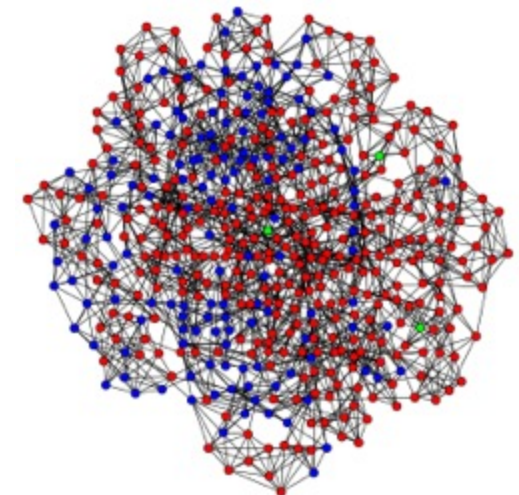
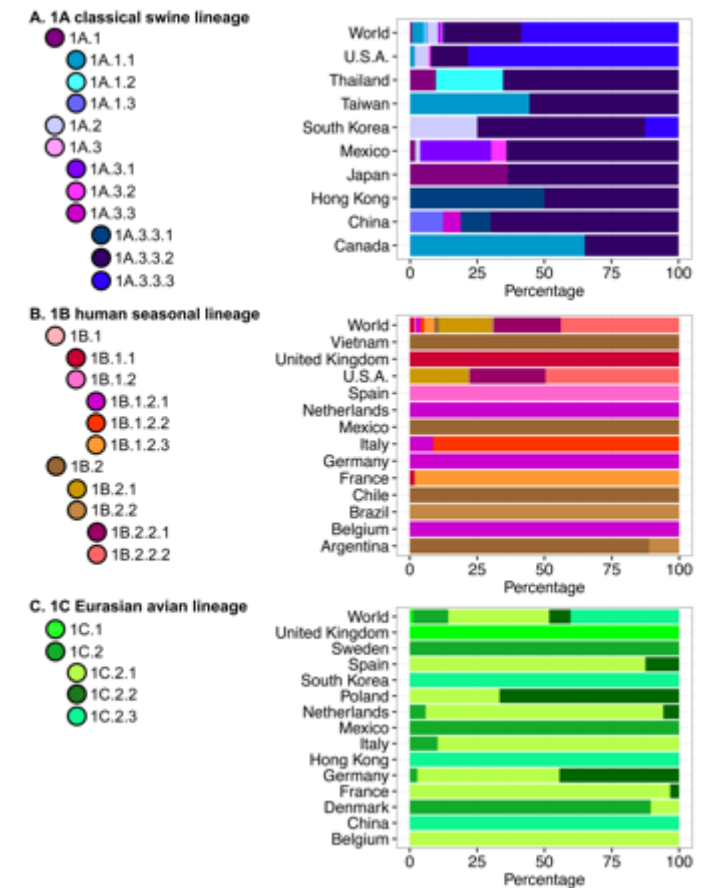


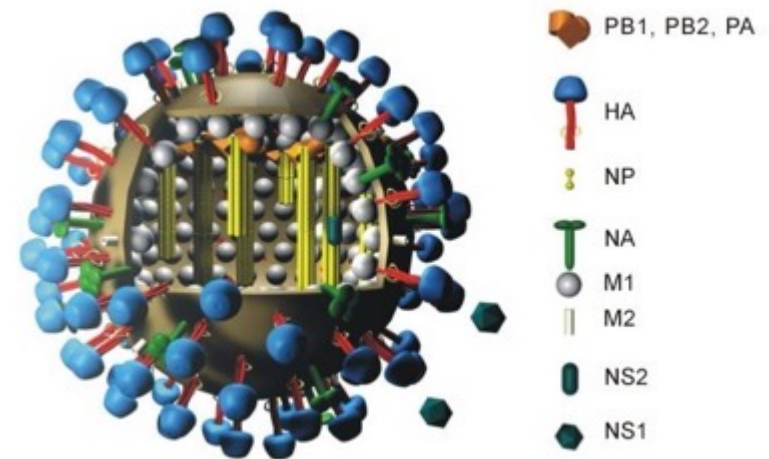
Influenza A virus at the human-animal interface

Tavis Anderson
Virus and Prion Research Unit
National Animal Disease Center
Agricultural Research Service
United States Department of Agriculture



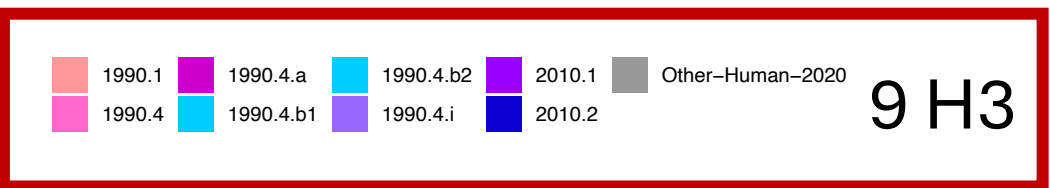
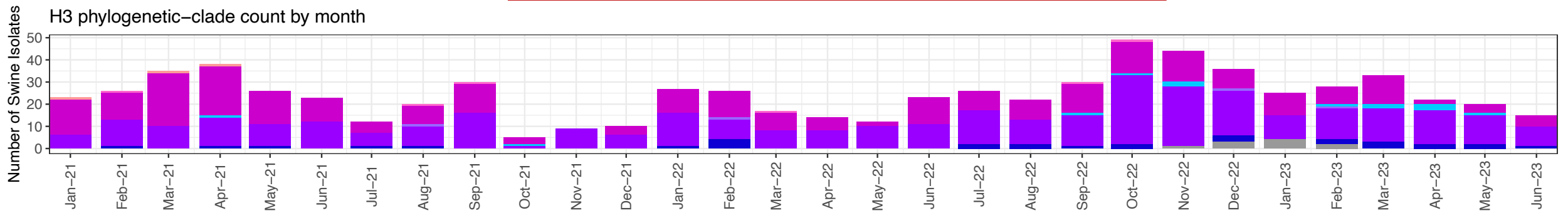
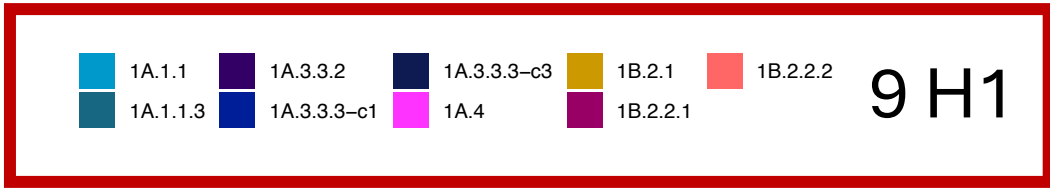
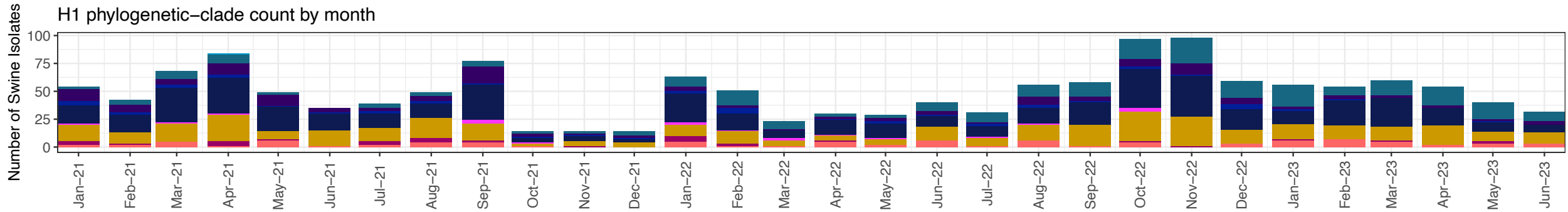
Only 3 influenza A virus subtypes in swine

- Negative-sense, single-stranded RNA virus
- HA is target of neutralizing antibodies
 - Antigenic drift
- Co-infection and reassortment
 - Antigenic shift
- Swine H1N1, H1N2, and H3N2



As surveillance systems were established,
detection of significant within-subtype IAV diversity

