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Spirochetes: Evolution, Genome Analyses and Physiology

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This short symposium is devoted to structural, molecular, physiological and evolutionary aspects of spirochetes. The spirochetes are a small cohesive group of chemoheterotrophic bacteria, readily distinguishable from other bacteria on the basis of their unique cell structures. Spirochete cells are generally long and narrow, helical in form, and surrounded by delicate flexible walls. All known spirochetes can swim actively in liquid media by virtue of their axial fibrils: periplasmic flagelli that underlie the cell wall. The cells often bend or flex during movement, and they can attain remarkable directed velocities and even swim through highly viscous solutions (see review by Li, Motaleb, Sal, Goldstein and Charon). The motile behavior of these bacteria allows them to respond to chemical and physical stimuli in their environments (see review by Lux, Moter and Shi). These organisms comprise a relatively close-knit group of organisms that, based on 16S RNA analyses, diverged from other bacteria during early evolutionary history. They exhibit unusual prokaryotic characteristics such as linear chromosomes and a cytoskeleton. They also are the targets of spirochete-specific bacteriophage which have co-evolved with their hosts over evolutionary time. For this reason, the study of phage can provide clues to the ecology and molecular biology of their host organisms (see review by Eggers, Casjens, Hayes, Garon, Damman, Oliver and Samuels).

Spirochetes are currently divided into nine genera (see article by Paster and Dewhirst). While some of these genera include free living organisms of bright colors and unusual physiological properties, others are pathogens of humans and animals, the causative agents of syphilis, Lyme disease, relapsing fever, leptospirosis and peridontitis. The pathogens responsible for these diseases exhibit tremendous structural and physiological variability. For example, although they are considered Gram-negative bacteria with a double envelope membrane, many spirochetes including *Treponema* and *Borrelia* lack outer membrane lipopolysaccharides (LPS). Others including *Leptospira* and *Brachyspira* do synthesize LPS, and LPS is the principle surface antigen displayed by these organisms, of considerable importance to diagnostics and immunity. The review by Bulach, Kalambaheti, de la Peña-Moctezuma and Adler discusses these important antigens from structural and biosynthetic standpoints. The importance of vector-host interactions, particularly with respect to tick-borne borreliae, is discussed by Nuttall, Paesen, Lawrie and Wang. The pathogenic properties of many spirochetes have provided much of the scientific impetus for their study.

Genome analyses of two spirochetes, *Treponema pallidum* and *Borrelia burgdorferi*, the bacterial determinants of syphilis and Lyme disease, respectively, have revealed a wide range of protein structures. Most protein folds identified in these two organisms have been shown to be common to many other organisms, but a few spirochete-specific folds have been identified (see article by Das, Hegyi and Gerstein). Additionally, the metabolic capabilities of these two spirochetes are limited. For example, they rely primarily on glycolysis for energy generation. Transport systems in these two pathogens are highly restricted, showing patterns of transporter types that differ from those found in all other bacteria for which complete genomes are currently available (see article by Saier and Paulsen). Information obtained by analyzing the genome of *T. pallidum* is analyzed in terms of the known biological properties of this important pathogen. Genome analyses of *Borrelia* species have revealed features unusual to bacteria, often more frequently associated with eukaryotes (see article by Casjens). Thus, housekeeping genes are maintained primarily on the large chromosome of *B. burgdorferi* while the numerous circular and linear plasmids (or small chromosomes) of this organism bear spirochete-specific genes that may prove to be important for pathogenesis. They may be rapidly evolving as compared to the chromosomal genes. These plasmids are greatly enriched for repetitive sequences, the most obvious of which are found in the family of cp32 plasmids (see article by Stevenson, Zückert and Akins). Hypervariability within these plasmids as well as the presence of multiple paralogues undoubtedly has survival value for the bacteria in their host organisms. These molecular features may provide mechanisms for avoiding the animal's immune system.

This symposium thus summarizes important overall aspects of spirochetes as a phylogenetic group of organisms, but it also surveys a few key representative pathogenic spirochetes in greater detail with respect to specific traits. To what extent the specific findings reported will prove to be relevant to other less well studied spirochetes has yet to be determined. However, genome sequences have for the first time provided detailed information about the life processes of two of these important and interesting microorganisms, and genome sequencing projects for other spirochetes that will allow comparative studies are currently in progress. It is an exciting time in the discipline of spirochetology!

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