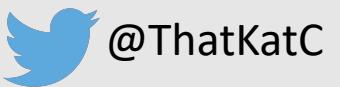


MADDOG: Updated Classifications for Genomic Surveillance of Rabies

- Kathryn Campbell
- Kathryn.Campbell@Glasgow.ac.uk



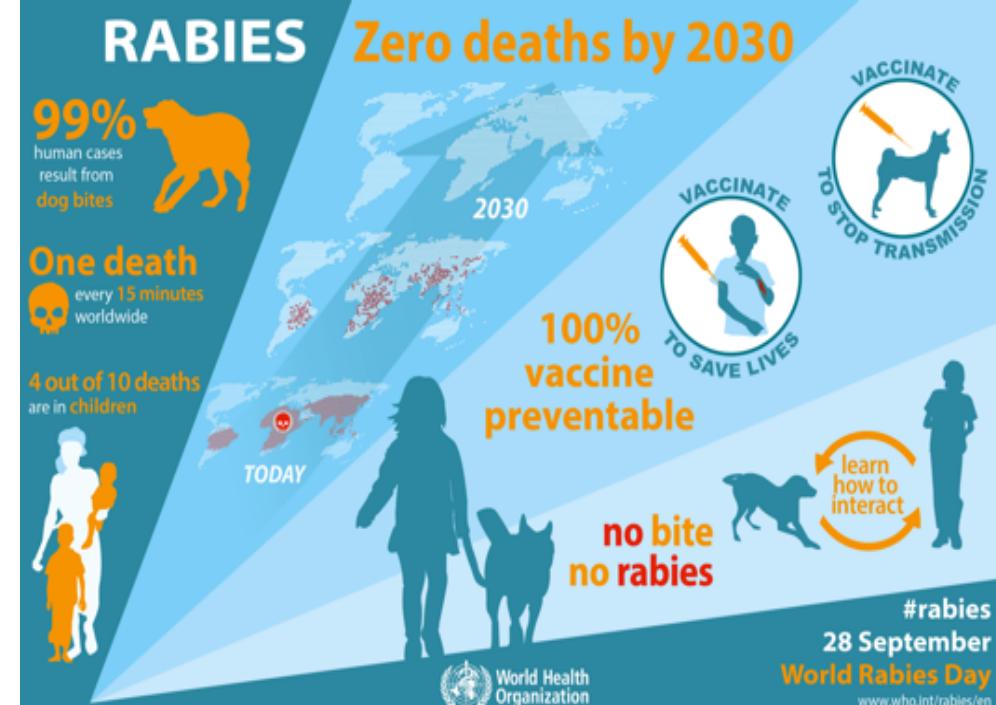
University
of Glasgow



Rabies elimination

“Zero by 30”

- Huge global collaboration
 - Implementation
 - Monitoring and evaluation
 - Policy updates



#rabies
28 September
World Rabies Day
www.who.int/rabies/en

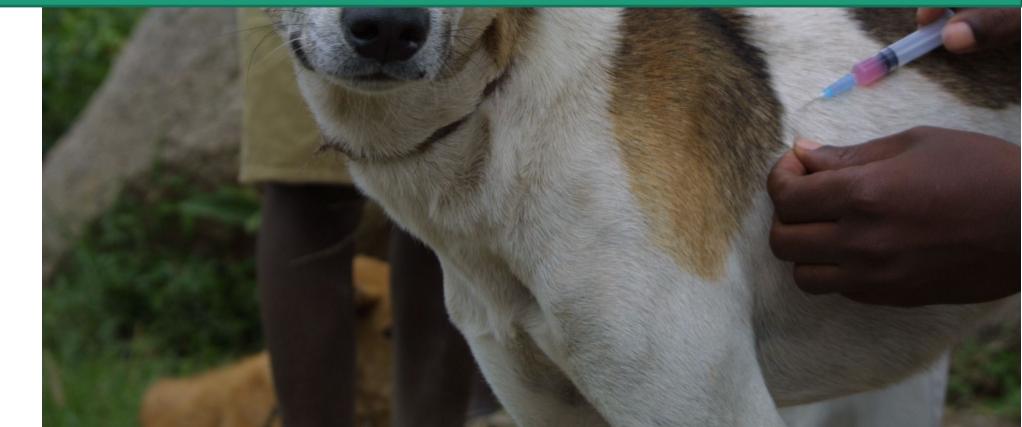
Rabies elimination

“Zero by 30”



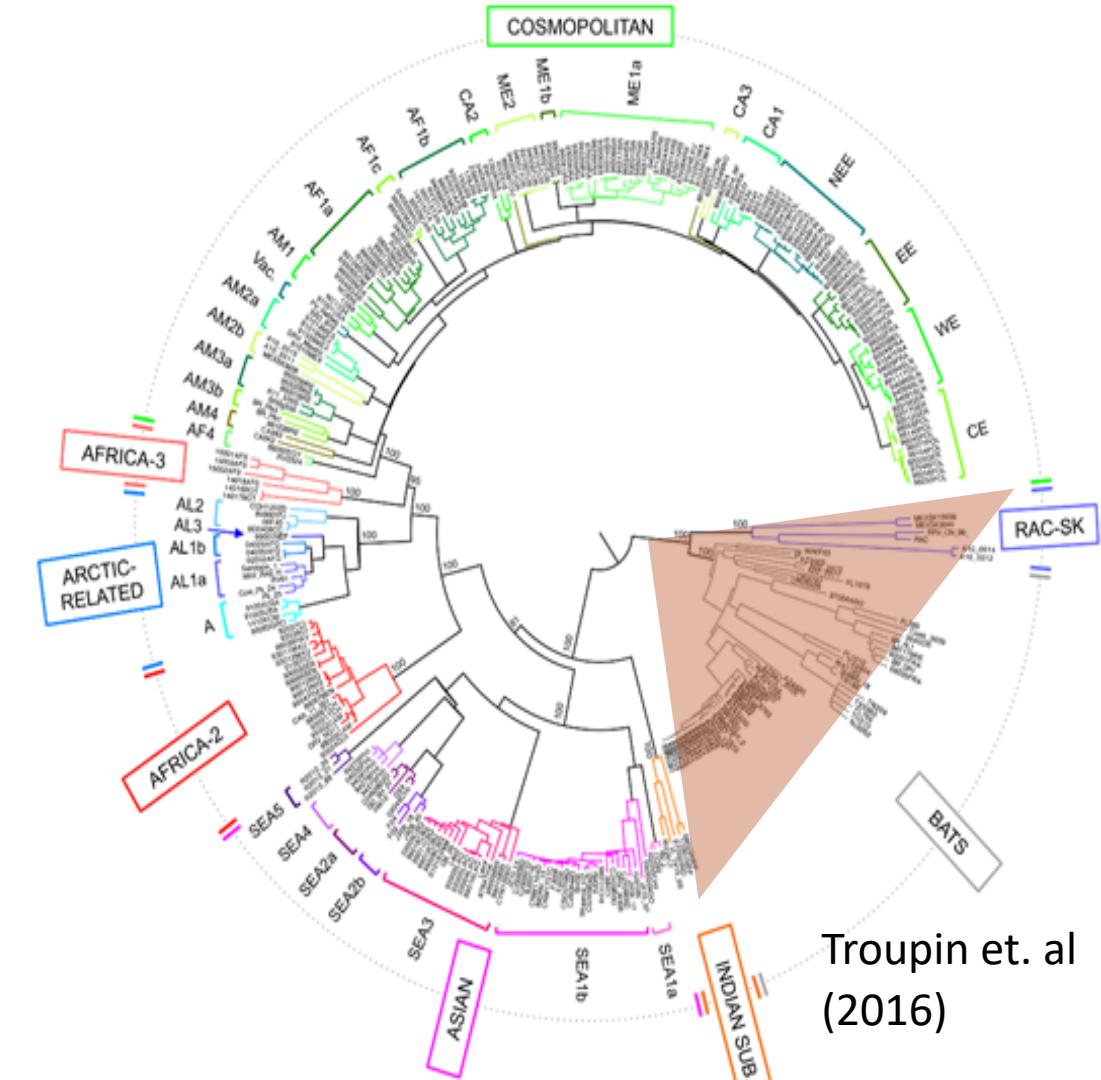
- Huge global collaboration
 - Implementation
 - Monitoring and evaluation
 - Policy updates

- What is circulating?
- Where is it coming from?
- Why is it persisting?
- How can we stop it?