From 3 subtypes to 18 different H1 and H3 HA



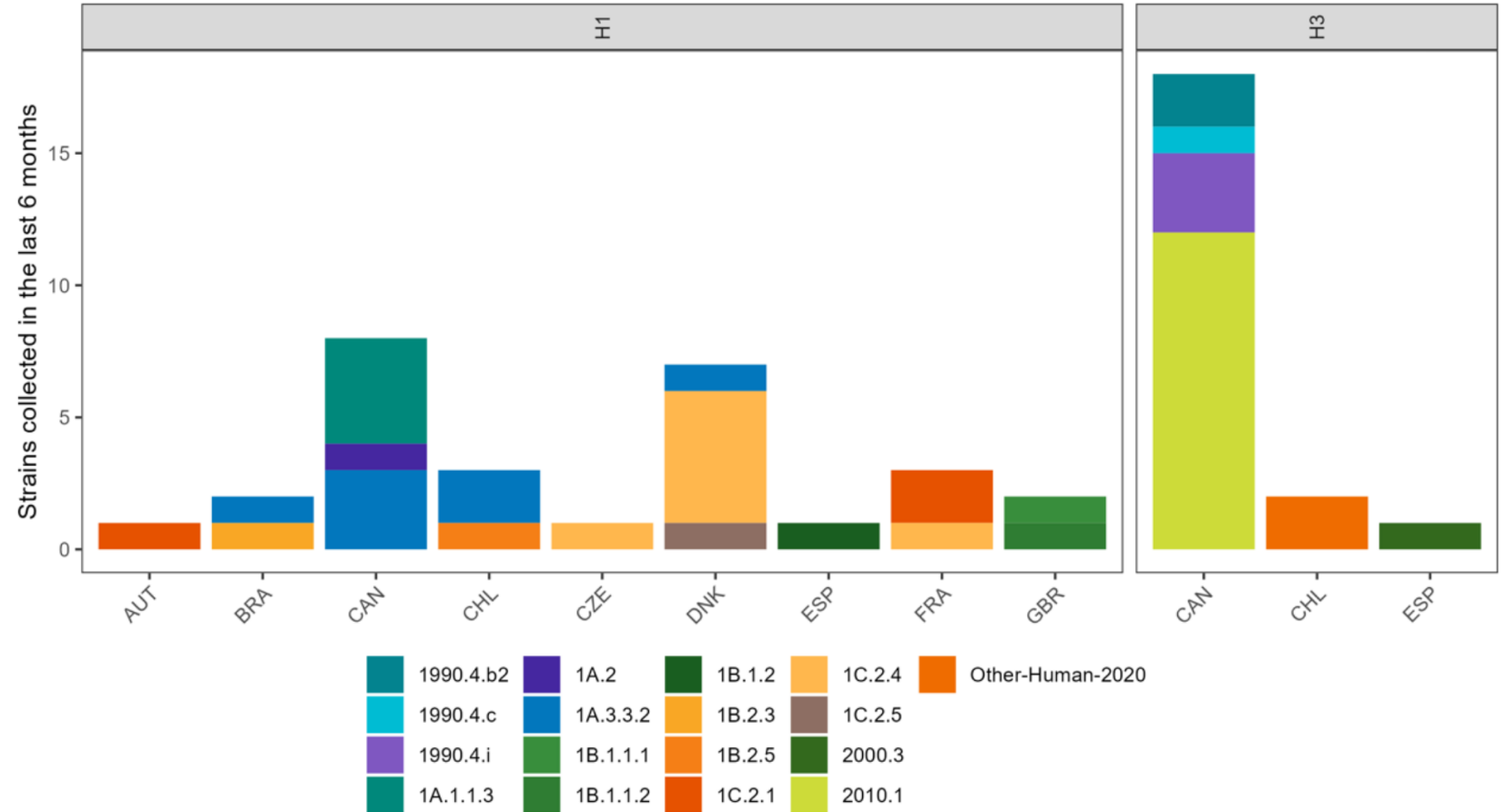
IAV in swine isn't restricted to the USA

Another 17 H1 and H3 HA detected (in 6 months)



World Organization for Animal Health/Food and Agriculture
Organization Network of
Expertise on Animal Influenza

<https://www.offlu.org/>



~15 countries currently sharing data

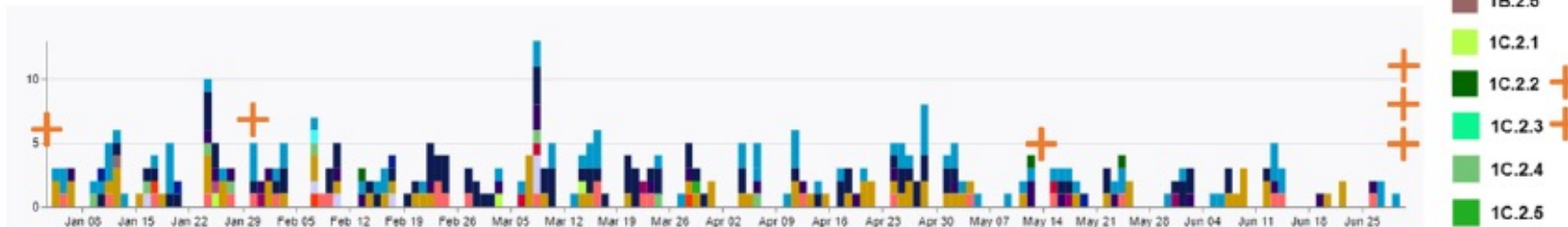
OFFLU team (February 2024)

IAV in swine is generally undersurveilled...

