

Lyme disease causing *Borrelia* are genetically distinct from their relapsing fever causing cousins

Lyme disease, a tick-borne infection caused by the bacterium *Borrelia burgdorferi* and its relatives, is currently the most prevalent vector-borne disease in North America and temperate regions of Eurasia. Increasing temperatures have expanded the habitat range for the tick vectors of Lyme disease and estimates now suggest that over 300,000 people in North America are afflicted by the disease annually, making Lyme disease a growing public health concern. Members of the genus *Borrelia* are also the causative agents of relapsing fever, another vector-borne infection which is characterized by recurring episodes of fever, headache, aches, and nausea. Currently, the members of the genus *Borrelia* are separated into two main groups based upon their pathogenicity profiles, the Lyme disease *Borrelia* and the relapsing fever *Borrelia*. The two groups are difficult to distinguish morphologically and are primarily distinguished from each other based on the arthropod vectors which transmit them, their pathogenicity, and by a limited number of biochemical and genetic tests in clinical environments. Previous research into the evolutionary relationships among the *Borrelia* species suggests that the Lyme disease *Borrelia* and the relapsing fever *Borrelia* form two distinct groups within the genus. However, due to a lack of reliable molecular, morphological, or biochemical characteristics that can distinguish these groups, the two groups of *Borrelia* were not separated into distinct genera.

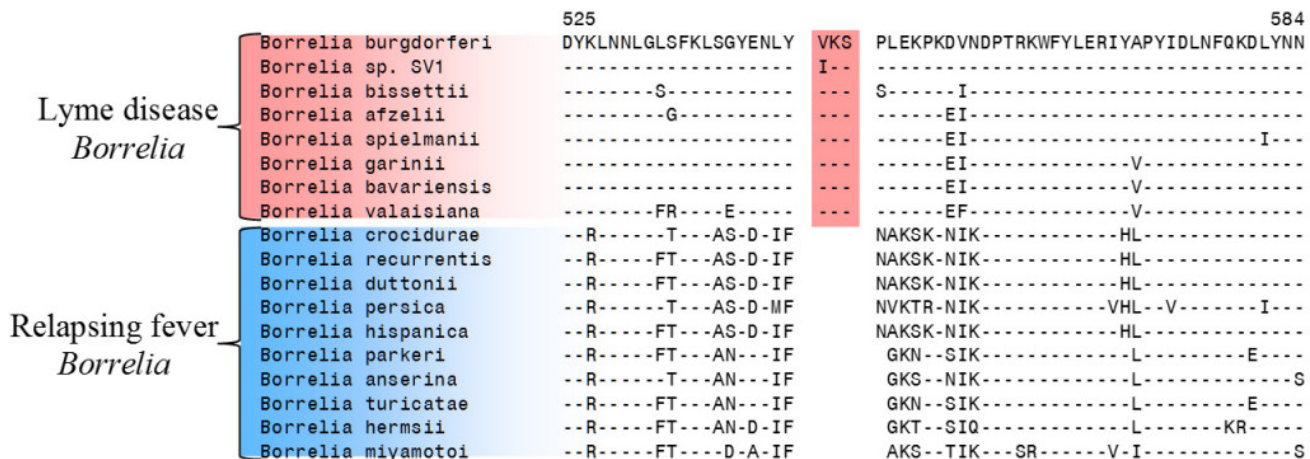


Fig. 1. An example of a unique genetic trait, a 3 amino acid indel in a protein sequence (viz. a CSI), that distinguishes the Lyme disease *Borrelia* (*Borrelia*) from the relapsing fever *Borrelia*. The indel is identified in a chromosomal protein that is uniquely and ubiquitously found in *Borrelia* species (viz. a CSP).

In this study, we have compared the genomic sequences of 38 genomes from 18 species of *Borrelia* to identify genetic traits, which can distinguish the Lyme disease *Borrelia* from the

relapsing fever *Borrelia*. The two types of differentiating traits we have focussed on are known as conserved signature insertions/deletions (CSIs), which are insertions or deletions only present in the protein sequences of a related group of organisms (Fig. 1), and conserved signature proteins (CSPs), which are proteins found only in a related group of organisms.

Our work has identified many unique genetic traits (53 CSIs and 25 CSPs) which clearly distinguish the Lyme disease *Borrelia* and the relapsing fever *Borrelia* from each other (Fig. 2). The distinctness of these two groups of *Borrelia* species was also supported by the results of an average nucleotide identity analysis of *Borrelia* genomes and by phylogenetic trees constructed based upon the 16S rRNA gene and protein sequences.

The results reported in our work, from multiple lines of investigations, provides compelling evidence that the *Borrelia* species are comprised of at least two distinct groups of organisms corresponding to the Lyme disease *Borrelia* and the relapsing fever *Borrelia*. Of the two groups, we would have liked to retain the genus name *Borrelia* for the Lyme disease *Borrelia*, which includes the best known species from this genus, *B. burgdorferi*. However, the type species of the genus *Borrelia*, *B. anserina*, is a part of the relapsing fever group. Hence, according to the rules governing the description of new bacterial names, the genus name *Borrelia* must be retained by the relapsing fever group. To minimize confusion among scientists and other health care professionals, we proposed that the species that are part of the Lyme disease *Borrelia* should be transferred to a new genus, *Borrelia*. The name *Borrelia* retains much of the original name of the genus *Borrelia*, thus, it is unlikely that the species with the new names (e.g. *Borrelia burgdorferi* and *B. burgdorferi*) could be confused with any other unrelated species and the name should be instantly recognizable by researchers or clinicians working on Lyme disease.

