Monoclonal Antibodies against Bacteria

Volume III

Edited by

Alberto J. L. Macario

Everly Conway de Macario

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Wadsworth Center for Laboratories and Research
New York State Department of Health
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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]

Volume II

Contents

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

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

4 Monoclonal Antibodies against *Campylobacter* Strains

Timo U. Kosunen and Mikko Hurme

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

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

6 Monoclonal Antibodies against Surface Components of *Streptococcus pneumoniae*

Larry S. McDaniel and David E. Briles

7 Monoclonal Antibodies to *Bordetella pertussis*

Charlotte D. Parker

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

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

Hiroko Sato

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

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

Joseph M. DiRienzo

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

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

1

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

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I. INTRODUCTION

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

MONOCLONAL ANTIBODIES
AGAINST BACTERIA
Volume III

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 pertenue*, the causative agent of yaws (51). Based on these studies, the pathogenic treponemes were recently reclassified