

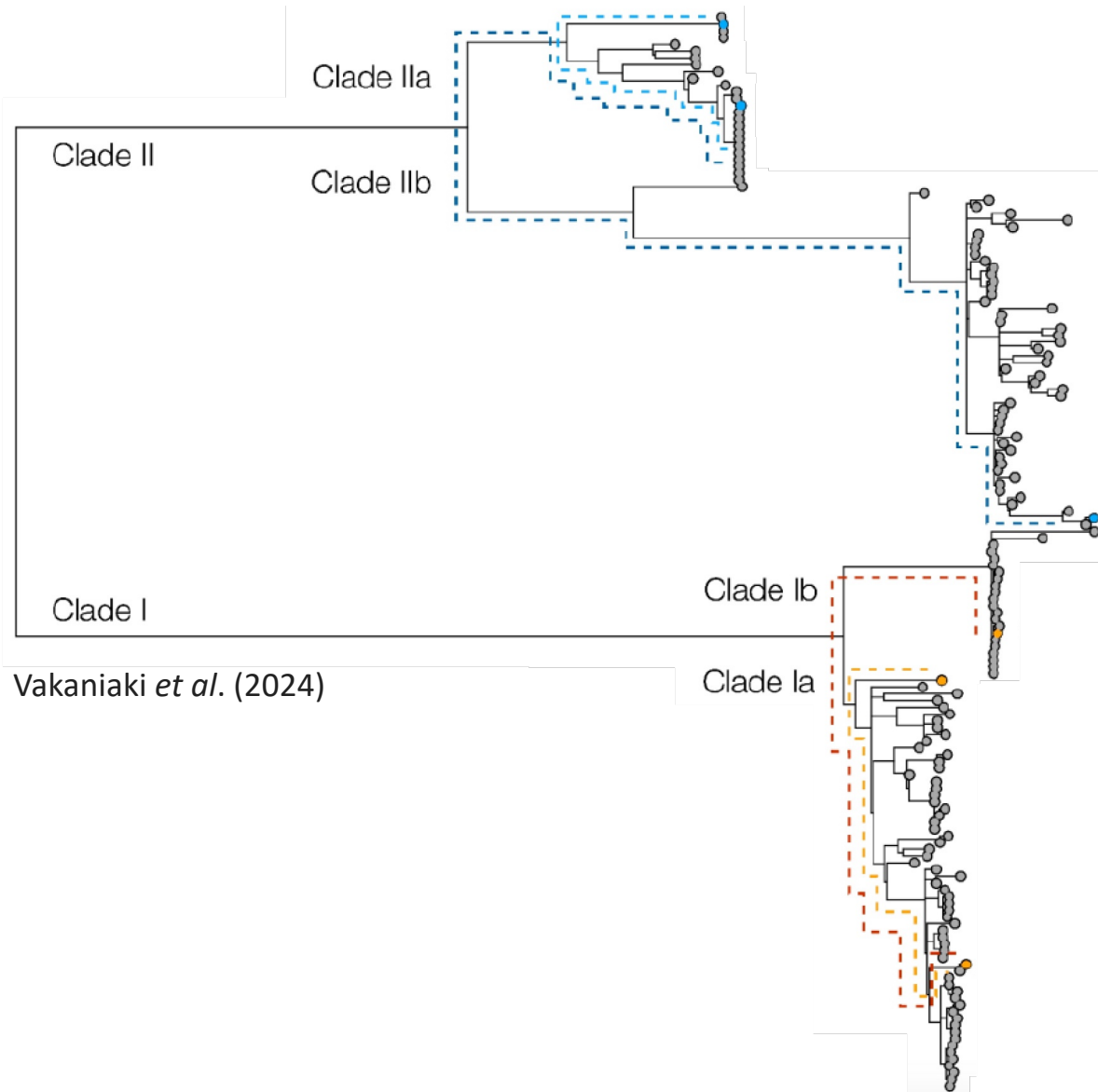
Why do we need to sequence MPXV genomes from *Funisciurus* squirrels?

