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Molecular Biology of *Borrelia burgdorferi*

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1. Introduction

*Borrelia* may be unique among prokaryote in having a genome that is mainly linear DNA physical and genetic map of linear chromosome of *B. burgdorferi* has been published, it consist of 946 to 952 kb Linear DNA (Sherwood *et al*; 1993, Davidson *et al*; 1992, Barbour *et al*; 1982).

This bacteria also contains several circular and specially linear plasmids from 5 to 55 kb. Recently analysis of entire *Agrobacterium tumefaciens* C58 genome revealed presence of one 2.1-Mb linear and one 3-Mb circular plasmid (Servent *et al*; 1993) and it has been shown that *rhodococcus fascians* contains 4 Mb linear chromosome (Crespi *et al*; 1992). Presence of several linear plasmids seems the segmentation of *Borrelias* DNA to several linear pieces has led to the suggestion that the relatively small linear chromosome and the linear plasmids actually are minichromosomes. In *B. hermsii* it has been shown that total cellular DNA organized into several complete gnomes (Kitten *et al*; 1992) and it suggests that linear plasmids are like small chromosomes (Ferdows *et al*; 1989). Plasmid profile of *B. burgdorferi* from different geographical area has been revealed significant heterogeneity a feature that can be used for classification of bacteria within given species (Barbour *et al*; 1987, 1989). Another related spirochete *B. hermsii* like *B. burgdorferi* has several linear and circular plasmids and the genes responsible for antigenic variation are located in linear plasmids. In *B. burgdorferi* a 49 kb linear plasmid carries the genes for Outer Surface Protein A and B (OspA and OspB) (Barbour *et al*; 1987, Baril *et al*; 1989). It has been shown that passage of *B. burgdorferi* in BSK medium changes the plasmid profile and loss of plasmids may change the infectivity of organism (Schwan *et al*; 1988, Simpson, *et al*; 1990). Structure of Linear plasmids of *B. burgdorferi* shows similarity to eukaryotic virus such as vaccinia and African swine fever virus in having covalently closed ends like hairpin loops (Hinnebusch *et al*; 1991).

1.1 Taxonomy and classification

*Borrelia burgdorferi* belongs to the phylum Spirochaetes. The members of this phylum are long, thin, helically coiled bacteria that have flagella (*axial filaments*) running lengthwise between the peptidoglycan layer and the outer membrane. Movement of the flagellum produces a screw-like motion that propels the organism.

The phylum Spirochaetes contains a single class (Spirochaetes), a single order (Spirochaetales), and three families: Brachyspiraceae, Leptospiraceae, and Spirochaetaceae.
The Spirochaetaceae family includes the genus *Treponema* and the genus *Borrelia*. *Treponema pallidum* is the causative agent of the sexually-transmitted disease syphilis.

The three members of the *Borrelia* genus *Borrelia burgdorferi* sensu stricto, *Borrelia garinii*, and *Borrelia afzelii* are collectively known as *Borrelia burgdorferi* sensu lato, and are the causative agents of Lyme disease.

### 1.2 Structure and morphology

*Borrelia* cells average 0.2 to 0.5 µm by 4 to 18 µm, and have fewer coils than *Leptospira*. The periplasmic flagella originate from either end of the spirochete (where they are anchored to the cytoplasmic membrane) and wind around the protoplasmic cylinder, imparting both motility and shape to the organism—in contrast to other bacteria, in which the peptidoglycan layer determines the shape.

The role of flagella in imparting *Borrelia* ’s helical shape was established by inactivation of the *flaB* gene, which encodes the major flagellar filament protein, FlaB. This produced bacteria that lacked periplasmic flagella, were non-motile and rod-shaped.

Whereas the motility of externally-flagellated bacteria is hindered in viscous substances, that of spirochetes is enhanced, and about 6% of the chromosomal genome encodes proteins involved in motility and chemotaxis.
Fig. 2.

Fig. 3.
1.3 Genome organization of *Borrelia burgdorferi*

All members of the *Borrelia* genus that have been examined harbor a linear chromosome that is about 900 kbp in length as well as a plethora of both linear and circular plasmids in the 5-220 kbp size range. Genome sequences have been determined for *B. burgdorferi*, *B. garinii*, *B. afzelii*, *B. duttonii* and *B. recurrentis*. The chromosomes, which carry the vast majority of the housekeeping genes, appear to be very constant in gene content and organization across the genus. The content of the plasmids, which carry most of the genes that encode the differentially-expressed surface proteins that interact with *Borrelia*’s arthropod and vertebrate hosts, are much more variable. *B. burgdorferi* strain B31, the *B. burgdorferi* type strain, has been studied in the most detail and harbors twelve linear and nine circular plasmids that comprise about 612 kbp. The plasmids are unusual, as compared to most bacterial plasmids, in that they contain many paralogous sequences, a large number of pseudogenes and, in some cases, essential genes. In addition, a number of the plasmids have features suggesting that they are prophages. Some correlations between genome content and pathogenicity have been deduced and comparative whole genome analyses promise future progress in this arena.

The highly unusual segmented genomes of *Borrelia* species can contain over 20 autonomously replicating DNA molecules. Many of the molecules, including the chromosome, are linear with covalently closed hairpin ends.

2. Molecular biology

2.1 The *Borrelia burgdorferi* genome

The genome of *Borrelia burgdorferi* consists of a single linear chromosome and several plasmids, both linear and circular. To date—as of January 2005—only the genome of *Borrelia burgdorferi* sensu stricto B31 strain has been fully sequenced.

| Distribution of cellular functions of *E. coli* and *B. burgdorferi* genes [1] |
|-----------------------------------------------|---------------------|
| Category                                      | *B. burgdorferi* genes (%) |
| Intermediary metabolism                      | 4.9%                |
| Biosynthesis of small molecules              | 3.1%                |
| Macromolecule metabolism                     | 22.2%               |
| Cell Structure                                | 37.0%               |
| Cellular processes                            | 7.4%                |
| Other functions                               | 5.6%                |
| Unknown functions                             | 19.8%               |

Table 1.
2.2 Chromosomal genome

*B. burgdorferi* contains a single linear chromosome of approximately 900 kb, and about 90% of it is comprised of coding sequences. Most of the genes encoded by the chromosomal genome are homologous to genes of known function.

