Genetic features of Mycobacterium avium subsp. paratuberculosis strains circulating in the West of France deciphered by Whole-Genome Sequencing

Cyril Conde, Thierry Cochard, Marie-Noëlle Rossignol, Christine Fourichon, Arnaud Delafosse, Aurore Davergne, Alain Joly, David Ngwa-Mbot, Laurent Journaux, Raphaël Guatteo, et al.

Genetic features of strains of *Mycobacterium avium* subsp. *paratuberculosis* circulating in the West of France deciphered by Whole-Genome Sequencing

Condé C[1], Cochard T[1], Rossignol MN[2], FourichonC[3], Delafosse A[4], Davergne A[5], Joly A[6], Ngwa-Mbot D[7], Journaux L[8], Guatteo R[3], Schibler L[9], Bannantine J[10], Biet F[1]

[1]INRAE, ISP, Université de Tours, Nouzilly, France ; [2]INRAE, GABI, Université Paris-Saclay, Jouy-en-Josas, France ; [3]INRAE, UMR 1300 BIOEPAR, Nantes, France ; [4]Groupement de Défense Sanitaire Orne, Alençon, France

[5]GDMA, Bois Guillaume, France ; [6]Groupement de Défense Sanitaire Bretagne, Vannes, France ; [7]GDS France, Paris, France ; [8]Idele, Paris, France ; [9]Allice, Paris, France ; [10]USDA-Agricultural Research Service, National Animal Disease Center, Ames, Iowa, USA

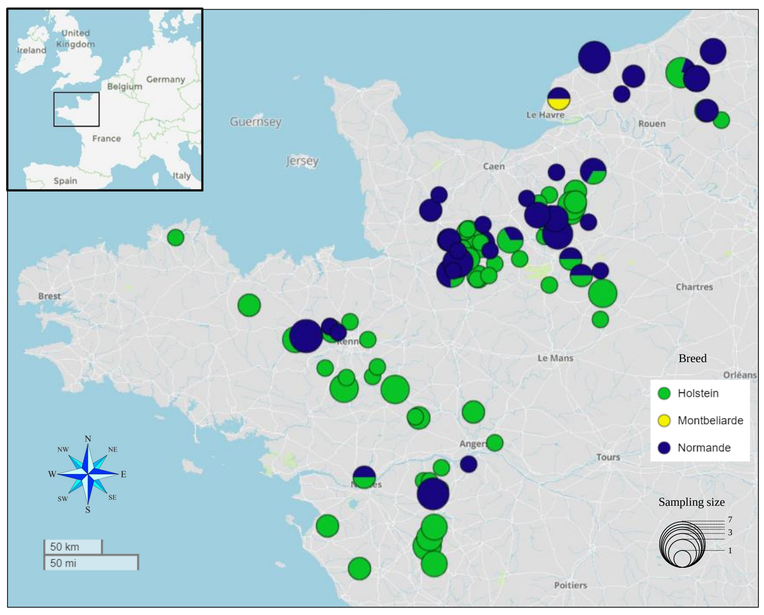
Background & Objective

Paratuberculosis is a chronic infection of the intestine, mainly the ileum, caused by *Mycobacterium avium* subsp. *paratuberculosis* (Map) in cattle and other ruminants. This enzootic disease is present worldwide and has a strong impact on the dairy cattle industry.

For this species, the typing tools do not make it possible to investigate the genetic diversity of the strains. These limitations can be overcome by the application of Whole Genome Sequencing (WGS), particularly for clonal populations such as Map. WGS analyses can provide comprehensive genetic information, including information on genome evolution, discrimination of closely related strains and virulence determinants.