Alexandre Hassanin

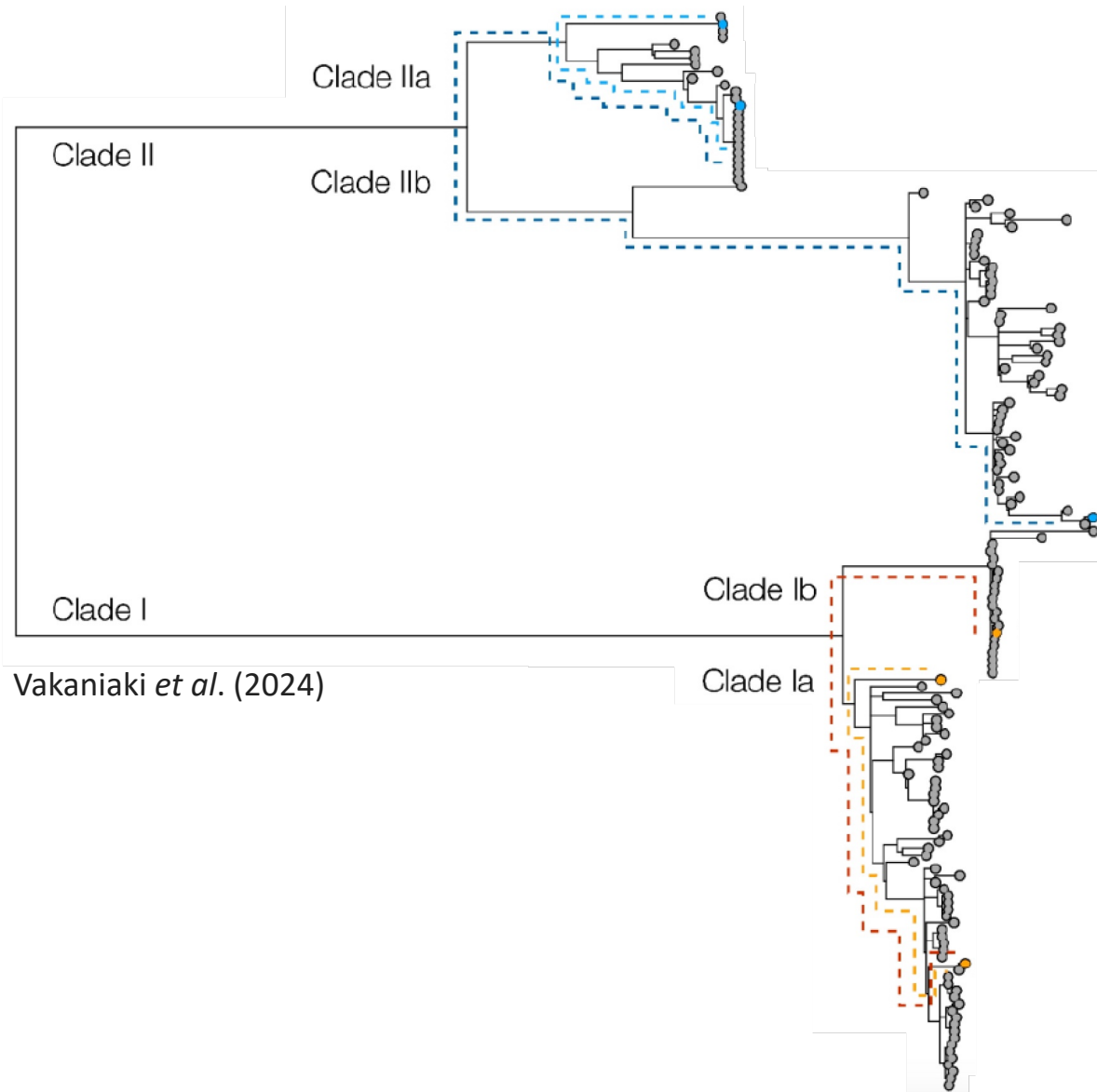
Institut de SYstématique, Évolution, Biodiversité



The MPXV genome has evolved with wide variation in substitution rates between lineages



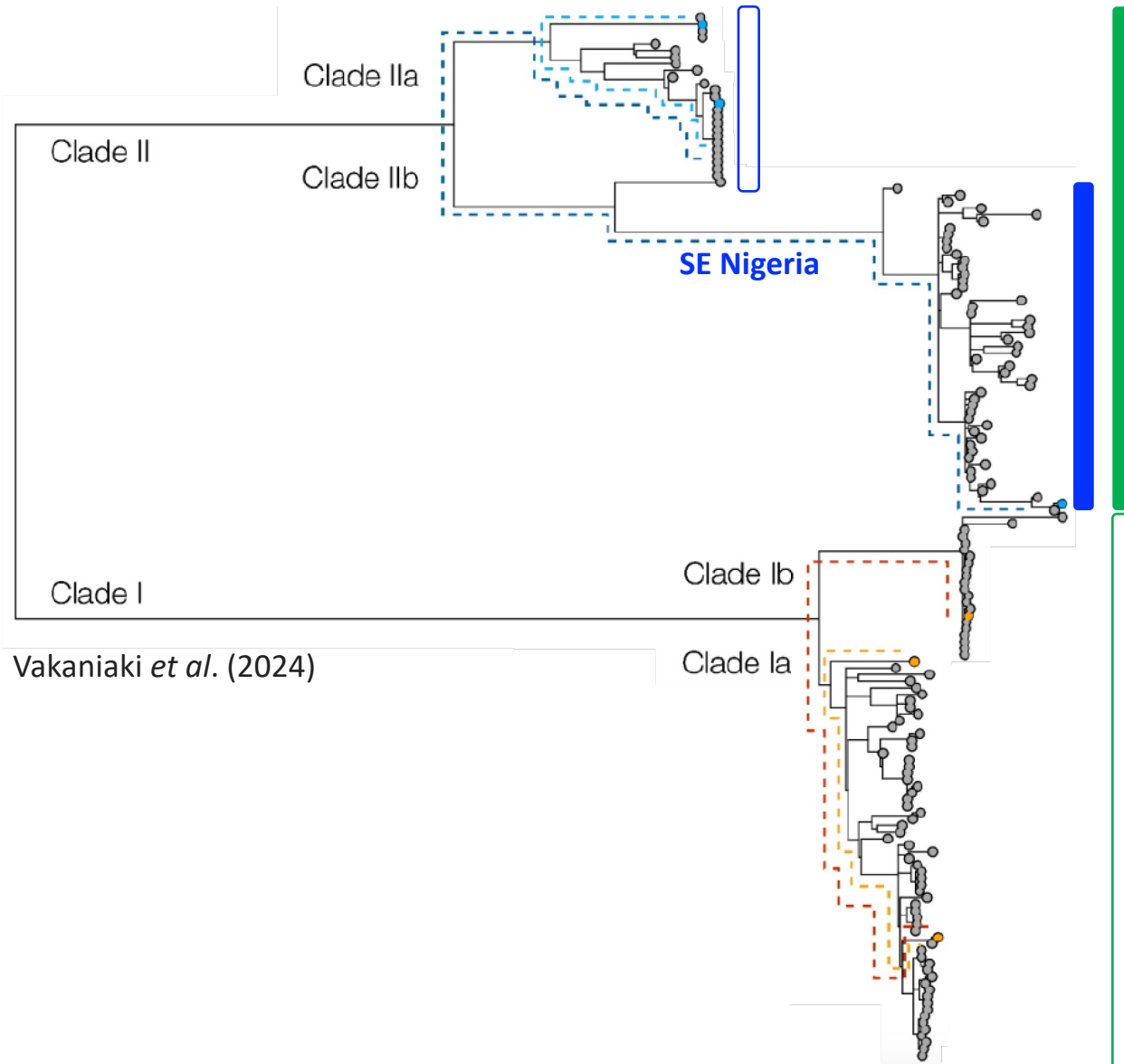
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Evidence of higher rates in three human MPXV clades