Zoonotic events as markers for swine IAV



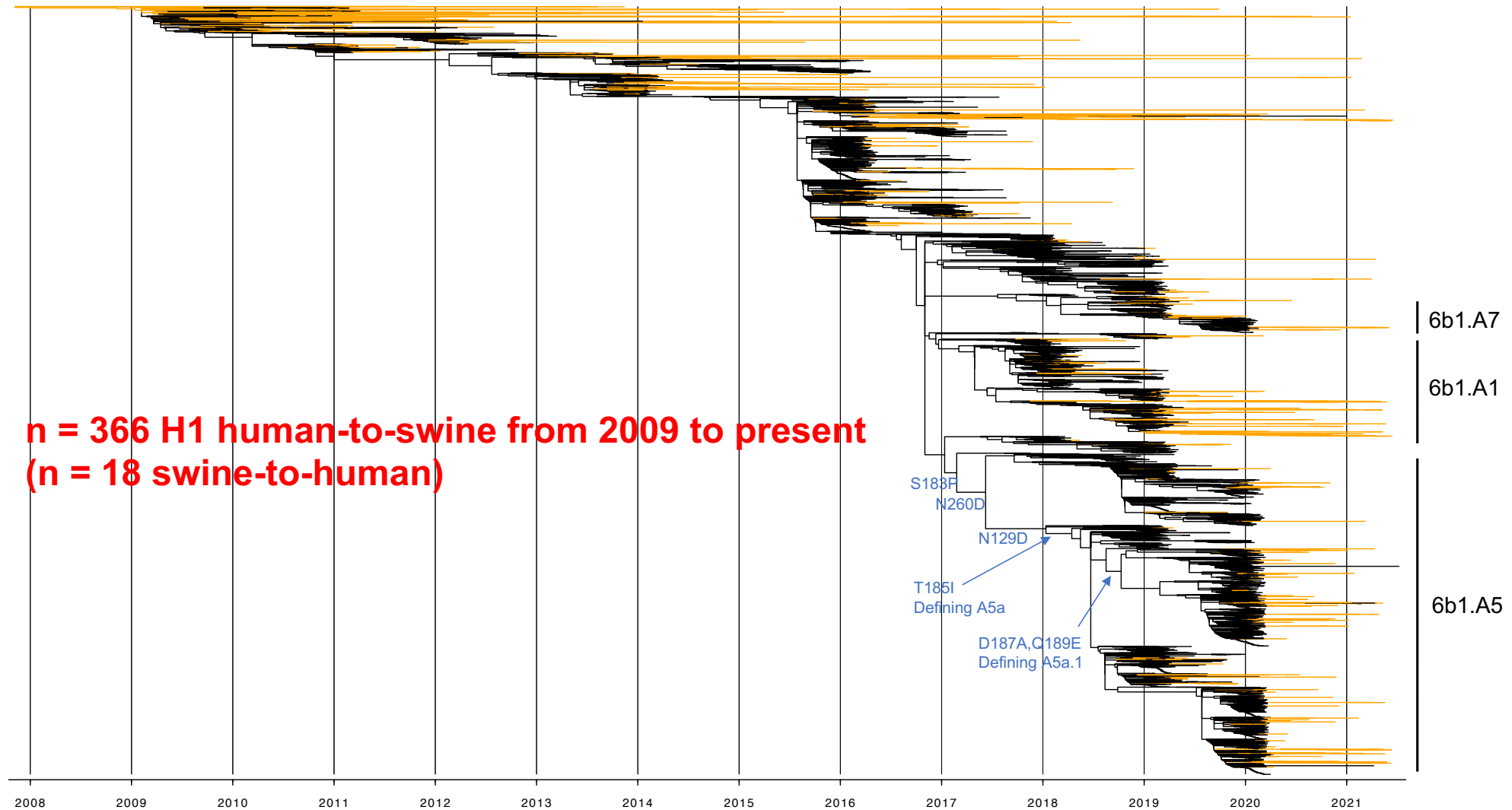
No Taiwan swine IAV data since 2013



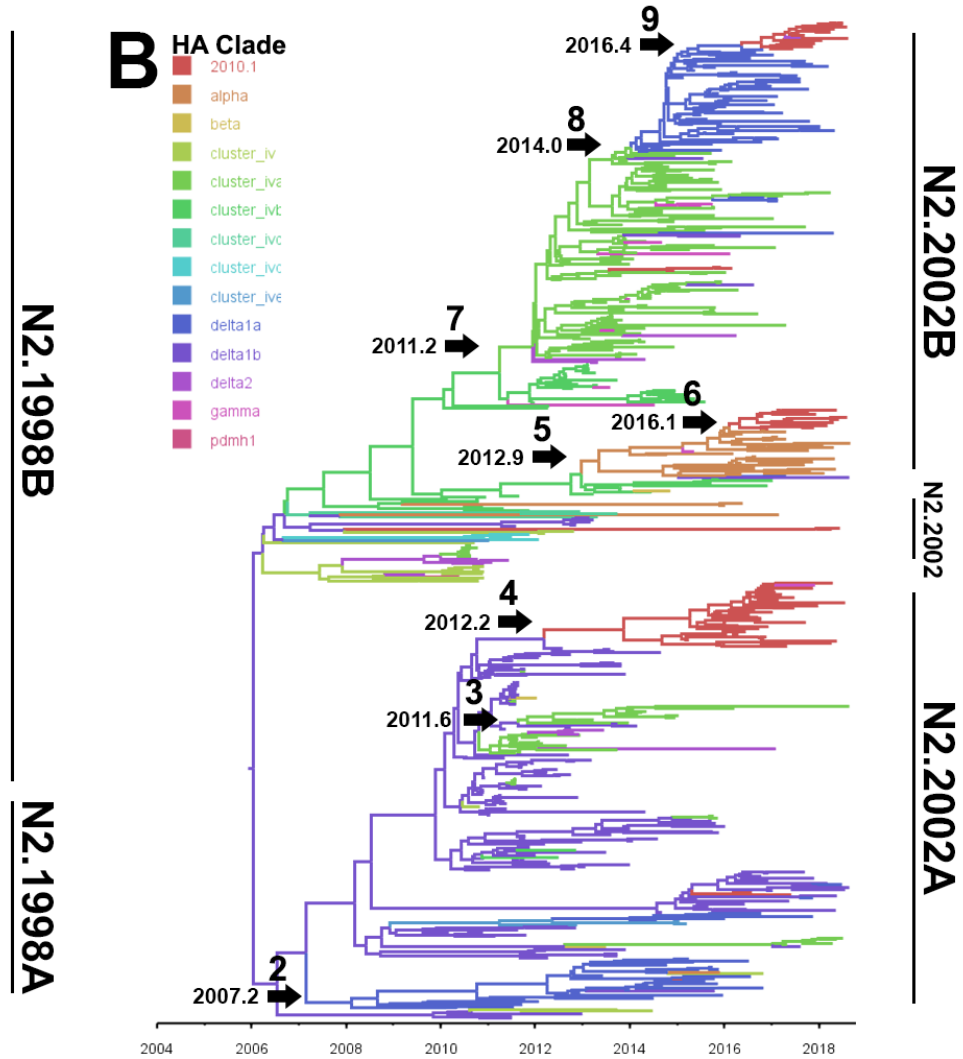
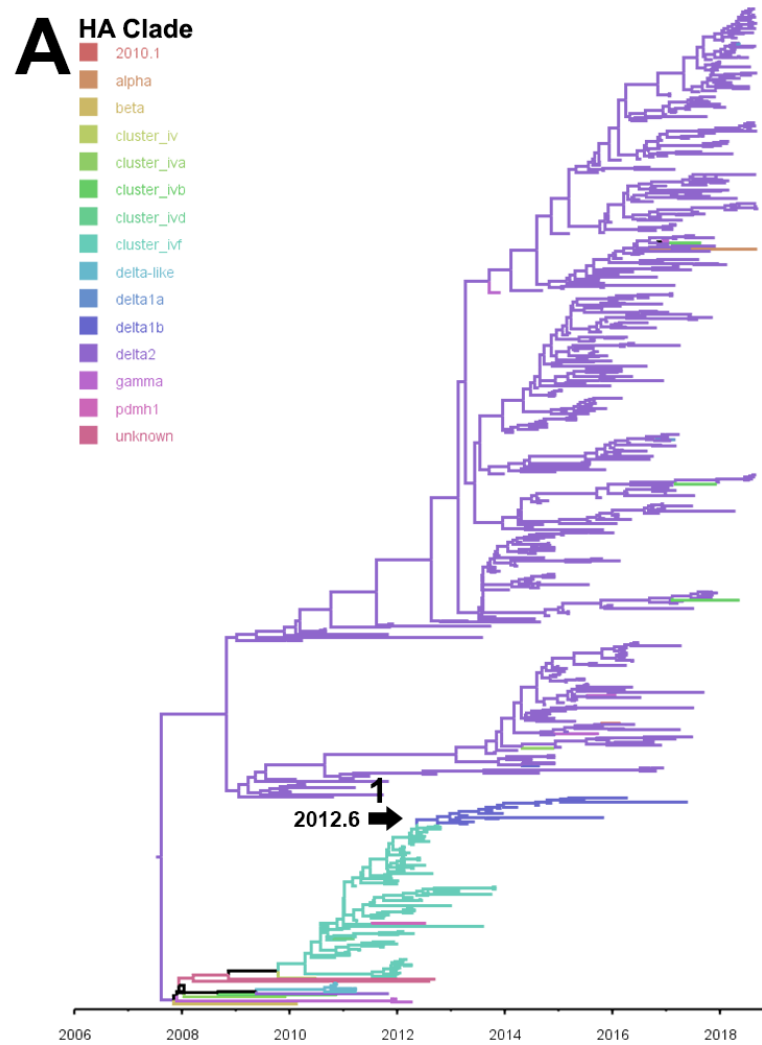
Human “variant” infections detected by public health in regions without IAV in swine data

The number of swine IAV groups is not static

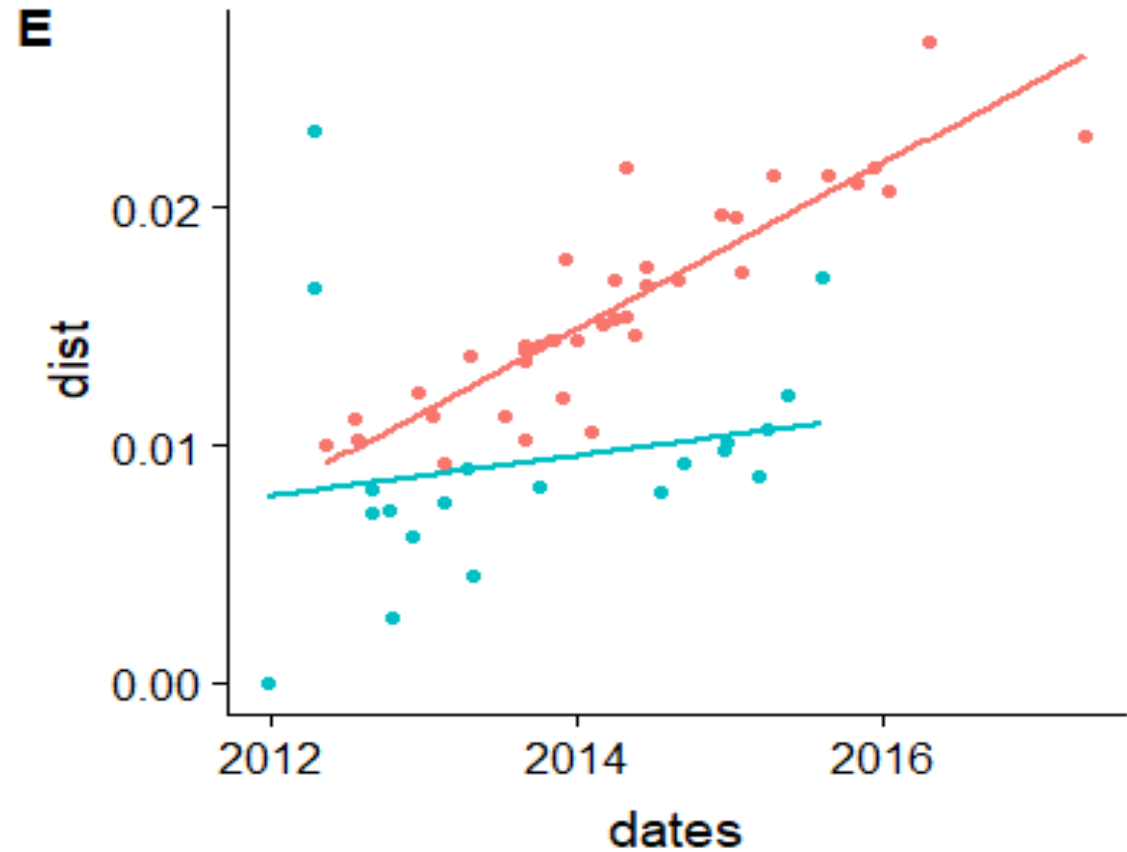
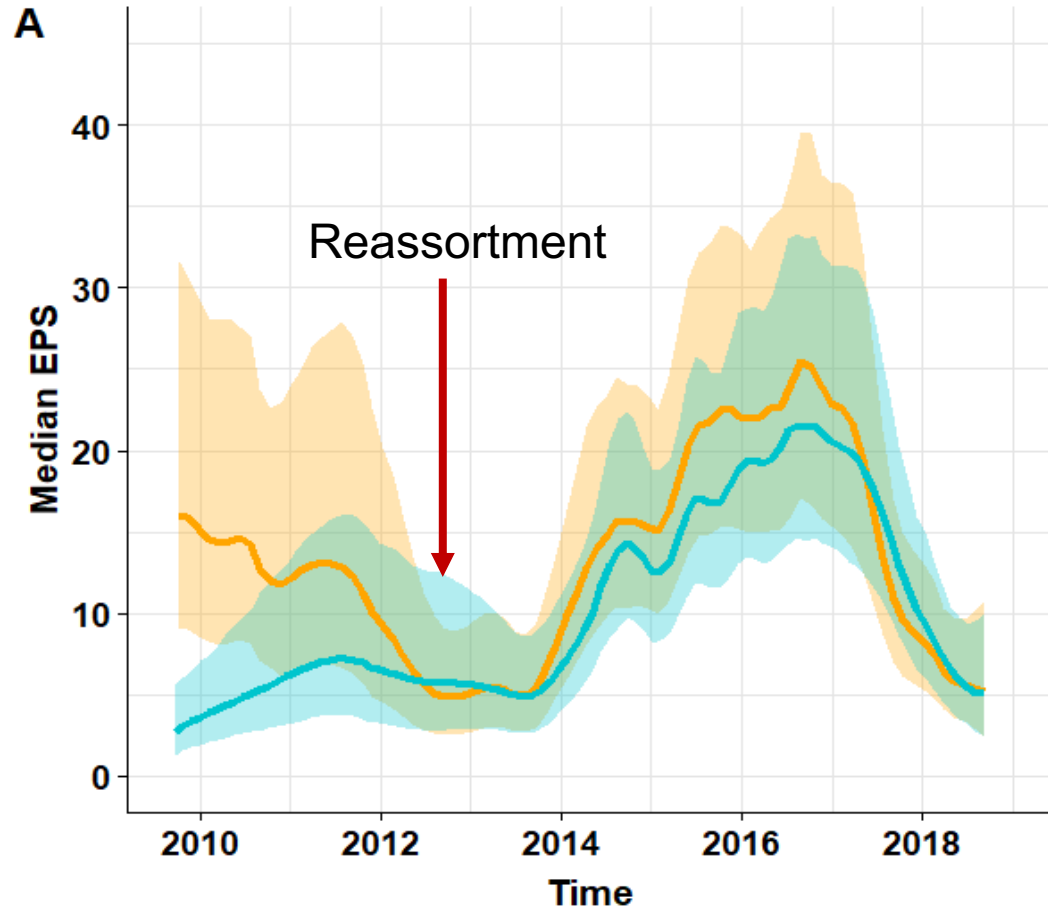
Human-to-swine spillovers, some establish new lineages



