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New *Mycobacterium bovis* complete genomes of different clonal complexes to improve molecular epidemiology studies of French field strains

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Bovine Tuberculosis (bTB) is a zoonotic disease due to *Mycobacterium bovis* (*M. bovis*). France has a bTB-free status, but the disease has not been eradicated yet and a worryingly steady increase of bTB outbreaks has been observed in some regions (1). This could be explained by the detection of bTB in wildlife that spills it back to livestock in the same territories. The transmission link within these multi-host systems remains difficult to establish given that they share the same *M. bovis* genotypes (2). Obtaining new reference genomes for each of these genotypes could improve the knowledge of clonal groups and refine molecular field epidemiology studies based on whole genome sequencing.

Goal

The aim of the study was to obtain ten new complete *M. bovis* genomes closer to French field strains.

Method

Ten strains representing each French *M. bovis* clonal group and responsible for the main current French outbreaks were selected (Fig 1). These genomes were *de novo* assembled using both long-reads (MiniON) and short-reads (Illumina) with a hybrid assembly method. New genomes were blast against previous genome reference (Mb3601) with BRIG platform (Fig 2). The precise comparison of genomic structures was performed with Mauve and allow the identification of region of differences (RD) between genomes. Annotation of these RDs was performed using prokka tool.

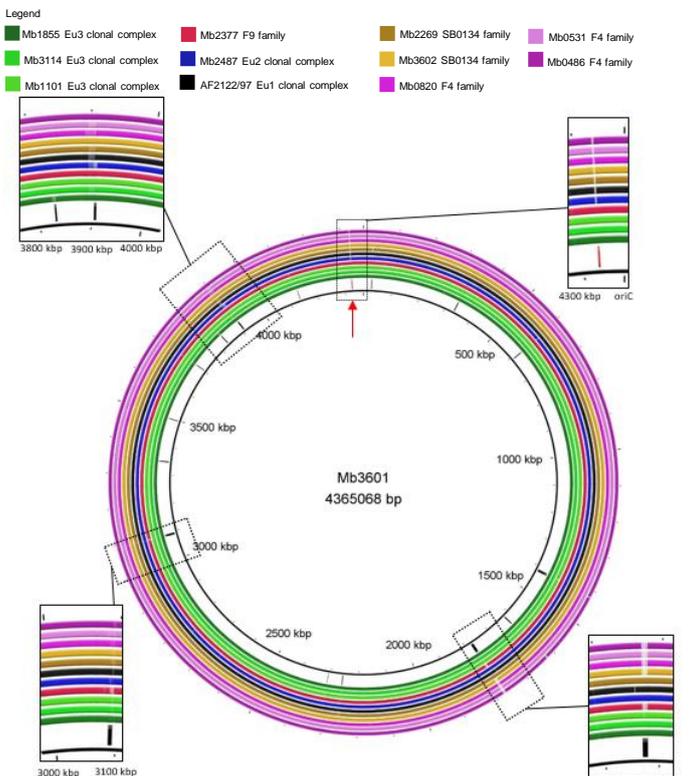
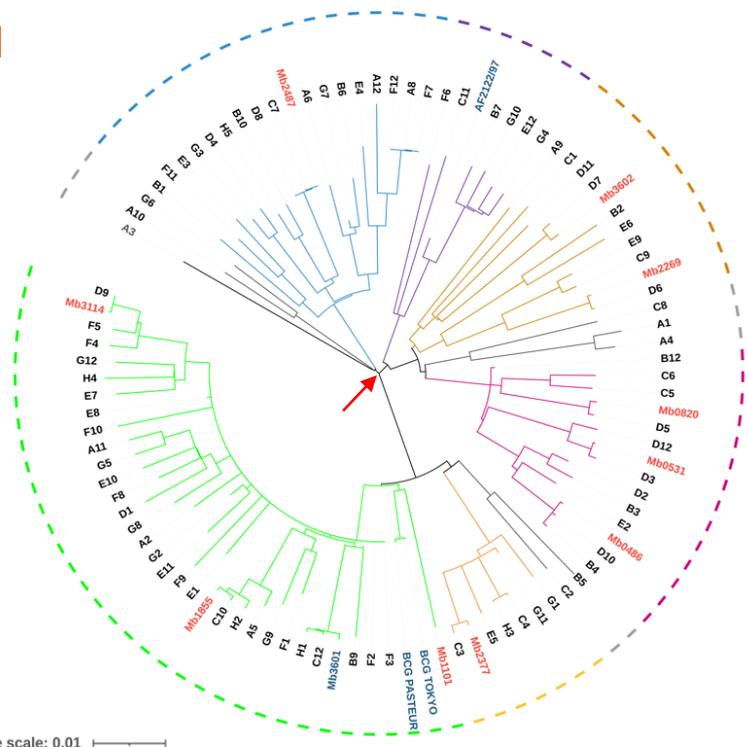


Fig 2. Genomes alignment of complete *M. bovis* genomes including AF2122/97 reference genome shown in black. Genomes were blast against Mb3601 reference genome. The representation was obtained using BRIG platform on complete genome sequences. Four interesting regions have been expand. Region of differences (RDs) for each sequence are indicated by white parts. The first circle shows major RD between the 11 genomes and Mb3601. The red arrow indicates specific RD of F4 family, SB0134 family, Eu1 and Eu2 clonal complex strains.

Conclusions

Obtaining these new reference genomes allows us to better describe clonal groups identified in France. These genomic data will help to better understand the bTB transmission dynamics in multi-host systems through precise molecular epidemiological studies and thus to implement more effective control measures to eradicate the disease in these areas.

Mycobacterium bovis group
Cluster F / Eu3 clonal complex Cluster C / SB0134 family Cluster G / F9 family Other
Cluster D / Eu1 clonal complex Cluster A / F4 family Cluster I / Eu3 clonal complex



Tree scale: 0.01

Fig 1. Circular phylogenetic tree of 100 *Mycobacterium bovis* genomes from various host species (89 cattle, 2 wildboars, 2 deer, 1 goat, 1 sheep and 2 vaccine strains), 86 of them provided by Hauer study (2). The two previous reference genomes (Mb3601 and AF2122/97) and 2 complete sequence of BCG vaccine strains (BCG Pasteur and BCG Tokyo) are marked in blue. The 10 new complete genome are indicated in red. The strains are grouped in 7 clusters which have been previously defined (2). The phylogenetic tree is based on 7424 whole genome single nucleotide polymorphism. Red arrow show the phylogenetic node who isolated strains with the specific RD describe in Fig 2.

Results

- Ten new complete genomes of French *M. bovis* strains were obtained (Fig 1).
- As expected, *M. bovis* is highly clonal and shows great stability in its genomic structure (Fig 2).
- However, 361 RDs of more than 10 bases were identified for specific genome or group. For example, the RD indicated by the red arrow shows the absence of 2409 bp specific to F4 family, SB0134 family, Eu1 and Eu2 clonal complex strains (Fig 2). This genetic event involves partial deletion of genes implied in secretion system named *eccD2* and *espG2*.

REFERENCES

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