2.3 Extra-chromosomal genome

The extra-chromosomal genome of *B. burgdorferi* B31 consists of 12 linear plasmids and nine circular plasmids that total 610 kb in size.

2.3.1 Linear plasmids

There are two linear plasmids in *B. burgdorferi* that are absolutely necessary for persistent infection of a mammalian host. These plasmids, known as lp25 and lp28-1, are relatively unstable in culture, and are commonly lost after a few generations of *in vitro* growth. Bacteria that have lost either of these two plasmids remain capable of *in vitro* growth, but lose their ability to cause persistent infection even in immunocompromised mice. The lp25 plasmid contains a gene, *pncA*, which encodes a nicotinamidase whose function is most likely the biosynthesis of NAD; by all appearances its activity is dispensable growth *in vitro*, but crucial for growth within a host. Transforming the lp25- spirochetes with *pncA* on a shuttle vector replaces the requirement of lp25 *in vivo*. Likewise, reintroduction of the entire lp25 plasmid (by transformation) into lp25- spirochetes successfully rescues infectivity. [2]

2.3.2 Circular plasmids

An unusual feature of *B. burgdorferi* is a series of related 32-kb circular plasmids, termed cp32s. These have been found to be prophage genomes, and it is believed that they play a role in the horizontal transfer of DNA among spirochetes that share a common geographical and ecological niche. [3, 4]

2.3.3 OuterSurface Proteins (Osps)

The Outer Surface Proteins (Osps) of *B. burgdorferi* are lipoproteins that play an important role in interacting with interstitial and cellular components of insect and mammalian hosts. OspA, the most studied of the Osps, is expressed on spirochetes in unfed nymphs and adult ticks, as well as in culture. OspA mediates adherence to the cells of the tick midgut, which presumably allows spirochetes to avoid endocytosis by tick gut cells during digestion of the blood meal. The ability of *Borrelia* to regulate expression of OspA indicates that it also plays a role in detachment from the midgut, which allows the bacteria to enter the mammalian host when the tick takes a second bloodmeal.

During tick feeding, *Borrelia* in the midgut upregulate expression of another outer surface protein, OspC, and begin to move toward the salivary glands. This evident correlation suggests that OspC might play a role in transmission. Once it has entered the mammalian host, *Borrelia* downregulates OspA and exhibits variable OspC upregulation patterns. Although *B. burgdorferi* possesses only one copy of the *ospC* gene, sequences vary significantly from one strain to the next, which accounts for the observed antigenic variation.
between OspC proteins. The host immune system plays an important role in selecting for certain strains by eliminating the immunodominant ones.

![Physical map of the linear chromosome of *Borrelia burgdorferi* 212](image)

3. **Genome features in *Borrelia burgdorferi***

Chromosome 910,725 bp (28.6% G+C)

- Coding sequences (93%)
- RNAs (0.7%)
- Intergenic sequence (6.3%)

853 coding sequences
- 500 (59%) with identified database match
- 104 (12%) match hypothetical proteins
- 249 (29%) with no database match

**Plasmids**

- cp9 9,386 bp (23.6% GC)
- cp26 26,497 bp (26.3% GC)
lp17 16,828 bp (23.1% GC)  
lp25 24,182 bp (23.3% GC)  
lp28-1 26,926 bp (32.3% GC)  
lp28-2 29,771 bp (31.5% GC)  
lp28-3 28,605 bp (25.1% GC)  
lp28-4 27,329 bp (24.4% GC)  
lp36 36,834 bp (26.8% GC)  
lp38 38,853 bp (26.1% GC)  
lp54 53,590 bp (28.1% GC)  
Coding sequences (71%)  
Intergenic sequence (29%)  
430 coding sequences  
70 (16%) with identified database match  
110 (26%) match hypothetical proteins  
250 (58%) with no database match  

Ribosomal RNA Chromosome coordinates  
16S 444581–446118  
23S 438590–441508  
5S 438446–438557  
23S 435334–438267  
5S 435201–435312  

Stable RNA  
tmRNA 46973–47335  
mpB 750816–751175  

Transfer RNA  
34 species (8 clusters, 14 single genes)  
*The telomeric sequences of the nine linear plasmids assembled as part of this study were not determined; estimation of the number of missing terminal nucleotides by restriction analysis suggests that less than 1,200 bp is missing in all cases. Comparisons with previously determined sequences of lp 16.9 and one terminus of lp28-1 indicate that 25, 60 and 1,200 bp are missing, respectively.  

Chromosomally-encoded genes  
- rRNA sequences  
- fla sequences  
- hbb sequences  
- fesmid sequences
### 3.1 *Borrelia burgdorferi* rRNA sequences