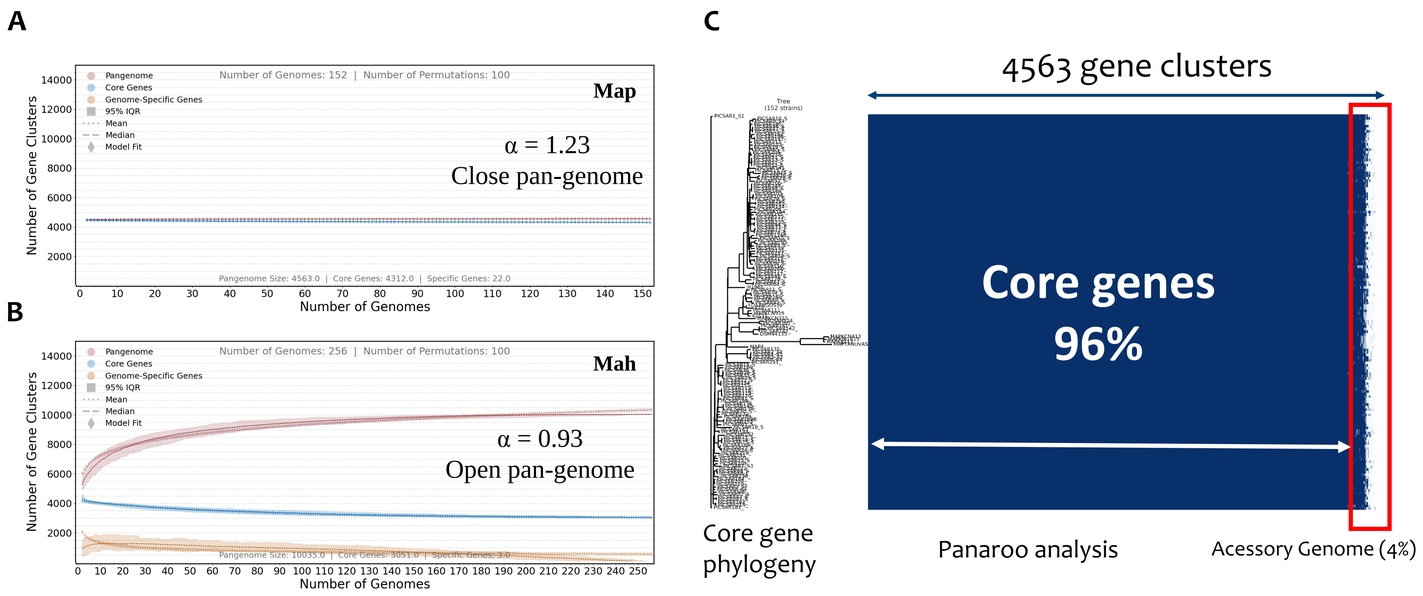
The purpose of the present study was to undertake a whole-genome analysis of Map strains isolated from herds in western France. This allowed us to identify accurate phylogenetic relationships between isolates and further, establish correlations between genomic traits and epidemiological data within a population of well documented-strains.

Figure 1. Material and methods



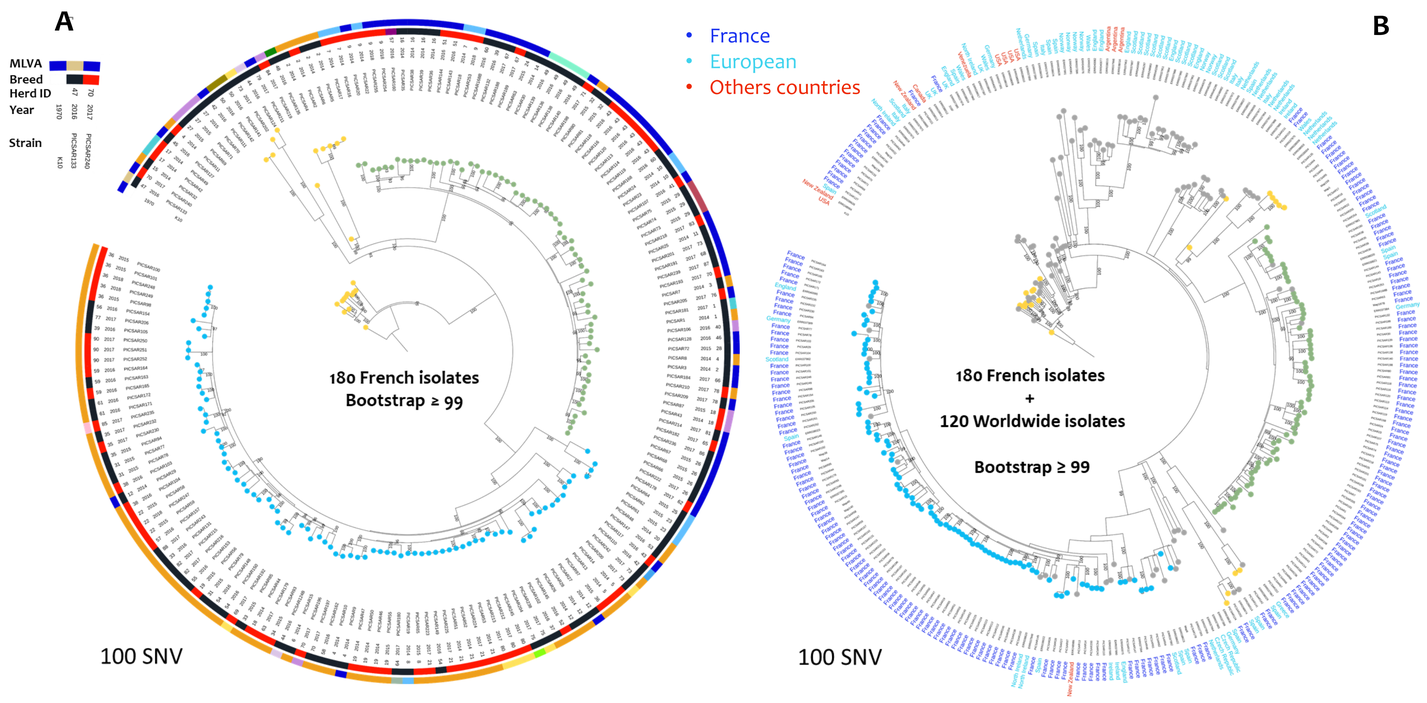
Geographic location of herds sampled including breed and number of isolates (n= 200) selected from a large genetic study on the trait of animal sensitivity to paratuberculosis disease (1,2)

