Section 5 is dedicated to the detection of gene transfer in the environment. A wide range of bacteria express competence (the physiological ability to take up DNA) during normal growth, and plasmid DNA without homology to the host may be recircularized, allowing for transformation of different genera. This horizontal transfer endows microbes with an enormous genetic flexibility that allows them to respond and rapidly adapt to changing environmental conditions, in addition to having enormous phylogenetic implications. Section 6 deals with methods for tracking specific (target) microbes in the environment. The expression of genes that encode useful characteristics (key enzymes) in relation to environmental factors can be analyzed to obtain information about the ecology of functional bacterial groups and then applied to the recovery of genetically modified microorganisms from the environment. Section 7, on the quantitative assessment of data and the methods to couple microbial identity and function, aids researchers in determining the significance of molecular data pertaining to patterns of microbial diversity and thus to go beyond the simple detection of populations, to quantitative determination. Methods based solely on 16S rRNA analysis provide extensive information on the taxa present in an environment; but little insight into the functional role of each phylogenetic group. Therefore, other methods are needed to link specific functions with the group responsible for them. Molecular techniques such those explained in the *Manual*, including in situ use of microelectrodes, whole-cell biosensors, stable-isotope labeling, and proteomic analysis, equip us with the tools to understand the functional diversity of microbial communities, and ultimately of the ecosystem as a whole.

Molecular approaches promise fuller and more accurate descriptions of the real diversity, structure, and dynamics of complex microbial communities. While the *Molecular microbial ecology manual* describes most of the techniques a microbial ecologist might currently wish to use, it is more than just a manual; rather it seeks to provide the reader with the insight behind the theory and application of each protocol, and thus to answer the "why" of each method. Moreover, with its on-line format, emerging methodological developments can be periodically included, so that the *Manual* can continue to keep pace with advances in microbial ecology.

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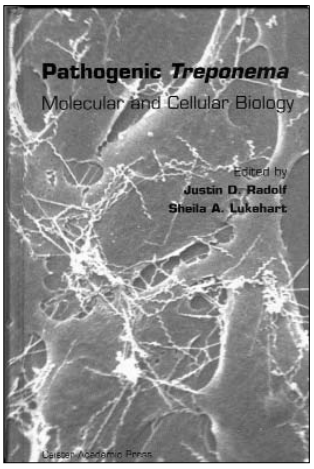

Pathogenic *Treponema.* Molecular and cellular biology

JUSTIN D. RADOLF, SHEILA A. LUKEHART (eds)

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Nearly 350 years ago, Anton van Leeuwenhoek, using microscopes he constructed himself, began to explore the human body. Several years after observing protists in water, he discovered bacteria on his teeth and recorded the diversity of these *beesjes* (beasties) or *cleijne Schepsels* (little creatures), as he wrote in Dutch (the Latin *animalculi*, in the translations of his time). One of his letters, published by the Royal Society, contains the first written description of what we know to be spirochetes. This new and "invisible" microbial world had no apparent function. Microorganisms existed, they had definite shapes and movement, but they were considered mere "curiosities". Of all the treponemes (a type of spirochete), the one that causes syphilis has, historically, been the greatest focus of attention, not only because of its disease manifestations but also due to the complex and still unsolved medical, social, and historical questions that surround it. The book *Pathogenic Treponema* highlights recent major advances in our understanding of *Treponema* biology, such as the organism's phylogenetic diversity, morphological features, metabolism, and motility.

The book is organized into 18 chapters, comprising four parts. Part I (Chapters 1-8), "The *Treponema* world", contains basic information about the genus *Treponema*. Part II (Chapters 9-13), "*Treponema pallidum*", discusses the history, pathogenesis, and immunology of syphilis. Treponemes exhibit enormous diversity and, appropriately, this book also includes many "non-syphilis" chapters, such as those in Part III (Chapters 14-16), "Oral treponemes", and Part IV (Chapters 17-18), "Other treponemes."

Chapter 1 reviews the phylogenetic relationships among members of the genus *Treponema*, including those which cannot be cultivated in vitro. It also illustrates the vast diversity of these spirochetes. Chapter 2 compares the sequenced genomes of several spirochetes: *Treponema pallidum*, *Treponema denticola*, two *Borrelia* species, and two *Leptospira interrogans* strains. Current information indicates