1. clade II (West Africa) >> clade I (Central Africa)

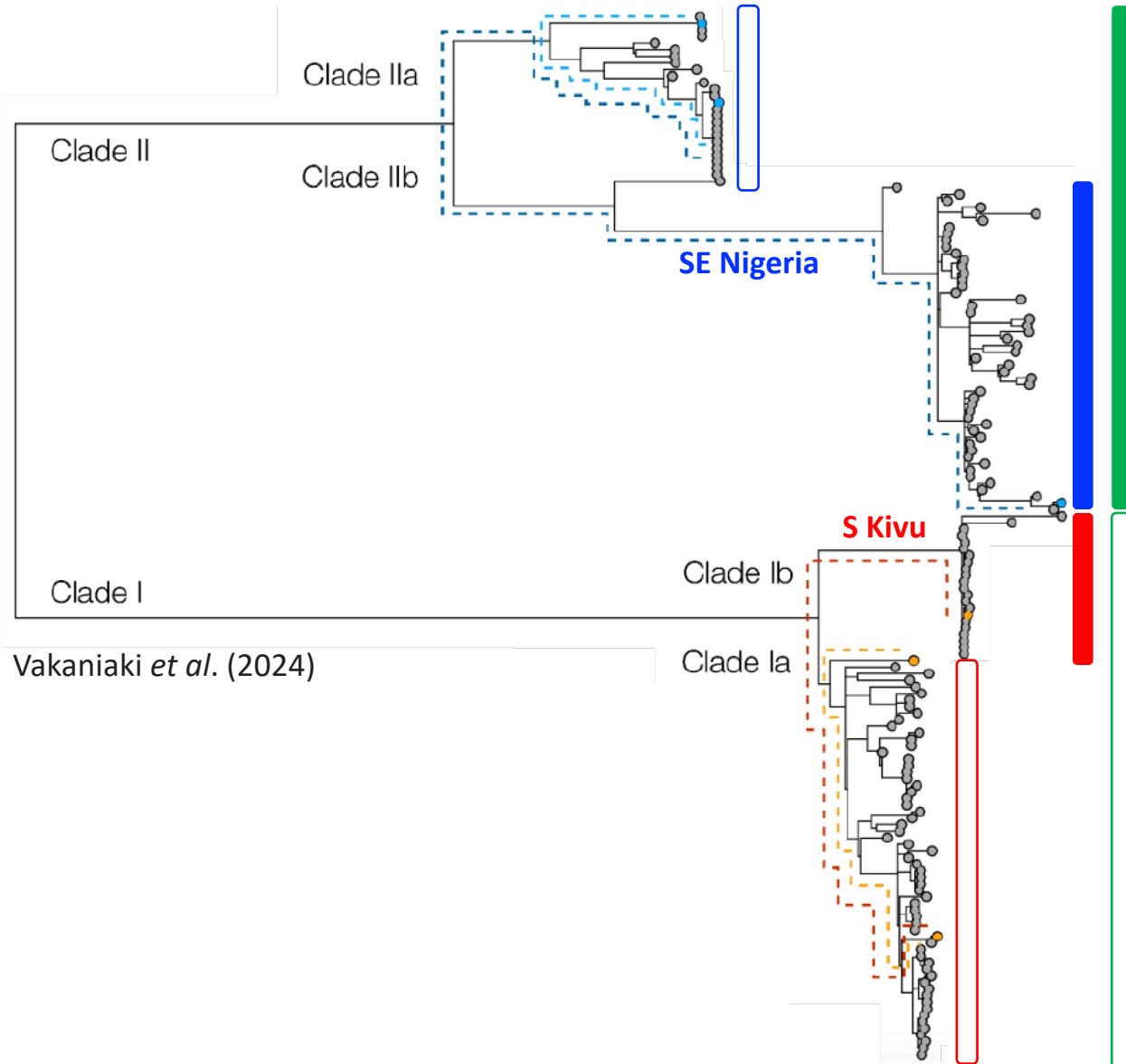
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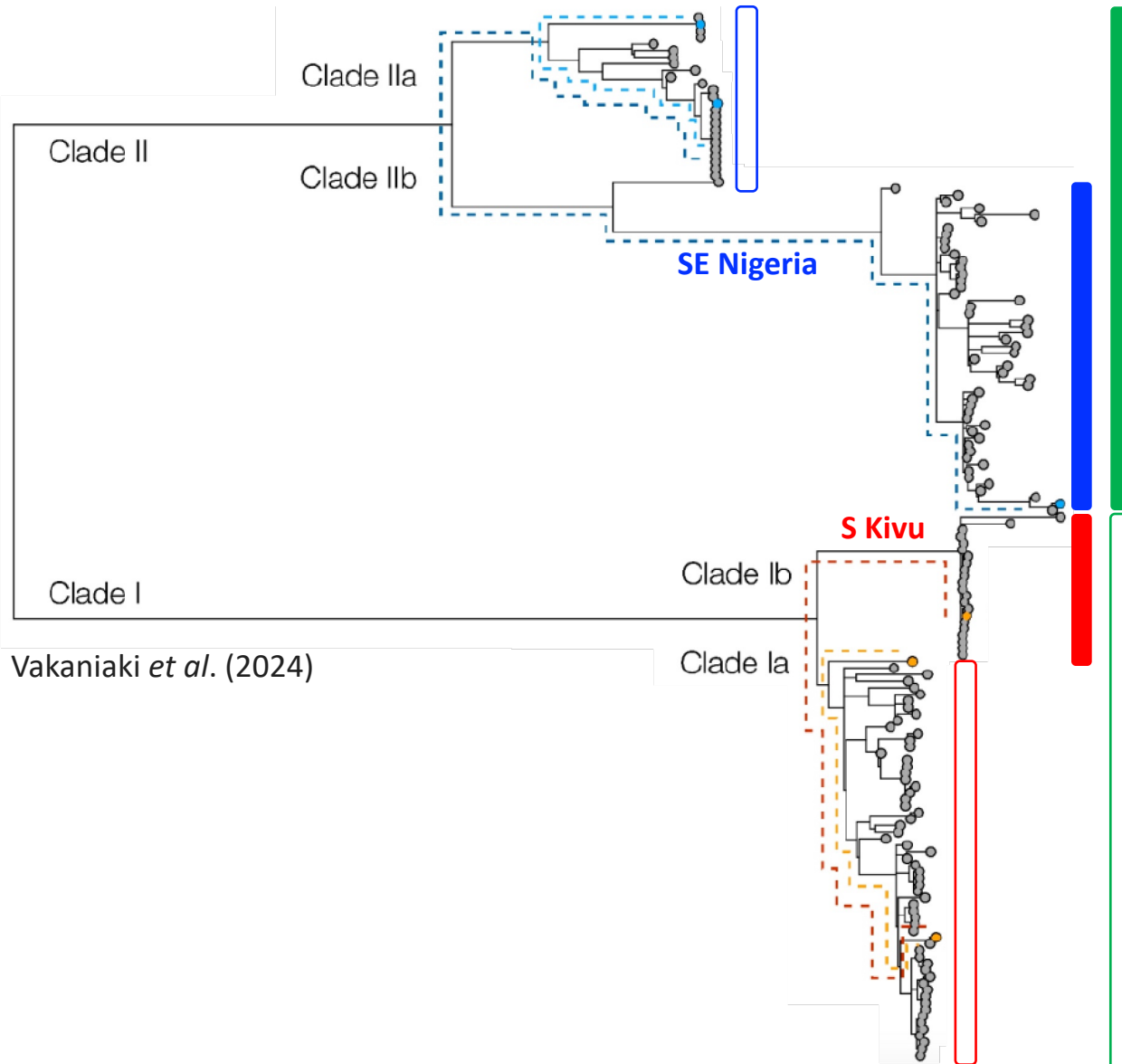