| Genbank mnemonic | Accession number | Description          | Strain   | Date of entry | Size     |
|------------------|------------------|----------------------|----------|---------------|----------|
| Gb_ba:Bbrnaopr   | U03396           | *alaT* (Ala-tRNA), *ileT* (Ile-tRNA), *rrs* (16S rRNA), *rrlA* & *rrlB* (23S rRNA) *rrfA* & *rrfB* (5S rRNA) | B31      | 10/93         | 11955bp  |
| Gb_ba:Bbu44938   | U44938           | *rrs* (16S rRNA)     | 5MT      | 5/96          | 1,533bp  |
| Gb_ba:Bor16rg    | L39080           | *rrs* (16S rRNA)     | 9MT      | 3/95          | 1,533bp  |
| Gb_ba:Bbu44939   | U44939           | *rrs* (16S rRNA)     | 917Y     | 5/96          | 1,533bp  |
| Gb_ba:Bb16s297   | X85204           | *rrs* (16S rRNA)     | 297      | 5/95          | 1,488bp  |
| Gb_ba:Borrrd     | L36160           | *rrs* (16S rRNA)     | 934U     | 9/94          | 1,536bp  |
| Gb_ba:Bor16rga   | L39081           | *rrs* (16S rRNA)     | 935T     | 3/95          | 1,542bp  |
| Gb_ba:Borrrdq    | M64309           | *rrs* (16S rRNA)     | 1352     | 4/92          | 1,481bp  |
| Gb_ba:Borrrd     | M64310           | *rrs* (16S rRNA)     | 20004    | 4/92          | 1,480bp  |
| Gb_ba:Bb16srrna  | X57404           | *rrs* (16S rRNA)     | B31      | 3/92          | 1,465bp  |
| Gb_ba:Borssrna   | M59293           | *rrs* (16S rRNA)     | B31      | 4/92          | 1,480bp  |
| Gb_ba:Borrnaca   | M89935           | *rrs* (16S rRNA)     | CA2-87   | 1/93          | 1,291bp  |
| Gb_ba:Bb16sdk7   | X85195           | *rrs* (16S rRNA)     | DK7      | 5/95          | 1,488bp  |
| Gb_ba:Bb16sdk29  | X85202           | *rrs* (16S rRNA)     | DK29     | 5/95          | 1,488bp  |
| Gb_ba:Bb16sdunk  | X85201           | *rrs* (16S rRNA)     | DUNKIRK  | 5/95          | 1,488bp  |
| Gb_ba:Bbu28501   | U28501           | *rrs* (16S rRNA)     | ESP-1    | 7/95          | 1,488bp  |
| Gb_ba:Borr16sa   | M60967           | *rrs* (16S rRNA)     | G2       | 4/92          | 1,483bp  |
| Gb_ba:Borrnail   | M89936           | *rrs* (16S rRNA)     | Illinois 1 | 1/93         | 1,291bp  |
| Gb_ba:Bb16skipp  | X85196           | *rrs* (16S rRNA)     | KIPP     | 5/95          | 1,488bp  |
| Gb_ba:Bb16slipz  | X85203           | *rrs* (16S rRNA)     | LIPITZ   | 5/95          | 1,488bp  |
| Gb_ba:Borr16sc   | M60969           | *rrs* (16S rRNA)     | Sh-2-82  | 4/92          | 1,476bp  |
| Gb_ba:Borrvavs  | M89938           | *rrs* (16S rRNA)     | VS219    | 1/93          | 1,350bp  |
| Gb_ba:Borr16s    | L40596           | *rrs* (16S rRNA)     |          | 3/95          | 1,492bp  |
### Table 2.

#### 3.2 *Borrelia burgdorferi* fla sequences

| Genbank mnemonic | Accession number | Description                  | Strain | Date of entry | Size   |
|-------------------|------------------|------------------------------|--------|---------------|--------|
| Gb_ba:Borflas     | L29234           | *fla* (flagellin)            | 212    | 7/94          | 193bp  |
| Gb_ba:Bbflaa      | X16833           | *fla* flagellum-associated 41kD antigen (flagellin) | B31    | 9/93          | 1,435bp|
| Gb_ba:Bbfla2      | X15661           | *fla* (flagellin)            | B31    | 2/94          | 1,011bp|
| Gb_ba:Borflab31a  | L29200           | *fla* (flagellin)            | B31    | 7/94          | 193bp  |
| Gb_ba:Borflag     | M34710           | *fla* (flagellin)            | B31    | 5/95          | 684bp  |
| Gb_ba:Bbbo41      | X69607           | *fla* flagellum-associated 41kD antigen (flagellin) | BO     | 5/94          | 1,008bp|
| Gb_ba:Bbgehofla   | X56334           | *fla* (flagellin)            | GeHo   | 4/93          | 1,426bp|
| Gb_ba:Bbfla       | X15660           | *fla* (flagellin)            | GeHo   | 2/94          | 1,011bp|
### Table 3.

#### 3.3 *Borrelia burgdorferi* hbb sequences

| Genbank mnemonic | Accession number | Description | Strain     | Date of entry | Size   |
|------------------|------------------|-------------|------------|---------------|--------|
| Gb_ba:Bbu48650   | U48650           | *hbb* (Histone like protein HBbu) | A44S       | 4/96          | 327bp  |
| Gb_ba:Bbu48648   | U48648           | *hbb* (Histone like protein HBbu) | B31        | 4/96          | 327bp  |
| Gb_ba:Bbu48652   | U48652           | *hbb* (Histone like protein HBbu) | IP1        | 4/96          | 327bp  |
| Gb_ba:Bbu48653   | U48653           | *hbb* (Histone like protein HBbu) | IP2        | 4/96          | 327bp  |
| Gb_ba:Bbu48648   | U48648           | *hbb* (Histone like protein HBbu) | B31        | 4/96          | 327bp  |
| Gb_ba:Bbu48649   | U48649           | *hbb* (Histone like protein HBbu) | NY13-87    | 4/96          | 327bp  |
| Gb_ba:Bbu48654   | U48654           | *hbb* (Histone like protein HBbu) | IP3        | 4/96          | 327bp  |
| Gb_ba:Bbu35673   | U35673           | *hbb* (Histone like protein HBbu) | Sh-2-82    | 10/95         | 3,399bp|

Table 4.
3.4 *Borrelia burgdorferi* fesmid sequences

| Genbank mnemonic | Accession number | Description                     | Strain | Date of entry | Size   |
|-------------------|------------------|---------------------------------|--------|---------------|--------|
| Gb_ba:Bbu43739    | U43739           | Genes noted below               | B31    | 1/96          | 34,817bp |

Table 5.