The global rabies phylogeny reveals large-scale geographic structure

- 2 major phylogenetic groups; bat related and dog related (5-7 clades)
- Same geographical area group closely together
 - Host species also important but less so
 - Major clades are segregated by barriers
 - Oceans, mountain ranges, human factors



Greater phylogenetic resolution is needed to guide control programmes

- Progress towards elimination, should see reduction in viral diversity
- Need to see if any lineages have become extinct, or if any are persisting
 - Use this to direct elimination efforts
 - Monitor how we are progressing towards elimination

BUT

- Needs a high-definition classification system
 - Current system is very broad – often only 1 subclade circulating
 - Can't track changes
 - Needs to be universal
 - Lots of studies, but all define and name lineages differently
 - Can't compare and communicate these

Need one, high definition system to classify all rabies globally



SCAN ME

MAD DOG

Method for Assignment, Definition
and Designation Of Global Lineages

Increase the resolution

See the patterns

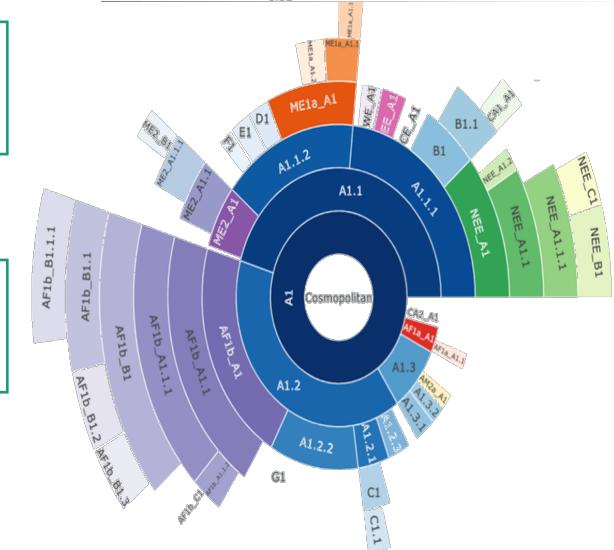
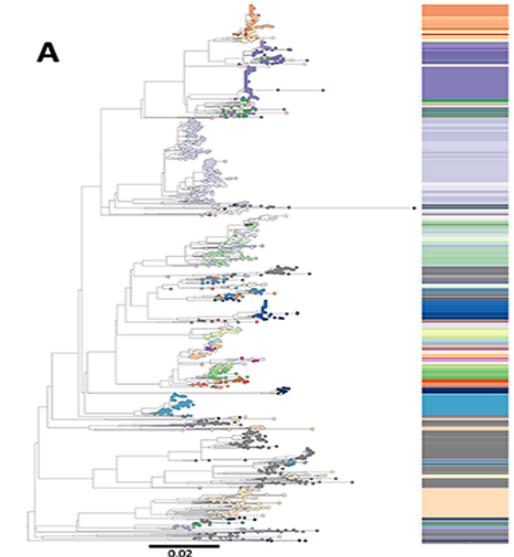
Stop the Spread

Phylogeny based classification tool

- Command line and R package

Over 4 fold increase in resolution

Does the analysis for you!