They reassort and shape the evolutionary landscape...



... through epistatic changes and (sometimes) rate changes



A team has developed an approach to address these challenges for IAV in swine



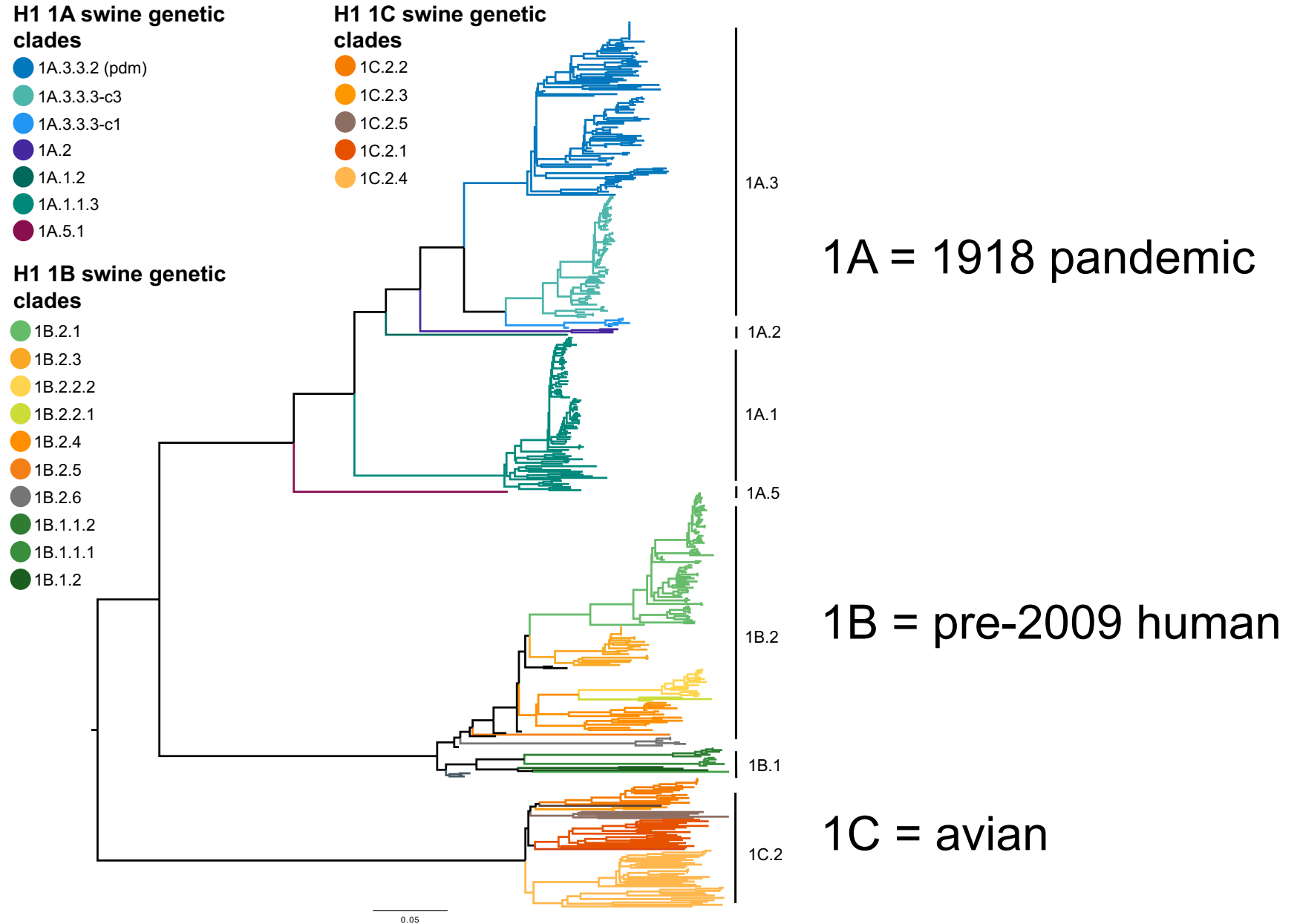
World Organization for Animal
Health/Food and Agriculture
Organization Network of
Expertise on Animal Influenza

<https://www.offlu.org/>

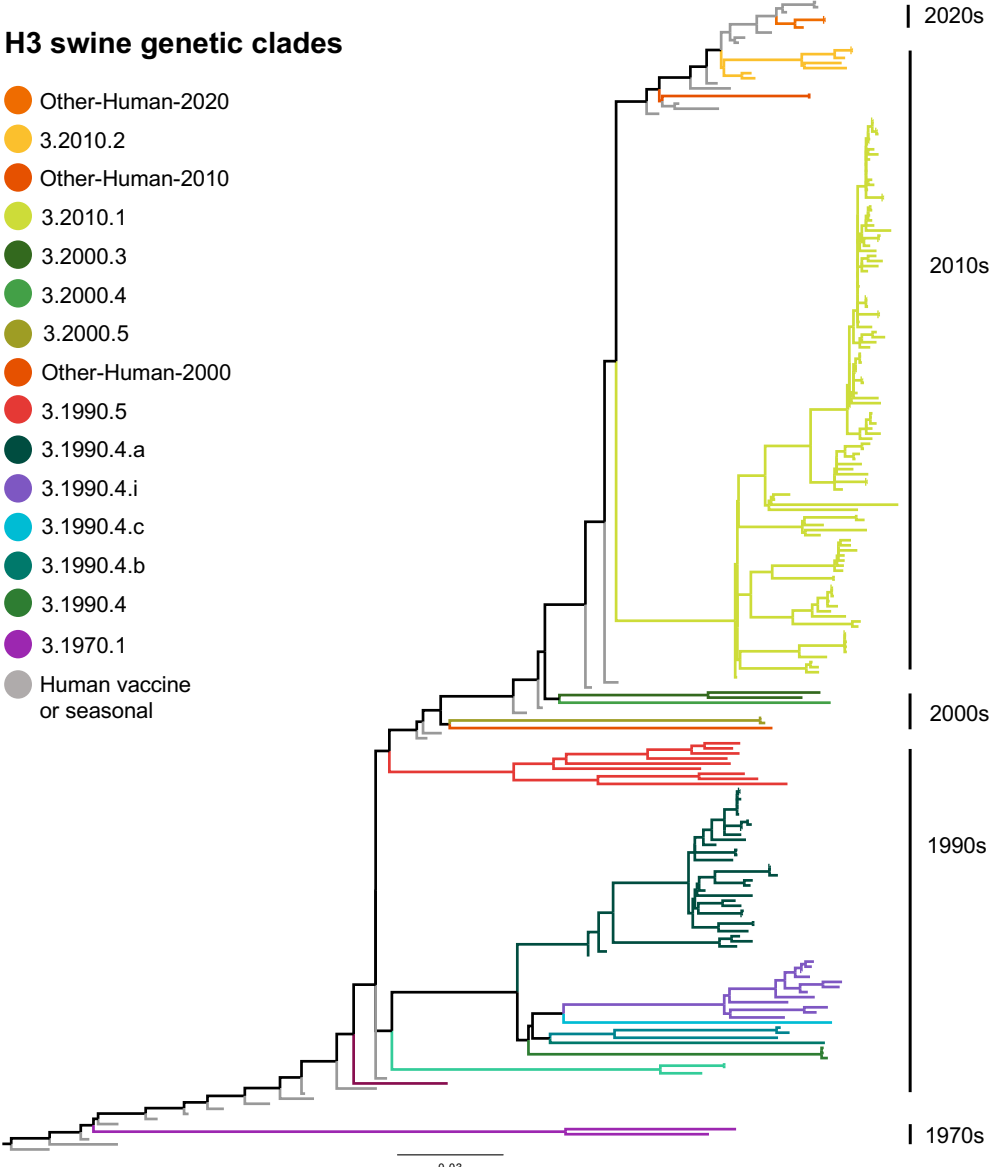
The basic criteria for H1 and H3 HA clade naming