*orf38* (open reading frame);  
*orf37* (open reading frame);  
*orf36* (open reading frame);  
*ylxH* (putative ATP-binding protein);  
*fhlF* (flagella associated putative GTP-binding protein);  
*fhlA* (flagellar protein required for flagellar formation);  
*fhlB* (flagellar protein required for flagellar formation);  
*fliR* (flagellar protein required for flagellar formation);  
*fliQ* (flagellar protein required for flagellar formation);  
*fliP* (flagellar protein required for flagellar formation);  
*fliZ* (flagellar protein required for flagellar formation);  
*fliN* (flagellar switch protein);  
*fliM* (flagellar switch protein);  
*orf25* (open reading frame);  
*motB* (flagellar motor rotation protein B);  
*motA* (flagellar motor rotation protein A);  
*fge* (flagellar hook protein);  
*ylxG* (flagellar synthesis);  
*orf20* (open reading frame);  
*orf19* (open reading frame);  
*orf18* (open reading frame);  
*fliI* (flagellar synthesis);  
*fliH* (flagellar synthesis);  
*fliG* (flagellar switch protein);  
*fliF* (flagella basal-body M ring protein);  
*fliE* (flagella basal-body protein);  
*fge* (flagella associated rod protein);  
*fge* (flagella associated rod protein);  
*hslU* (heat shock protein);  
*hslV* (heat shock protein);  
*smg* (?);  
*orf7* (open reading frame);  
*ftsZ* (cell division protein);  
*ftsA* (cell division protein);  
*dieIB* (cell division protein);  
*ftsW* (cell division protein);  
*mraY* (phosphotransferase);  
*murF* (pentapeptide presynthetase)
### 3.5 *Borrelia burgdorferi* chromosomal sequences (Except rrn & fla genes)

| Genbank mnemonic | Accession number | Description | Strain | Date of entry | Size    |
|-------------------|------------------|-------------|--------|---------------|---------|
| Gb_ba:Borp39ant   | L24194           | *bmpA* *bmpB* (immunodo-minant antigen P39 gene) | Sh-2-82 | 7/94          | 2,304bp |
| Gb_ba:Borbmpa     | L35050           | *bmpA* *bmpB* (membrane lipoproteins A & B) | 212    | 12/94         | 904bp   |
| Gb_ba:Borbmpc     | L34547           | *bmpC* (membrane lipoprotein C) | 297    | 11/94         | 1,293bp |
| Gb_ba:Bbu35450    | L34547           | *bmpD* (membrane lipoprotein D) | 297    | 4/96          | 1,525bp |
| Gb_ba:BBcheagen   | X91907           | *cheA1* (histidine kinase) | 212    | 9/95          | 332bp   |
| Gb_ba:Bbu28962    | U28962           | *cheA1* (histidine kinase) | CT-1   | 6/95          | 2,491bp |
| Gb_ba:Borchea     | L39965           | *cheA2* (histidine kinase) | B31    | 8/95          | 2,410bp |
|                   | U34384           | *cheW* (Positive regulator of CheA activity) | CT-1   | 9/95          | 660bp   |
| Gb_ba:Bbu04527    | U04527           | *dnaA* (DNA replication initiation), *dnaN* (DNA polymerase III beta subunit), *gyrB* (DNA gyrase B subunit), *rpmH* (ribosomal protein L34) and *rnpA* (ribonuclease P protein component) | 212    | 2/94          | 4943bp  |
| Gb_ba:Borgrpepl   | M96847           | *dnaJ* *dnaK* and *grpE* (heat shock proteins) |       | 2/93          | 3913bp  |
| Gb_ba:Bordnaj     | M97914           | *dnaJ* (heat-shock protein) | CA12   | 12/92         | 1,094bp |
| Gb_ba:Borhsp70a   | M97912           | *dnaK* (70 kDa heat shock protein) | CA12   | 10/92         | 1,928bp |
| Gb_ba:S42385      | S42385           | *dnaK* (70 kDa heat shock protein) | CA12   | 10/92         | 1,911bp |
| Gb_ba:BBhsp60     | X67646           | *dnaK* (70 kDa heat-shock protein) | ZS7    | 8/92          | 2,116bp |
| Gb_ba:Bbu12870    | U12870           | *filE* (flagellar hook polypeptide) | N40    | 4/95          | 1,552bp |
| Gb_ba:Bbu19712    | U19712           | *filE* (flagellar hook polypeptide) | B31    | 1/95          | 571bp   |
| Gb_ba:Burhflge    | L43849           | *filE* (flagellar hook polypeptide) | HB19   | 8/95          | 1499bp  |
| Gb_ba:Burhflif    | L40501           | *flfF* (Flagellar MS-ring protein) | 212    | 2/96          | 1717bp  |
| Gb_ba:BBU09711    | U09711           | *flfG* (Flagellar switch protein) | 212    | 7/95          | 1035bp  |
| Gb_ba:Burhflh    | L40502           | *flfH* (export of flagellar proteins?) | 212    | 1/96          | 921 bp  |
| Gb_ba:Burhflh    | L43325           | *flil* (export of flagellar proteins?) | 212    | 1/96          | 1311 bp |
| Genbank mnemonic | Accession number | Description                                                                 | Strain | Date of entry | Size     |
|------------------|------------------|------------------------------------------------------------------------------|--------|---------------|----------|
| Gb_ba:Bbftszg    | Z12164           | ftsZ (cell division protein)                                                | 212    | 5/94          | 261bp    |
|                  | U28760           | gapDH (glyceraldehyde-3-phosphate dehydrogenase); pgk phosphoglycerate kinase; tpi triose-phosphate isomerase |        |               |          |
|                  | Z12160           | gidA (glucose inhibited division protein)                                    | 212    | 5/94          | 196bp    |
|                  | X65139           | groEL (common antigen)                                                       | ZS7    | 5/92          | 1,931bp  |
|                  | Z12165           | gyrA (DNA gyrase subunit A)                                                 | 212    | 5/94          | 289bp    |
|                  | Z12166           | gyrB (DNA gyrase subunit B)                                                 | 212    | 5/94          | 253bp    |
|                  | L32145           | htpG (C62.5 heat shock protein)                                              | 212    | 12/94         | 236bp    |
|                  | L77216           | lon ATP-dependent protease                                                   | B31    | 4/96          | 2,946bp  |
|                  | L32146           | metG (methionyl tRNA synthetase)                                            | 212    | 12/94         | 346bp    |
|                  | L32861           | parE (topoisomerase IV, B subunit), plsC (1-acyl-sn-glycerol-3-phosphate acetyltransferase) | 212    | 5/94          | 677bp    |
|                  | X78708           | pep APE1 (aminopeptidase 1 homologue)                                        | ZS7    | 4/94          | 1,776bp  |
|                  | L32595           | pgk (phosphoglycerate kinase), tpi (triose-phosphate isomerase)             | 212    | 5/94          | 370bp    |
|                  | L32144           | pth (peptidyl-tRNA hydrolase)                                               | 212    | 4/94          | 910bp    |
|                  | U23457           | recA General recombination & DNA repair                                     | Sh-2-82| 4/96          | 2,025bp  |
|                  | L07656           | rho (Rho protein)                                                            | Sh-2-82| 9/93          | 1,499bp  |
|                  | L48488           | rpoB rpoC (RNA polymerase, beta & beta prime subunits)                      | B31    | 11/95         | 3,682bp  |
|                  | L46347           | rho (Rho protein)                                                            | 212    | 8/95          | 571bp    |
|                  | U35673           | rpsT (30S ribosomal protein S20)                                             | Sh-2-82| 10/95         | 3,399bp  |
|                  | U17591           | rpoD (primary sigma factor)                                                  | B31    | 12/94         | 4,165bp  |
|                  | L23125           | tuf (elongation factor EF-Tu)                                                | B31    | 8/93          | 1,230bp  |

