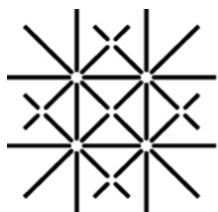


Rapid, Relatable, and Real-Time: Pathogen Tracking with Nextstrain

Dr. Emma B Hodcroft

Neher Lab



Universität
Basel

BIOZENTRUM

University of Basel
The Center for
Molecular Life Sciences

Thanks...



Richard
Neher



Trevor
Bedford



James
Hadfield



John
Huddleston



Tom
Sibley



Sidney
Bell



Robert Dyrdak

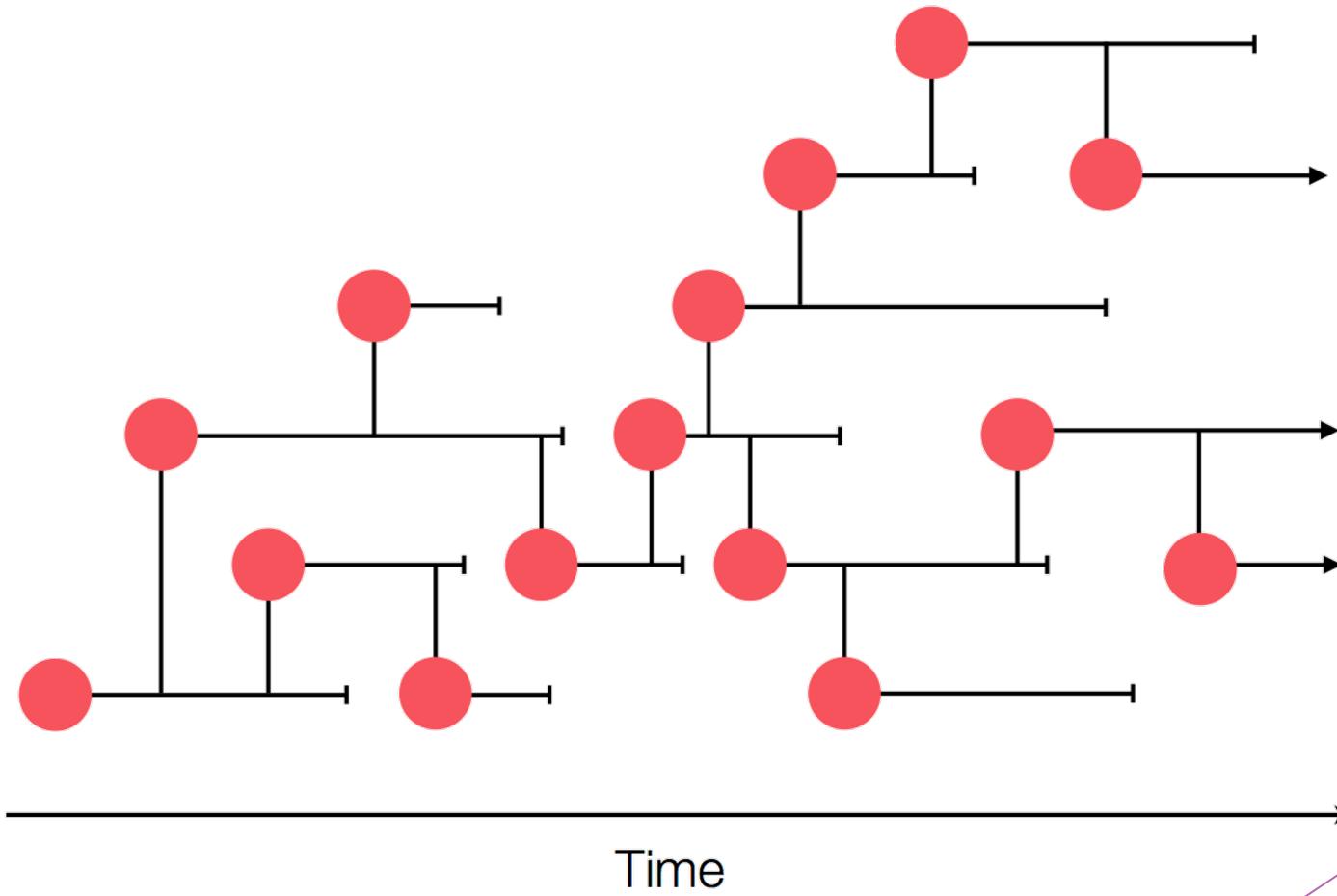


Monika Mastafa

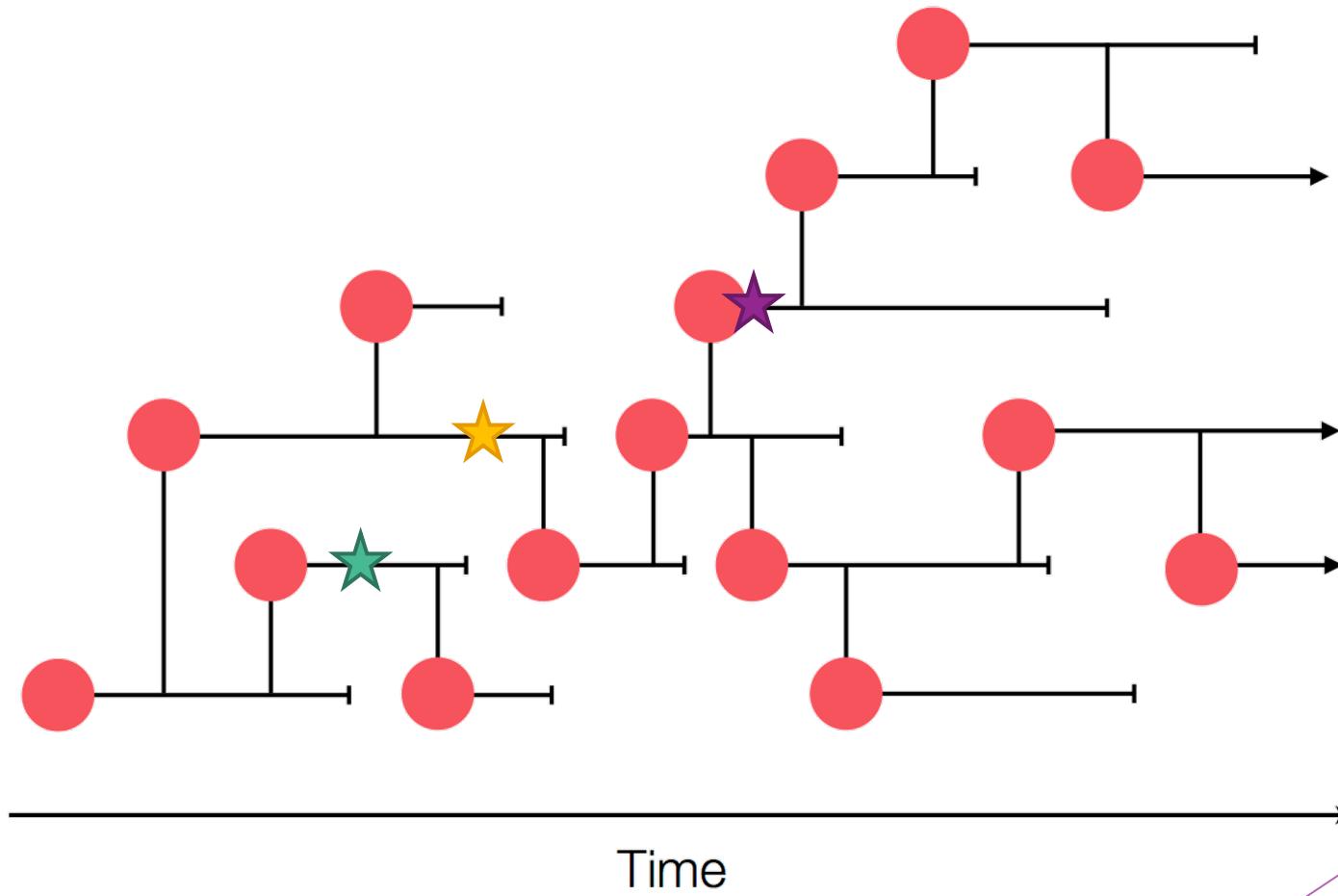


Jan Albert

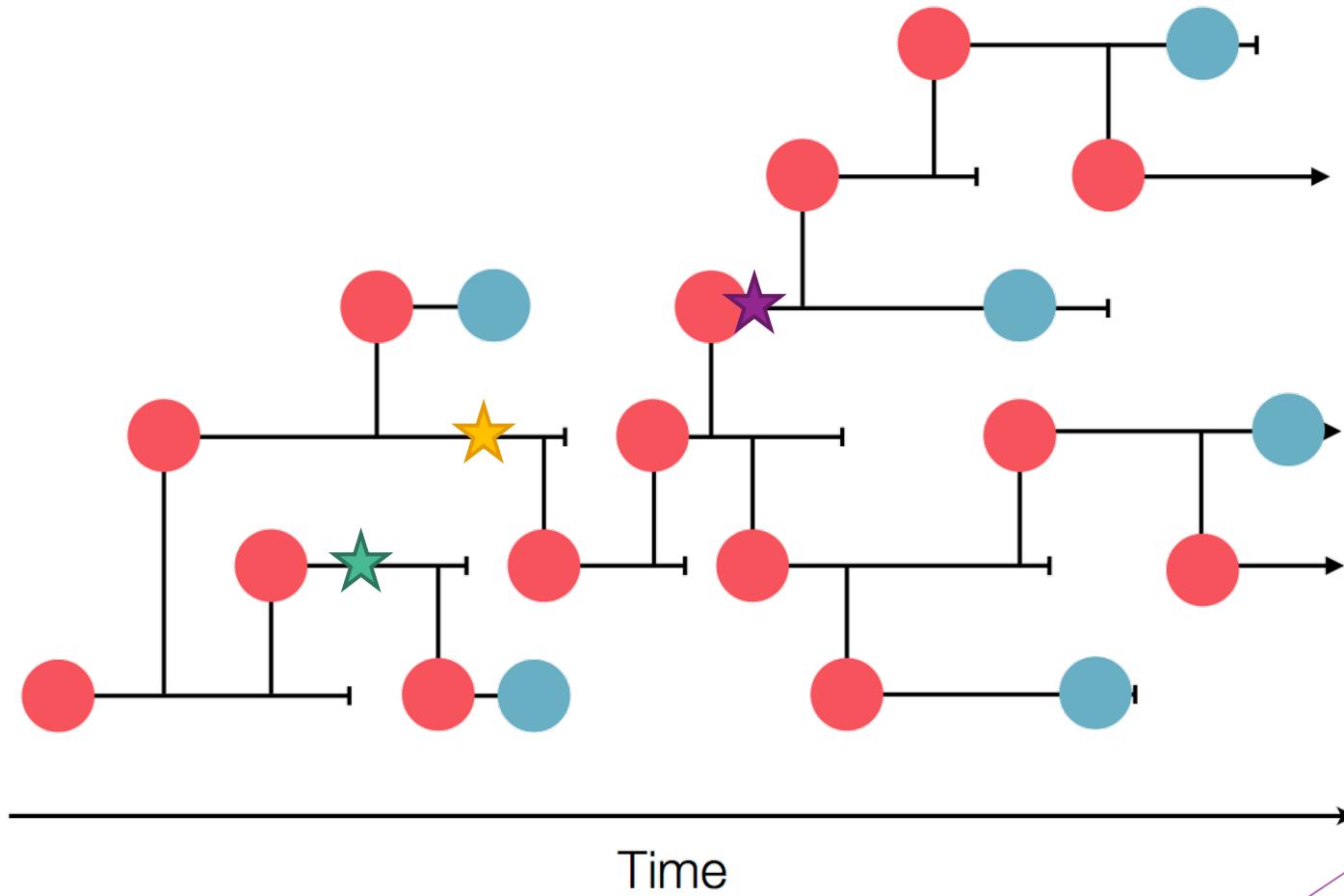
Sequencing Pathogens



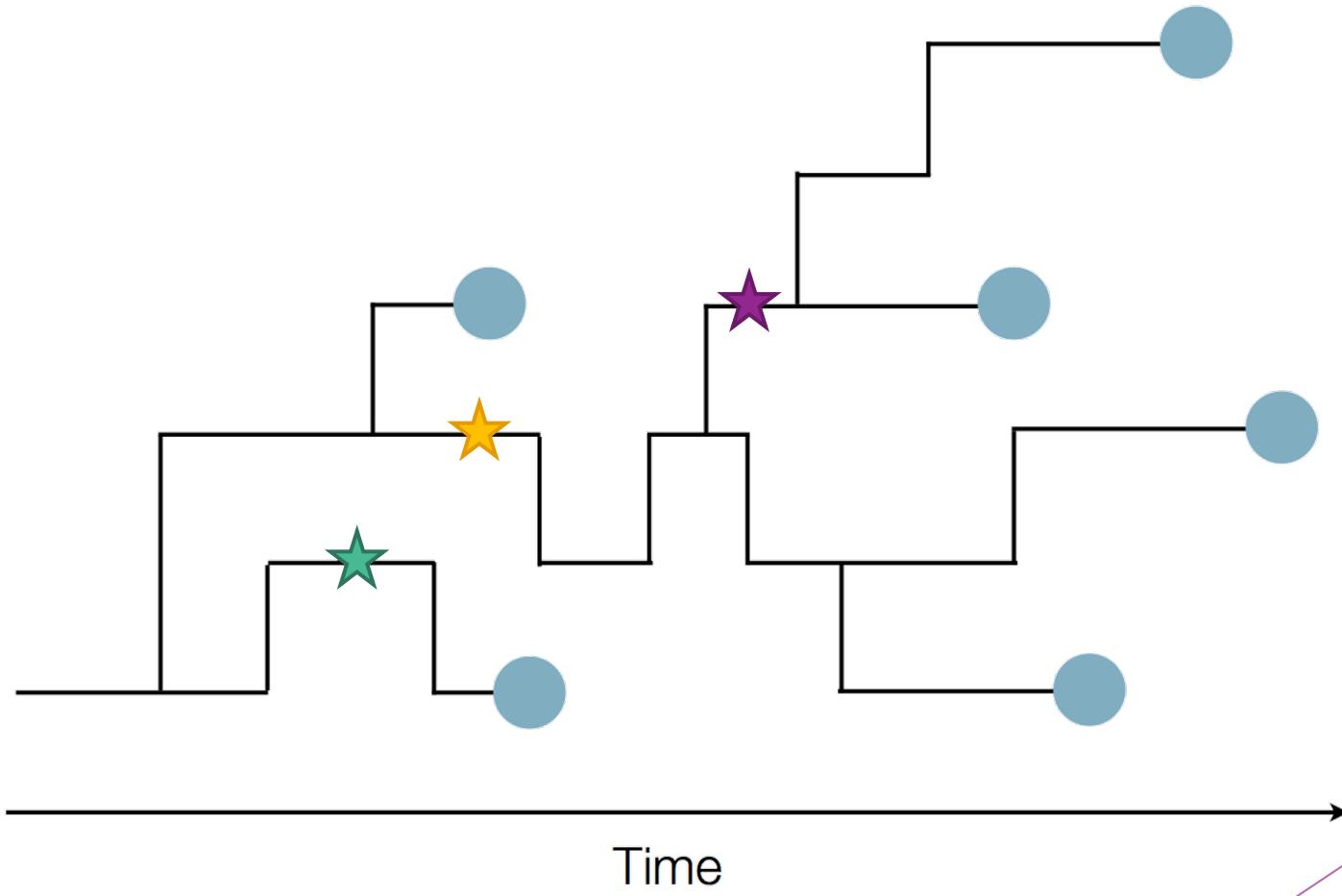
Sequencing Pathogens



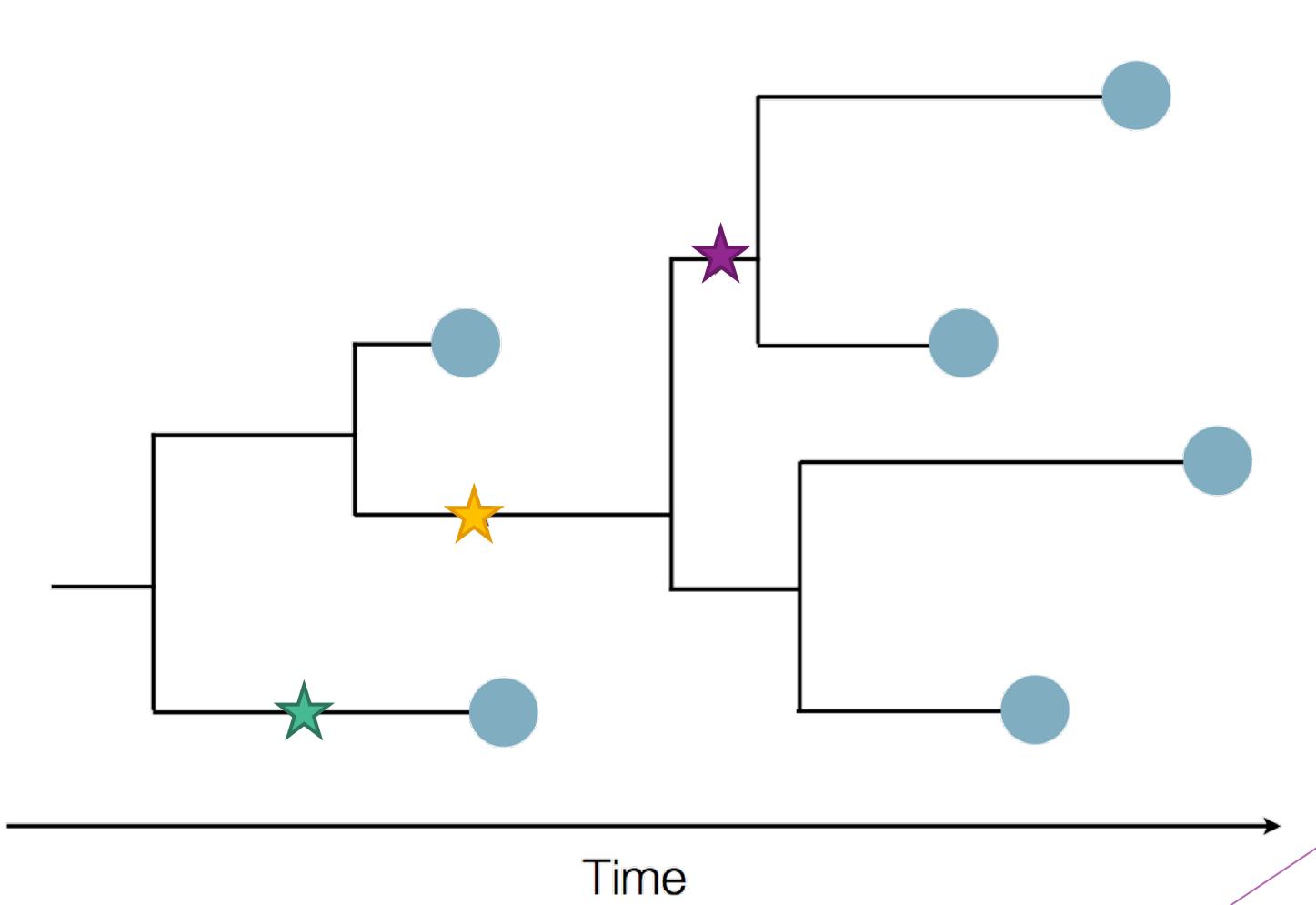
Sequencing Pathogens



Sequencing Pathogens



Sequencing Pathogens



A pathogen phylogenetic analysis tool
should be...