Vakaniaki *et al.* (2024)

Evidence of higher rates in three human MPXV clades

1. clade II (West Africa) >> clade I (Central Africa)
2. In West Africa: clade IIb >> clade IIa
3. In Central Africa: clade Ib >> clade Ia

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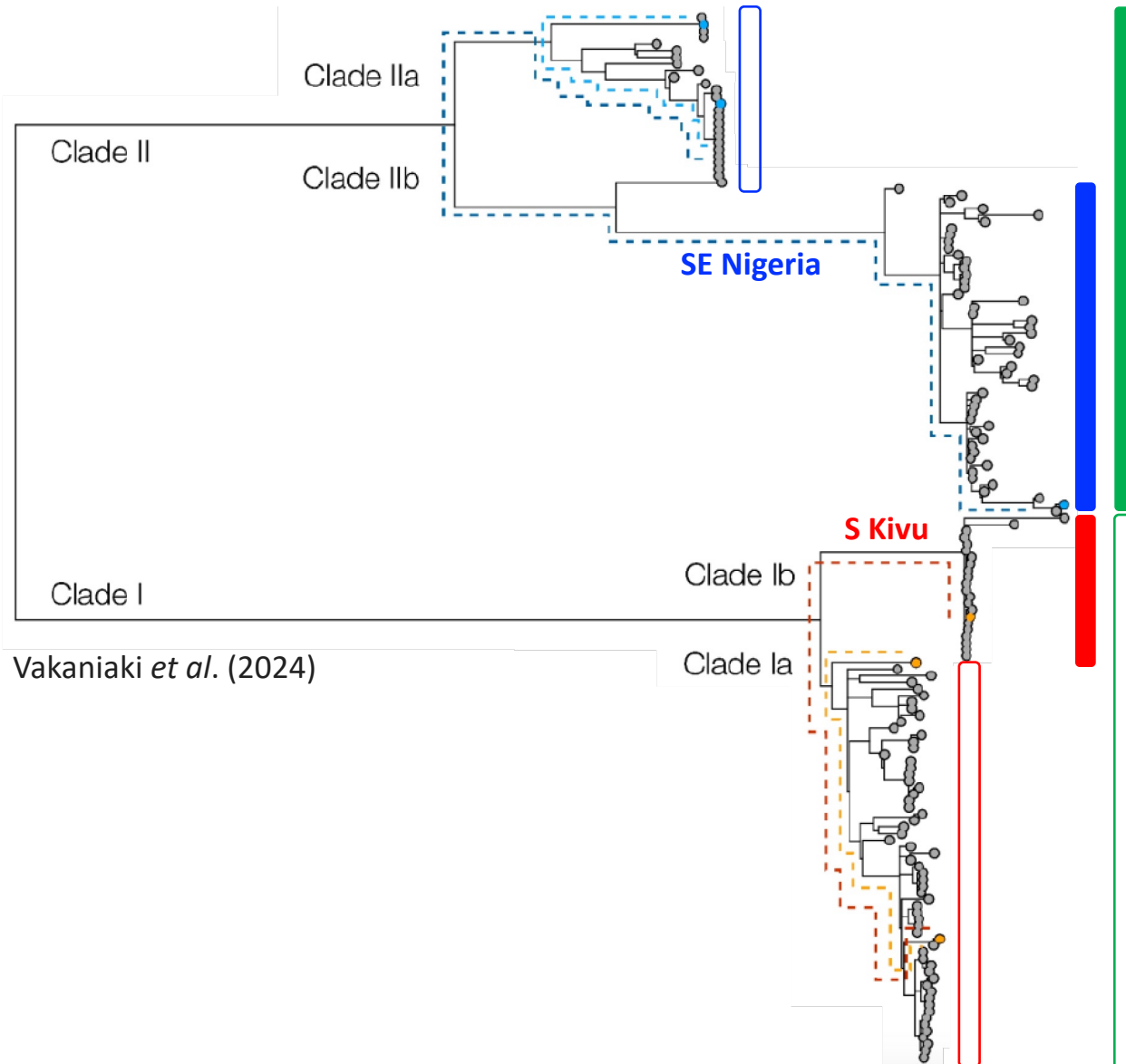
3. In Central Africa: clade Ib >> clade Ia