SCAN ME

MAD DOG

Method for Assignment, Definition and Designation Of Global Lineages

Increase the resolution

See the patterns

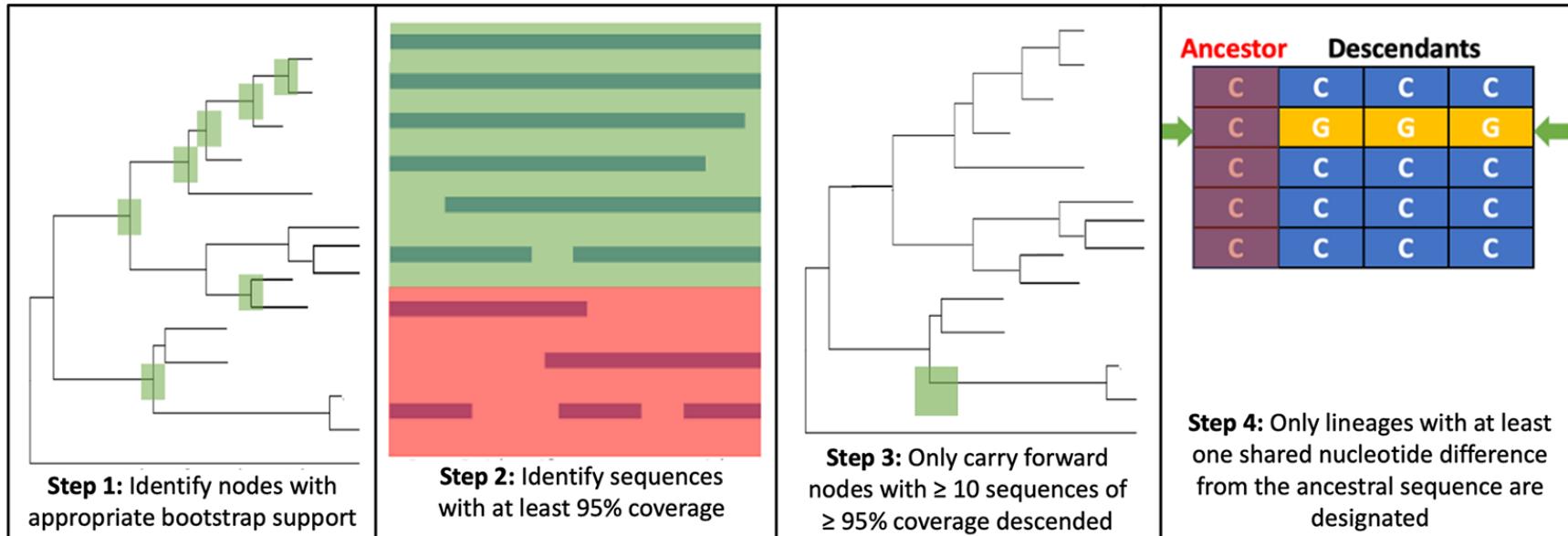
Stop the Spread

METHODS

Data Processing

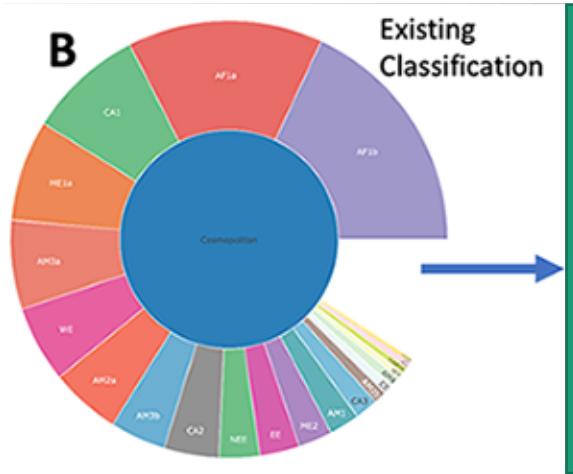


Lineage Designation

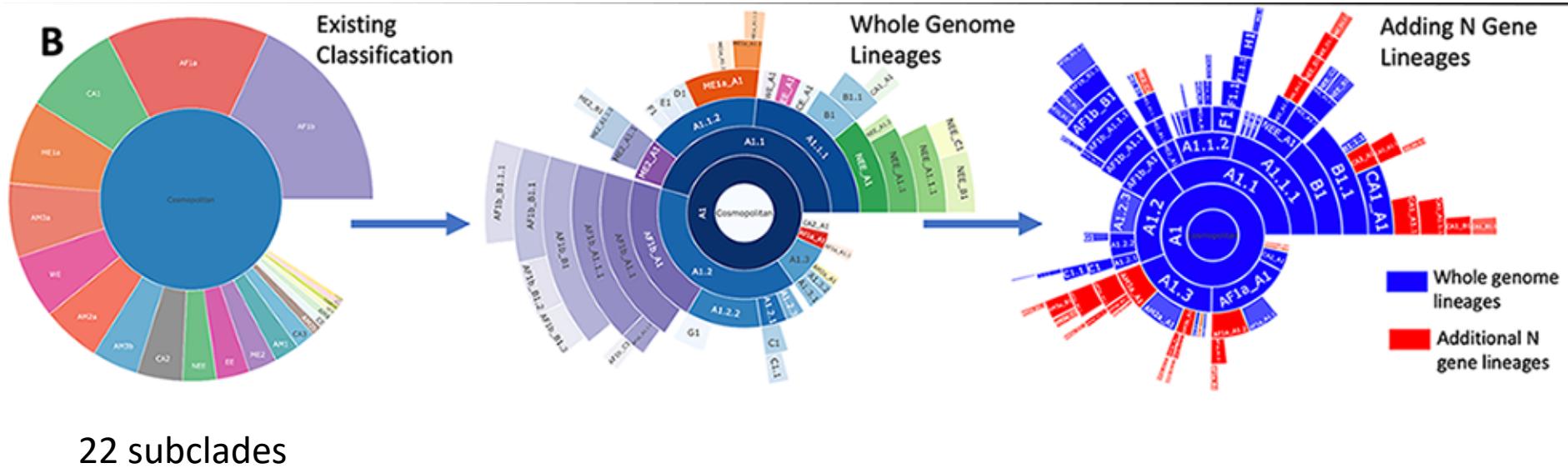


- Modelled after SARS-CoV-2 lineage designation
- Different parameters to consider for rabies!
 - Time scale
 - Existing classifications
 - Tracked since emergence vs decades of endemic circulation