Relevant

Flexible

Communicable

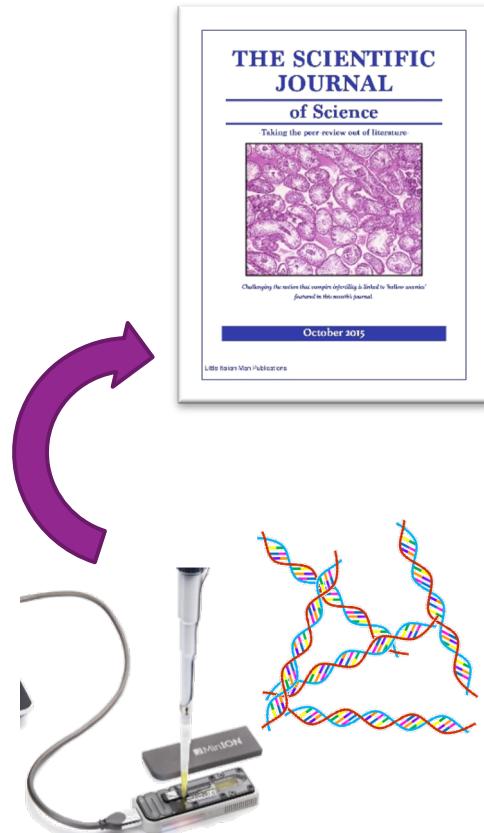
Useful Phylogenetic Analyses

Updatable • Real-time • Repeatable

Relevant

Flexible

Communicable



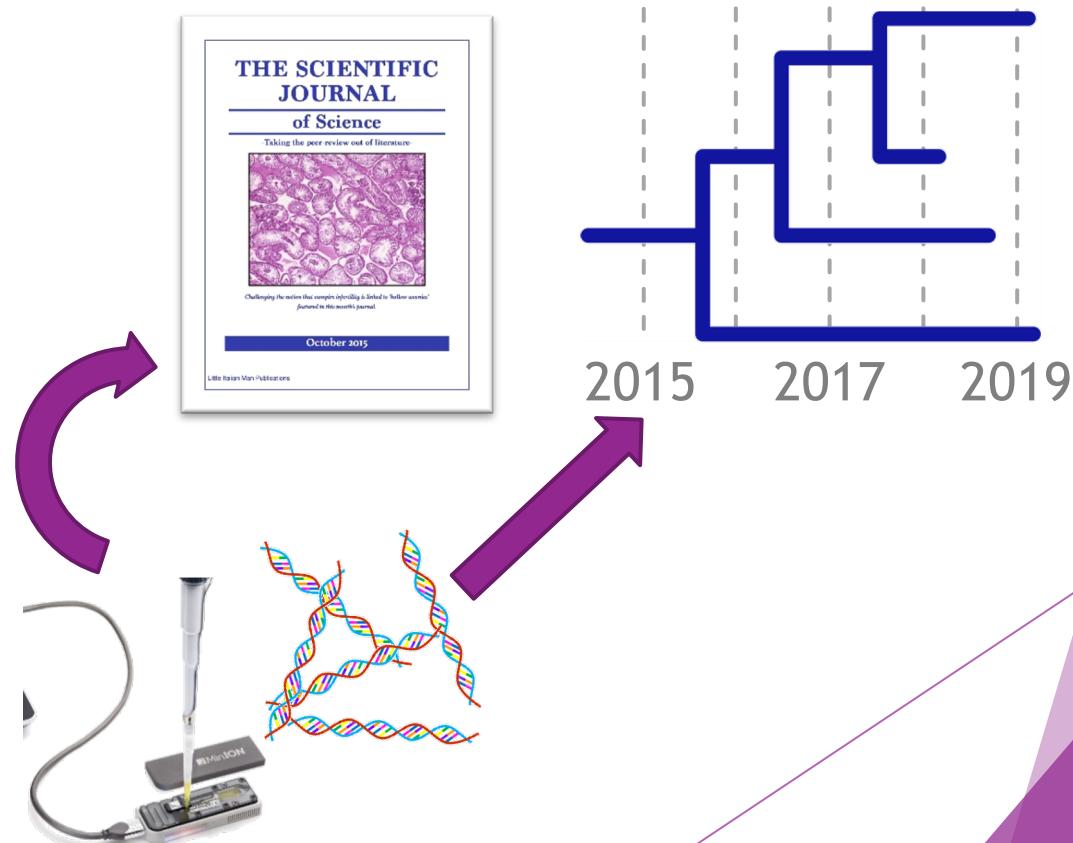
Useful Phylogenetic Analyses

Updatable • Real-time • Repeatable

Relevant

Flexible

Communicable



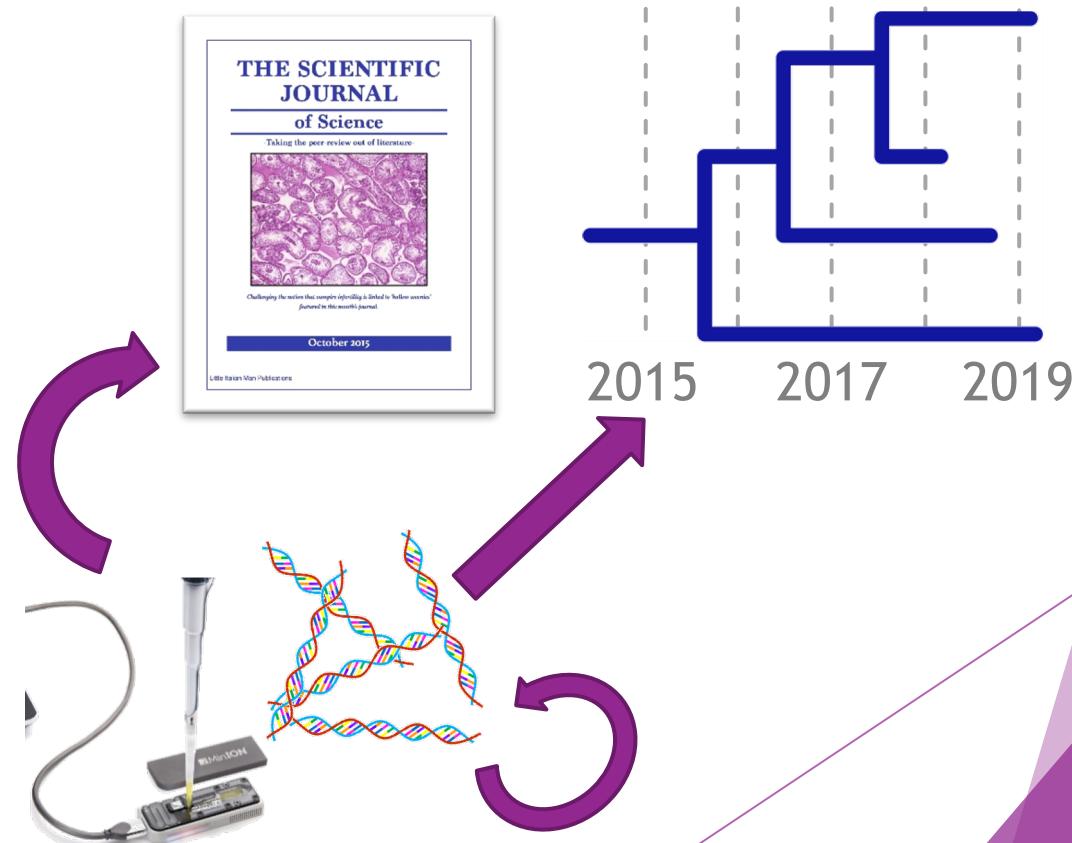
Useful Phylogenetic Analyses

Updatable • Real-time • Repeatable

Relevant

Flexible

Communicable



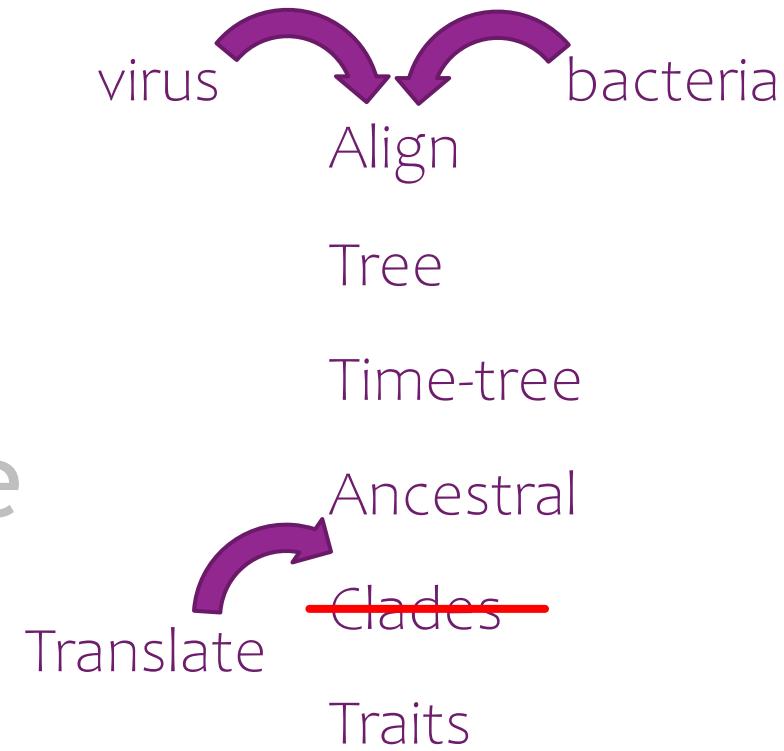
Useful Phylogenetic Analyses

Composable • Compatible • Controllable

Relevant

Flexible

Communicable



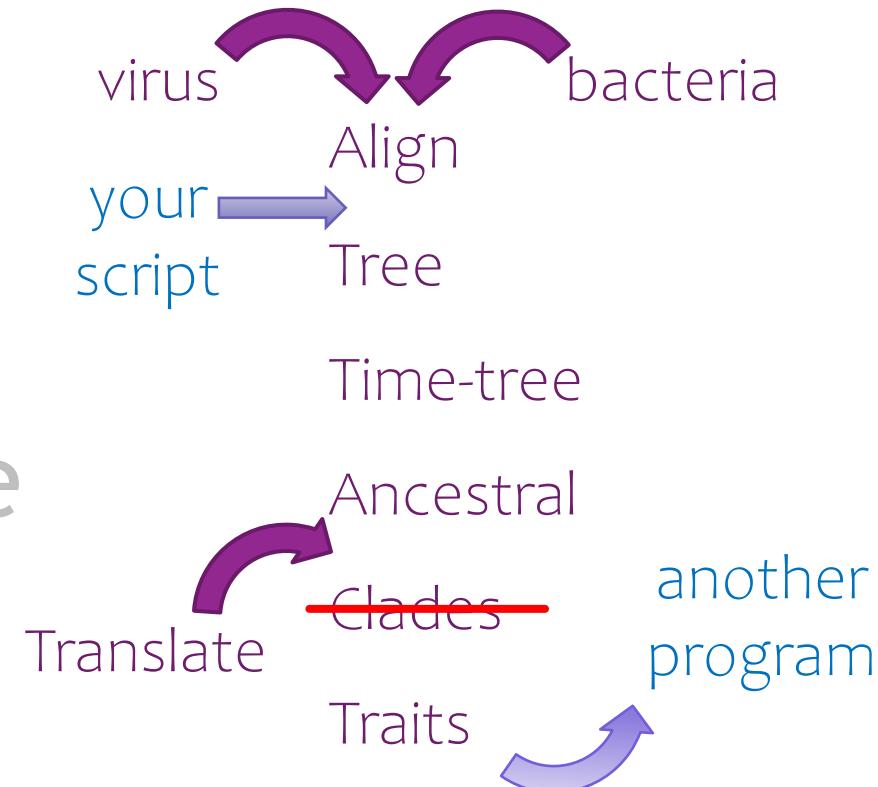
Useful Phylogenetic Analyses

Composable • Compatible • Controllable

Relevant

Flexible

Communicable



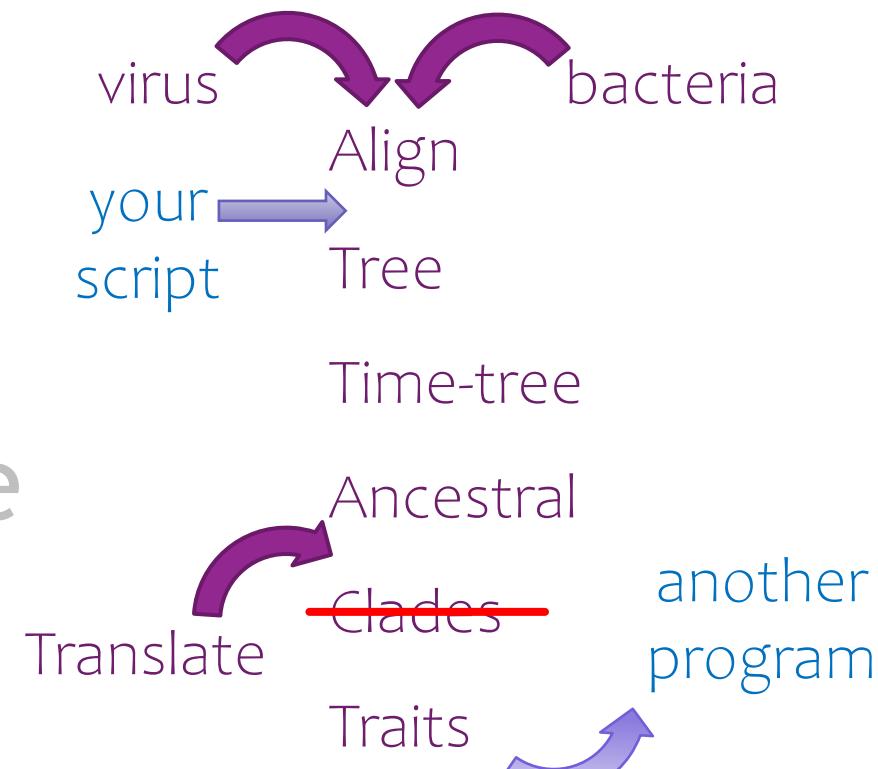
Useful Phylogenetic Analyses

Composable • Compatible • Controllable

Relevant

Flexible

Communicable



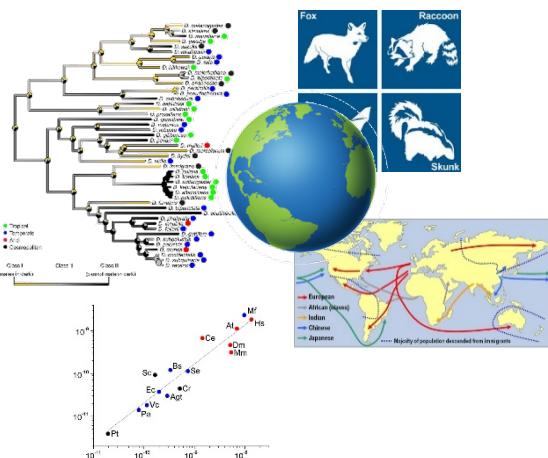
Useful Phylogenetic Analyses

Relevant

Flexible

Communicable

Comprehensive • Intuitive
Shareable • Explainable



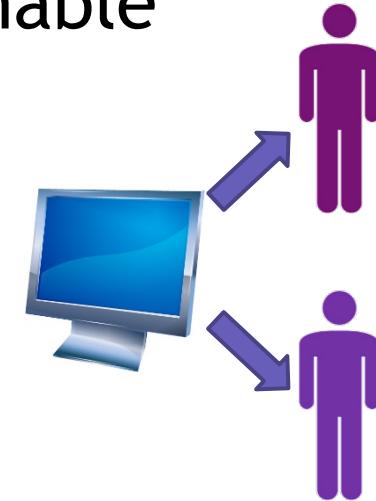
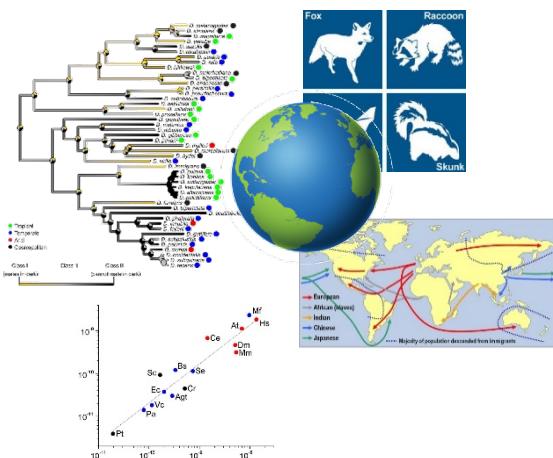
Useful Phylogenetic Analyses

Relevant

Flexible

Communicable

Comprehensive • Intuitive
Shareable • Explainable



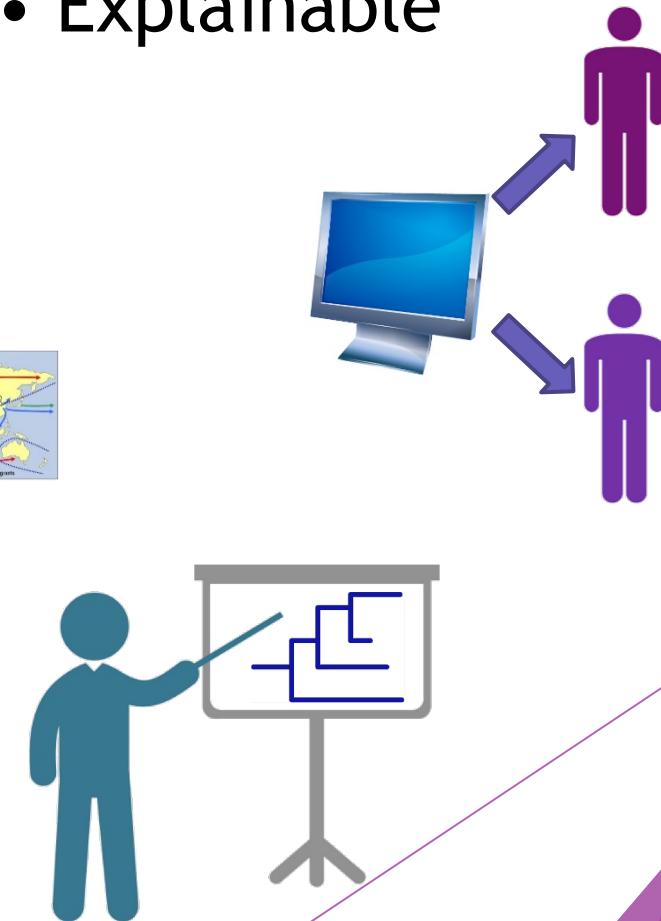
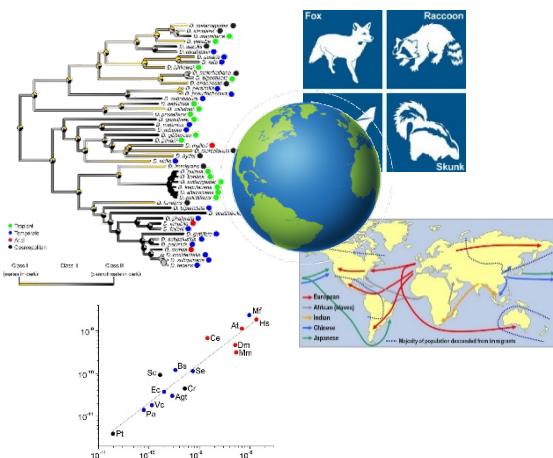
Useful Phylogenetic Analyses

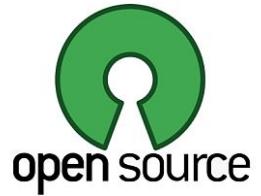
Relevant

Flexible

Communicable

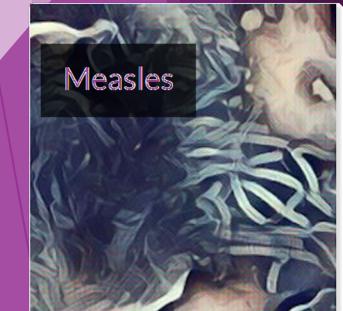
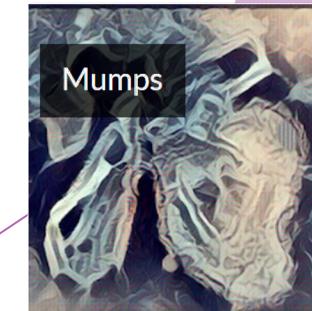
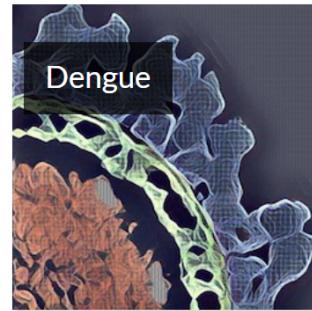
Comprehensive • Intuitive
Shareable • Explainable





nextstrain

- Innovative and intuitive interface
- Track epidemics/pandemics in real-time
- Mutations, antigen change, traits, geography



- Free! Open-source!
- University-associated



Nextstrain examples...



Nathan Grubaugh