Table 6.
### 3.6 *Borrelia burgdorferi* chromosomal sequences (Antigens and proteins of unknown function)

| Genbank mnemonic | Accession number | Description | Strain       | Date of entry | Size     |
|-------------------|------------------|-------------|--------------|---------------|----------|
| Gb_ba:Bororf      | L32797           | p21 (21 kDa protein) | 5/95         | 1,152bp      |
| Gb_ba:Borunk      | L31615           | p21A (21 kDa protein) | 297          | 700bp        |
| Gb_ba:Bor22kdant  | M90084           | p22 (22 kDa antigen) | B31          | 795bp        |
| Gb_ba:Borp22x     | L22530           | p22X (22 kDa outer surface lipoprotein) | N40          | 585bp        |
| Gb_ba:Borp23a     | L31616           | p23 (23kDa protein) | 297          | 686bp        |
| Gb_ba:Bbhyp     | X63898           | p38 (38 kDa ATP-binding protein) | GeHo         | 1,435bp      |
| Gb_ba:BDna66kd    | X87725           | p66 (66 kDa protein) | B31          | 2,180bp      |
| Gb_ba:Borlyme     | L32596           | p66 (66 kDa protein) | 212          | 240bp        |
| Gb_ba:Bbp831001   | X81514           | p93/p100 (93 kDa protein) | 297          | 287bp        |
| Gb_ba:Bbbop93     | X69601           | p93 (93 kDa protein) | BO           | 1,991bp      |
| Gb_ba:Bbp97       | X77749           | p97 (97 kDa protein) | GOE2         | 2,082bp      |
| Gb_ba:Bbp831002   | X81520           | p93/p100 (93 kDa protein) | pacificus    | 269bp        |
| Gb_ba:Bbp83100    | X81357           | p83/p100 (100 kDa protein) | PBre         | 287bp        |
| Gb_ba:Bbp831003   | X81528           | p93/p100 (93 kDa protein) | PKa2         | 287bp        |
| Gb_ba:Bbp831004   | X81531           | p93/p100 (93 kDa protein) | T255         | 287bp        |
| Gb_ba:Bbtrop93    | X69604           | p93 (93 kDa protein) | TRO          | 2,081bp      |
| Gb_ba:Borsurant   | L36037           | surface antigen | Dk1          | 185bp        |
| Gb_ba:Bbla7       | X70826           | LA7 (21 kDa lipoprotein) | ZS7          | 821bp        |
| Gb_ba:abp         | X91965           | *abp* (probable ATP binding protein) | 212          | 285bp        |
| Gb_ba:Boraaa      | M60802           | immunogen gene | 12/92        | 2,258bp      |
| Gb_ba:Bbu18292    | U18292           | "bbk2.10 gene" | 297          | 1,799bp      |
| Gb_ba:Bbu19105    | U19105           | "bbk2.10 gene" | N40          | 832bp        |
| Gb_ba:Borlyme     | L32596           | PCR target    | 212          | 240bp        |
### Table 7.

**Plasmid-encoded genes**

- ospA genes
- ospB genes
- ospC genes
- ospD genes

**3.7 Borrelia burgdorferi** Plasmid-encoded sequences (Except ospA, ospB, ospC & ospD)

| Genbank mnemonic | Accession number | Description | Plasmid | Strain | Date of entry | Size |
|------------------|-----------------|-------------|---------|--------|---------------|------|
| Gb ba:Borseqa    | M58429          | PCR target  |         |        | 3/91          | 379bp|
| Gb ba:Borseqc    | M58431          | PCR target  |         |        | 3/91          | 1725bp|
| Gb ba:Borseqd    | M58432          | PCR target  |         |        | 3/91          | 381bp|
| Gb ba:Borseqe    | M58433          | PCR target  |         |        | 3/91          | 379bp|
| Gb ba:Bbu35673   | U35673          | orfH, orfR and hbbU (putative proteins) |         | Sh-2-82 | 10/95 | 3,399bp |