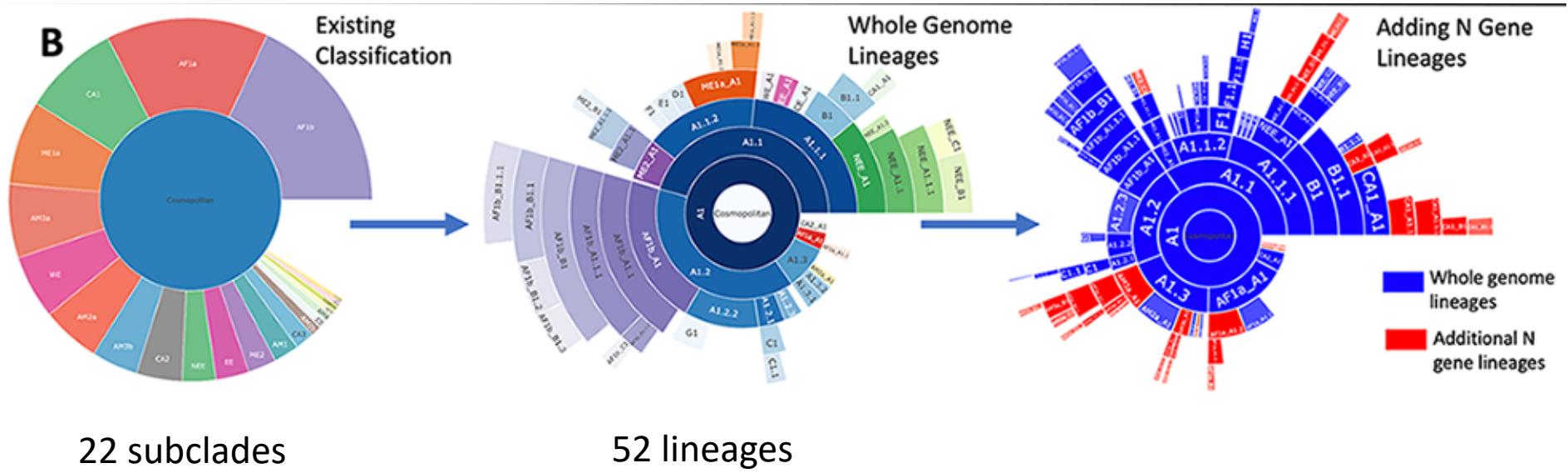
MAD DOG- Partial Genomes



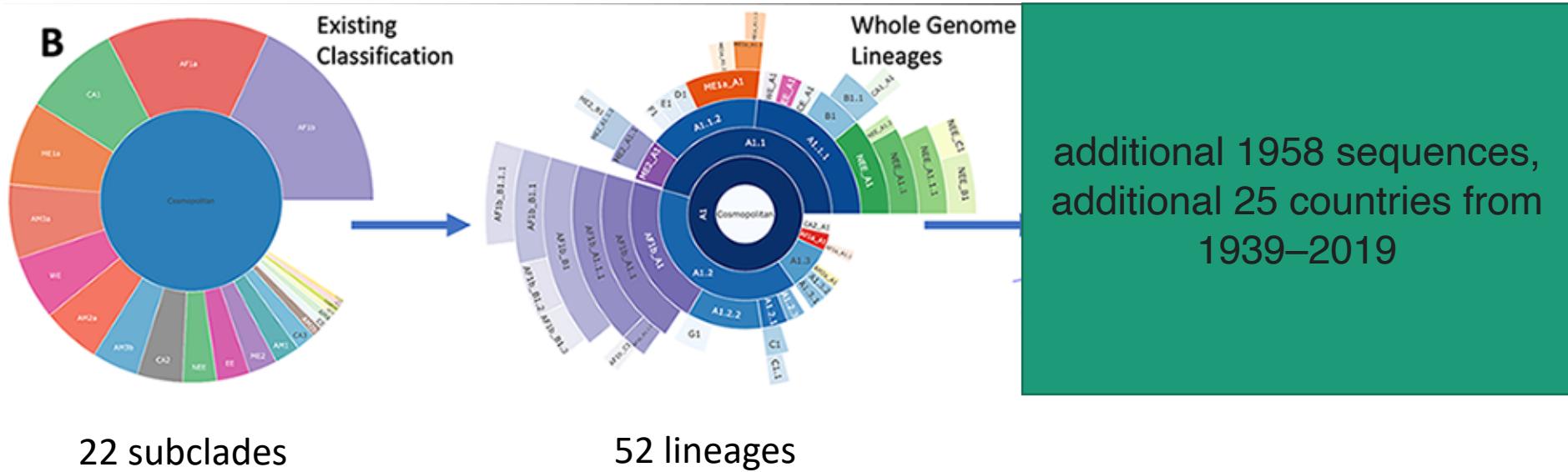
MAD DOG- Partial Genomes



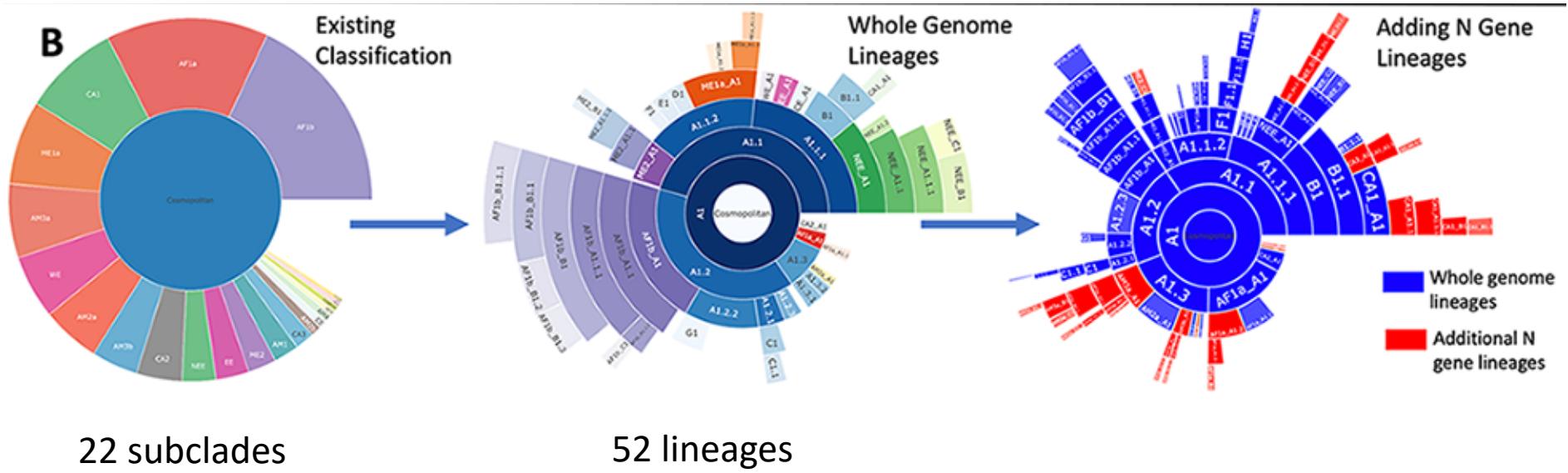
MAD DOG- Partial Genomes



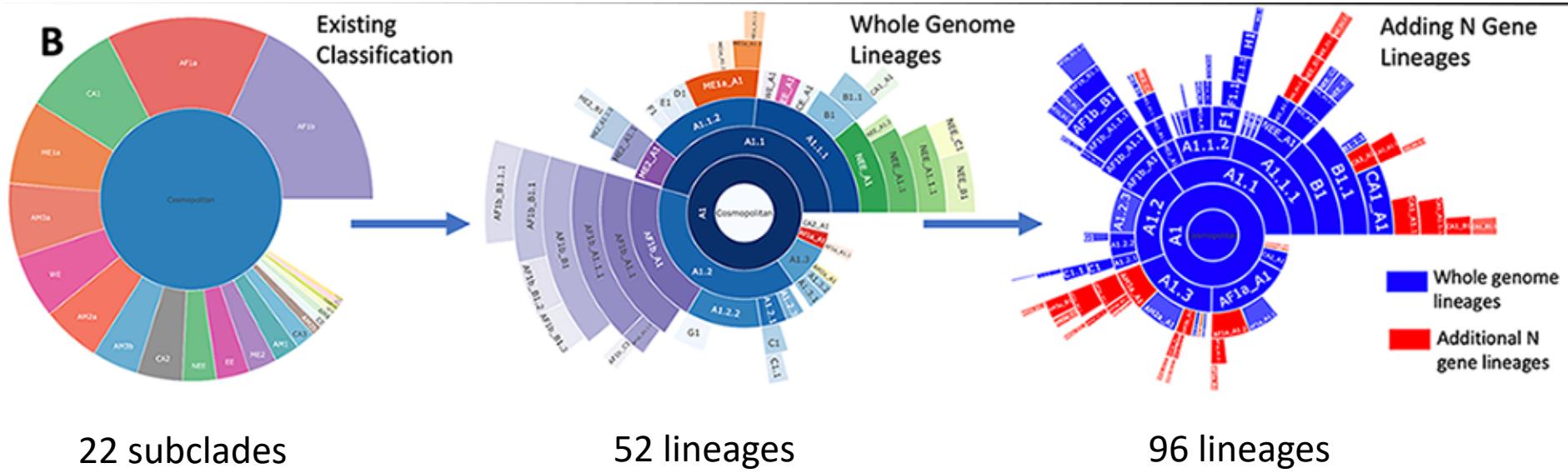
MAD DOG- Partial Genomes



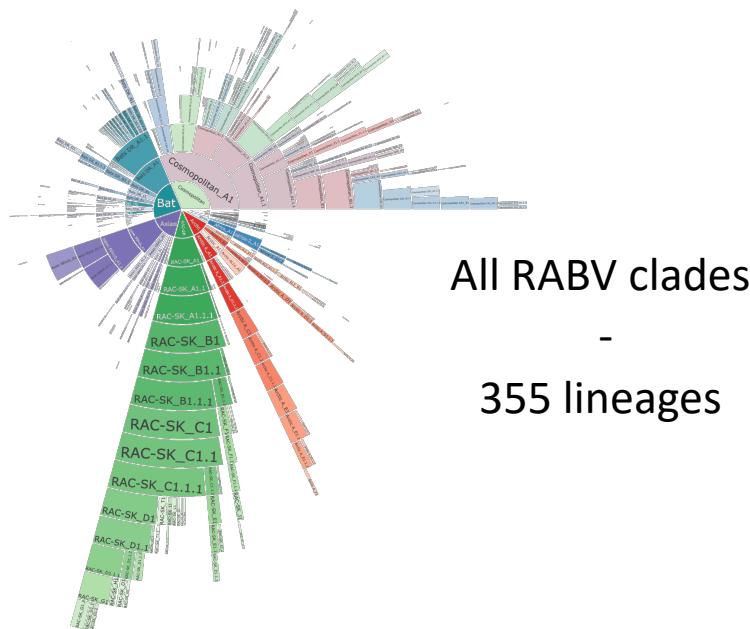
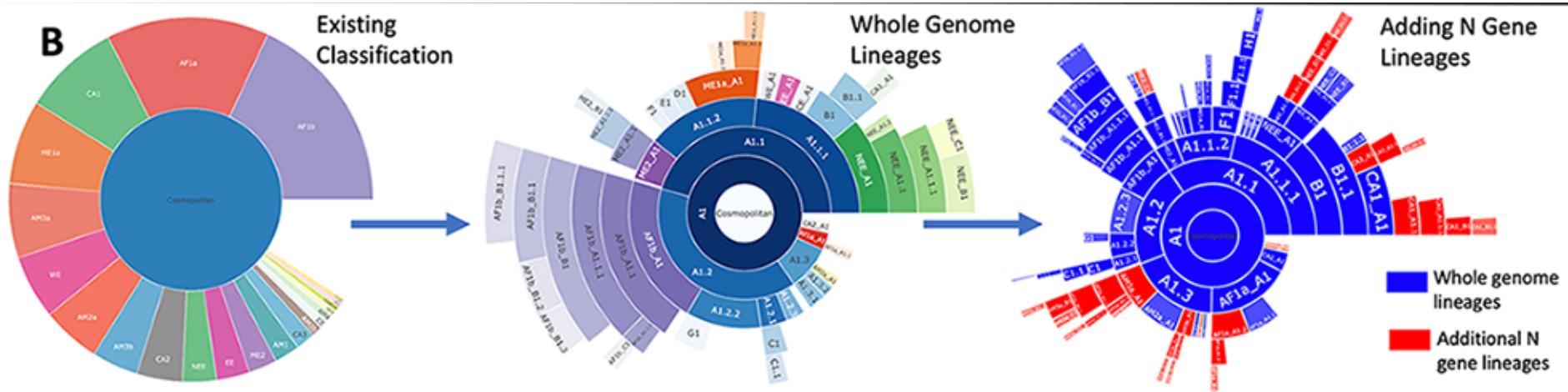
MAD DOG- Partial Genomes