- Maintain established clades
 - Remove stigmatizing and/or incriminating toponyms
- Evolutionary history
- Statistical support and genetic diversity
- Minimum time period (>1 year)
- Minimum number of contemporary genes
 - and/or incorporate antigenic support based on HI cross-reactivity or serosurveillance
 - and/or reflect human variant detections

H1 HA can be traced to human- or avian-origin IAV



H3 HA can be traced to human-origin IAV



Grouping by the decade of human-to-swine spillover

How can we determine when we need to make new or refine old names?

Responding to human “variants” with new IAV clades

1C Eurasian avian lineage

★ H1v candidate vaccine virus

Reported H1v cases

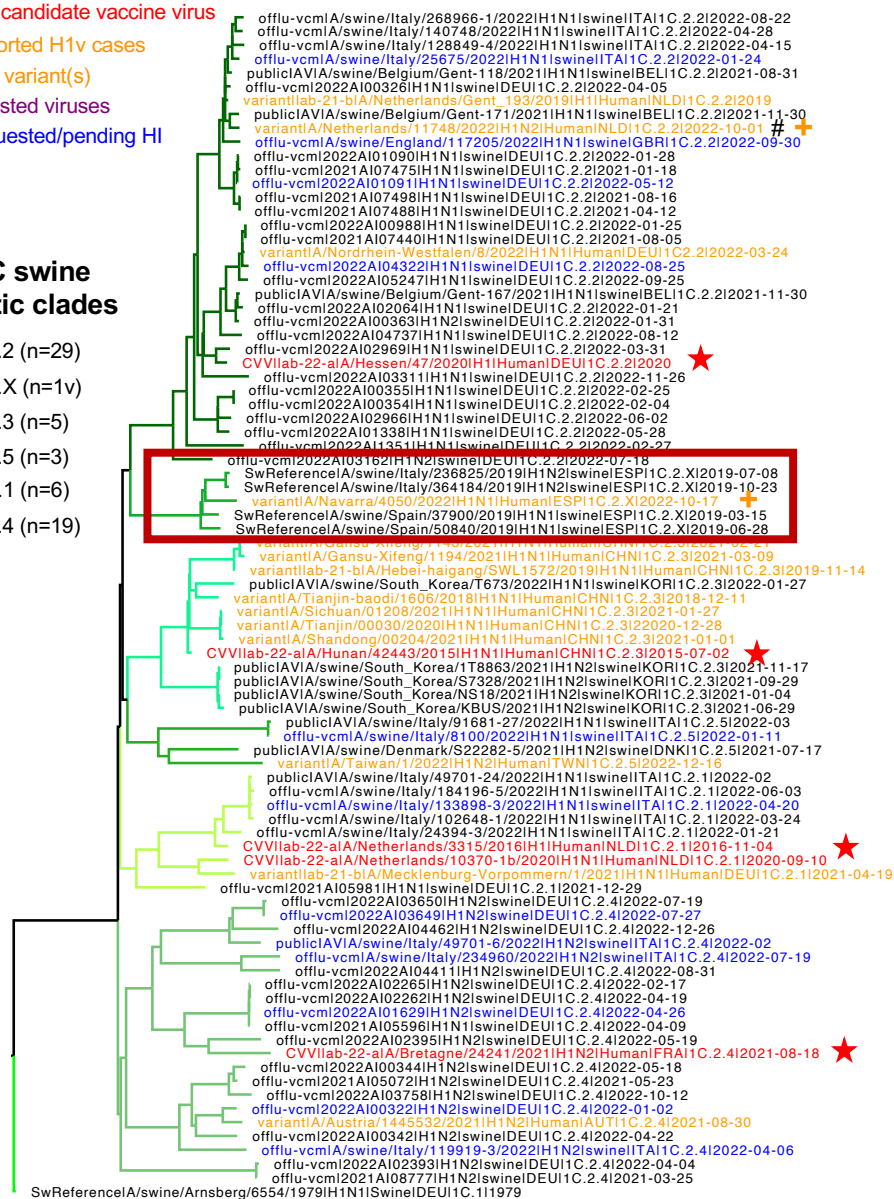
+ New variant(s)

HI tested viruses

Requested/pending HI

H1 1C swine genetic clades

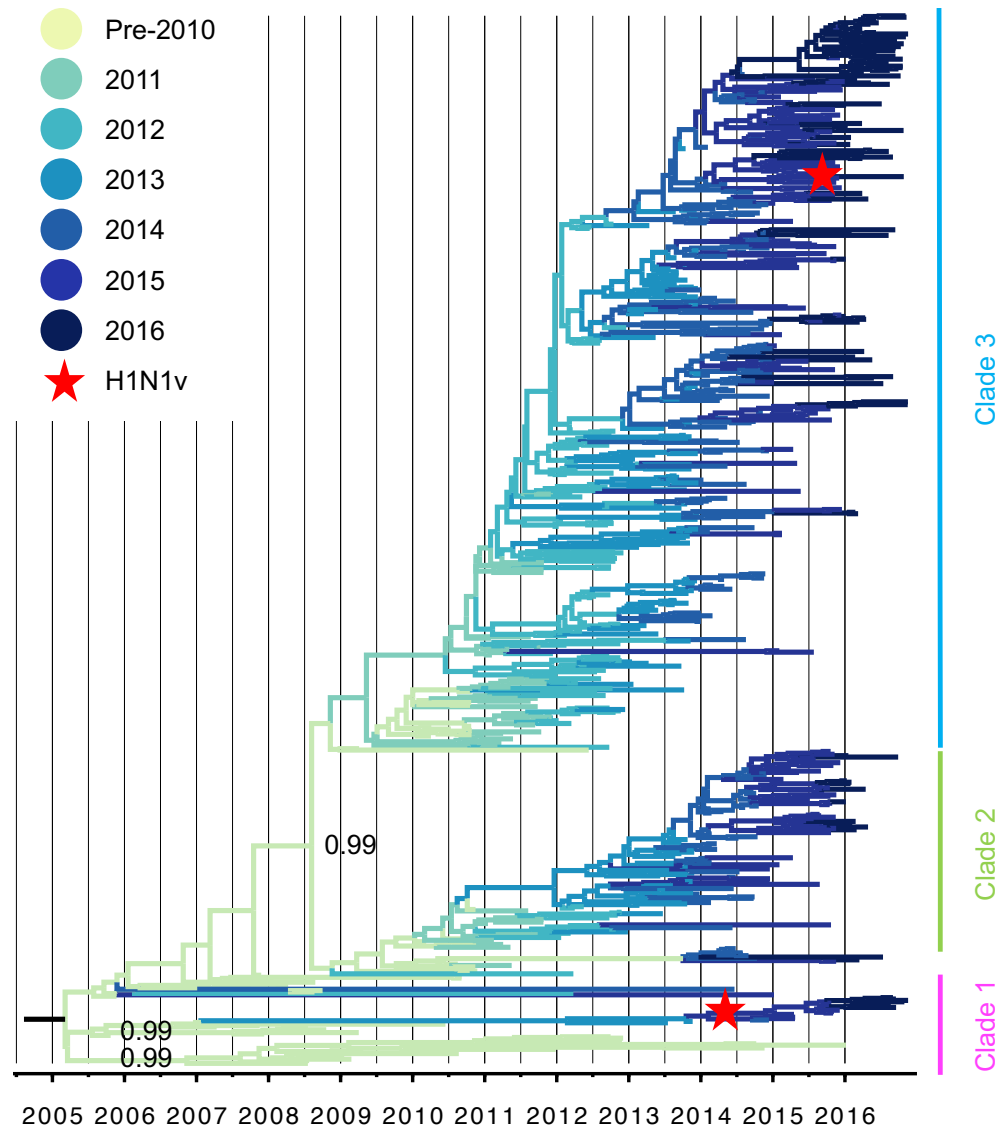
- 1C.2.2 (n=29)
- 1C.2.X (n=1v)
- 1C.2.3 (n=5)
- 1C.2.5 (n=3)
- 1C.2.1 (n=6)
- 1C.2.4 (n=19)