@NathanGrubaugh

What is going on with EEE? It's not like there are hundreds of cases, but with a high fatality rate, this is scary.

Getting texts from family in Michigan very worried about this virus. Not sure what to say (other than protective practices).

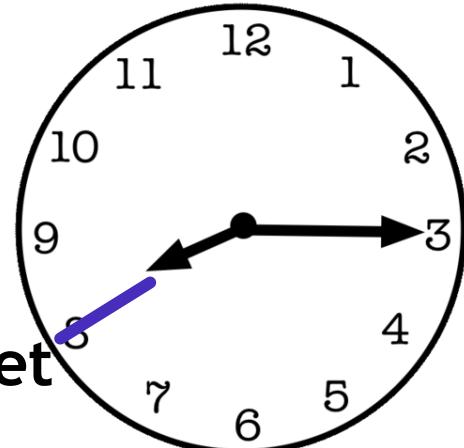


Derek Trobaugh @Alphalimmune · Sep 21

9th person diagnosed with EEE in Mass., health officials say boston.com/news/health/20... via @BostonDotCom

5:35 PM · Sep 21, 2019 · Twitter Web App

See tweet



Eastern Equine Encephalitis



Nathan Grubaugh
@NathanGrubaugh

What is going on with EEE? It's not like there are hundreds of cases, but with a high fatality rate, this is scary.

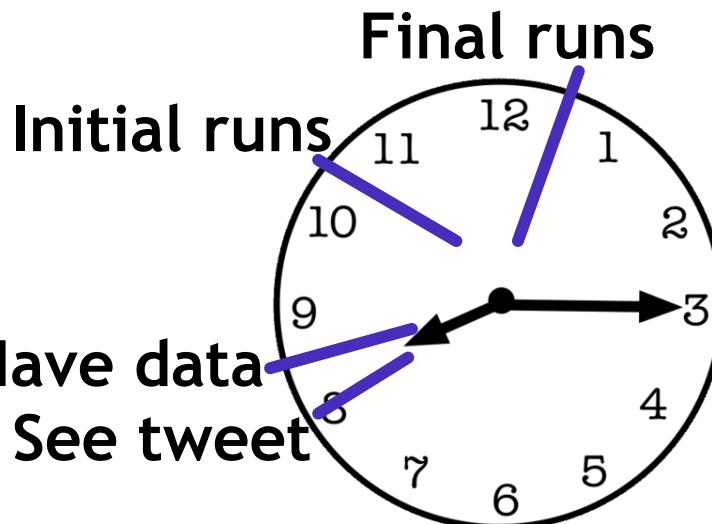
Getting texts from family in Michigan very worried about this virus. Not sure what to say (other than protective practices).



Derek Trobaugh @Alphalimmune · Sep 21

9th person diagnosed with EEE in Mass., health officials say boston.com/news/health/20... via @BostonDotCom

5:35 PM · Sep 21, 2019 · Twitter Web App



Eastern Equine Encephalitis



Nathan Grubaugh
@NathanGrubaugh

What is going on with EEE? It's not like there are hundreds of cases, but with a high fatality rate, this is scary.

Getting texts from family in Michigan very worried about this virus. Not sure what to say (other than protective practices).

Derek Trobaugh @
9th person diagnosed w
boston.com/news/health

5:35 PM · Sep 21, 2019 · T



Dr Emma Hodcroft @firefoxx66 · Sep 23

Replies to @NathanGrubaugh

I couldn't find anything really past 2014, but if anyone turns up more recent sequences just shout and I'll throw them in...

nextstrain.org/community/emma...

1 reply · 1 retweet · 5 likes



Dr Emma Hodcroft @firefoxx66 · Sep 23

This is a pull of all full-genome EEE on ViPR as of 22 Sept, minus some highly divergent ones throwing things off.