that the genus *Treponema* evolved from a common ancestor early in bacterial evolution. Chapter 3 describes treponemal morphology. All treponemes are gram-negative bacteria, with a characteristic number of flagella (between 1 and 8) located in the periplasmic space. The cytoplasmic filament of *Treponema* is a ribbon-like structure of two to six filaments that are located beneath the flagellar filament bundle. It has been suggested that these filaments are involved in the maintenance of cell structure and shape as well as transport, cell motility, and cell division. Chapter 4 compares the metabolism of *Treponema pallidum* with that of *Treponema denticola* by genomic studies and explains the problems arising from attempts to cultivate *T. pallidum*. *T. denticola* has almost 2000 genes that are absent in *T. pallidum*; many of them are predicted to code for proteins involved in DNA repair, oxygen metabolism, stress, and transport capabilities. Chapter 5 discusses metal utilization and oxidative stress. It compares the mechanisms present in *T. denticola* and *L. interrogans* with the more limited systems observed in *T. pallidum* and *Borrelia burgdorferi*. Chapters 6 and 7 are devoted, respectively, to treponemal motility and chemotaxis, both of which account for a considerable portion of these organisms' genomic information. *Borrelia* and *T. pallidum*, which are only ca. 1 Mb in chromosomal size, "spend" 5–6% of their genomes on motility. In *T. denticola* (ca. 2.7 Mb) and *L. interrogans* (ca. 4.8 Mb), the proportion of the chromosome dedicated to genes encoding motility and chemotaxis functions is equivalent to that of other motile bacteria with a comparable genome size. Chapter 8 focuses on the genetic manipulation of cultivable treponemes, such as the oral spirochete *T. denticola*. Until recently, treponemal genes were cloned into *Escherichia coli*, a nonspirochete. Now *T. denticola* can be used for cloning purposes, thereby allowing the expression and characterization of genes from noncultivable treponemes in selected cultivable treponemes.

Syphilis, which is caused by *T. pallidum*, has a long and complicated history, reviewed in Chapter 9. What are the origins of the disease? Why did a syphilis epidemic occur during the French invasion of Italy, in 1494, and the Spanish defense of Naples, in 1495? Chapter 10 describes the pathogenesis of syphilis. Our current knowledge derives from clinical and epidemiological observations as well as autopsy studies and the results of experimental animal models (e.g., rabbits, but not mice). The advent of molecular techniques has allowed direct analysis of the *T. pallidum* genome, which have shed light on the spirochete's virulence properties and determinants. This chapter also explains individual steps in the disease process and specific disease manifestations in terms of the cellular and molecular properties of *T. pallidum*. Chapter 11 assigns the pathogenic potential of *T. pallidum* to its outer membrane and describes the latter's ultrastructure, lipid composition, and permeability. *T. pallidum* is called the "stealth pathogen" due to its remarkable ability to evade the host immune response and to remain quiescent for extended periods of time. Chapter 12 explains the ability of *T. pallidum* to exert antigenic variation within the host. Chapter 13 focuses on the immunology of syphilis. One of the main paradoxes of syphilis is that the immune system has the capacity to eliminate millions of treponemes from the primary site of infection, but some of them evade these defenses and become persistent in the body.

Chapters 14 to 16 provide an overview of the characteristics of oral spirochetes as important members of oral biofilms and their role in periodontal disease. Oral spirochetes are distinct from those associated with the genital and intestinal tracts and from free-living spirochetes. Although oral spirochetes are frequently detected, they to represent ≤0.5% of the microbial population of healthy people. Oral treponemes concentrate at a specific site, the gingival sulcus. It seems that innate immunity plays an important role in the pathogenesis of periodontitis (local inflammation, destruction of periodontal ligaments, and bone resorption).

Chapter 17 describes a bovine skin disease associated with the intensive housing of cattle and the prolonged exposure of their hooves to moist, unhygienic conditions. The lesions contain both anaerobic bacteria and spirochetes. Currently, it is unclear whether spirochetes are the primary pathogens or secondary opportunists. In any case, comparative 16S rRNA analysis of treponema isolated from affected cattle shows that the pathogenic spirochetes cluster with human oral spirochetes. However, further research is necessary to clarify their taxonomic position and basic biology. Chapter 18 discusses the spirochetes inhabiting the termite gut. Spirochetes constitute an unusually abundant component of the hindgut microbiota of termites and contribute to the nutrition and viability of their host. The chapter also summarizes the phylogenetic and physiological diversity of spirochetes.

Nothing is easy in the world of spirochetes, and within this group *Treponema* are the most challenging to study in the laboratory. This book includes a discussion of genomics with respect to improving our knowledge of the structural, physiological, pathogenetic, and immunological aspects of treponemes. *Pathogenic Treponema* is a book especially recommended for advanced students in the field, senior researchers, physicians, and dentists; but all microbiologists will find in the book an exceptional opportunity for extending their understanding of an unusual and unique microbial group.

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