Interpretation

■ High rates of MPXV evolution: epidemic spreading
= human-to-human transmissions (with APOBEC3 editing)

□ Low rates of MPXV evolution: zoonotic spillover
= independent host jumps from animals to humans

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Only a few MPXV genomes from wild animals

1985: *Funisciurus anerythrus* (Thomas's squirrel) - Yambuku, DRC

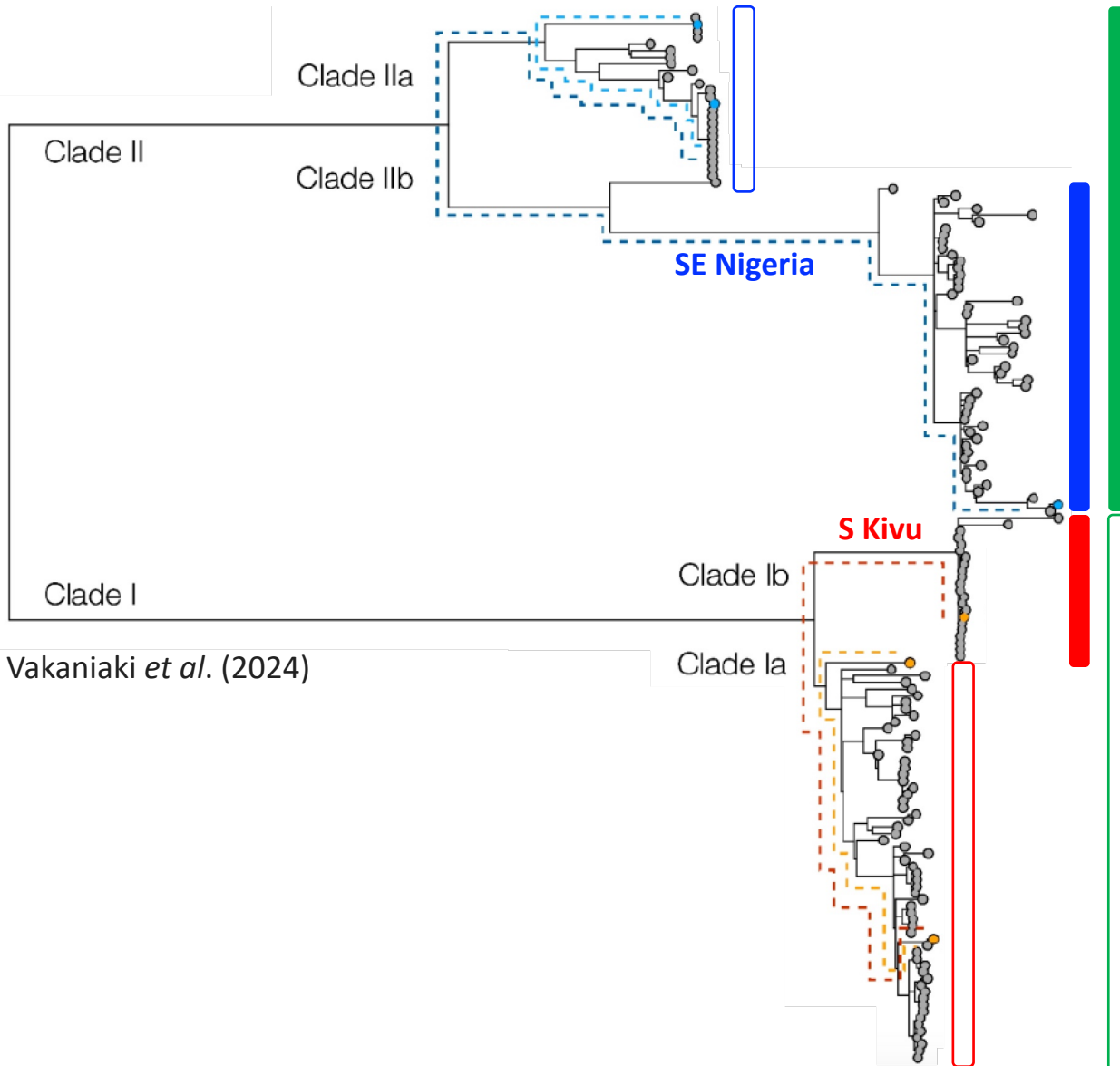
2012: *Cercocebus atys* (Sooty mangabey) - Taï NP, Côte d'Ivoire

2016: *Pan troglodytes* (chimpanzee) - Mefou Park, Cameroon

2018: *Pan troglodytes* (chimpanzee) - Taï NP, Côte d'Ivoire

Radonić et al. (2014); Nakazawa et al. (2015); Patrono et al. (2020);
Brien et al. (2024).