Figure 2. Overview of pan-genomic characteristics of Map isolates



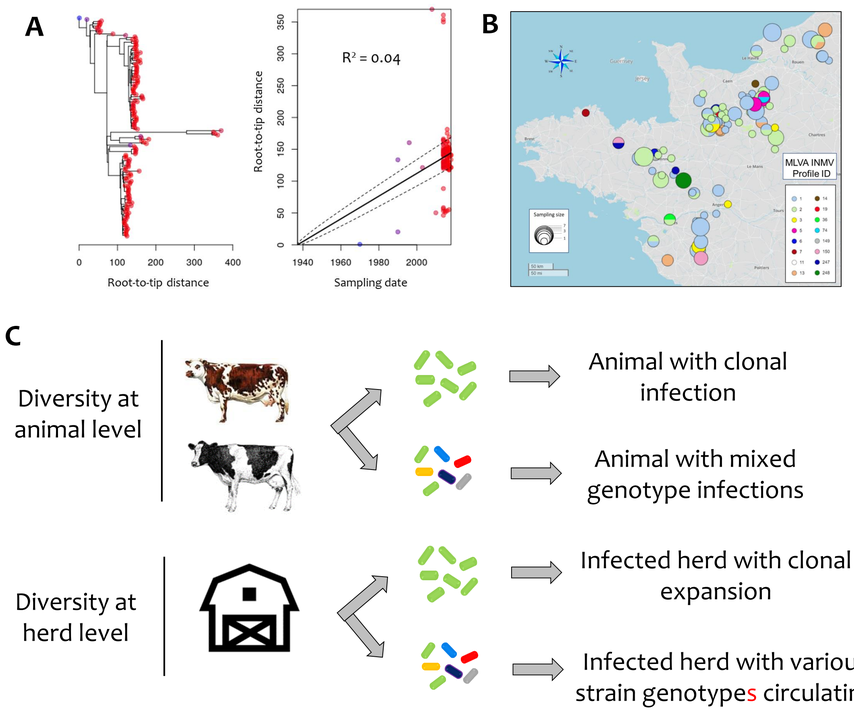
(A) Genome size evolution curves of pan-genome (red) and core genome (blue) analysis inferred with the French Map strains (unique genes are indicated in orange) **(B)** Comparison analysis inferred with the closely related Mah genomes. **(C)** Core gene phylogeny and pan-genome overview inferred with the French Map isolates and the 10 Map complete genomes available in GenBank. Data show Map has a very stable genome.

Figure 3. SNP Phylogeny of French Map isolates



(A) SNP phylogeny was inferred using the French genomes and include the Map K10 genome. **(B)** Global SNP phylogeny was inferred using the French genomes and a worldwide panel previously described (3).

Figure 4. Particular traits of French Map isolates



(A) Temporal signal by Root-to-tip analysis (4) **(B)** Geo-distribution of the MLVA genotype **(C)** Strain diversity observed at animal level and at herd level.

Results

- More than new 180 Map French genomes are available from well-documented cases of bovine paratuberculosis.
- The genomic phylogeny revealed that French strains are divided in 3 different clusters. Two main clusters are well defined and one is very heterogeneous.
- The global distribution highlight that French isolates constitute specific clusters with an occasional strain from close neighboring country encrusted.
- No association with breed/strain type.
- No molecular clock observed.
- We observed in some case animals with mixed infection and herds with different infectious status.

Conclusion & Perspectives

- This study provide an ultimate degree of resolution of Map diversity thanks to WGS
- First description of the population structure of French Map-isolates at genomic level.
- In progress, combine epidemiological information to study the dynamic of transmission of this pathogen circulating in the west of France.
- Propose a model of risk linked to the movement of animals

References : 1. Navaro-Gonzalez, J.Dairy Sci, 2019 ; 2. Sanchez MP, GSE, 2020 ; 3. Bryant J, BMC Genomics 2016 ; 4. Didelot X , NAR 2018

Cyril Conde – INRA
cyril.conde@tours.inra.fr

Franck Biet – INRA
Franck.biet@tours.inra.fr