antibodies

Sheila A. Lukehart

I. Introduction	1
II. Background	2
III. Results and Discussion	10
IV. Conclusions	20
V. Prospects for the Future	21
VI. Summary	22
References	22

2 Diagnostic Uses of Monoclonal Antibodies to *Salmonella*

Pak Leong Lim

I. Introduction	29
II. Background	31
III. Results and Discussion	51

IV. Conclusions	63
V. Prospects for the Future	64
VI. Summary	67
References	68

3 Monoclonal Antibodies and Immunodetection Methods for *Vibrio cholerae* and *Escherichia coli* Enterotoxins

Ann-Mari Svennerholm, Marianne Wikström, Lëif Lindholm, and Jan Holmgren

I. Introduction	77
II. Background	78
III. Results and Discussion	80
IV. Conclusions and Prospects for the Future	92
V. Summary	94
References	94

4 Monoclonal Antibodies against *Campylobacter* Strains

Timo U. Kosunen and Mikko Huume

I. Introduction	99
II. Background	100
III. Results and Discussion	104
IV. Conclusions	110
V. Prospects for the Future	112
VI. Summary	114
References	114

5 Monoclonal Antibodies to the Lipopolysaccharide and Capsular Polysaccharide of *Bacteroides fragilis*

Matti K. Viljanen, Linnëa Linko, Pertti Arstila, Olli-Pekka Lehtonen, and Andrej Weintraub

I. Introduction	120
II. Background	120
III. Results and Discussion	124
IV. Conclusions	137
V. Prospects for the Future	138
VI. Summary	139
References	140

6 Monoclonal Antibodies against Surface Components of *Streptococcus pneumoniae*

Larry S. McDaniel and David E. Briles.

I. Introduction	143
II. Background	145
III. Results and Discussion	147
IV. Conclusions	157
V. Prospects for the Future	158
VI. Summary	159
References	160

7 Monoclonal Antibodies to *Bordetella pertussis*

Charlotte D. Parker

I. Introduction	165
II. Background	166
III. Results and Discussion	170
IV. Conclusions	174
V. Prospects for the Future	176
VI. Summary	176
References	177

8 Molecular Structures of Bacteria Elucidated by Monoclonal Antibodies with Special Reference to Antigenic Determinants of the Methanogens' Envelopes

Everly Conway de Macario and Alberto J. L. Macario

I. Introduction	181
II. Background	182
III. Results and Discussion	190
IV. Conclusions	196
V. Prospects for the Future	198
VI. Summary	199
References	200

9 Monoclonal Antibodies against *Clostridium perfringens* θ Toxin (Perfringolysin O)

Hiroko Sato

I. Introduction	203
II. Background	206
III. Results and Discussion	210

IV. Conclusions	221
V. Prospects for the Future	222
VI. Summary	224
References	225

10 Monoclonal Antibodies against Diphtheria Toxin: Their Use in Analysis of the Function and Structure of the Toxin and Their Application to Cell Biology

T. Yoshimori and T. Uchida

I. Introduction	229
II. Background	231
III. Results and Discussion	232
IV. Conclusions	244
V. Prospects for the Future	245
VI. Summary	246
References	246

11 Application of Monoclonal Antibodies to the Study of Oral Bacteria and Their Virulence Factors

Joseph M. DiRienzo

I. Introduction	250
II. Background	251
III. Results and Discussion	255
IV. Conclusions	280
V. Prospects for the Future	283
VI. Summary	284
References	285

12 Current and Future Applications of Monoclonal Antibodies against Bacteria in Veterinary Medicine

David M. Sherman and R. J. F. Markham

I. Introduction	295
II. Background	296
III. Results and Discussion	298
IV. Conclusions	328
V. Summary	331
References	331

Index	341
-------------	-----

1

Identification and Characterization of *Treponema pallidum* Antigens by Monoclonal Antibodies

SHEILA A. LUKEHART

Department of Medicine
University of Washington School of Medicine
Seattle, Washington

I. Introduction	1
II. Background	2
A. Taxonomy	2
B. Growth and Morphology	3
C. Clinical Course of Treponemal Infections	3
D. Pathogenesis and the Immune Response	4
E. Identification and Characterization of <i>Treponema pallidum</i> Antigens Using Polyvalent Antisera	6
F. Unanswered Questions	10
III. Results and Discussion	10
A. Production of Monoclonal Antibodies	10
B. Characterization of Monoclonal Antibody Reactivity to <i>Treponema</i> <i>pallidum</i> and Related Organisms	14
C. Location and Function of Antigens Defined by Monoclonal Antibodies	17
D. Diagnostic Applications of Monoclonal Antibodies	18
IV. Conclusions	20
V. Prospects for the Future	21
VI. Summary	22
References	22

I. INTRODUCTION

Treponemal infections in humans are complex, chronic, systemic diseases with protean clinical manifestations and the risk of serious late sequelae. Syph-

ilis, which is the most widely known, is a sexually transmitted disease with worldwide distribution, while the nonvenereal treponematoses (yaws, bejel, and pinta) occur primarily in tropical or semiarid regions of the developing world, particularly in Africa and Southeast Asia. These diseases progress from an initial, primary skin or mucous membrane lesion to the secondary disseminated and destructive tertiary stages, interrupted by long periods of latency. The numerous and varied clinical manifestations of syphilis have been recognized for centuries, but little real progress has been made in understanding the pathogenesis of the disease or the role of the host's immune response in modifying disease progression. The definition of the antigenic structure of pathogenic treponemes has been limited by the inability to cultivate the organisms continuously *in vitro*, and consequently, much of our knowledge of the antigenic structure of members of the genus *Treponema* is based on studies of cultivable nonpathogenic treponemes and cumbersome absorption of polyvalent antisera. Major advances have been made since 1980 in the identification of the major antigens of *Treponema pallidum* and in the definition of the host's immune response to those molecules. This chapter briefly reviews the current knowledge of treponemal biology and antigenic structure, and will detail the recent production of monoclonal antibodies to *T. pallidum* as well as the potential contributions of monoclonal antibodies to the study of treponemal infections.

II. BACKGROUND

A. Taxonomy

The genus *Treponema* includes the etiologic agents of venereal and endemic syphilis, yaws, and pinta, as well as numerous nonpathogenic commensal species which are found on the mucosal surfaces of the mouth, genitalia, and gastrointestinal tract (73). The pathogenic treponemes are distinguishable from the nonpathogens by their morphology, motility, and inability to be cultured *in vitro*. Although a considerable degree of antigenic relatedness exists between the pathogenic and nonpathogenic treponemes, no DNA homology has been reported between virulent *T. pallidum* (Nichols strain) and the nonpathogenic *Treponema phagedenis* or *Treponema refringens* (50).

The four human pathogens are morphologically identical and, to date, are indistinguishable serologically. Historically, they have been classified as separate species on the basis of the characteristic diseases they cause and, to some degree, their animal host ranges. Recent DNA sequence homology studies revealed 100% reassociation of DNA from *T. pallidum* Nichols strain (venereal syphilis) with that of *Treponema pertenuis*, the causative agent of yaws (51). Based on these studies, the pathogenic treponemes were recently reclassified