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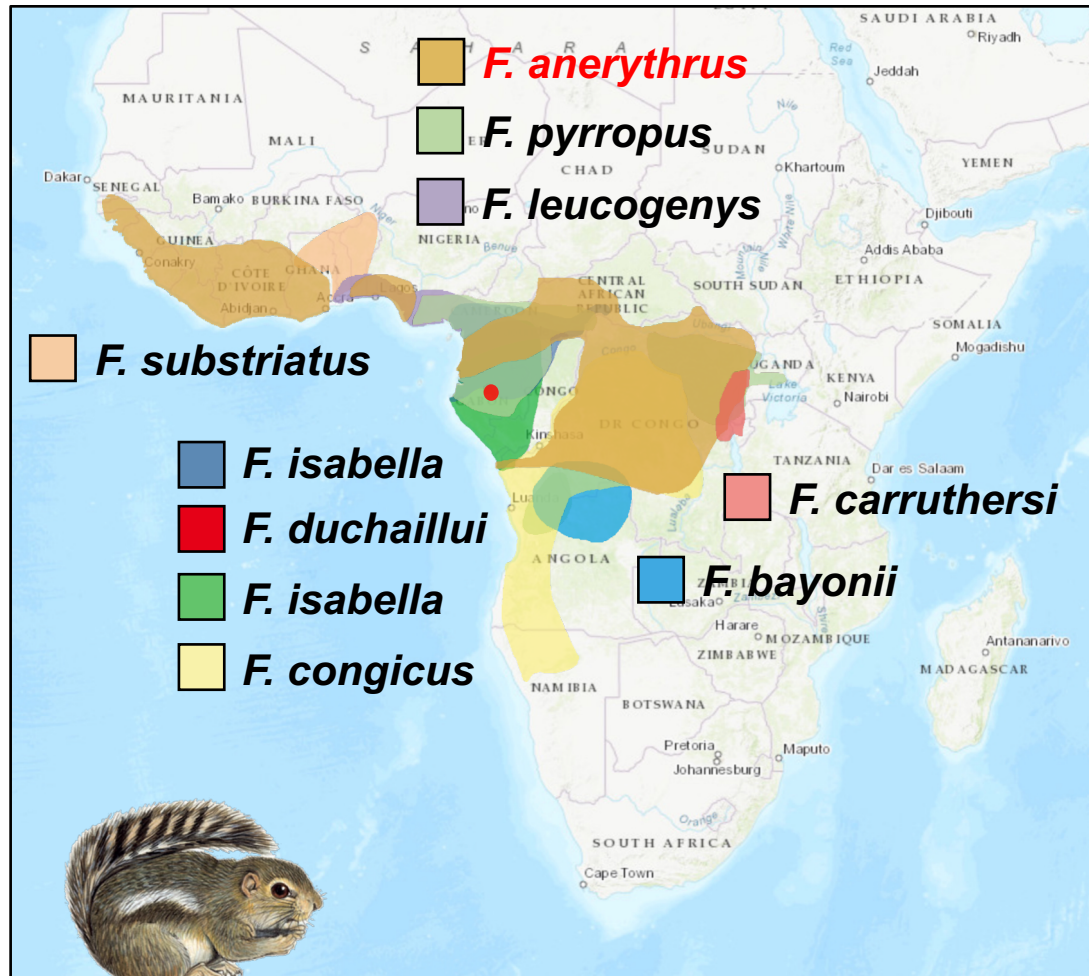
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=> New data from mammalian hosts are needed to better estimate the "natural rates" of MPXV evolution.

MPXV detection and sequencing based on museomics

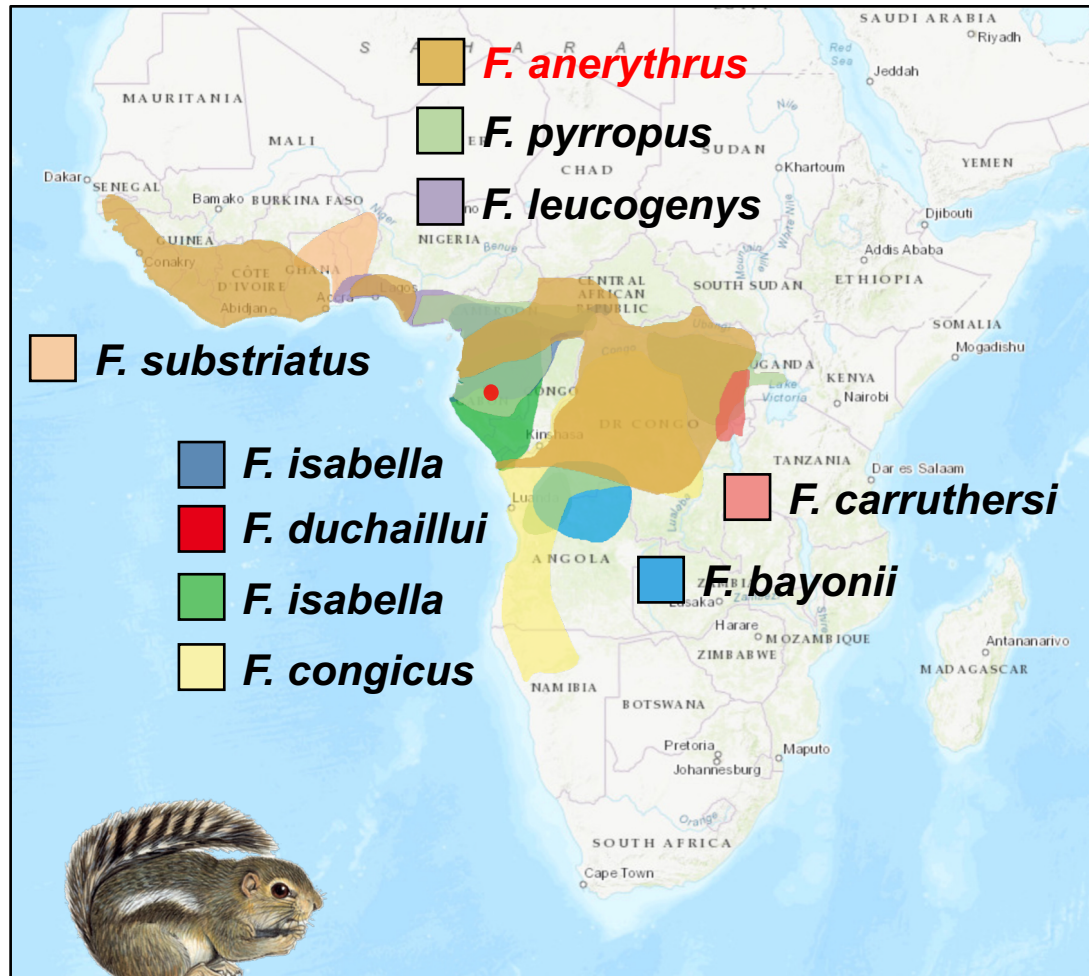
Funisciurus anerythrus and other species of *Funisciurus*