1C.2-like

- Only in Spain, detected in 2019
- Human variant in 2022
- Established 1C.2.6

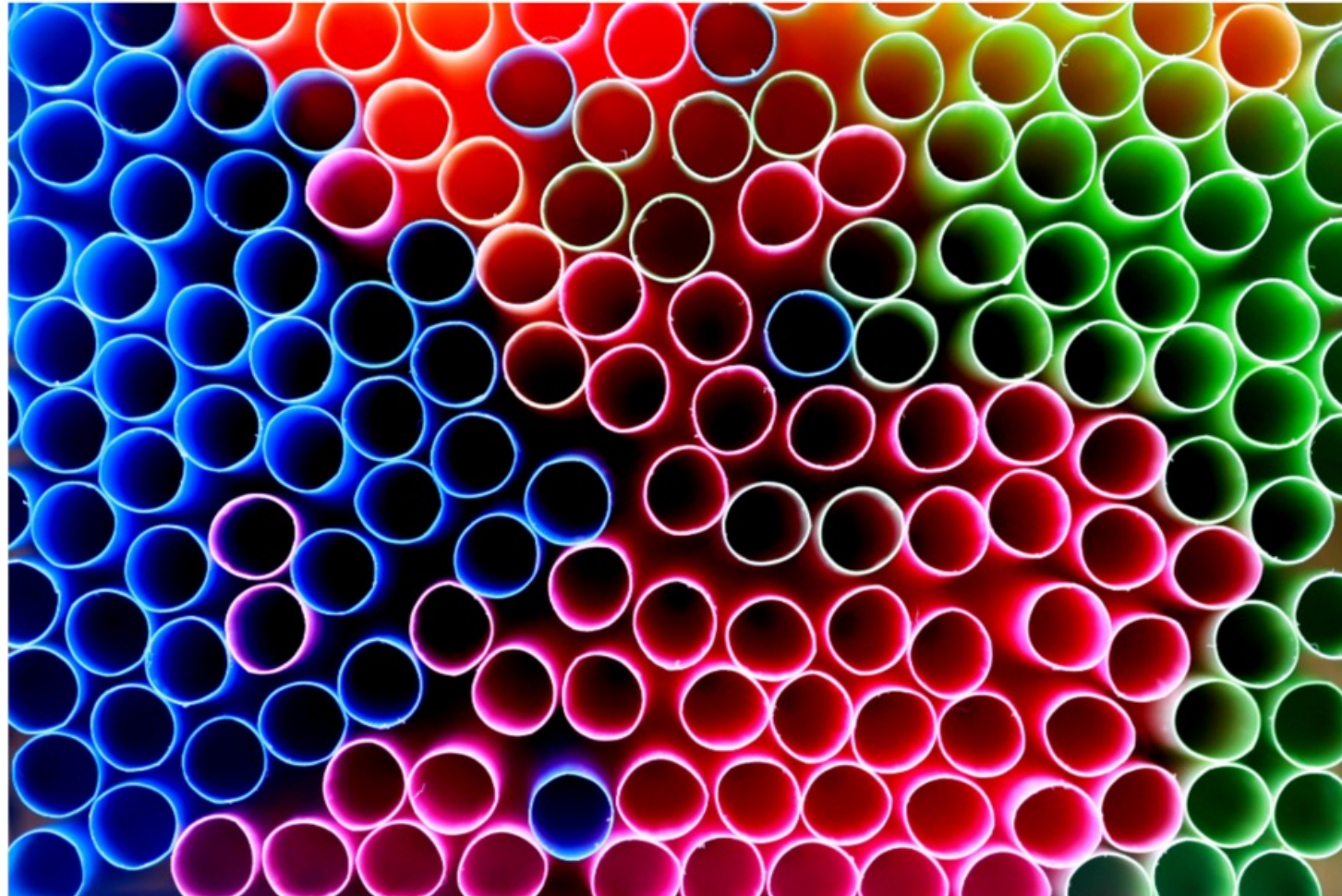
Splitting existing IAV clades to reflect phenotypic diversity



1A.3.3.3.x

- ~300-400 detections a year
- USA and South Korea
- Statistical support but low diversity
- HI tested with 4-fold or greater loss in cross-reactivity
- Human variants detected in 2 clades
- 1A.3.3.3 split into 3 groups

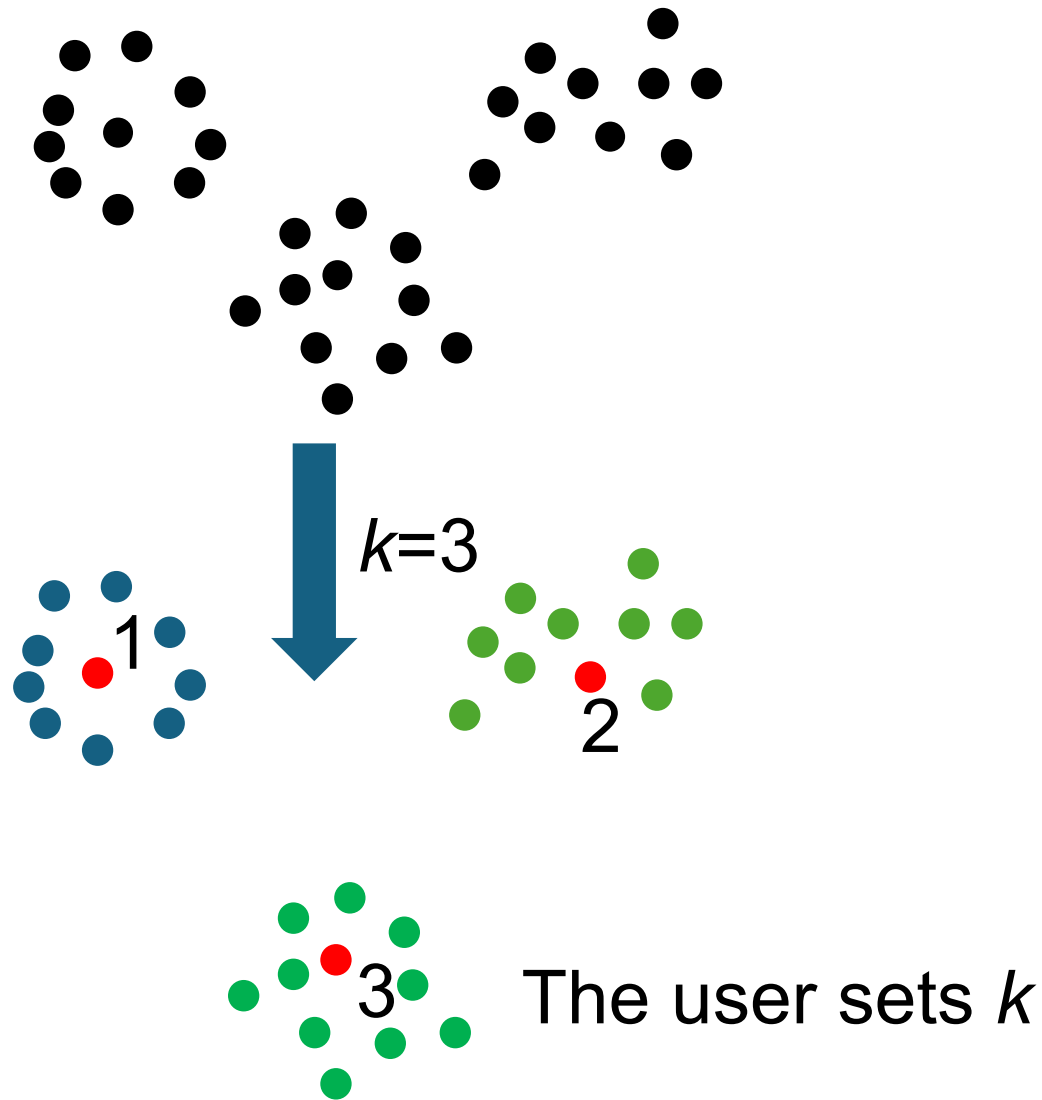
Identifying when IAV clades require revision with PARNAS