1 reply · 1 retweet · 1 like



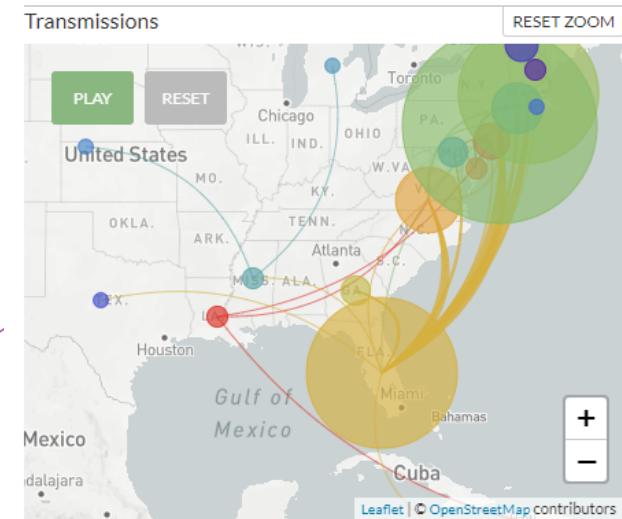
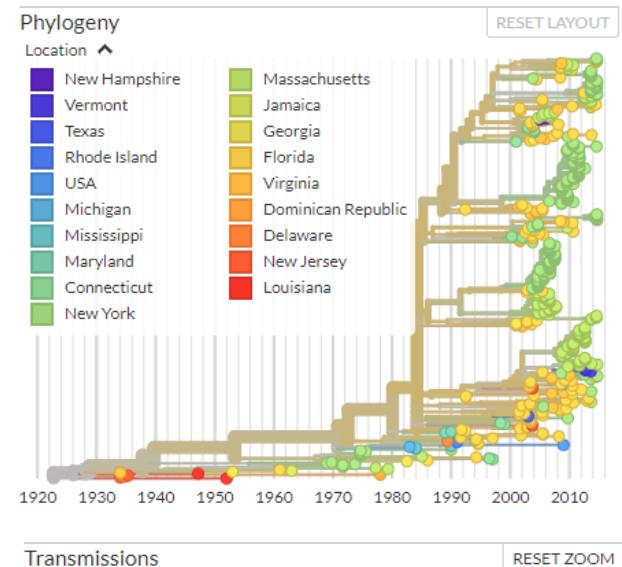
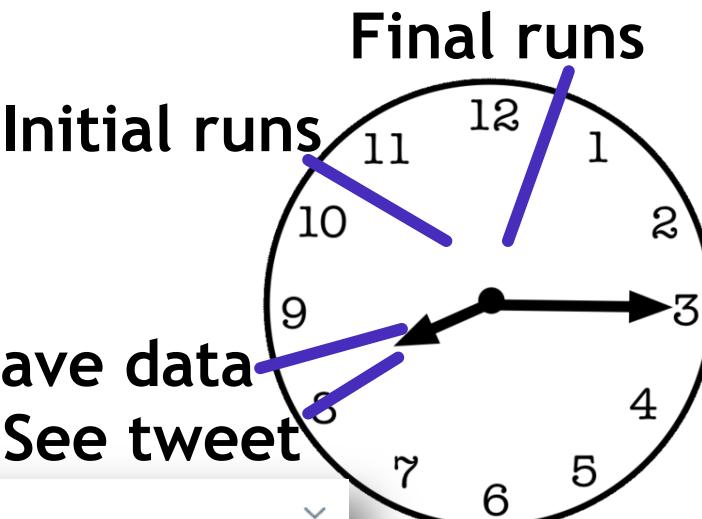
Nathan Grubaugh @NathanGrubaugh · Sep 23

so... let me get this straight. We're having this twitter conversation about EEE, then you just, um...

[this is where things are getting fuzzy]

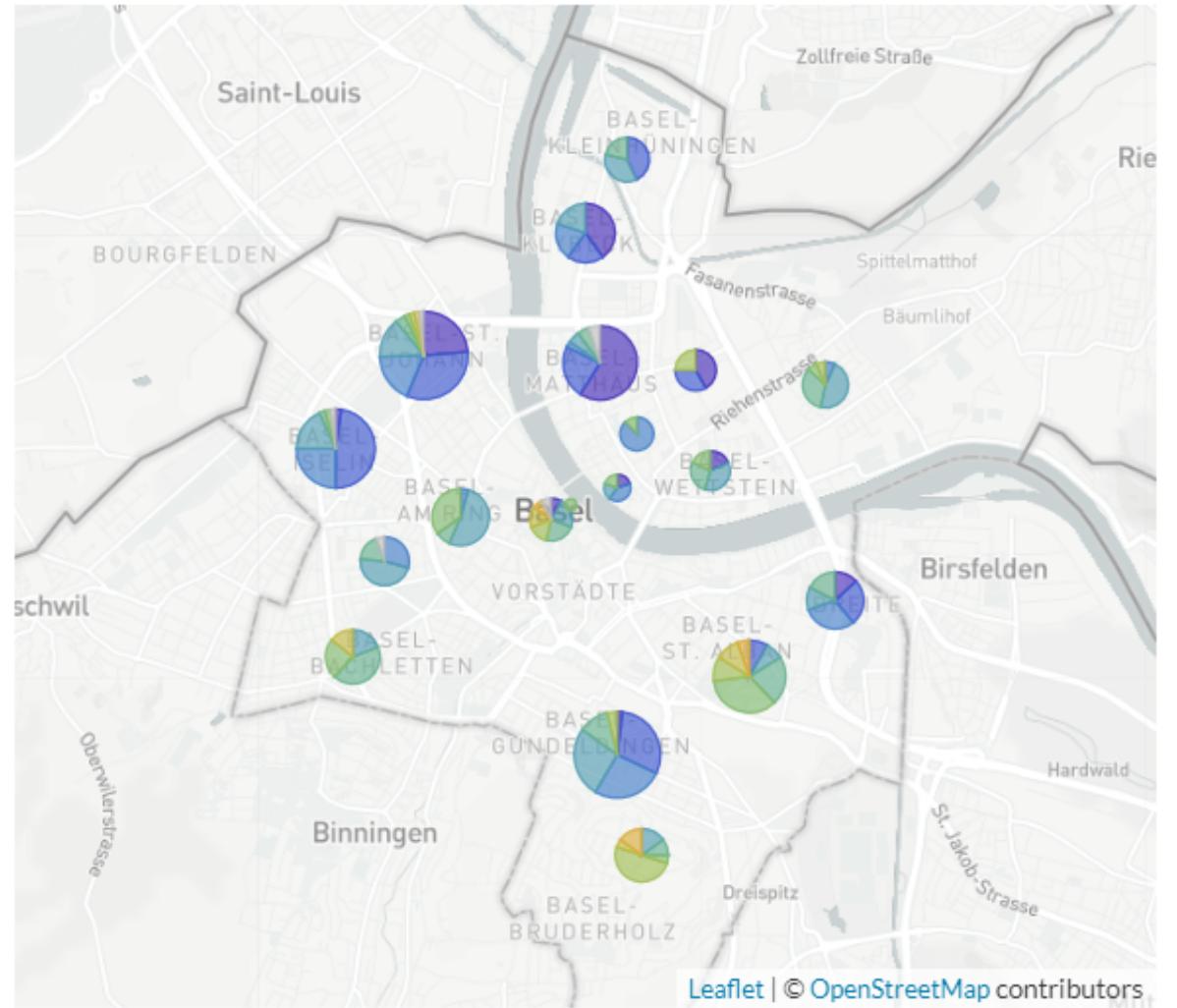
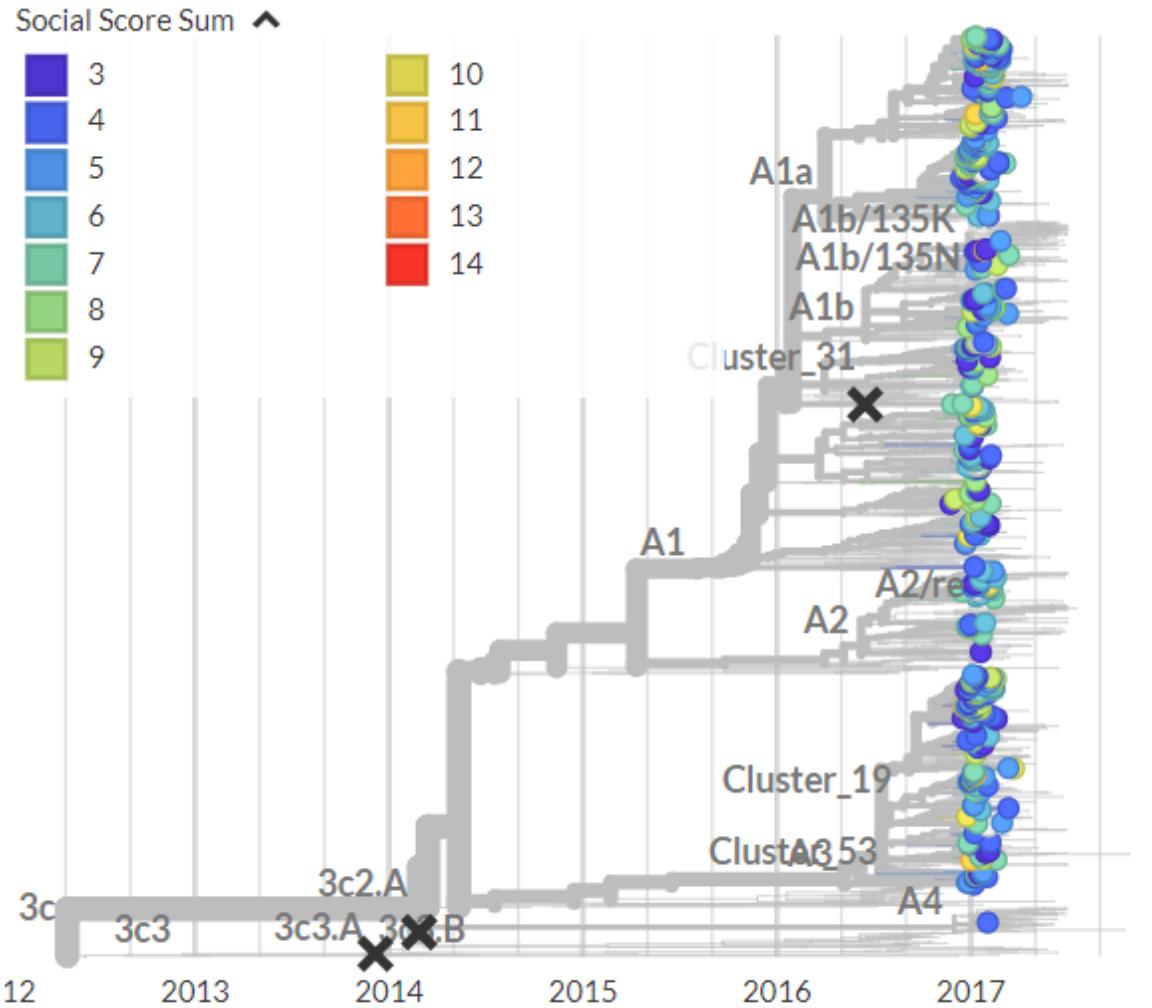
download all of the EEE data and whip together a Nextstrain community build

and, ah, just casually drop it in the thread??

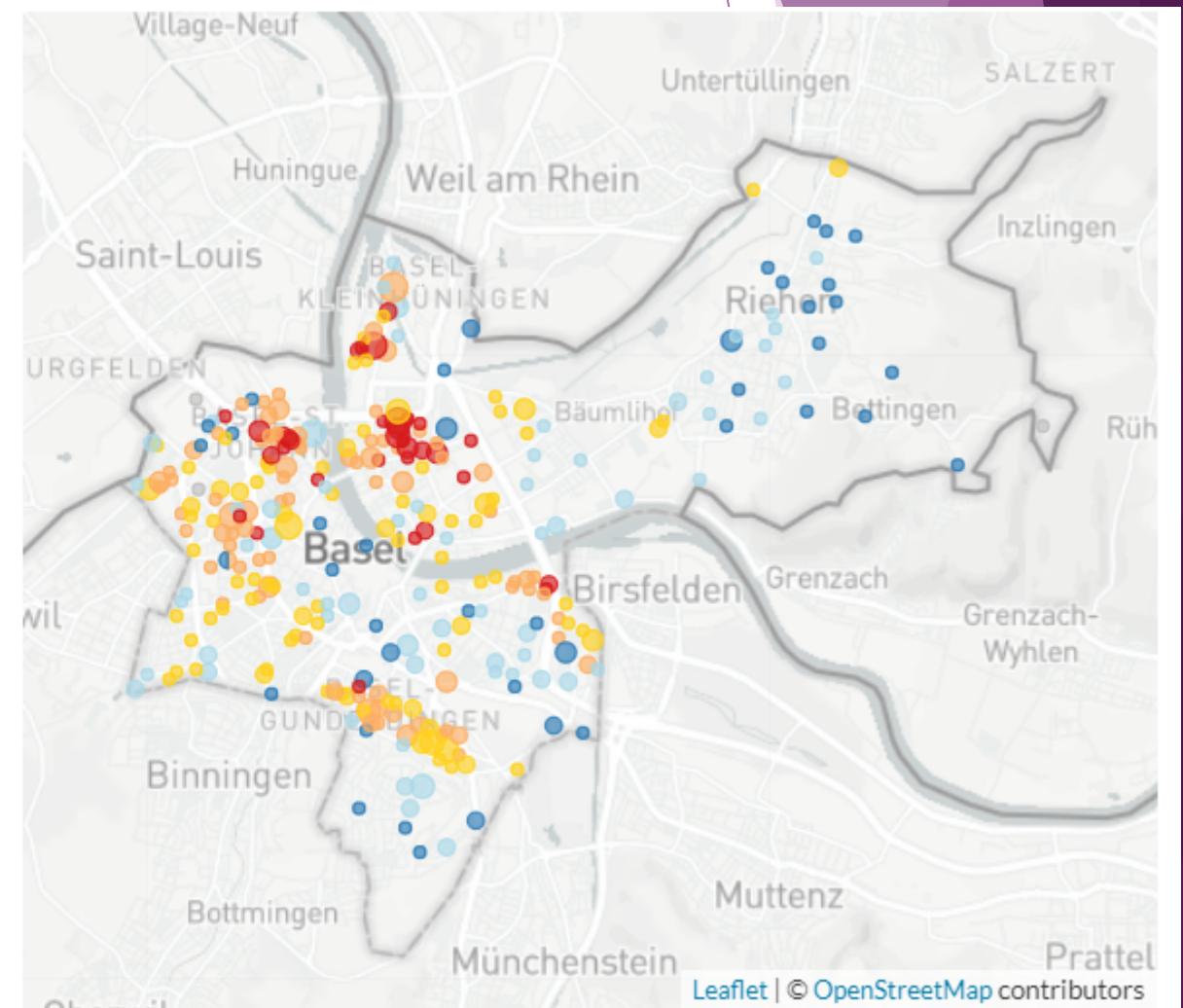
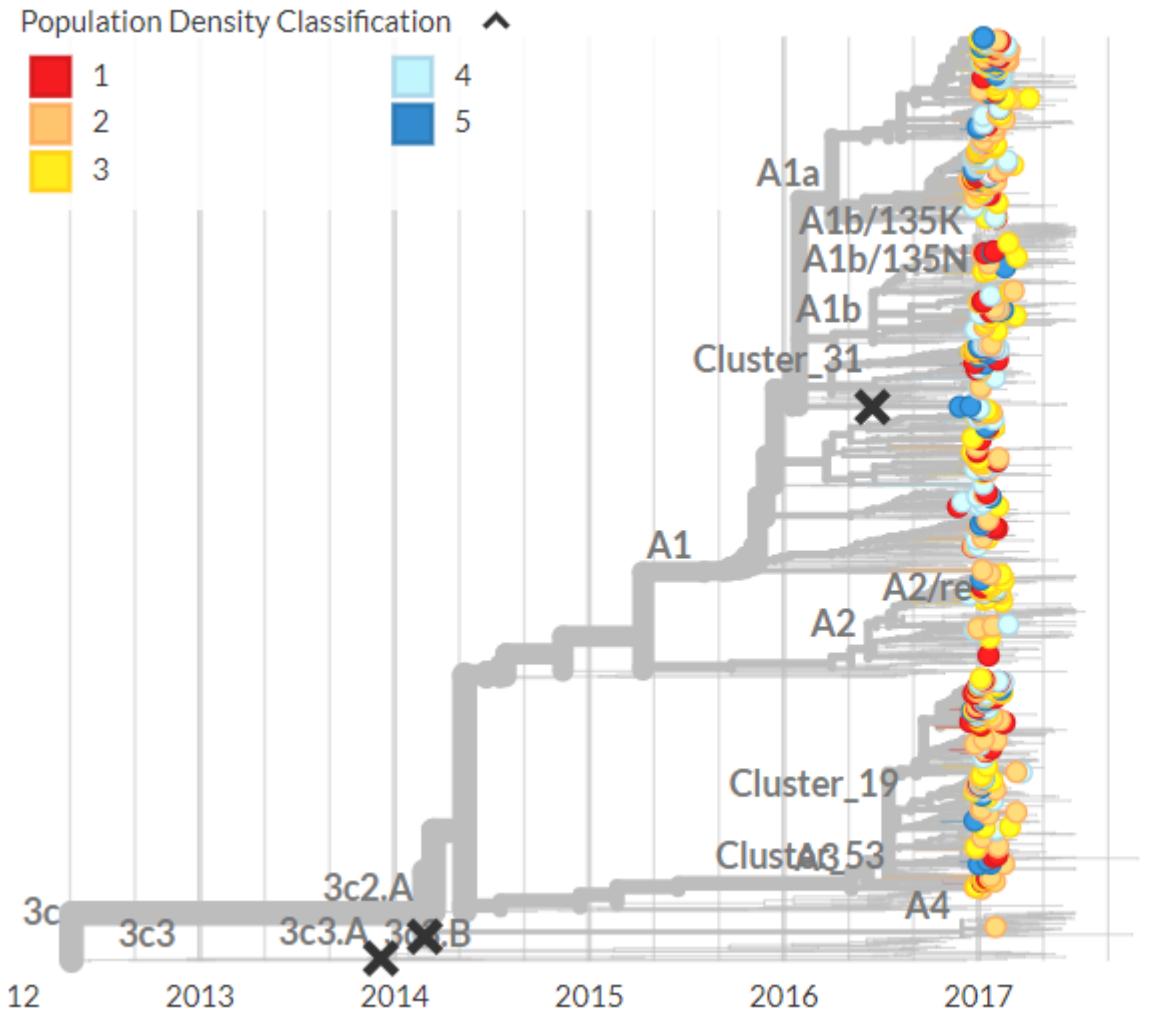