| Genbank mnemonic | Accession number | Description | Plasmid | Strain | Date of entry | Size |
|------------------|-----------------|-------------|---------|--------|---------------|------|
| Gb ba:Borgmpguaa | L25883          | guaA (GMP synthetase) | 26 kb cp | CA-11.2A | 11/94 | 1,599bp |
| Gb ba:Bbu13372   | U13372          | guaB (IMP dehydrogenase) | 26 kb cp | CA-11.2A | 11/94 | 1,212bp |
| Gb ba:Borospea   | L13924          | ospE (outer surface protein E) | 45kb lp | N40 | 3/94 | 644bp |
| Gb ba:Borospfa   | L13925          | ospF (outer surface protein F) | 45kb lp | N40 | 3/94 | 785bp |
| Gb ba:Bbu19754   | U19754          | ospF (outer surface protein F) | 45kb lp | 297 | 7/95 | 690bp |
| Gb ba:Bbospg     | X82409          | ospG & bapA (outer surface protein G & associated protein A) | 48b lp | ZS7 | 11/95 | 1524bp |
| Gb ba:Bbu22451   | U22451          | p12 (12kDa lipoprotein) | 49kb lp | B31 | 3/95 | 285bp |
| Gb ba:Borexpprtn | L16625          | p20 (exported neuro-toxin-like protein) | 9kb cp | B31 | 8/94 | 720bp |
| Gb ba:S66708     | S66708          | PCR target sequence | 30kb cp | B31 | 11/95 | 416bp |
| Genbank mnemonic | Accession number | Description                                      | Plasmid | Strain | Date of entry | Size   |
|-------------------|------------------|--------------------------------------------------|---------|--------|---------------|--------|
| Gb Ba:Bors1a      | L34016           | S1 antigen                                       | 49kb lp | N40    | 11/95         | 1,421bp|
| Gb Ba:Bors2a      | L34016           | S2 antigen                                       | 49kb lp | N40    | 11/95         | 837bp  |
| Gb Ba:Bbptl4916   | X53311           | telomeres pTL16 and pTL49                        | 16kb lp & 49kb lp | N40 | 2/93         | 238bp  |
| Gb Ba:Bbptr16     | X53312           | telomere pTR16                                   | 16 kb lp | N40    | 2/93         | 191bp  |
| Gb Ba:S65114      |                 | left terminal repeat, telomeric fragment         | lp      | N40    | 7/92          | 38bp   |
| Gb Ba:            | X87127           | repeated DNA element                             | 30.5kb cp | N40 | 4/96         | 5,500bp|

Table 8.

3.8 *Borrelia burgdorferi* ospA sequences

| Genbank mnemonic | Accession number | Description                                      | Strain | Date of entry | Size   |
|-------------------|------------------|--------------------------------------------------|--------|---------------|--------|
| Gb Ba:Bb297ospa   | X85442           | *ospA* (outer surface protein A)                 | 297    | 8/95          | 822bp  |
| Gb Ba:Borospad    | L23138           | *ospA ospB* (outer surface proteins A & B)       | 19535NY2 | 8/94 | 1,653bp      |
| Gb Ba:Borospah    | L23141           | *ospA ospB* (outer surface proteins A & B)       | 21343WI | 8/94 | 1,653bp      |
| Gb Ba:Borospac    | L23137           | *ospA ospB* (outer surface proteins A & B)       | 27985CT2 | 6/94 | 1,653bp      |
| Gb Ba:Borospaf    | L23140           | *ospA ospB* (outer surface proteins A & B)       | 41552MA | 8/94 | 1,653bp      |
| Gb Ba:Borospae    | L23139           | *ospA ospB* (outer surface proteins A & B)       | 42373NY3 | 8/94 | 1,653bp      |
| Gb Ba:Borospaa    | L23136           | *ospA ospB* (outer surface proteins A & B)       | B19CT1  | 6/94 | 1,653bp      |
| Gb Ba:Bbosapab    | X14407           | *ospA ospB* (outer surface proteins A & B)       | B31    | 9/94 | 1,915bp      |
| Gb Ba:Boropsab    | L19701           | *ospA ospB* (outer surface proteins A & B)       | B31    | 6/93 | 1,916bp      |
| Genbank mnemonic | Accession number | Description | Strain | Date of entry | Size   |
|------------------|------------------|-------------|--------|---------------|--------|
| Gb_ba:Borospai   | L23142           | *ospA ospB* (outer surface proteins A & B) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Borospaj   | L23143           | *ospA ospB* (outer surface proteins A & B) | CA7    | 8/94          | 1,653bp|
| Gb_ba:Borospak   | L23144           | *ospA ospB* (outer surface proteins A & B) | CA8    | 8/94          | 1,653bp|
| Gb_ba:Bbdk6ospa  | X83622           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpospa    | X63412           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bormajospr | L19702           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbaspa     | X60300           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Borospa3   | X65600           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbu33179   | U33179           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbopsaa    | X70365           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbka0spa   | X69606           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbospcmul  | X84779           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Borfra     | L38657           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Borospa    | M57248           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbdnaospa  | X85739           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpheiosp  | X80251           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpkaospa  | X80182           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpwud1    | X80184           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpwudi    | X68540           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpwudl6   | X80185           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Gb_ba:Bbpwudll   | X80253           | *ospA* (outer surface protein A) | CA3    | 8/94          | 1,653bp|
| Genbank mnemonic | Accession number | Description                  | Strain         | Date of entry | Size    |
|------------------|------------------|------------------------------|----------------|---------------|---------|
| Gb_ba:Bbpwudii   | X68539           | ospA (outer surface protein A) | PWudII         | 3/93          | 333bp   |
| Gb_ba:Bor90ospa  | L42873           | ospA (outer surface protein A) | SIMON          | 6/95          | 582bp   |
| Gb_ba:Bbt25ospa  | X85443           | ospA (outer surface protein A) | T255           | 9/95          | 822bp   |
| Gb_ba:Borospaab  | D29660           | ospA (outer surface protein A) | tick isolate   | 4/95          | 911bp   |
| Gb_ba:Bbospa1    | X65598           | ospA (outer surface protein A) | TRO            | 1/94          | 822bp   |
| Gb_ba:Bbospa     | X16467           | ospA (outer surface protein A) | ZS7            | 9/93          | 942bp   |
| Gb_ba:A22442     | A22442           | ospA (outer surface protein A) | ZS7            | 12/94         | 822bp   |
| Gb_ba:Bbosproa   | X66065           | ospA (outer surface protein A) | ZQ1            | 7/93          | 825bp   |
| Gb_ba:A24006     | A24006           | ospA (outer surface protein A) | ZQ1            | 2/95          | 825bp   |
| Gb_ba:A04009     | A04009           | ospA ospB (outer surface proteins A & B) |             | 4/93          | 1,915bp |

Table 9.

