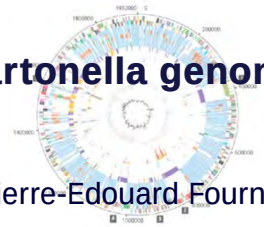
ESCMID Postgraduate Technical Workshop
Intracellular bacteria: from biology to clinic
Villars-sur-Ollon, 26-30 August 2013



Bartonella genomes

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The genomic era

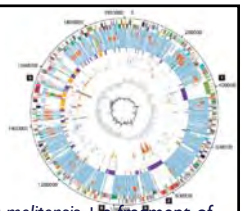
As of August 23rd, 2013

21 genomes from *Bartonella* species

B. alsatica, *B. australis*, *B. bacilliformis* (x2), *B. birtlesii*, *B. clarridgeiae*, *B. doshiae*, *B. gr ahamii*, *B. henselae*, *B. melophagi*, *B. quintana* (x2), *B. senegalensis*, *B. tamurae*, *B. taylorii*, *B. tribocorum*, *B. vinsonii* (x2), *B. washoensis* (x2)

How do genomes from facultative intracellular bacteria behave?

Pioneering work



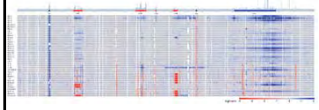
- ✓ *B. quintana* and *B. henselae*
- ✓ 1,58 and 1.93 Mb, ~27% non-coding
- ✓ High degree of synteny
- ✓ Similarity to chromosome I from *Brucella melitensis* + a fragment of chromosome II flanked by 2 rRNA operons
- ✓ Evidence of LGT and phage integration
- ✓ *B. henselae* has 1 prophage (similar to *Wolbachia*), 3 specific genomic islands encoding filamentous hemagglutinin and a partial pathogenicity island similar to *Photorhabdus*, all lost by *B. quintana*
- ✓ Reduced genomes from louse-associated bacteria («specialists») suggest that host restriction is associated to accelerated genome degradation

B. koehlerae

Characterization of the Genome Composition of *Bartonella koehlerae* by Microarray Comparative Genomic Hybridization Profiling†

- ✓ Same host (felids) as *B. henselae*, causes CSD
- ✓ Comparative genomic hybridization (microarray)
- ✓ 1.7 – 1.8 Mb
- ✓ Few unique genes
- ✓ Only remnants of prophage and genomic islands (as in *B. quintana*)
- ✓ Sequence variability in the chromosome II-like region
- ✓ As *B. koehlerae* is closely related to *B. henselae*, loss events are likely independents, although similar, to those of *B. quintana*
- ✓ Genomic islands are instable

Genomic diversity of *B. henselae*

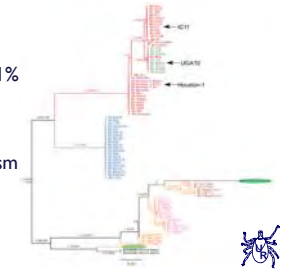


Genome Rearrangements, Deletions, and Amplifications in the Natural Population of *Bartonella henselae*†

- ✓ 38 *B. henselae* strains
- ✓ Comparative genomic hybridization (microarray)
- ✓ Variations confined to the prophage and genomic islands + extensive rearrangements across the terminus of replication
- ✓ No difference in gene content or structure in between feline and human isolates
- ✓ DNA amplification in the chromosome II-like region
- ✓ Has the variable gene pool a role in the establishment of long-term persistent infection by promoting antigenic variation and escape from the host immune response?

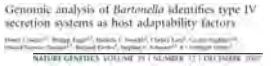
Genomic diversity of *B. henselae*

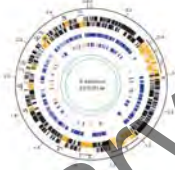
- ✓ 3 *B. henselae* strains
- ✓ Full genome sequencing
- ✓ Only minor gene content variation (closed pan genome)



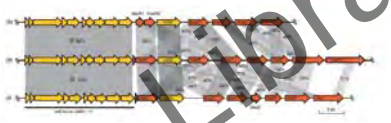
- ✓ Nucleotide sequence variation <1%
- ✓ Multiple recombinations in T4SS gene clusters (*virB*, trw genes) and for a gene involved in iron metabolism
- ✓ Possible LGT across *Bartonella* species

Genomic adaptation to hosts





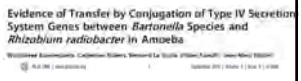
- ✓ *B. tribocorum* genome sequencing: 2.6 Mb
- ✓ Compared to *B. henselae* and *B. quintana*
- ✓ 959 core genes
- ✓ Genome extension in *B. tribocorum* (LGT acquisition of prophages and genome islands + gene duplications)
- ✓ Species-specific *virB* T4SS operons may play a role in host adaptability

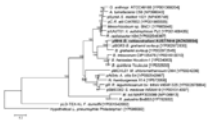


High genomic diversity of *B. grahamii*

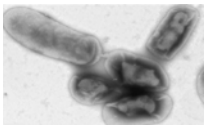
- ✓ *B. grahamii* genome sequencing ~2.3 Mb
- ✓ 27 strains from 11 rodent species in 7 countries
- ✓ High variability in genome content, especially in outer surface-exposed proteins, notably hemagglutinin (T5SS), and a plasmid encoding a T4SS operon
- ✓ Strong geographic patterns
- ✓ Lower sequence divergence in European and North American (98%) than Asian strains (95% and recombination events)
- ✓ The most variable the hosts, the most variable the strains

LGT in amoebal bacteria





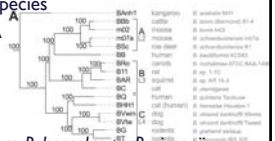
- ✓ *B. rattaustraliani* plasmid
- ✓ Encodes a tra cluster (T4SS)
- ✓ Evidence of LGT between *Bartonella* sp. and *Rhizobium radiobacter*



- ✓ Possible cross-talk between *Bartonella* species and plant pathogens within amoebae

Gene transfer agents in *Bartonella*

- ✓ Gene transfer agents (GTAs) transfer random genomic fragments <14kb (smaller than those transferred by phages)
- ✓ GTAs are present in *B. grahamii* (Berglund *et al.* PLoS Genet.2009;5:e1000546)
- ✓ Comparison of 16 genomes from 11 species
- ✓ 428 core genes, incl. 12 genes for GTA



- ✓ Recent transfer of 7 genes, incl. *virB* from *B. henselae* to *B. vinsonii*
- ✓ The GTA system from *B. henselae* is functional
- ✓ GTAs may facilitate host adaptation

Overall

- ✓ The genomic variation in *Bartonella* species depends on the diversity of their hosts (rodents +++)
- ✓ Genomic variability in *Bartonella* species occurs in only a few fragments : prophage, genomic islands, chromosome II-like region
- ✓ T4SS variability may play a role in host adaptation
- ✓ *Bartonella* species may exchange genes among species and with other genera, possibly thanks to gene transfer agents
- ✓ Human- and louse-associated bacteria have the most degraded genomes