Eastern Equine Encephalitis

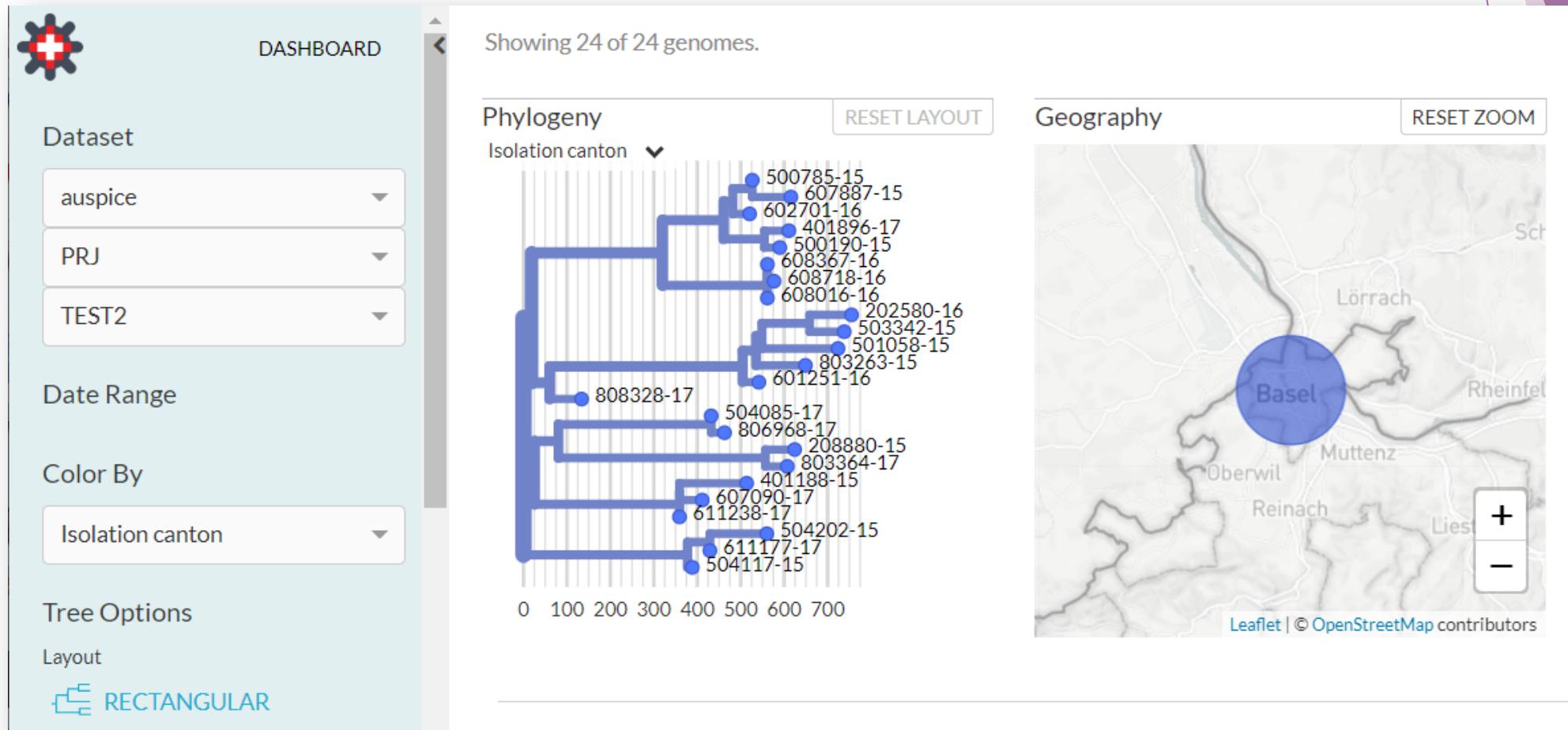
Fine-scale Location & Socioeconomic Data



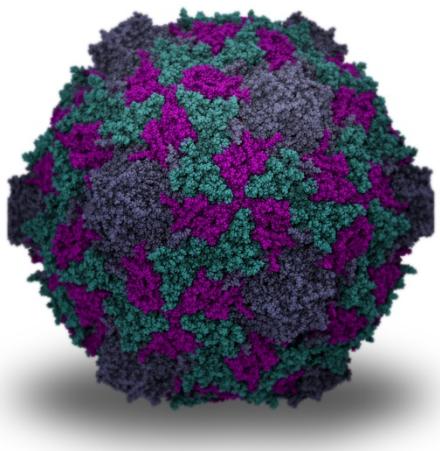
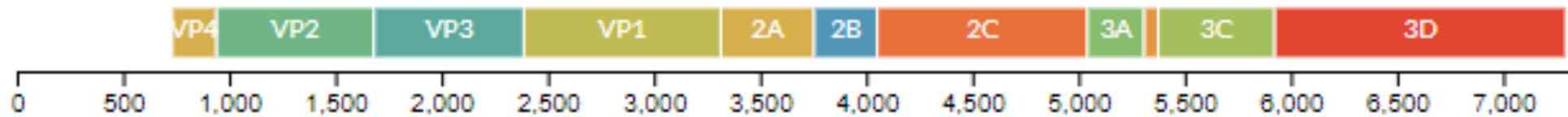
Fine-scale Location & Socioeconomic Data



Secure, Internal Setups

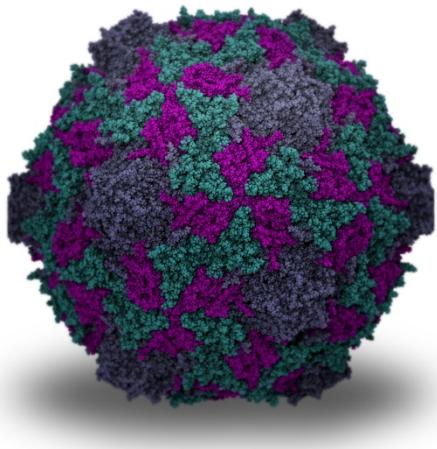
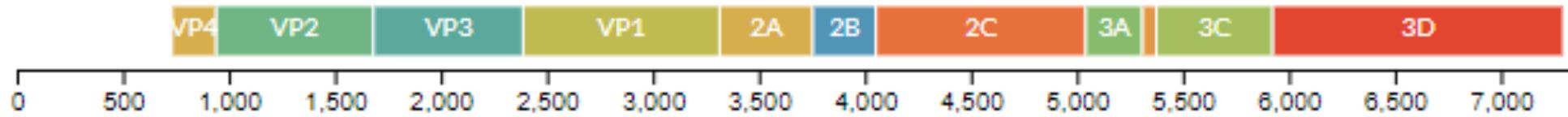


Enterovirus D68 (EV-D68)

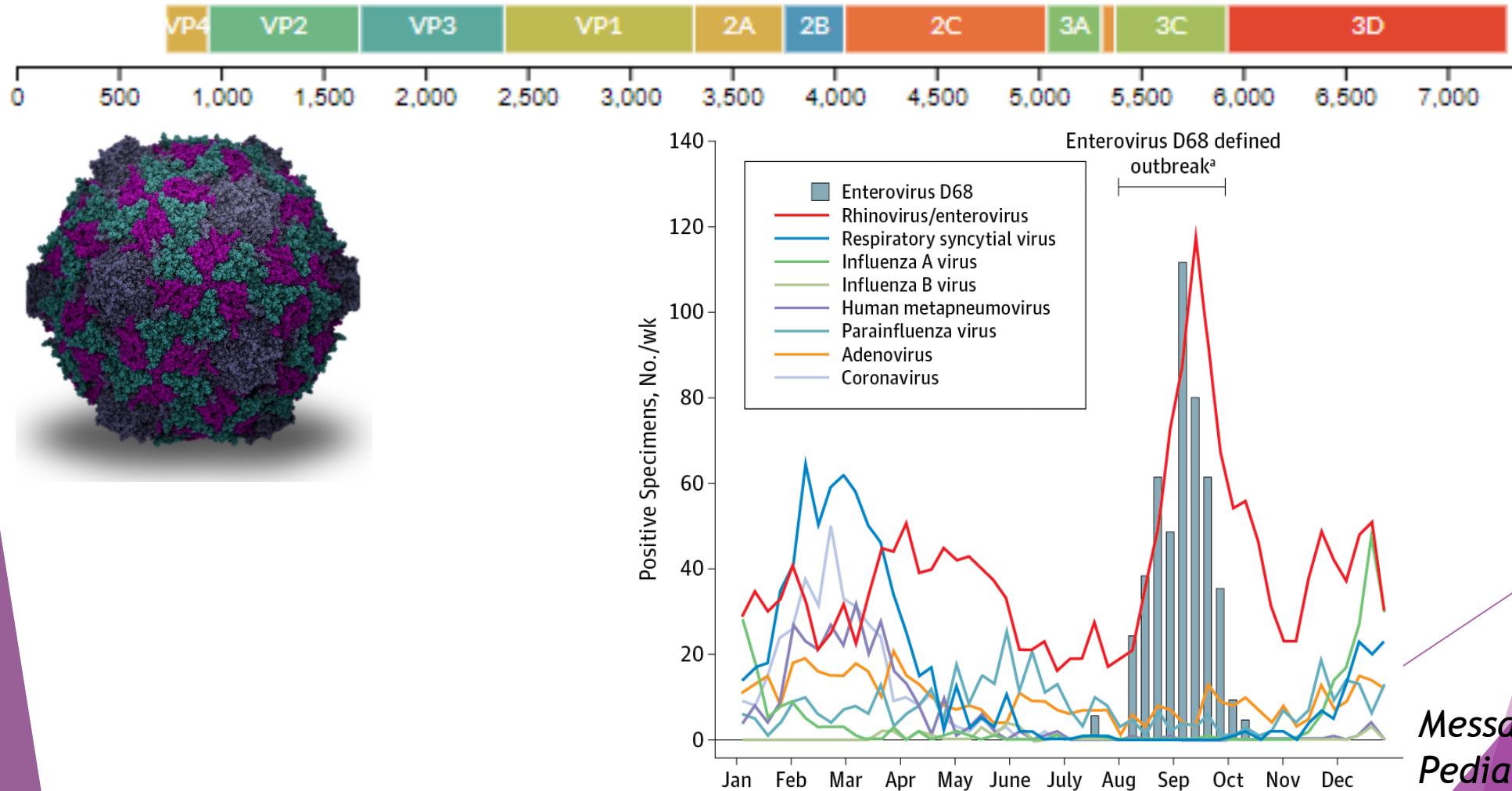


- ▶ Picornavirus
- ▶ Discovered 1962 California

Enterovirus D68 (EV-D68)

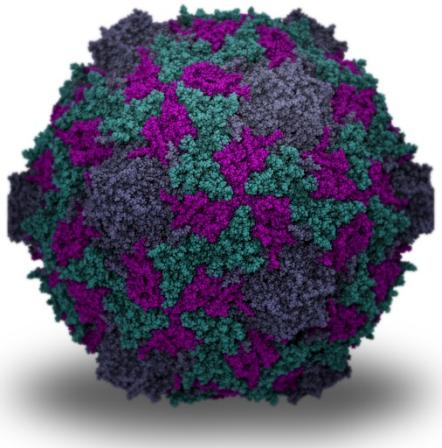
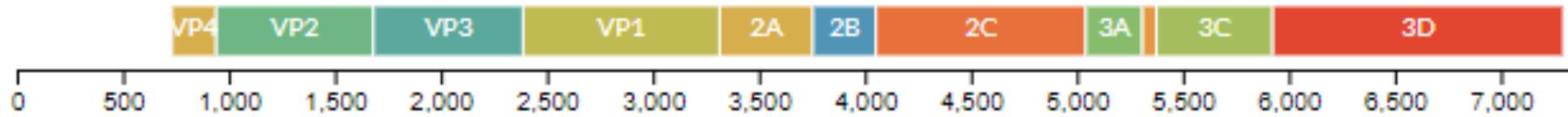


Enterovirus D68 (EV-D68)



Messacar et al. JAMA
Pediatrics. 170(3). 2016

Enterovirus D68 (EV-D68)



Symptoms of Acute Flaccid Myelitis (AFM)

AFM is a rare but serious condition that affects the nervous system.