Georeferenced specimens collected in Africa and conserved in museum collections



MPXV detection and sequencing based on museomics

Funisciurus anerythrus and other species of *Funisciurus*



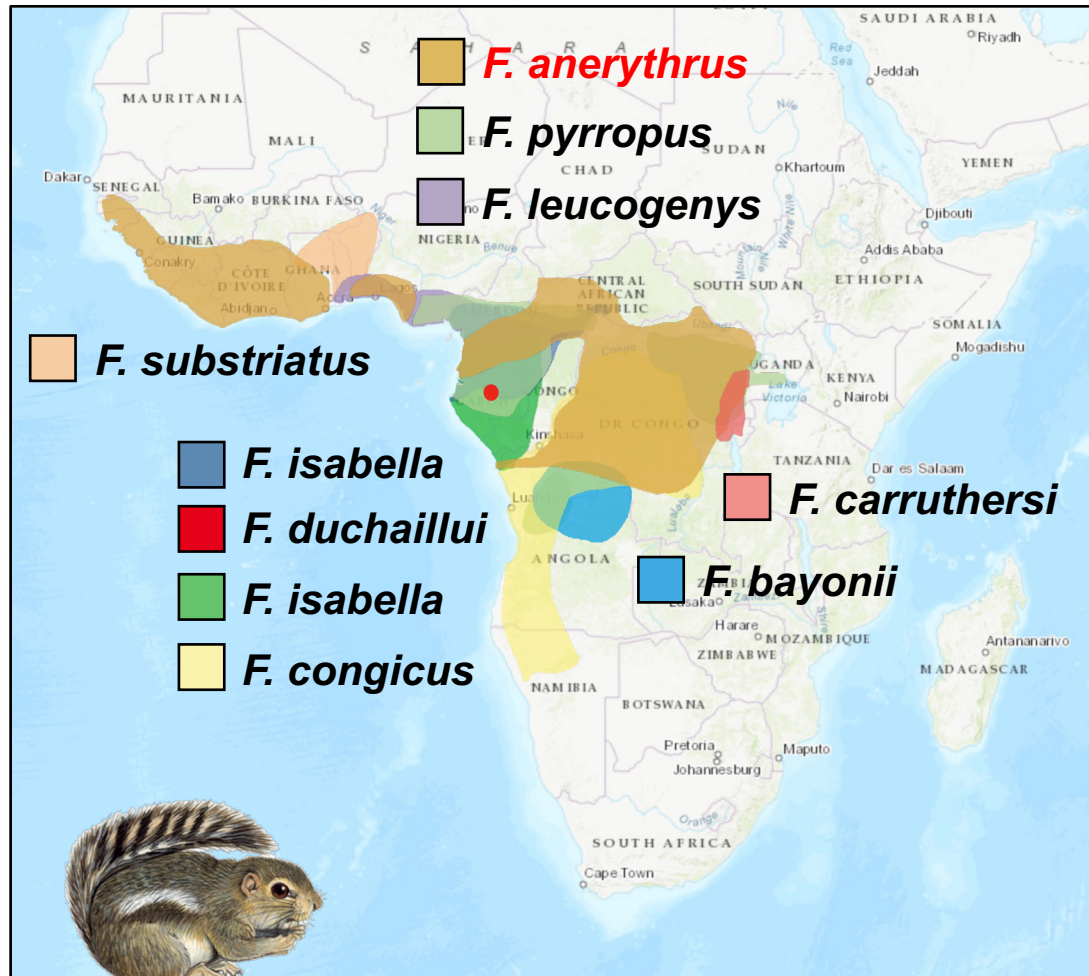
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Advantages

- A large diversity of specimens can be used for DNA extraction.
=> More comprehensive phylogeography of *Funisciurus* species
- Several squirrel MPXV could be found in these DNA extracts.