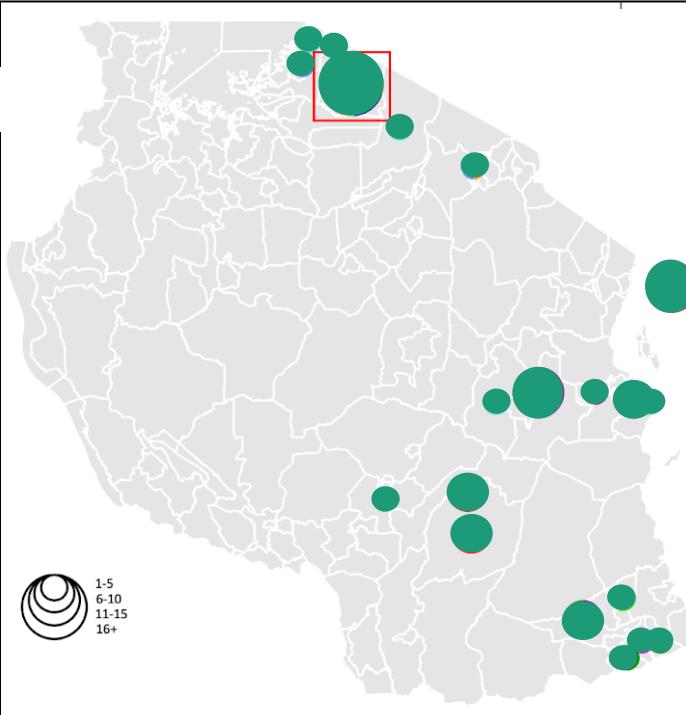


MAD DOG- Partial Genomes



MAD DOG- Partial Genomes

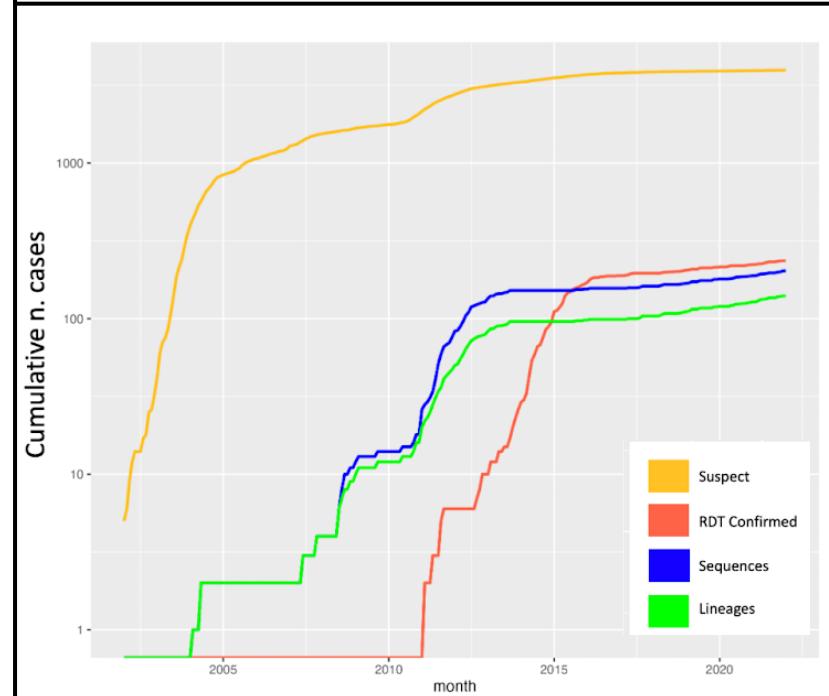
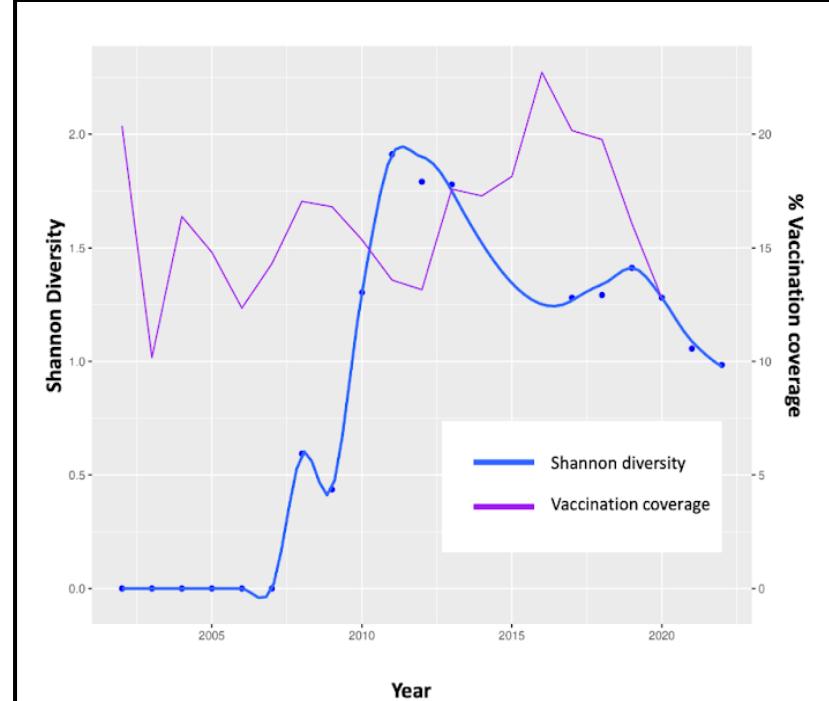
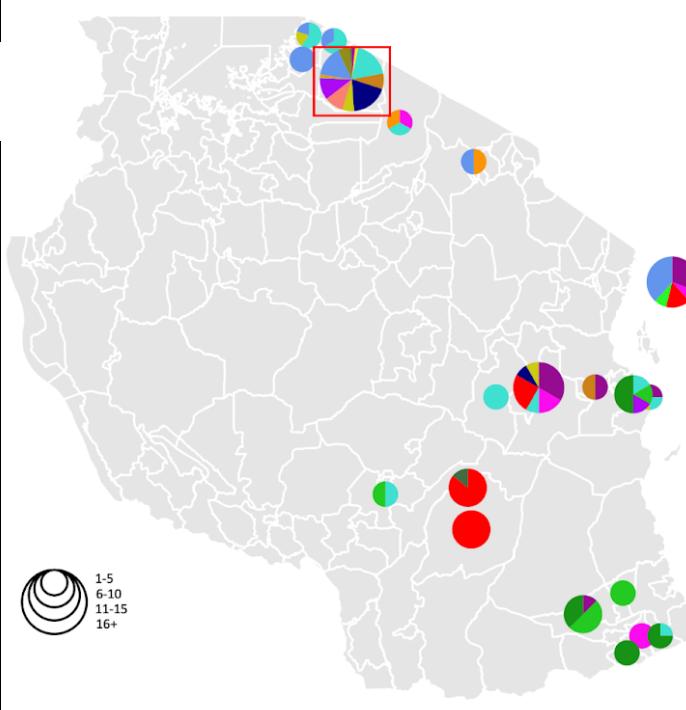


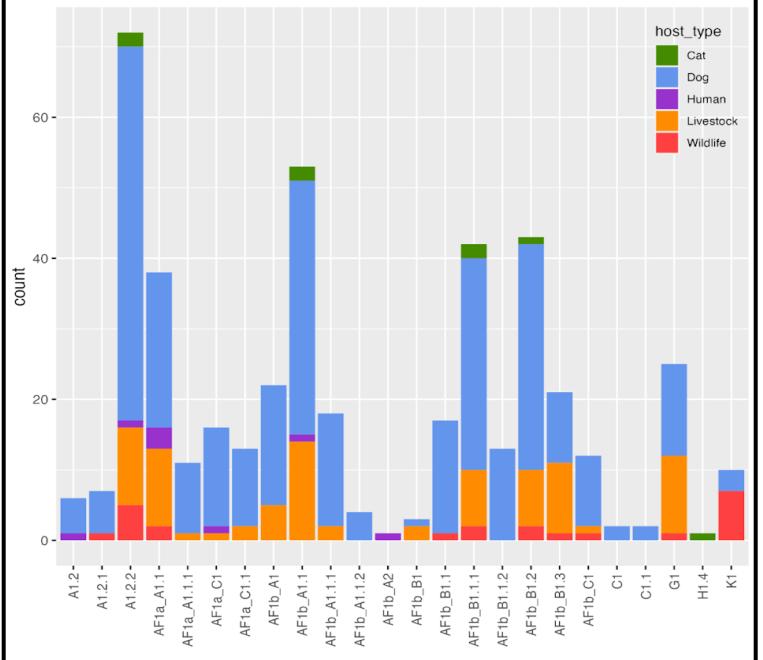
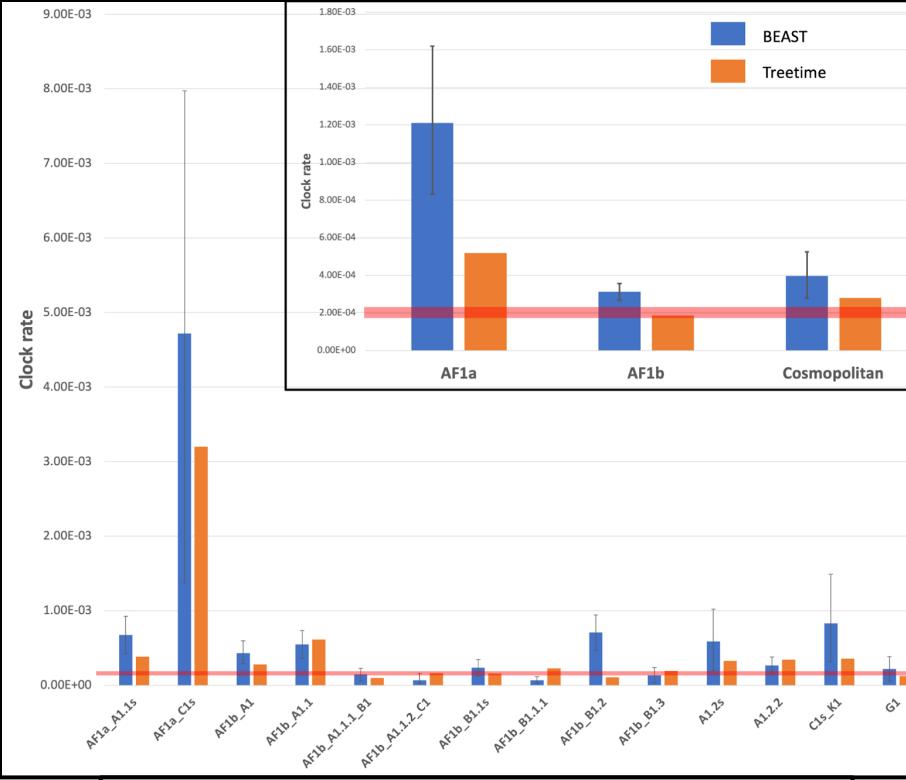