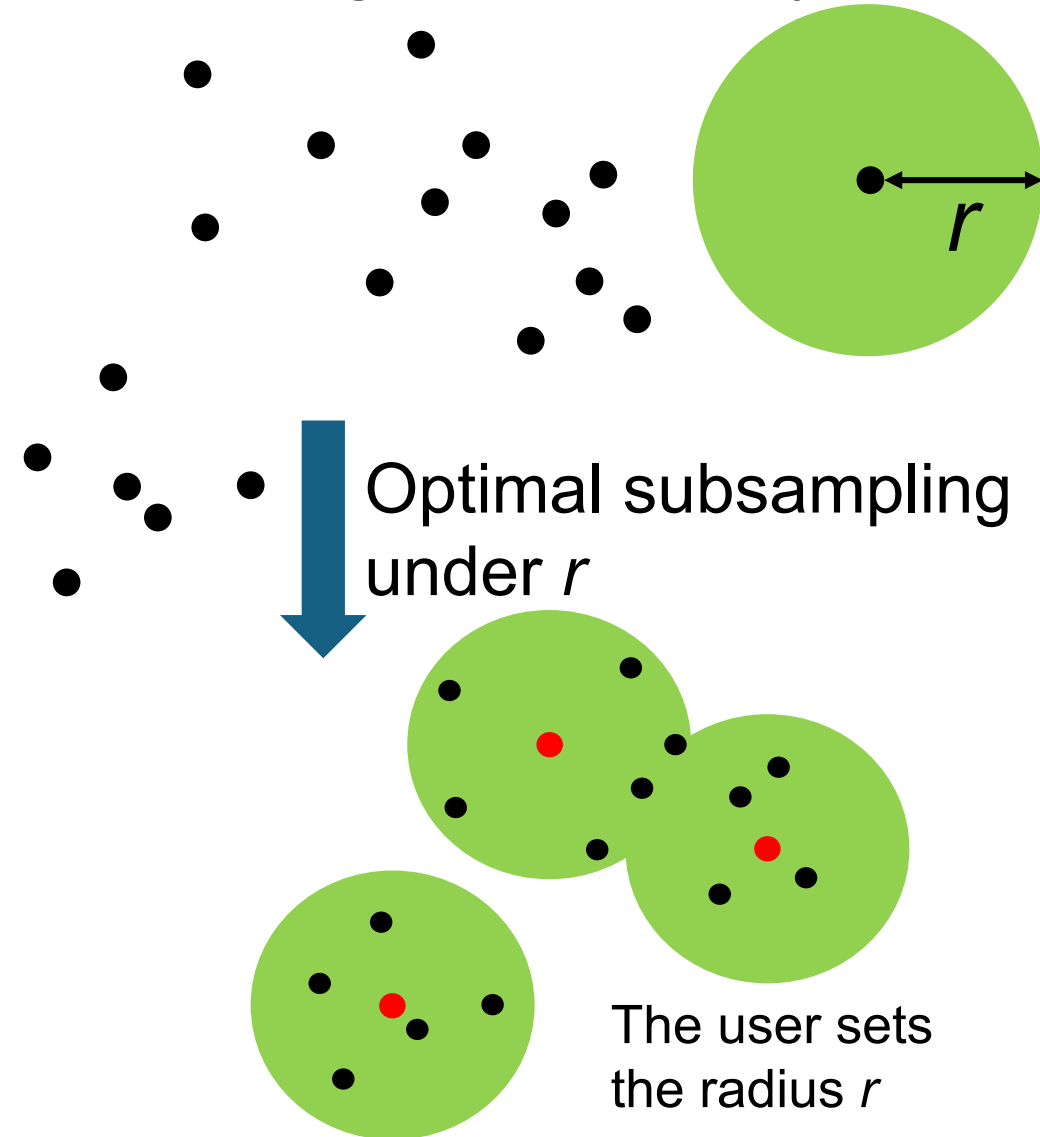
Markin et al. (2023) Systematic Biology
<https://github.com/flu-crew/PARNAS>