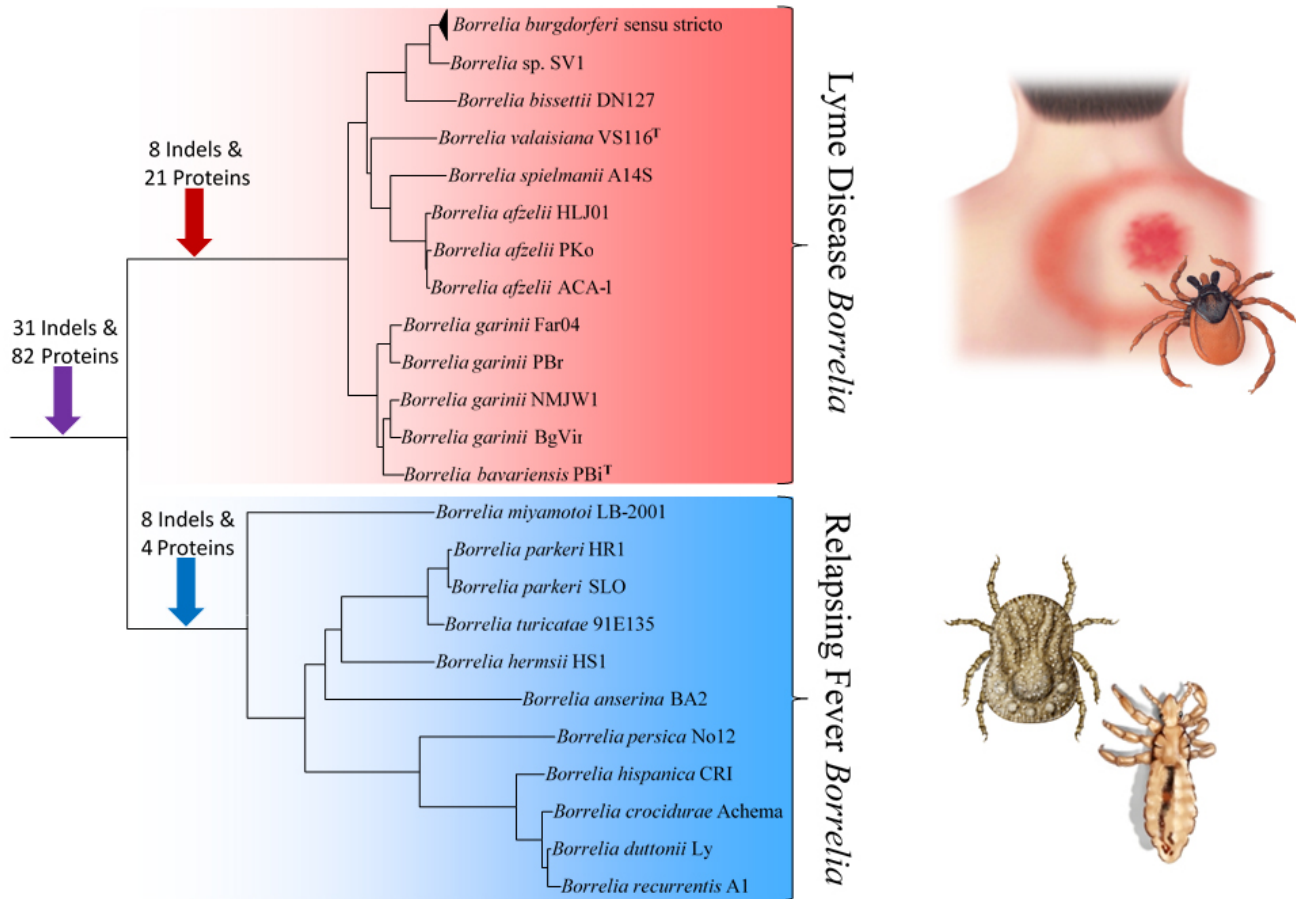


Fig. 2. The two groups of *Borrelia* species are distinguished by many unique genetic traits as shown here (CSIs located in *Borrelia* specific CSPs are not shown in this figure). The two groups of *Borrelia* species also differ in their arthropod vectors, associated diseases, and phylogeny. (Images adapted from universalmedicalinc.com, worksafebc.com, northwestmvd.org, and orkin.com).

In addition to distinguishing the two main groups of *Borrelia* species, the unique genetic traits identified here should lead to improved understanding of the two groups of *Borrelia* species and of their associated diseases. The genetic traits identified in the present work provide scientists, for the first time, novel means to rapidly and unambiguously distinguish between the two main groups of *Borrelia* species via PCR-based or immunological diagnostic assays. More importantly, the unique genetic characteristics for the two groups of *Borrelia* species identified here provide important targets for functional studies and their results should lead to novel biochemical and pathological insights into the aspects of these microbes that are responsible for causation of Lyme disease and relapsing fever.

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Publication

[A phylogenomic and molecular marker based proposal for the division of the genus *Borrelia* into two genera: the emended genus *Borrelia* containing only the members of the relapsing fever *Borrelia*, and the genus *Borrelia* gen. nov. containing the members of the Lyme disease *Borrelia* \(*Borrelia burgdorferi sensu lato* complex\).](#)

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