Increase the resolution

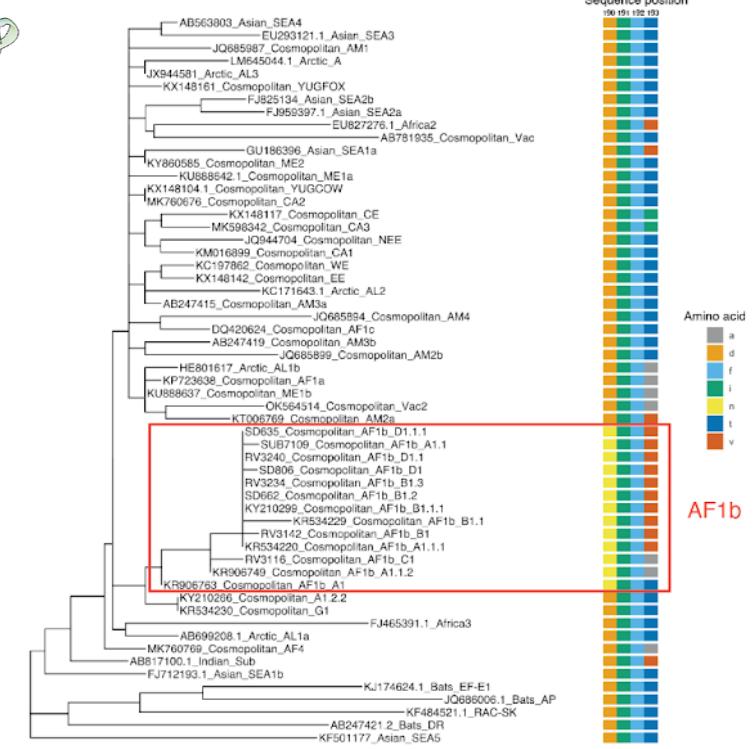
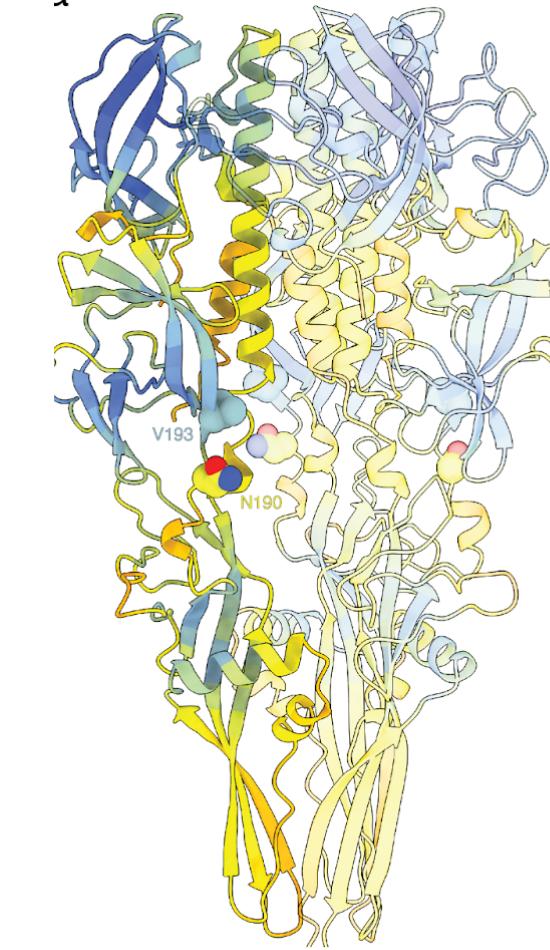
See the patterns

Stop the Spread





Identifying differences between lineages





showcase



Search

Favourites

Dropbox

AirDrop

Recents

Applicati...

Desktop

Documents

Downloads

OneDrive...

kathrync...

Zanzibar...

iCloud

iCloud Dri...

Tags

Red

Orange

Yellow

Green

Blue

Purple

Grey

All Tags...

Kenya.fasta Kenya_metadata.
csv



showcase



Search

Favourites

Dropbox

AirDrop

Recents

Applicati...

Desktop

Documents

Downloads

OneDrive...

kathrync...

Zanzibar...

iCloud

iCloud Dri...

Tags

Red

Orange

Yellow

Green

Blue

Purple

Grey

All Tags...

Kenya.fasta Kenya_metadata.
csv



showcase



Search

Favourites

Dropbox

AirDrop

Recents

Applicati...

Desktop

Documents

Downloads

OneDrive...

kathrync...

Zanzibar...

iCloud

iCloud Dri...

Tags

Red

Orange

Yellow

Green

Blue

Purple

Grey

All Tags...

Kenya.fasta Kenya_metadata.
csv

File Edit Insert Table Organise Format Arrange View Share Window Help

Kenya_metadata 2

125% View Zoom Add Category Pivot Table Insert Table Chart Text Shape Media Comment Collaborate Format Organise

Sheet 1

Kenya_metadata

Table data was imported. Adjust Settings

ID	country	year	assignment
Z0083249	Kenya	2022	
Z0083262	Kenya	2022	
Z0083263	Kenya	2022	
Z0083261	Kenya	2022	
Z0083265	Kenya	2022	
Z0629344	Kenya	2022	
Z0629343	Kenya	2022	
Z0629340	Kenya	2022	
Z0629341	Kenya	2022	
Z0629337	Kenya	2022	
Z0629335	Kenya	2022	
Z0629333	Kenya	2022	
Z0629334	Kenya	2022	
Z0629325	Kenya	2022	
Z0629323	Kenya	2022	
Z0629313	Kenya	2022	
Z00861836	Kenya	2022	
Z00861834	Kenya	2022	
Z00861832	Kenya	2022	
Z00861831	Kenya	2022	
Z00861829	Kenya	2022	
Z00861827	Kenya	2022	
Z00861826	Kenya	2022	
Z00861824	Kenya	2022	

Sheet

Sheet Name: Sheet 1

Background:

Duplicate Sheet

Delete Sheet

```
/Users/kathryncampbell/MADDDG — iqtree + sh designation.sh
```

```
Last login: Tue Oct 25 19:22:31 on ttys008  
(base) kathryncampbell@Kathryns-MacBook-Pro ~ % conda activate MADDDG  
(MADDDG) kathryncampbell@Kathryns-MacBook-Pro ~ % cd MADDDG  
(MADDDG) kathryncampbell@Kathryns-MacBook-Pro MADDDG % sh designation.sh  
What is the name of the folder containing your sequences and metadata?
```

```
/Users/kathryncampbell/MADDDG — sh designation.sh
```

```
/Users/kathryncampbell/MADDOG — iqtree + sh designation.sh  
Last Login: Tue Oct 25 19:22:31 on ttys008  
(base) kathryncampbell@Kathryns-MacBook-Pro ~ % conda activate MADDOG  
(MADDOG) kathryncampbell@Kathryns-MacBook-Pro ~ % cd MADDOG  
(MADDOG) kathryncampbell@Kathryns-MacBook-Pro MADDOG % sh designation.sh  
What is the name of the folder containing your sequences and metadata?  
showcase  
showcase/Kenya_metadata.csv -> showcase/showcase_metadata.csv  
showcase/Kenya.fasta -> showcase/showcase.fasta  
nadd = 43  
nthread = 8  
nthreadpair = 8  
nthreadtb = 8  
ppenalty_ex = 8  
stacksize: 8192 kb  
generating a scoring matrix for nucleotide (dist=200) ... done  
Gap Penalty = -1.63, +0.00, +0.00
```

Making a distance matrix ..

```
there are 123936 ambiguous characters.  
1 / 1287
```

```
/Users/kathryncampbell/MADDOG — disttbfast + sh designation.sh
```

Study Overview

Lineages Overview

Lineage Changes Over Time

Areas to Investigate

Lineage Dynamics

Study Overview

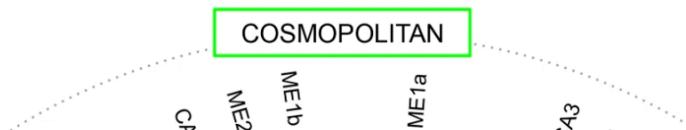
This study contains 56 sequences from between 2011 and 2019. This sequence data came from 1 different countries.