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Funisciurus anerythrus and other species of *Funisciurus*



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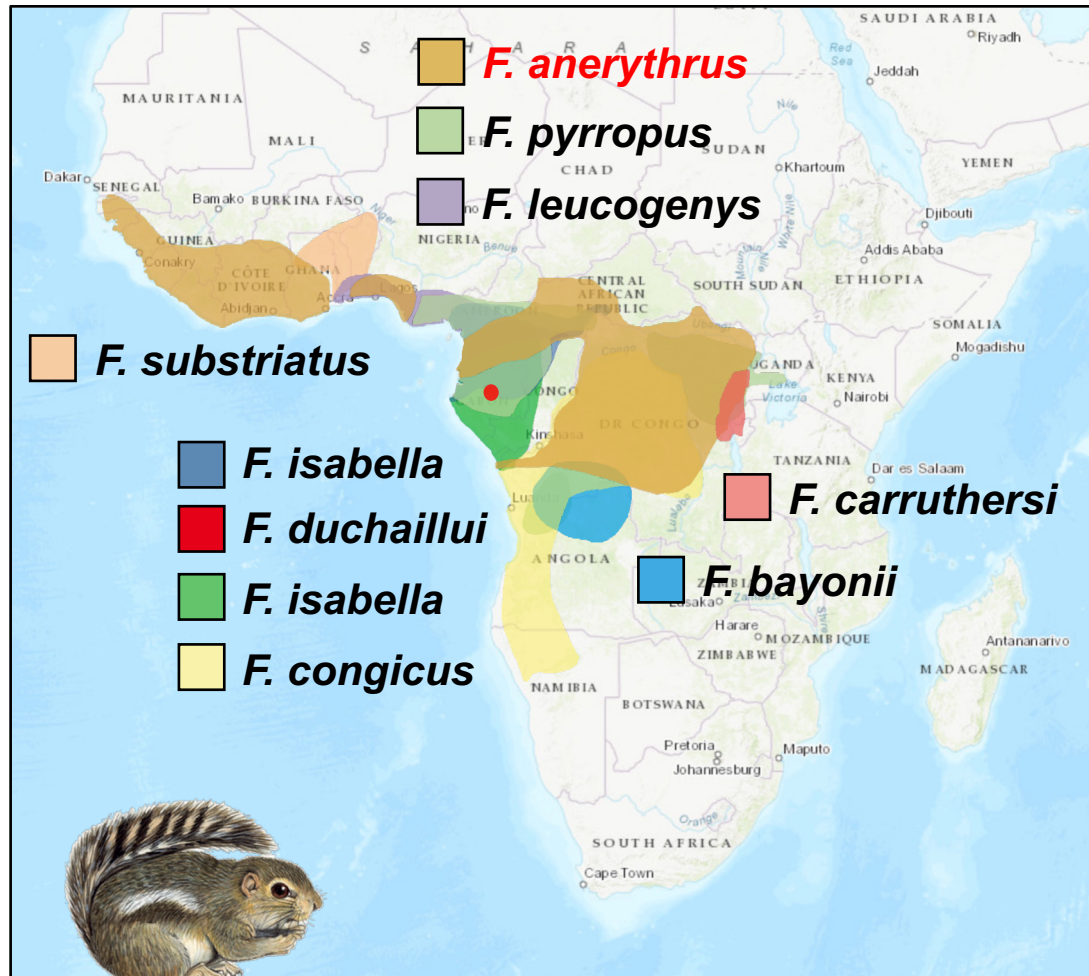
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- Low concentration
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Two main issues with ancient DNA

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Two methodological solutions

1. DNA hybridization captures with MPXV probes
=> DNA extracts enriched with MPXV fragments.
2. Next-generation sequencing based on short reads (75 bp)
=> The smallest MPXV fragments can be sequenced.

Conclusions

We need to sequence MPXV genomes from squirrels:

1. To provide full evidence that *Funisciurus anerythrus* is the main reservoir host of MPXV.
=> Prevention measure for villagers: simplified taxonomic key to identify the Thomas's rope squirrel.



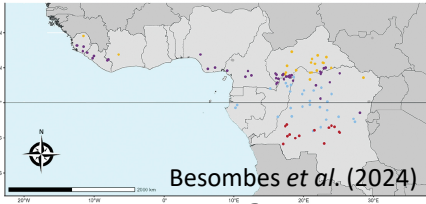
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2. To determine the geographical areas and seasons with higher MPXV prevalence in squirrels

=> Public prevention measure: hotspots and months of higher risks for humans.

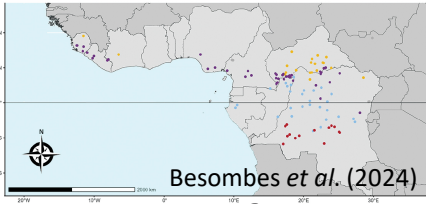
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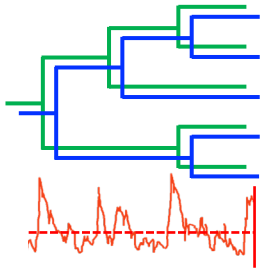
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in order to test whether MPXV diversification was driven by Pleistocene climatic changes.

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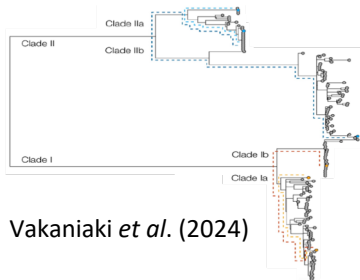
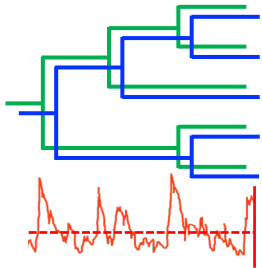
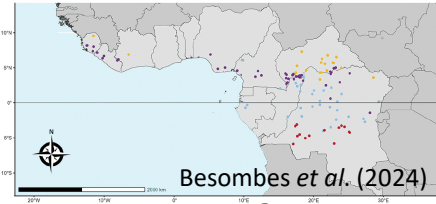
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4. To fully understand the history of MPXV epidemics in Africa

and in particular to test whether the higher rates of MPXV evolution in West Africa could be linked to unidentified past epidemics.



Thank you for your attention !

References

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