Difficulty moving eyes or drooping eyelids



Facial droop or weakness



Difficulty swallowing or slurred speech



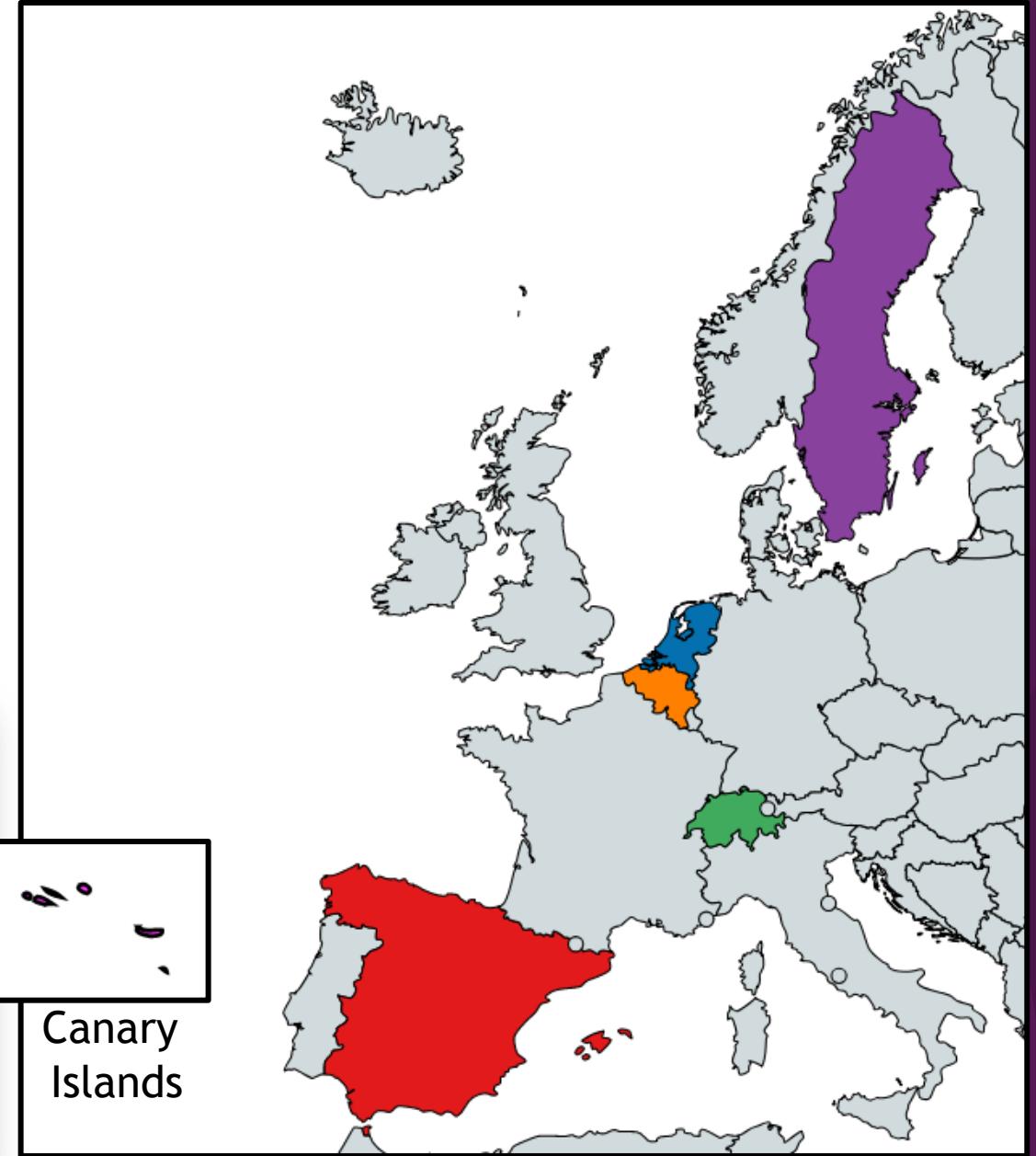
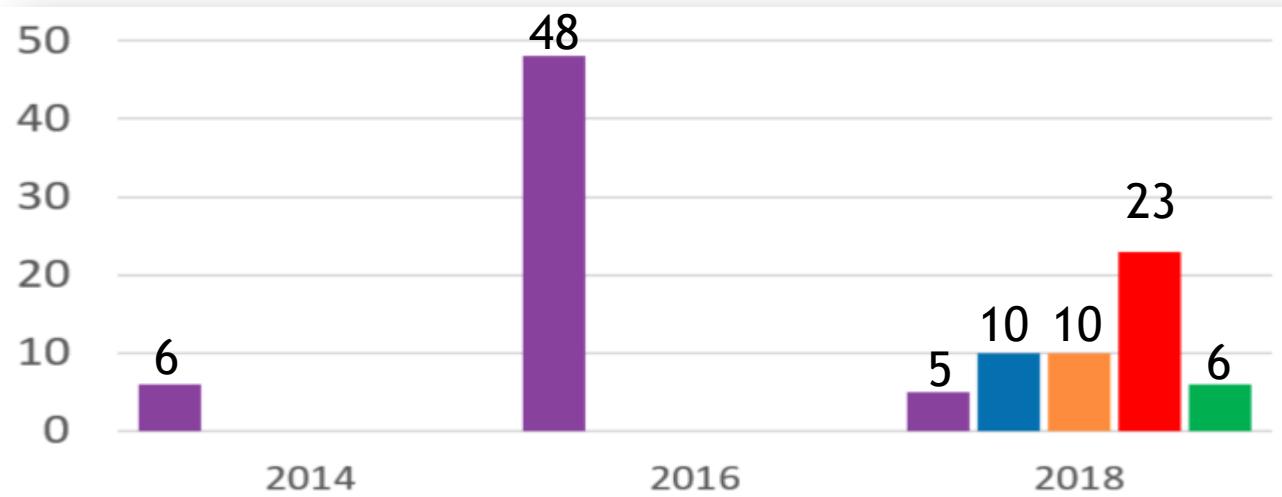
Sudden arm or leg weakness



pennsylvania
DEPARTMENT OF HEALTH

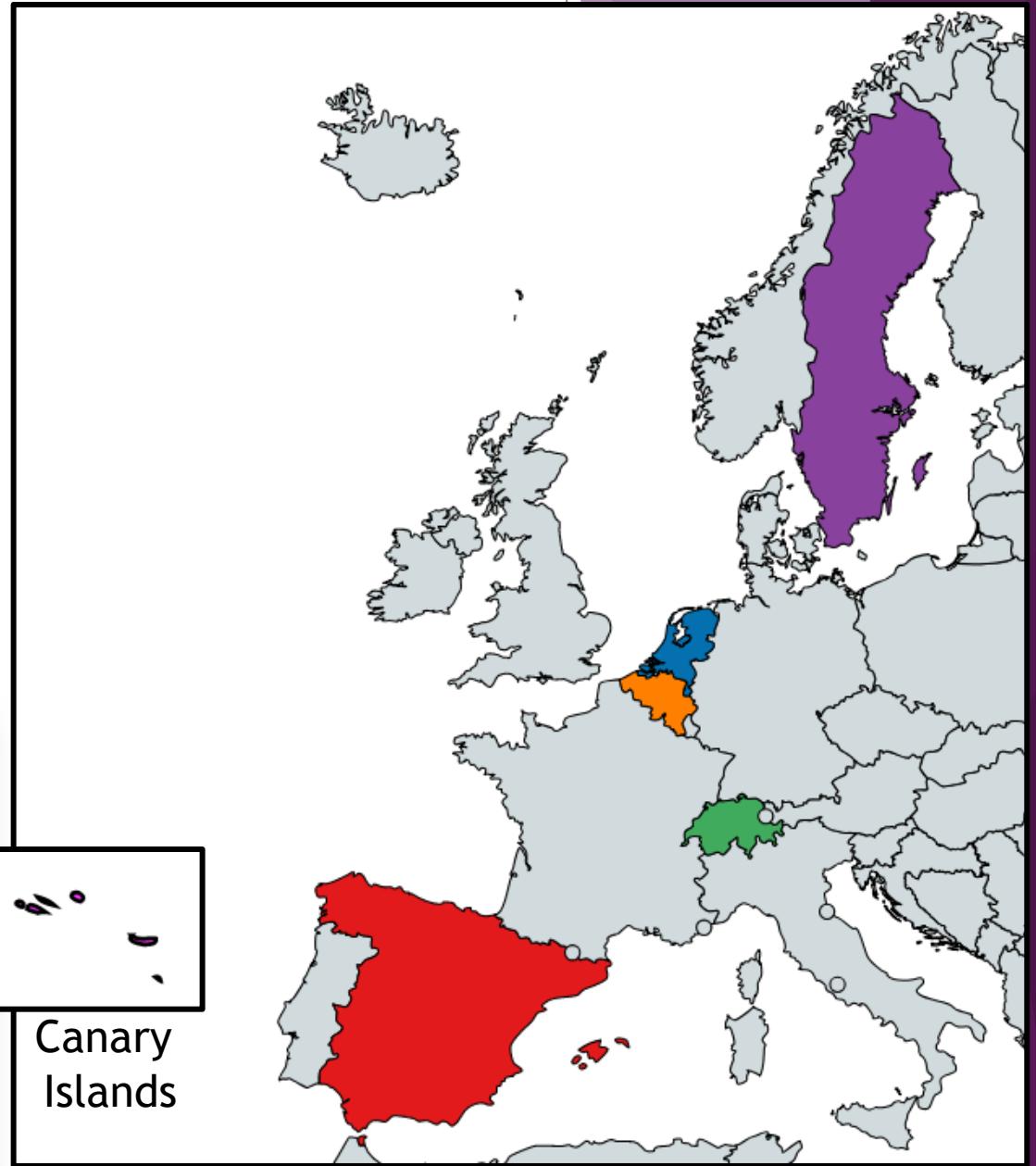
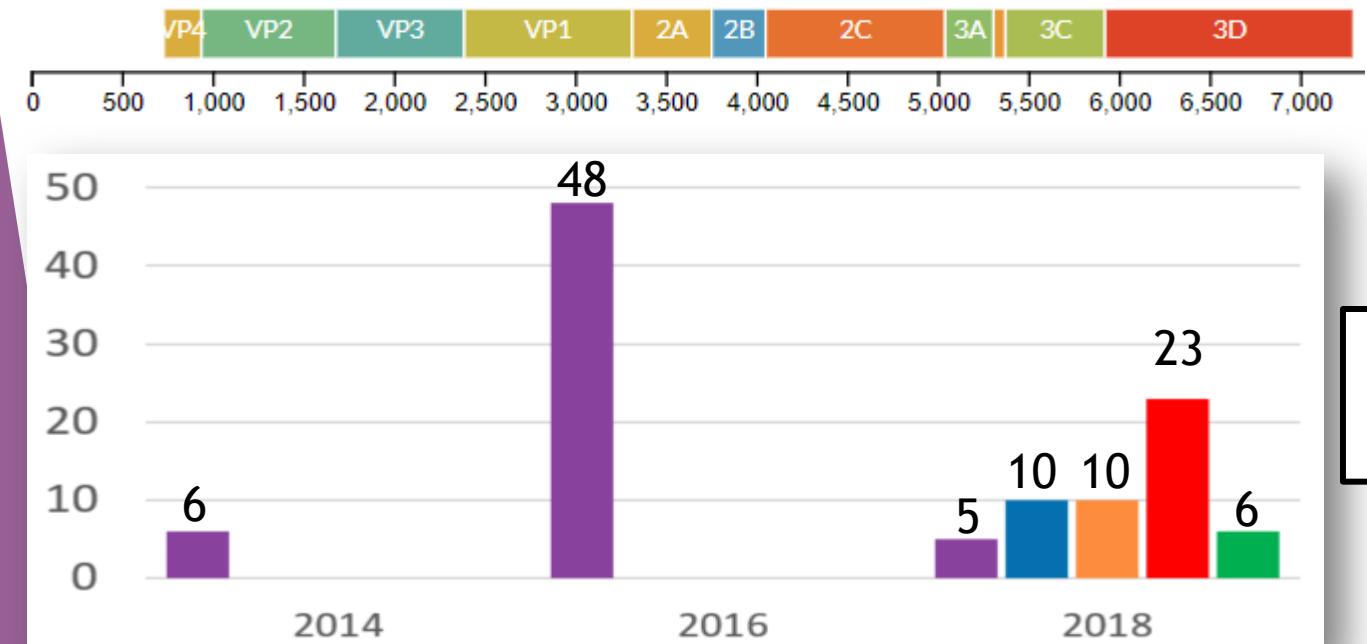
Our Samples