Country	Number of Sequences
Peru	56

Table 1. Numbers of sequences by area.

Lineages Overview

Several well-defined RABV clades circulate globally, within two major phylogenetic groups; bat-related and dog-related. The dog-related group is split into 6 different clades according to Troupin et al. (2016). These clades are: Africa 2, Africa 3, Cosmopolitan, Arctic, Asian and Indian. The majority of Nigerian sequences fall within the Africa 2 clade.



Study Overview

Lineages Overview

Lineage Changes Over Time

Areas to Investigate

Lineage Dynamics

Study Overview

This study contains 56 sequences from between 2011 and 2019. This sequence data came from 1 different countries.

Country	Number of Sequences
Peru	56

Table 1. Numbers of sequences by area.

Lineages Overview

Several well-defined RABV clades circulate globally, within two major phylogenetic groups; bat-related and dog-related. The dog-related group is split into 6 different clades according to Troupin et al. (2016). These clades are: Africa 2, Africa 3, Cosmopolitan, Arctic, Asian and Indian. The majority of Nigerian sequences fall within the Africa 2 clade.



Study Overview

Lineages Overview

Lineage Changes Over Time

Areas to Investigate

Lineage Dynamics

Study Overview

This study contains 56 sequences from between 2011 and 2019. This sequence data came from 1 different countries.

Country	Number of Sequences
Peru	56

Table 1. Numbers of sequences by area.

Lineages Overview

Several well-defined RABV clades circulate globally, within two major phylogenetic groups; bat-related and dog-related. The dog-related group is split into 6 different clades according to Troupin et al. (2016). These clades are: Africa 2, Africa 3, Cosmopolitan, Arctic, Asian and Indian. The majority of Nigerian sequences fall within the Africa 2 clade.



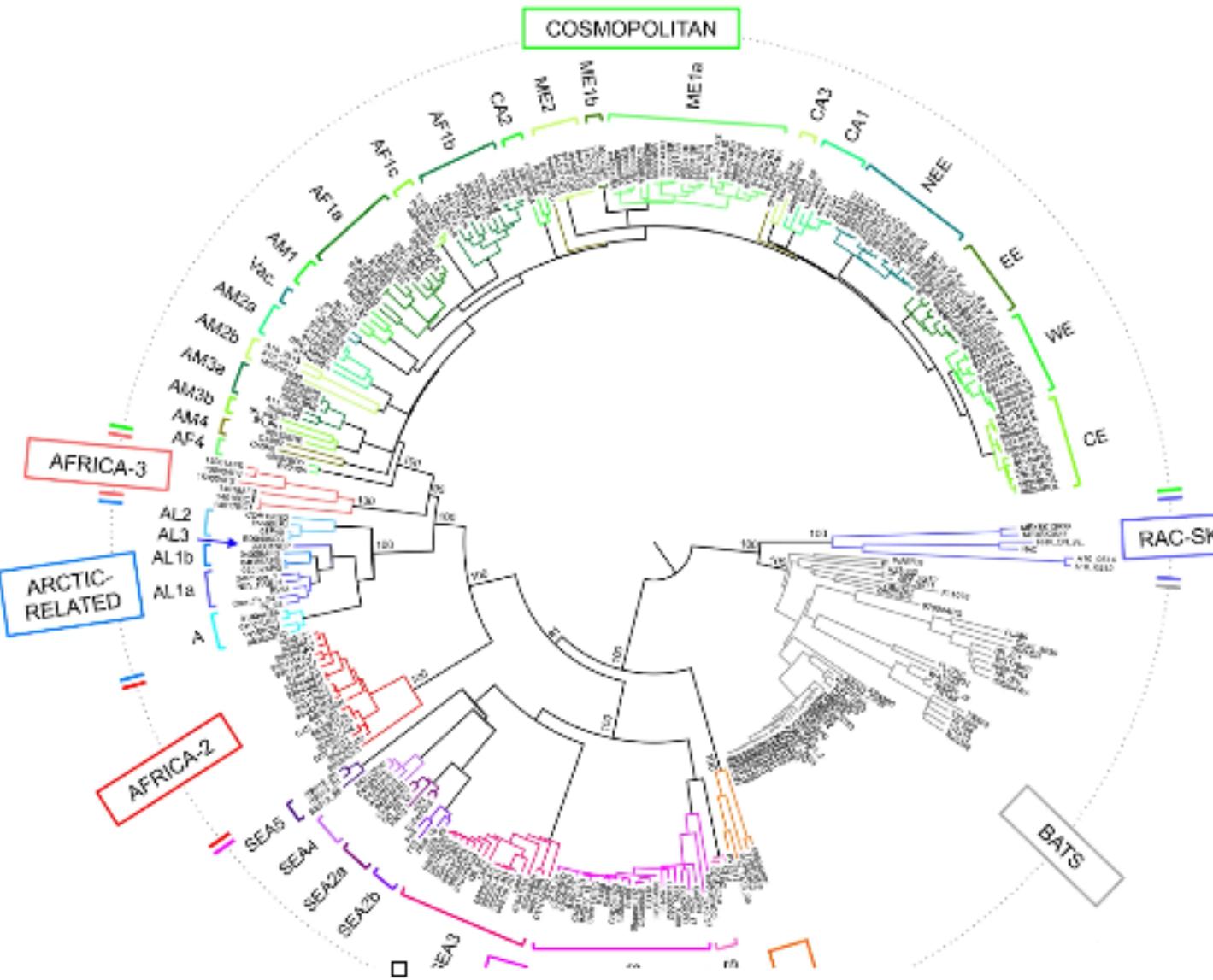
Study Overview

Lineages Overview

Lineage Changes Over Time

Areas to Investigate

related and dog-related. The dog-related group is split into 6 different clades according to Iroupin et al. (2016). These clades are: Africa 2, Africa 3, Cosmopolitan, Arctic, Asian and Indian. The majority of Nigerian sequences fall within the Africa 2 clade.

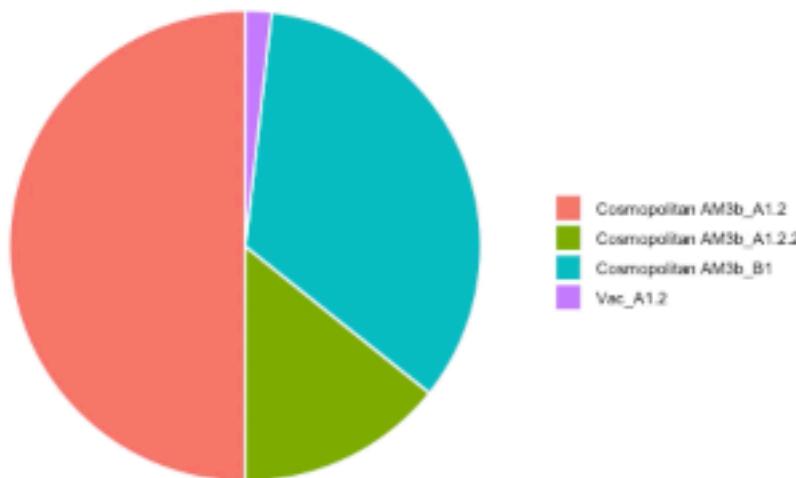
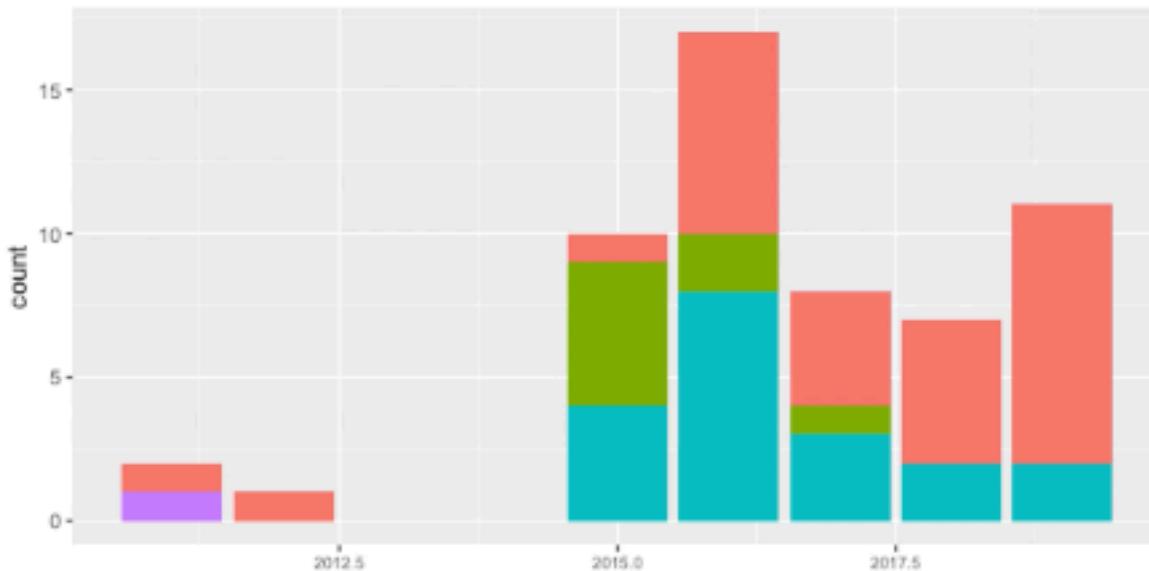