**3.9 *Borrelia burgdorferi* ospB sequences**

| Genbank mnemonic | Accession number | Description                  | Strain         | Date of entry | Size    |
|------------------|------------------|------------------------------|----------------|---------------|---------|
| Gb_ba:Borospad   | L23138           | ospA ospB (outer surface proteins A & B) | 19535NY2       | 8/94          | 1,653bp |
| Gb_ba:Borospha   | L23141           | ospA ospB (outer surface proteins A & B) | 21343WI        | 8/94          | 1,653bp |
| Gb_ba:Borospac   | L23137           | ospA ospB (outer surface proteins A & B) | 27985CT2       | 6/94          | 1,653bp |
| Gb_ba:BorospaF   | L23140           | ospA ospB (outer surface proteins A & B) | 41552MA        | 8/94          | 1,653bp |
| Gb_ba:BorospaE   | L23139           | ospA ospB (outer surface proteins A & B) | 42373NY3       | 8/94          | 1,653bp |
| Gb_ba:Boropsab   | L19701           | ospA ospB (outer surface proteins A & B) | B31            | 6/93          | 1,916b  |
| Gb_ba:Bbospaper  | X14407           | ospA ospB (outer surface proteins A & B) | B31            | 9/94          | 1,915bp |
### Table 10.

#### 3.10 *Borrelia burgdorferi* ospC sequences

| Genbank mnemonic | Accession number | Description                              | Strain  | Date of entry | Size  |
|-------------------|------------------|------------------------------------------|---------|---------------|-------|
| Gb_ba:Bbospc272   | X84785           | *ospC* (outer surface protein C)         | 272     | 5/95          | 534bp |
| Gb_ba:Bbu08284    | U08284           | *ospC* (outer surface protein C)         | 297     | 9/94          | 579bp |
| Gb_ba:Bor26ospc   | L42893           | *ospC* (outer surface protein C)         | 297     | 6/95          | 576bp |
| Gb_ba:Bbu01892    | U01892           | *ospC* (outer surface protein C)         | 2591    | 1/94          | 824bp |
| Gb_ba:Bor32ospc   | L42899           | *ospC* (outer surface protein C)         | 21347   | 6/95          | 576bp |
| Gb_ba:Bor30ospc   | L42897           | *ospC* (outer surface protein C)         | 26815   | 6/95          | 579bp |
| Gb_ba:Bor29ospc   | L42896           | *ospC* (outer surface protein C)         | 27579   | 6/95          | 573bp |
| Gb_ba:Bor28ospc   | L42895           | *ospC* (outer surface protein C)         | 28354   | 6/95          | 579bp |
| Gb_ba:Bor27ospc   | L42894           | *ospC* (outer surface protein C)         | 28691   | 6/95          | 573bp |
| Genbank mnemonic | Accession number | Description | Strain | Date of entry | Size  |
|------------------|------------------|-------------|--------|---------------|-------|
| Gb_ba:Bbb31ospc  | X69596           | *ospC* (outer surface protein C) | B31    | 5/93          | 633bp |
| Gb_ba:Bbu01894   | U01894           | *ospC* (outer surface protein C) | B31    | 1/94          | 980bp |
| Gb_ba:Borospca   | D49497           | *ospC* (outer surface protein C) | B31    | 5/95          | 633bp |
| Gb_ba:Bbospcbur  | X84765           | *ospC* (outer surface protein C) | BUR    | 5/95          | 534bp |
| Gb_ba:Borospc    | L25413           | *ospC* (outer surface protein C) | CA-11.2A | 7/94     | 1,150bp |
| Gb_ba:Bbospc     | X73626           | *ospC* (outer surface protein C) | DK6    | 2/94          | 609bp |
| Gb_ba:Bbospcd    | X73625           | *ospC* (outer surface protein C) | DK7    | 2/94          | 618bp |
| Gb_ba:Bbospcc    | X73624           | *ospC* (outer surface protein C) | DK26   | 2/94          | 624bp |
| Gb_ba:Bbospcb    | X73623           | *ospC* (outer surface protein C) | DK27   | 2/94          | 624bp |
| Gb_ba:Bbospcduk  | X84778           | *ospC* (outer surface protein C) | DUNKIRK | 5/95    | 528bp |
| Gb_ba:Bbu04281   | U04281           | *ospC* (outer surface protein C) | HB19   | 1/95          | 692bp |
| Gb_ba:Bor20ospc  | L42887           | *ospC* (outer surface protein C) | Ip2    | 6/95          | 576bp |
| Gb_ba:Bbospckip  | X84782           | *ospC* (outer surface protein C) | KIPP   | 5/95          | 534bp |
| Gb_ba:Bbu04240   | U04240           | *ospC* (outer surface protein C) | N40    | 8/94          | 689bp |
| Gb_ba:Bbdnaospc  | X83555           | *ospC* (outer surface protein C) | pacificus | 6/95    | 630bp |
| Gb_ba:Bbospc1    | X81522           | *ospC* (outer surface protein C) | PBre   | 6/95          | 636bp |
| Gb_ba:Bbpkaospc  | X69589           | *ospC* (outer surface protein C) | PKa    | 2/94          | 633bp |
| Gb_ba:Bbt25ospc  | X69592           | *ospC* (outer surface protein C) | T25    | 2/94          | 636bp |
| Gb_ba:Bbospc2    | X81524           | *ospC* (outer surface protein C) | T255   | 5/95          | 633bp |
| Gb_ba:Bbospctxw  | X84783           | *ospC* (outer surface protein C) | TXGW   | 5/95          | 531bp |
| Gb_ba:Bbwudospc  | X69590           | *ospC* (outer surface protein C) | WudI   | 2/94          | 639bp |
| Gb_ba:Bor40ospc  | L42868           | *ospC* (outer surface protein C) | ZS7    | 6/95          | 579bp |