- ▶ 99 samples WGS sequenced in Sweden



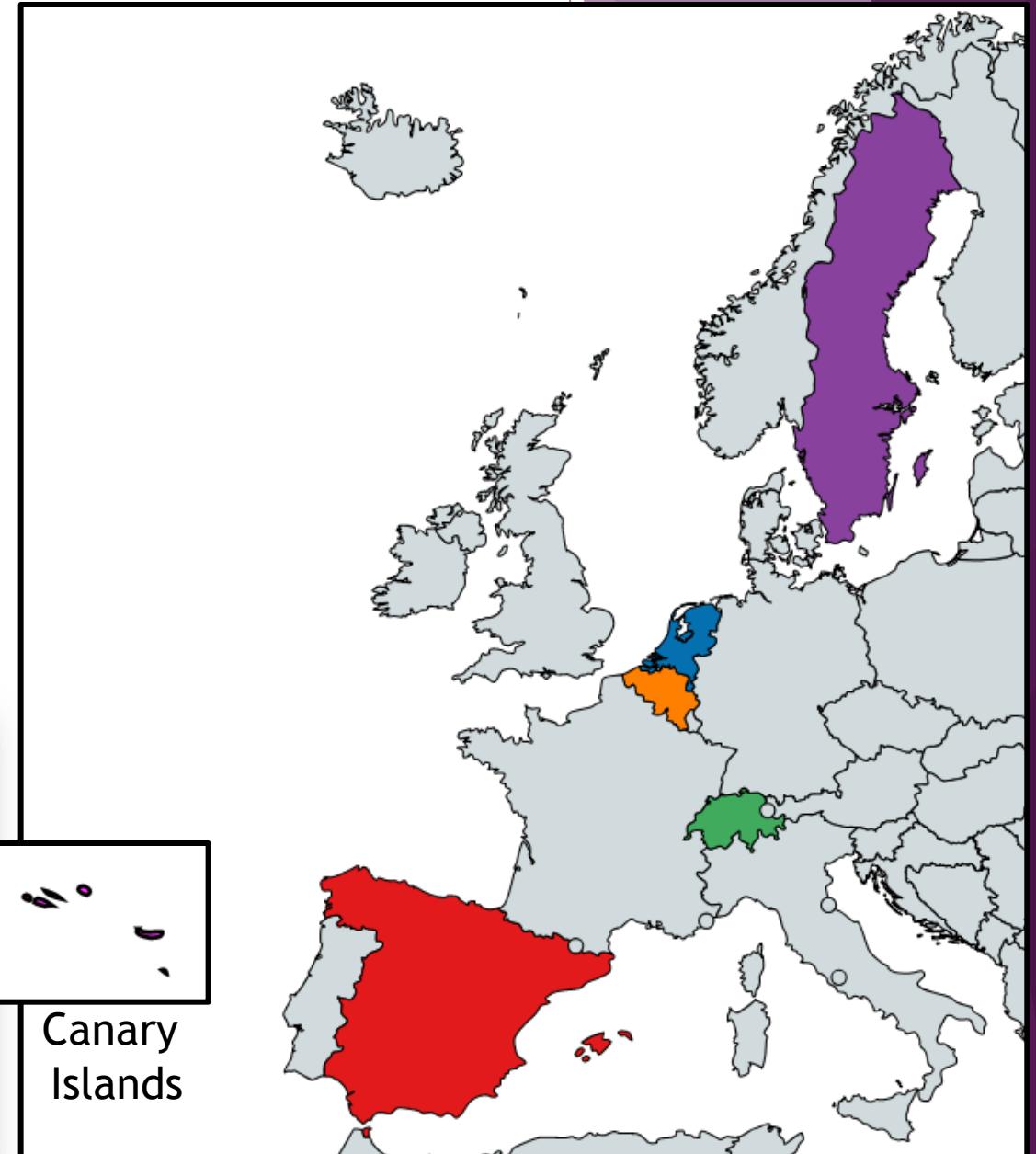
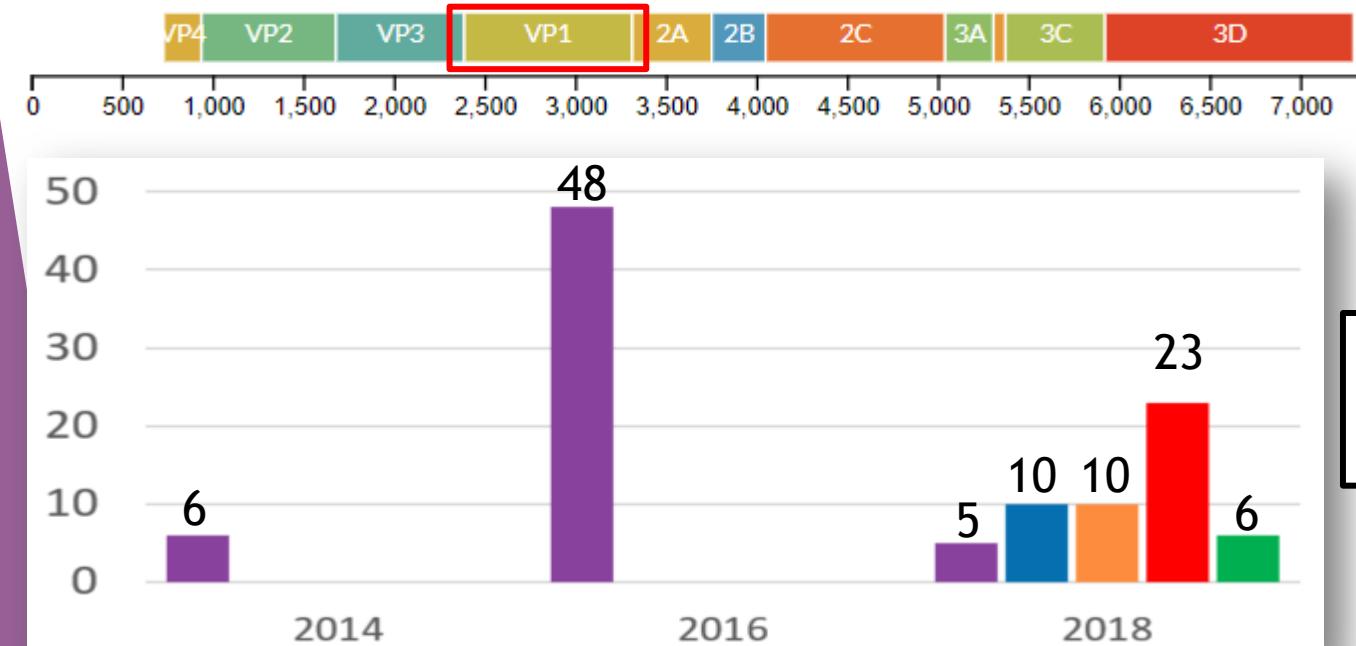
Our Samples

- ▶ 99 samples WGS sequenced in Sweden
- ▶ Combined with ~700 full length sequences from ViPR



Our Samples

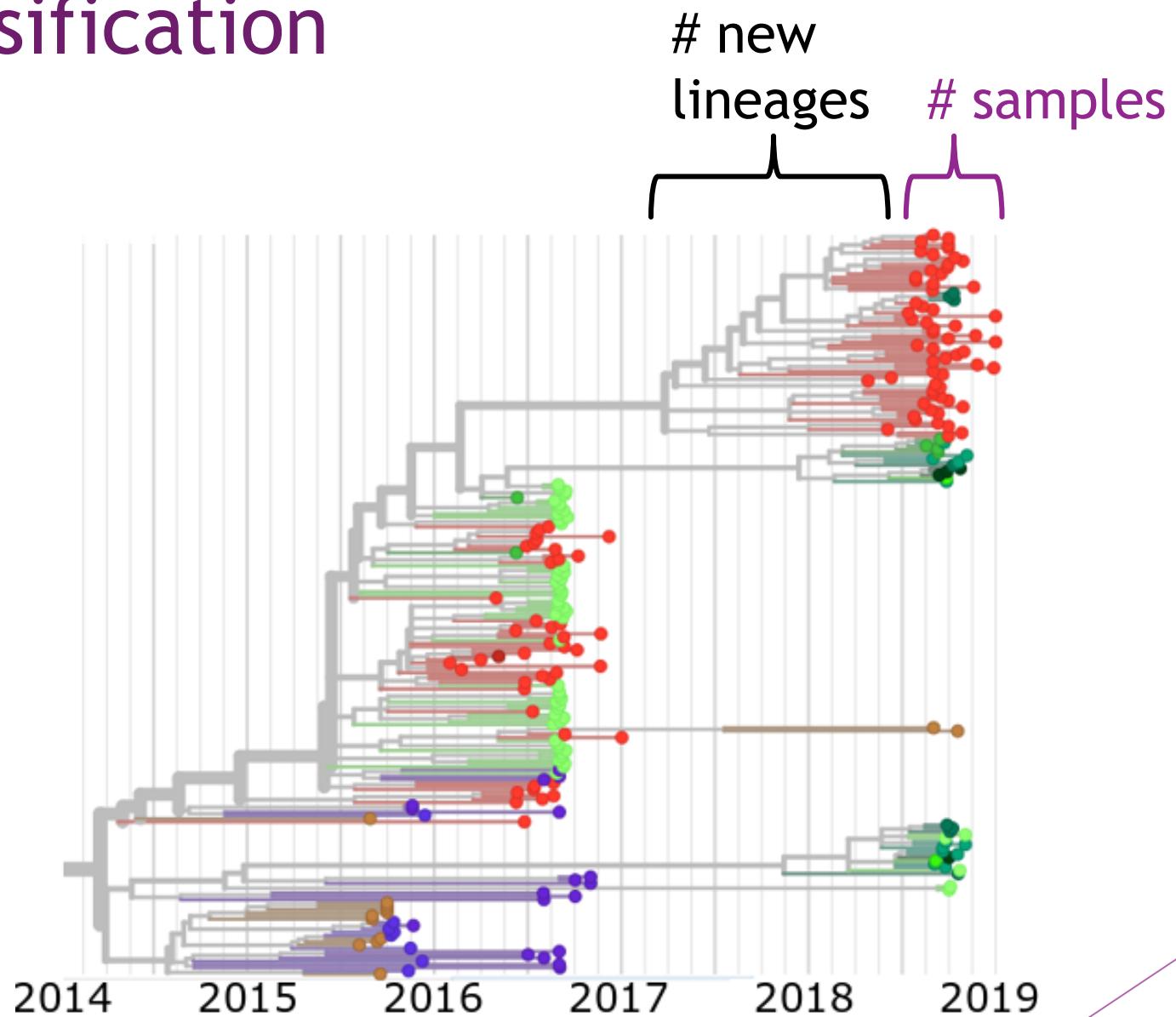
- ▶ 99 samples WGS sequenced in Sweden
- ▶ Combined with ~600 full length sequences from ViPR
- ▶ & ~1800 VP1 sequences



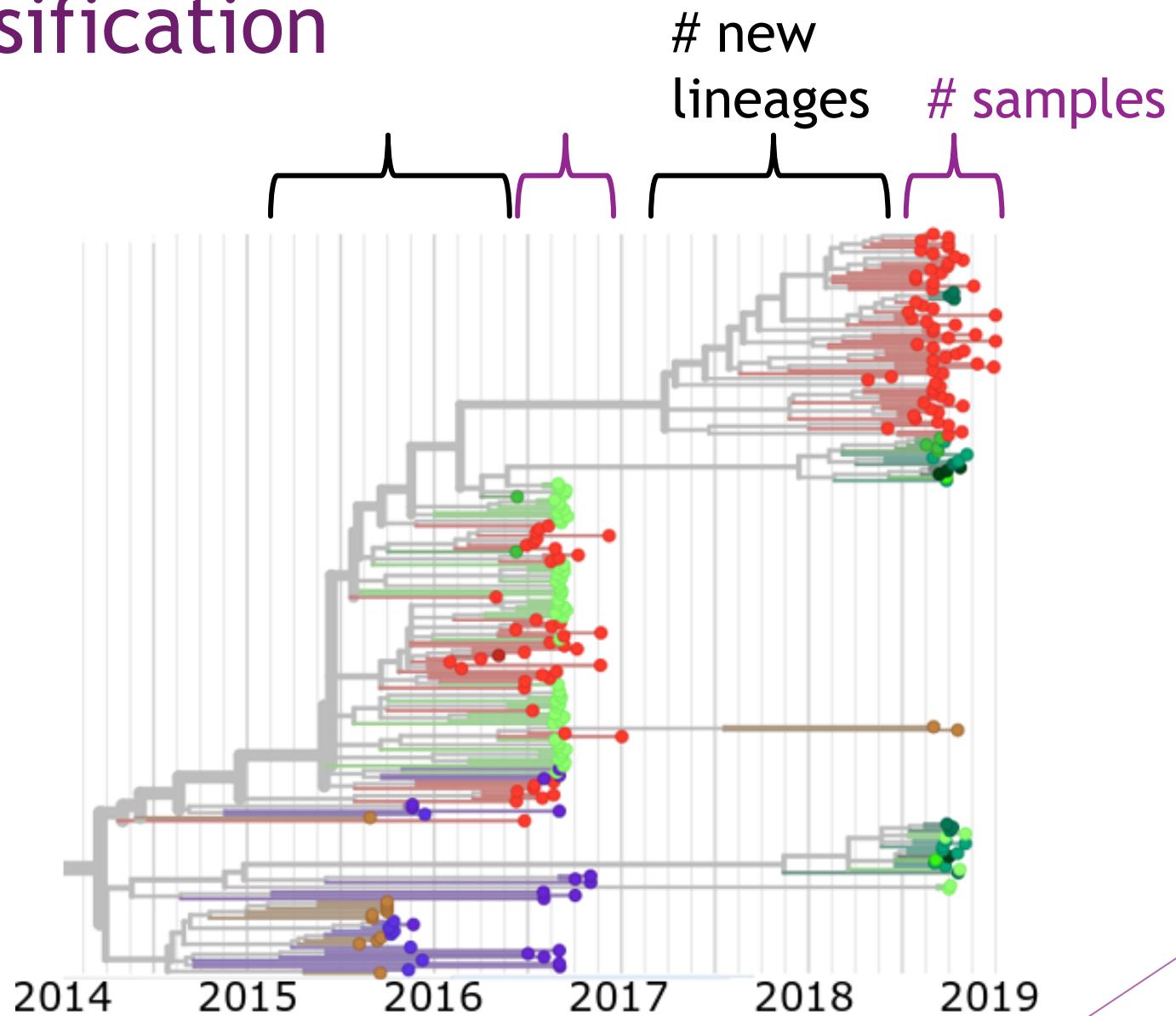
EV-D68 in Nextstrain...