The main PARNAS sampling strategies

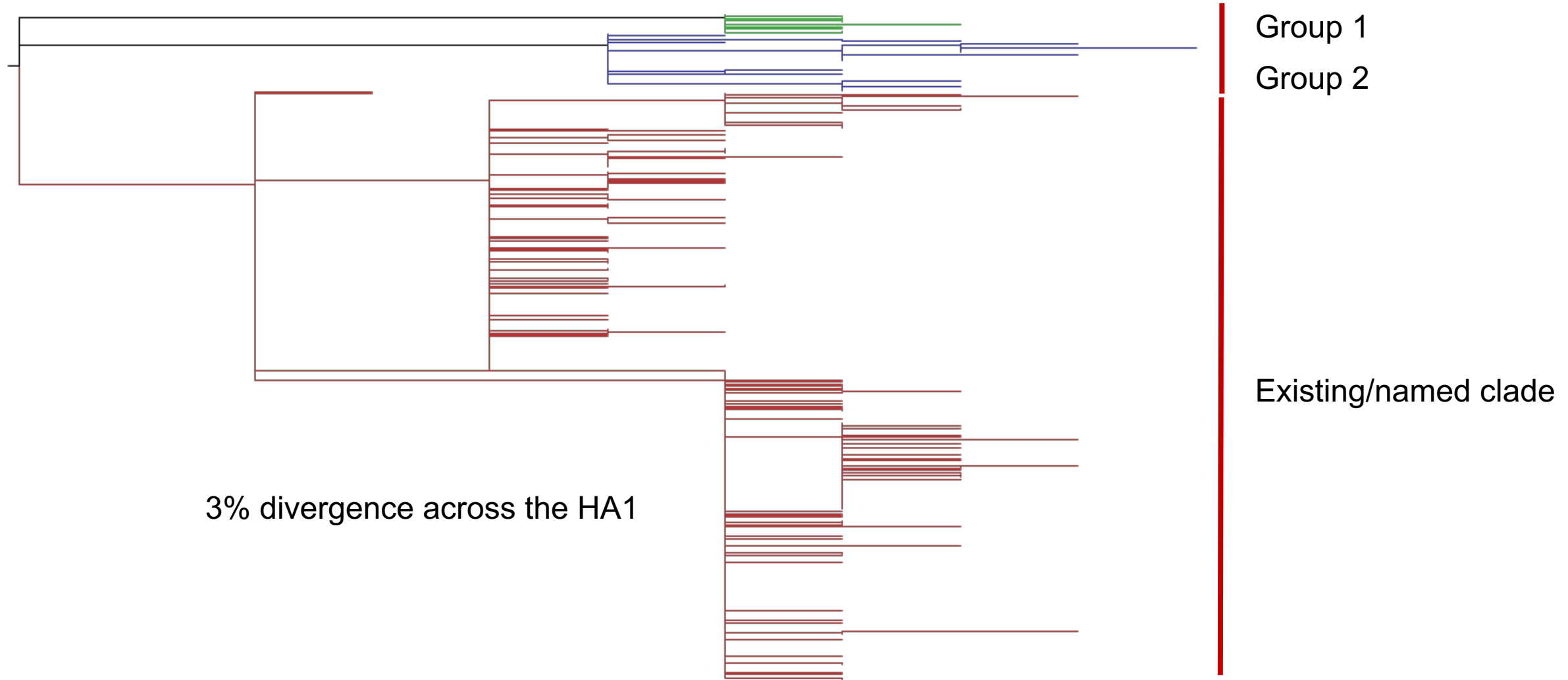
1) Selecting k best representatives



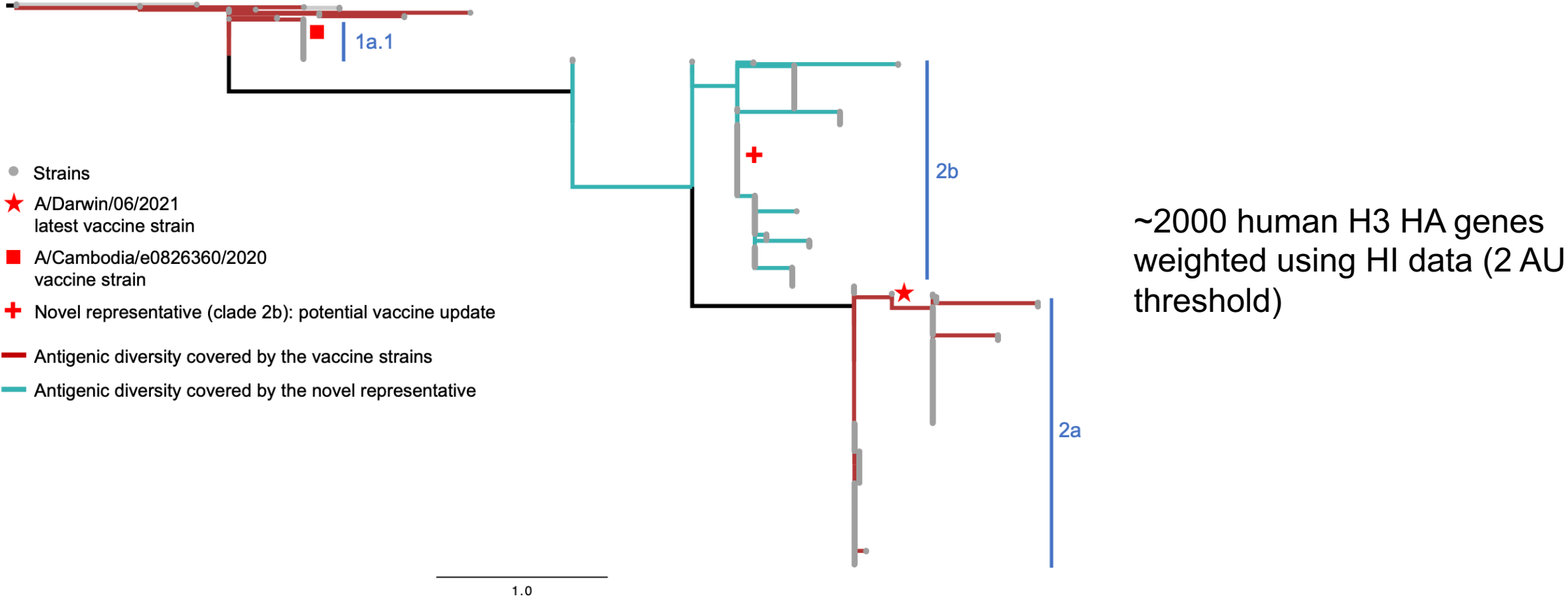
2) Covering all diversity



Using prior groupings, rapidly identify new groups



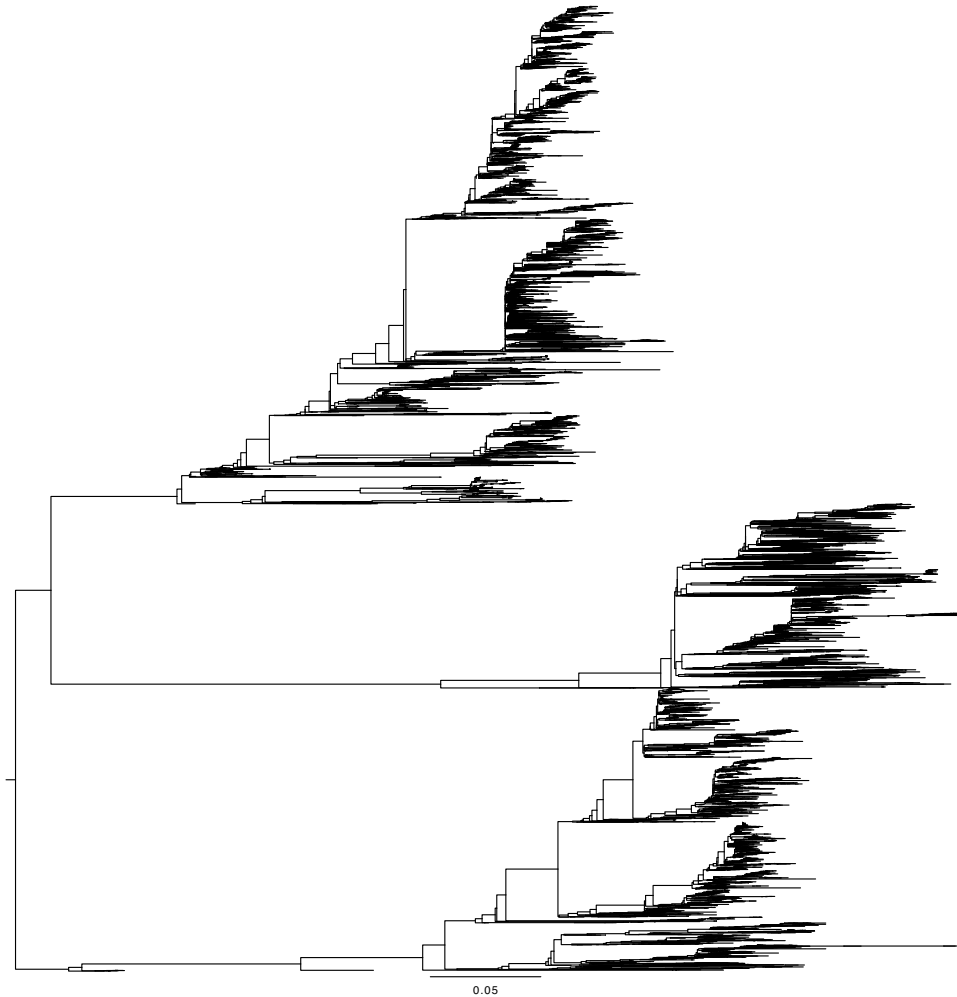
PARNAS can also work with “other” metadata and identify novel groups



Markin et al. (2023) Systematic Biology
<https://github.com/flu-crew/PARNAS>

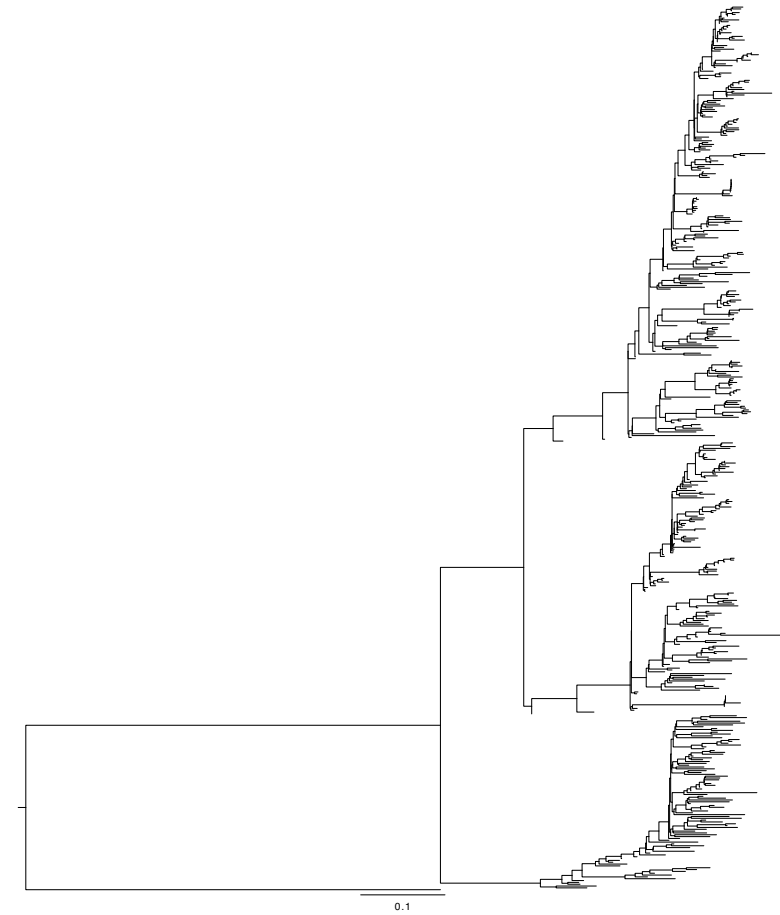
The H1 and H3 BV-BRC implementation

Objective selection of representative genes



14,378 H1 HA genes

PARNAS



482 H1 HA genes under a 0.5% divergence threshold

(similar process for the H3 HA – with human, swine, canine, equine, avian genes)

Classification of unknowns and database annotation

Services

Subspecies Classification

The Subspecies Classification tool assigns the genotype/subtype of a virus, based on the genotype/subtype assignments maintained by the International Committee on Taxonomy of Viruses (ICTV). This tool infers the genotype/subtype for a query sequence from its position within a reference tree. The service uses the pplacer tool with a reference tree and reference alignment and includes the query sequence as input. Interpretation of the pplacer result is handled by Cladinator. Link to [pplacer](#) and [Cladinator](#).

For further explanation, please see the Subspecies Classification Service [Quick Reference Guide](#) and [Tutorial](#).

Query source

Enter sequence Select FASTA file

Enter one or more query nucleotide or protein sequences to search. Requires FASTA format.

Species

Orthomyxoviridae - Swine influenza H3 (global classification, beta version) [Hemagglutinin gene, genomic RNA] ▼

Output Folder

Output Name

↓

oviridae » Alphainfluenzavirus » **Influenza A virus** (942006 Genomes)

Protein Structures **Domains and Motifs** **Epitopes** **Experiments** **Surveillance** **Serology**

1990.4.a

H3_CLADE x

Country	State Province	Geographic Group	Host Common Name	Host Group	H3 Clade
	Alabama (1)	Asia (17)	Environment (6)	Environment (6)	1990.4.a (1695)
	Arizona (1)	North America (1678)	Human (22)	Human (22)	1970.1 (449)
	Arkansas (8)		Lab reassortment (2)	Lab (2)	1970.1-like (3)
	California (2)		Mink (1)	Nonhuman Mammal (1695)	1980.1 (9)
	Colorado (2)		Pig (1664)		1980.1-like (22)
	Illinois (119)				1990 (1)
	Indiana (166)				1990-like (14)
	Iowa (304)				1990.1 (54)
	Kansas (13)				1990.1-like (1)
	Kentucky (2)				1990.2 (15)

Accession	H3 Clade	GenBank Accessions	Size	CDS	Collection Year	Isolation Country	Host Common Name
20/2022	1990.4.a	Q352236	1701	1	2022	USA	Pig
32/2022	1990.4.a	Q352175	1701	1	2022	USA	Pig
3-G20/2013	1990.4.a	Q350857	1701	1	2013	USA	Pig
HP-1/2014	1990.4.a	Q350087	1701	1	2014	USA	Pig
4/2013	1990.4.a	Q350016	1701	1	2013	USA	Pig

Summary

- Undersurveillance, human-to-swine transmission, and IAV evolution represent a challenge for naming swine IAV
- H1 and H3 HA system uses evolutionary history and epidemiological relevance to identify and name clades
- Objective selection of HA genes for characterization can have the objective flipped to:
 - Determine whether you have good genetic representation for reference datasets
 - Address when you need to update clade names
- All USDA-ARS-NADC software is available at <https://github.com/flu-crew>



USDA flucrew

- Amy Vincent Baker
- Tavis Anderson
- Bailey Arruda
- Meghan Wymore Brand
- Alexey Markin
- Megan Thomas
- Carine Souza
- Debora Goulart
- Katharine Young
- Celeste Snyder
- Giovana Zanella
- Garrett Janzen
- Blake Inderski
- Sid Grover
- Sanket Wagle
- Sriram Vijendran
- Carl Hutter
- Thao Nguyen

Collaborators

- BV-BRC team
- Phil Gauger
- Oliver Eulenstein
- Michael Zeller
- Joe Thomas
- Alicia Janas-Martindale
- Lauren Abrahamsen
- Nicola Lewis
- Daniela Rajao
- Daniel Perez
- John Barnes/CDC
- Han Di/CDC
- Todd Davis/CDC
- OFFLU

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