Table 11.
3.11 *Borrelia burgdorferi* ospD sequences

| Genbank mnemonic | Accession number | Description                  | Strain | Date of entry | Size   |
|------------------|------------------|------------------------------|--------|---------------|--------|
| Gb_ba:Bbu05304   | U05304           | *ospD* (outer surface protein D) | 3028   | 11/94         | 1,012bp |
| Gb_ba:Bbu05305   | U05305           | *ospD* (outer surface protein D) | 27985  | 11/94         | 1,012bp |
| Gb_ba:Borospd    | M97452           | *ospD* (outer surface protein D) | B31    | 2/93          | 1,079bp |
| Gb_ba:Bbu05324   | U05324           | *ospD* (outer surface protein D) | CA12   | 11/94         | 991bp   |
| Gb_ba:Borospdhhb | L34055           | *ospD* (outer surface protein D) | HB19   | 6/94          | 1,045bp |
| Gb_ba:Bbu05327   | U05327           | *ospD* (outer surface protein D) | lps    | 11/94         | 1,064bp |

Table 12.

3.12 *Borrelia burgdorferi* fusion sequences

| Genbank mnemonic | Accession number | Description | Strain | Date of entry | Size   |
|------------------|------------------|-------------|--------|---------------|--------|
| Gb_ba:A24010     | A24010           | *ospA* fusion | NS1   | 2/95          | 1,020bp |
| Gb_ba:A24012     | A24012           | *ospA* fusion | NS1   | 2/95          | 1,014bp |
| Gb_ba:A24014     | A24014           | *ospA* fusion | NS1   | 2/95          | 1,017bp |
| Gb_ba:A24016     | A24016           | *ospA* fusion | NS1   | 2/95          | 1,017bp |
| Gb_ba:Borbb1     | L31427           | *phoA* fusion | 297    | 4/95          | 279bp   |
| Gb_ba:Borbb10    | L31421           | *phoA* fusion | 297    | 4/95          | 319bp   |
| Gb_ba:Borbb11    | L31424           | *phoA* fusion | 297    | 4/95          | 248bp   |
| Gb_ba:Borbb13    | L31422           | *phoA* fusion | 297    | 4/95          | 354bp   |
| Gb_ba:Borbb14    | L31423           | *phoA* fusion | 297    | 4/95          | 361bp   |
| Gb_ba:Borbb16    | L31425           | *phoA* fusion | 297    | 4/95          | 135bp   |
| Gb_ba:Borbb17    | L31426           | *phoA* fusion | 297    | 4/95          | 615bp   |
| Gb_ba:Borbb4     | L31417           | *phoA* fusion | 297    | 4/95          | 294bp   |
| Gb_ba:Borbb4a    | L31419           | *phoA* fusion | 297.   | 4/95          | 221bp   |
| Gb_ba:Borbb5     | L31418           | *phoA* fusion | 297    | 4/95          | 341bp   |
| Gb_ba:Borbb9     | L31420           | *phoA* fusion | 297    | 4/95          | 233bp   |

Table 13.
3.13 *Borrelia burgdorferi* promoter sequences

| Genbank mnemonic       | Accession number | Description | Strain | Date of entry | Size  |
|------------------------|------------------|-------------|--------|---------------|-------|
| Gb_ba:BorpromA         | M28680           | promoter    | B31    | 6/90          | 194bp |
| Gb_ba:BorpromB         | M28681           | promoter    | B31    | 6/90          | 203bp |
| Gb_ba:BorpromC         | M28682           | promoter    | B31    | 6/90          | 78bp  |

Table 14.

Fig. 5. Electron microscopy of unfixed, negative stained DK1 strain (skin isolate). This strain consist of two morphologically distinct borrelia A. small and B. larger *borrelia*. Bar 1 mm. Magnification 10,260 x.
Fig. 6. Electron microscopy of unfixed, negative stained DK1 strain (skin isolate).
Fig. 7. Plasmids isolated from different strains of *Borrelia burgdorferi* : The Dk1 strain (B), Dk5 strain (C), DK6 strain (D), DK2 strain (E), DK7 strain (F) and a super coiled circular molecular weight marker (G). Linear molecular markers (A) (HindIII fragments of Lambda DNA). Samples were separated in 0.3% gel at 14°C for 20 hr then stained with ethidium bromide.

Fig. 8. Electron micrograph of 25 kb plasmid extracted from DK1 strain. One supercoiled plasmid. magnification 52000 x.
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Lyme disease, or Lyme borreliosis, is an emerging infectious disease caused by bacteria belonging to the genus borrelia. Borrelia burgdorferi, in the strict sense. This book deals mostly with the molecular biology of the Lyme disease agent orrelia burgdorferi. It has been written by experts in the relevant field and is tailored to the need of researchers, advanced students of biology, molecular biology, molecular genetics of microorganism. It will also be of use to infectious disease experts and people in other disciplines needing to know more about Lyme borreliosis. The book contains chapters on the molecular biology of the Lyme disease agent, zoonotic peculiarities of Bb, advancement in Bb antibody testing, the serology diagnostic schemes in Bb, discovering Lyme disease in ticks and dogs, adaptation to glucosamine starvation in Bb, and porins in the genus borrelia.

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