	AM3b_A1.2				AM3b_A1
Study Overview	Vac_A1.2	c("China", "Czechia", "France", "Germany", "Mexico", "Morocco", "Nepal", "Russia", "Slovenia")	1993	2019	1 Vac_A1
Lineages Overview	Cosmopolitan_AM3b_A1	Brazil	2002	2010	0 Cosmopolitan_A1.3
Lineage Changes Over Time	Vac_A1	c("Austria", "China", "Czechia", "France", "Mexico")	2007	2020	0 Vac
Areas to Investigate	Cosmopolitan_A1.3	c("Egypt", "Israel", "Mexico", "Peru", "United States")	1950	2017	0 Cosmopolitan_A1
	Vac	Mexico	2003	2009	0 RABV
	Cosmopolitan_A1	c("Brazil", "China", "Gabon", "Grenada", "Japan", "Mexico", "Nigeria", "Peru", "Russia")	1931	2020	0 Cosmopolitan
	Cosmopolitan		NA	NA	0 RABV

Table 2. Details of lineages relevant to this study. First and last years refer to the first and most recent years the lineage has been detected prior to this study.

sequences.

- Study Overview
- Lineages Overview
- Lineage Changes Over Time**
- Areas to Investigate



[Study Overview](#)[Lineages Overview](#)[Lineage Changes Over Time](#)[Areas to Investigate](#)

lineage	tips	distance	country	year_first	year_last
Cosmopolitan AM3b_B1_E1	6	0.1334107	Peru	2016	2019

Table 5. Details of potentially emerging or undersampled lineages relevant to this study. First and last years refer to the first and most recent years the lineage has been detected.

There are 3 singletons of interest detected. These reflect highly divergent sequences that could indicate sequencing errors, or the start of new lineages, especially in undersampled areas. Be aware these include ALL singletons of interest within the relevant lineages in your dataset; not just your data. This is to show there may be general gaps in the data.

lineage	n_singletons	singleton_countries	singleton_years
Cosmopolitan AM3b_A1	1	Brazil	2005
Cosmopolitan AM3b_A1.2	1	Mexico	2006
Cosmopolitan AM3b_A1.2.1	1	Georgia	2016

Table 6. Summary of singletons of interest relevant to this study.

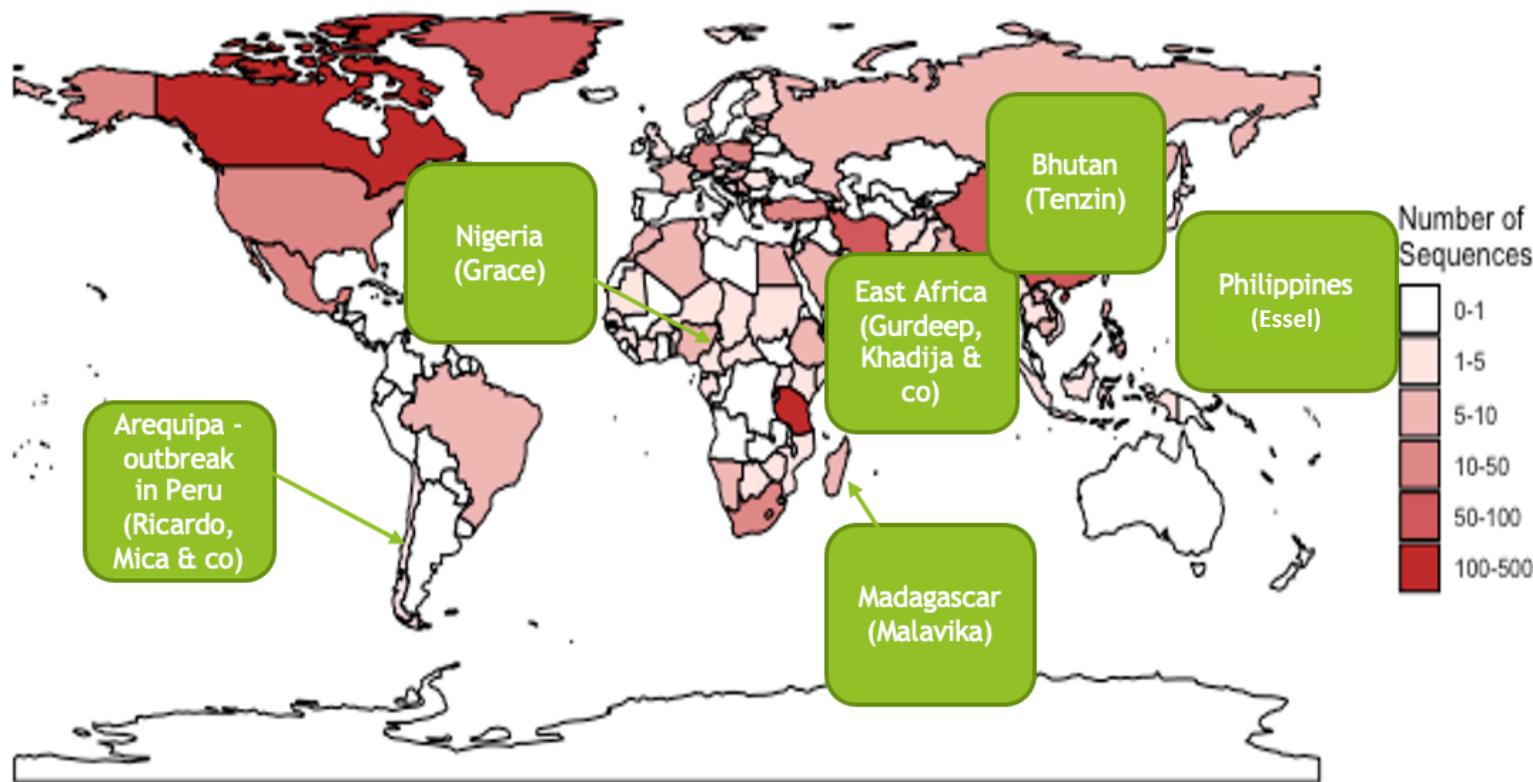
ID	closest relative	lineage	year	country
KJ001501	U22627	Cosmopolitan AM3b_A1.2	2006	Mexico
DQ149104	DQ875051	Cosmopolitan AM3b_A1	2005	Brazil
MW055108	OM971003	Cosmopolitan AM3b_A1.2.1	2016	Georgia

Table 7. Details of individual singletons of interest relevant to this study.



Moving forwards

- Detailed global analysis
 - Areas of persistence
 - Host associations
- Lineage specific differences
 - Evolutionary analysis
 - Amino acid substitutions
 - Impact



Acknowledgements



► Katie Hampson

► Kirstyn Brunker

► Rob Gifford

► Roman Biek

► Rowan Durrant

► Matt Arnold



THE UNIVERSITY
of EDINBURGH

► Andrew Rambaut

► Aine O'Toole

► Verity Hill



UNIVERSITY OF NAIROBI

► Gurdeep Jaswant



► Criselda Bautista