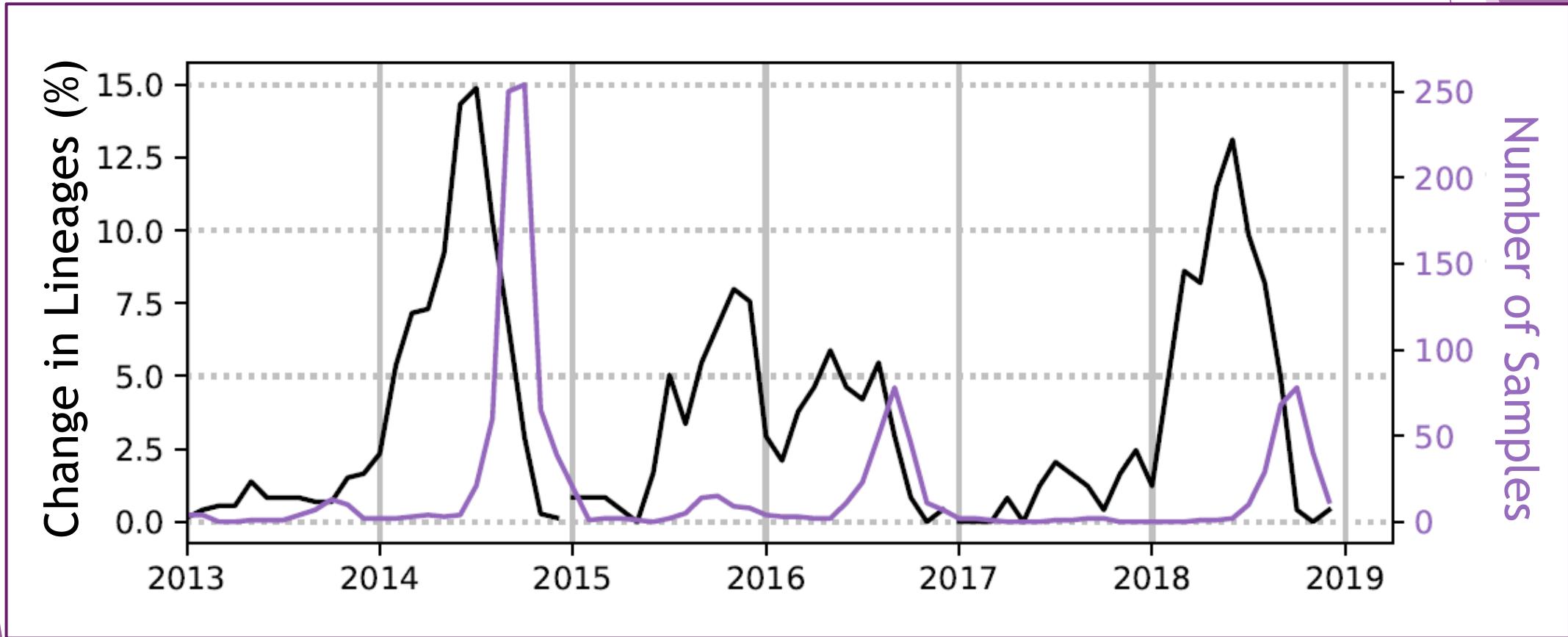
Diversification



Diversification

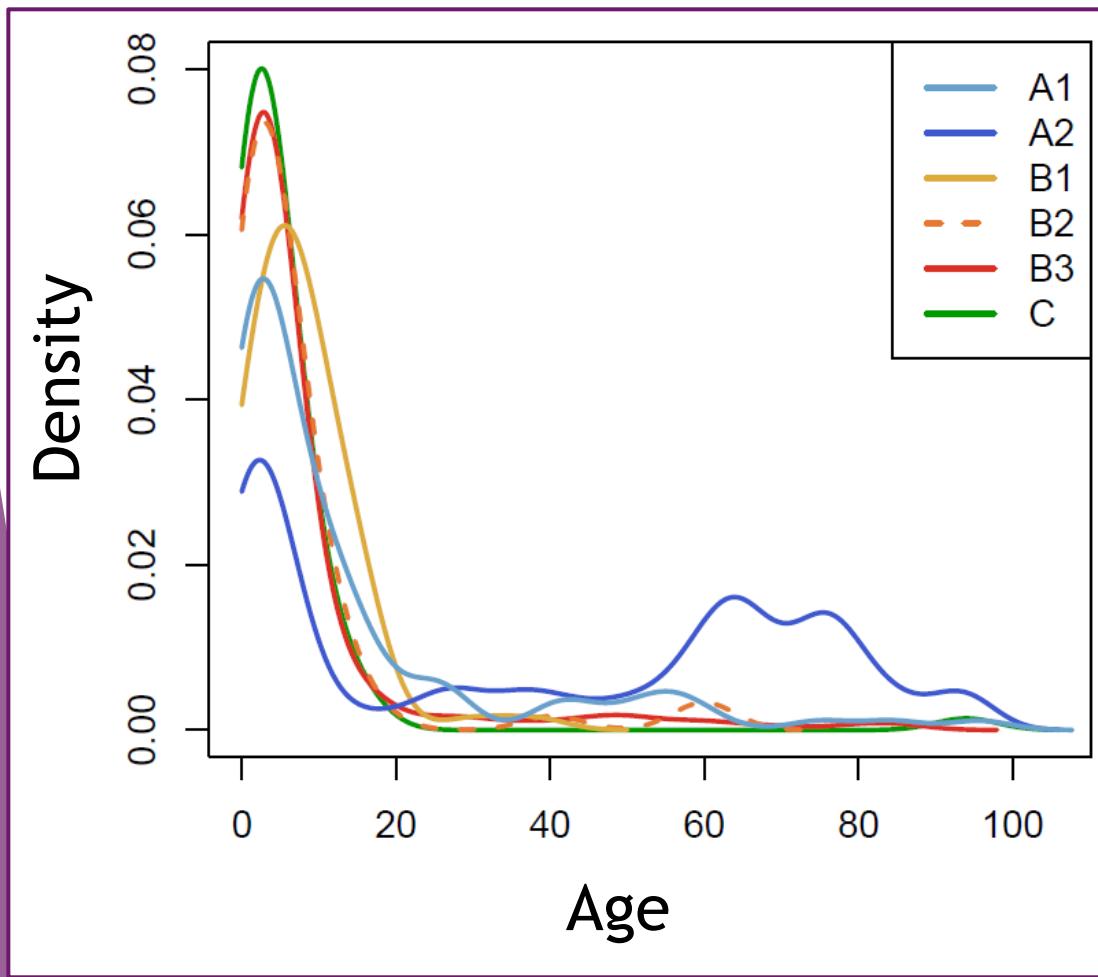


Signs of ‘Hidden Diversification’

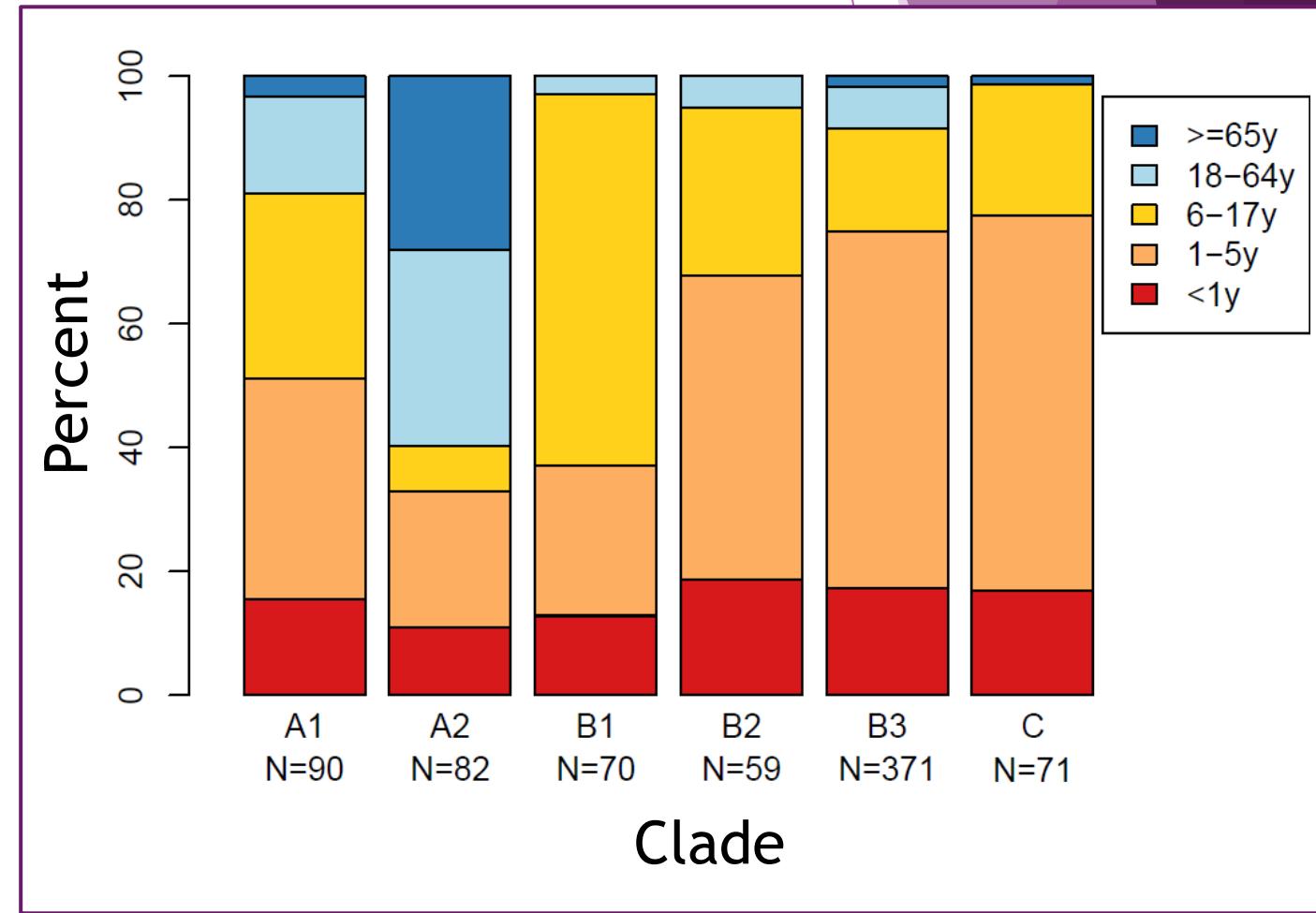
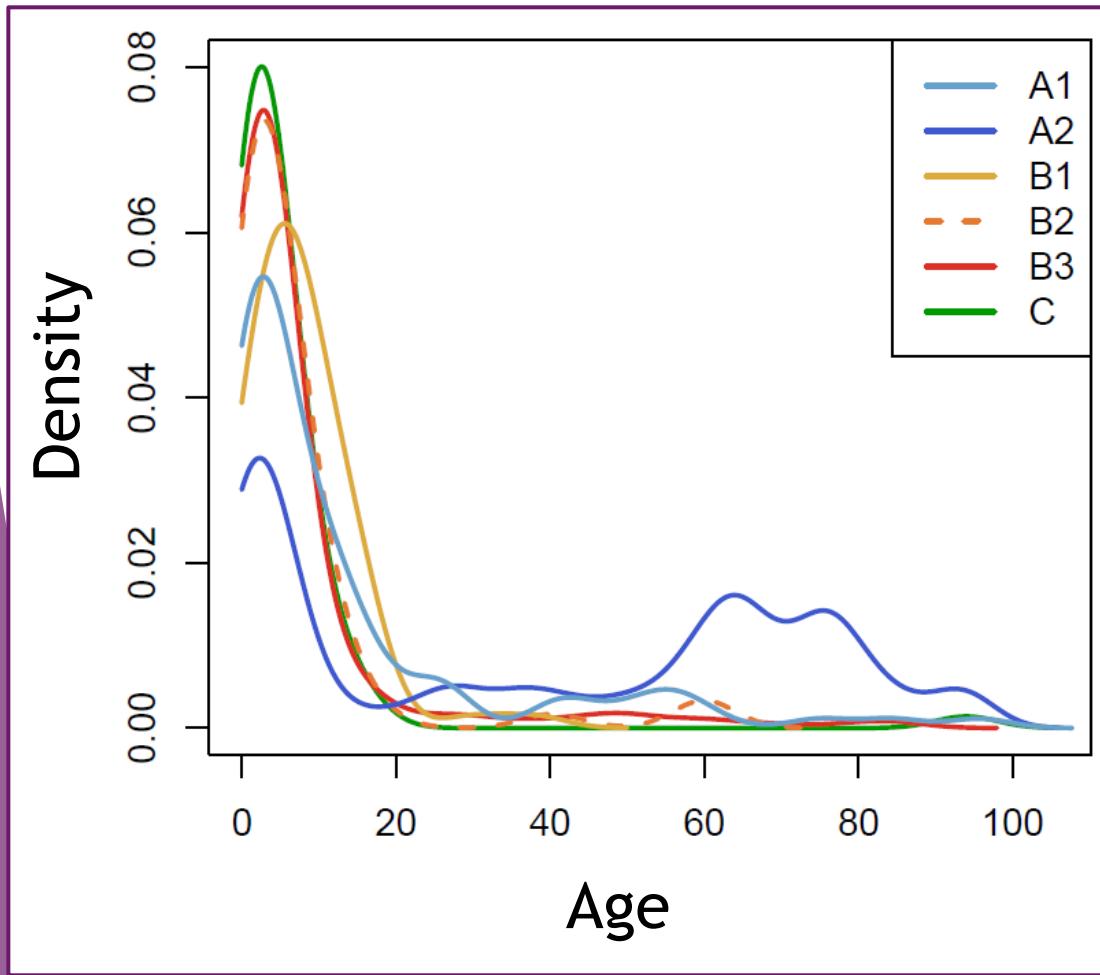


Age in EV-D68...

Age Distribution by Clade

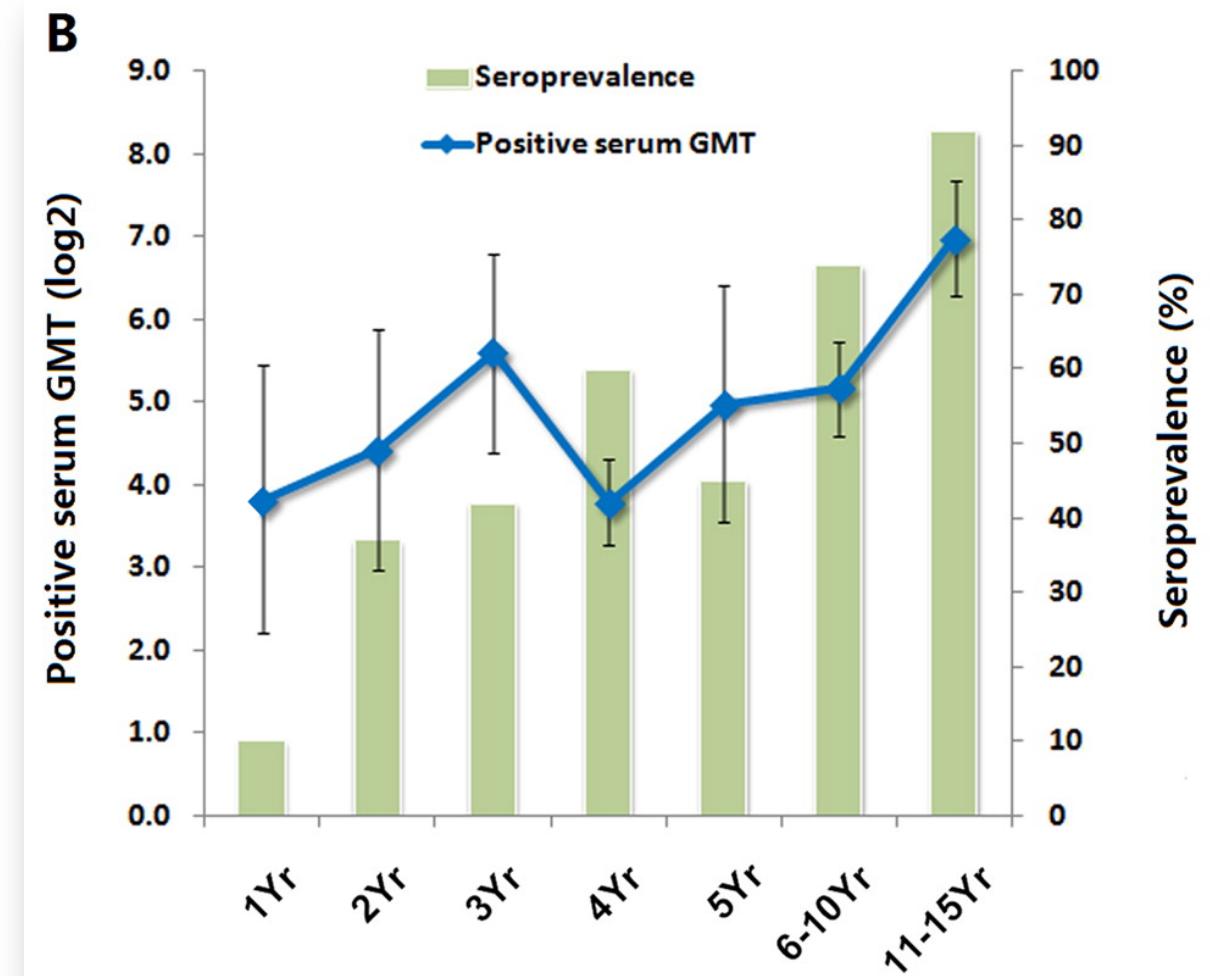


Age Distribution by Clade



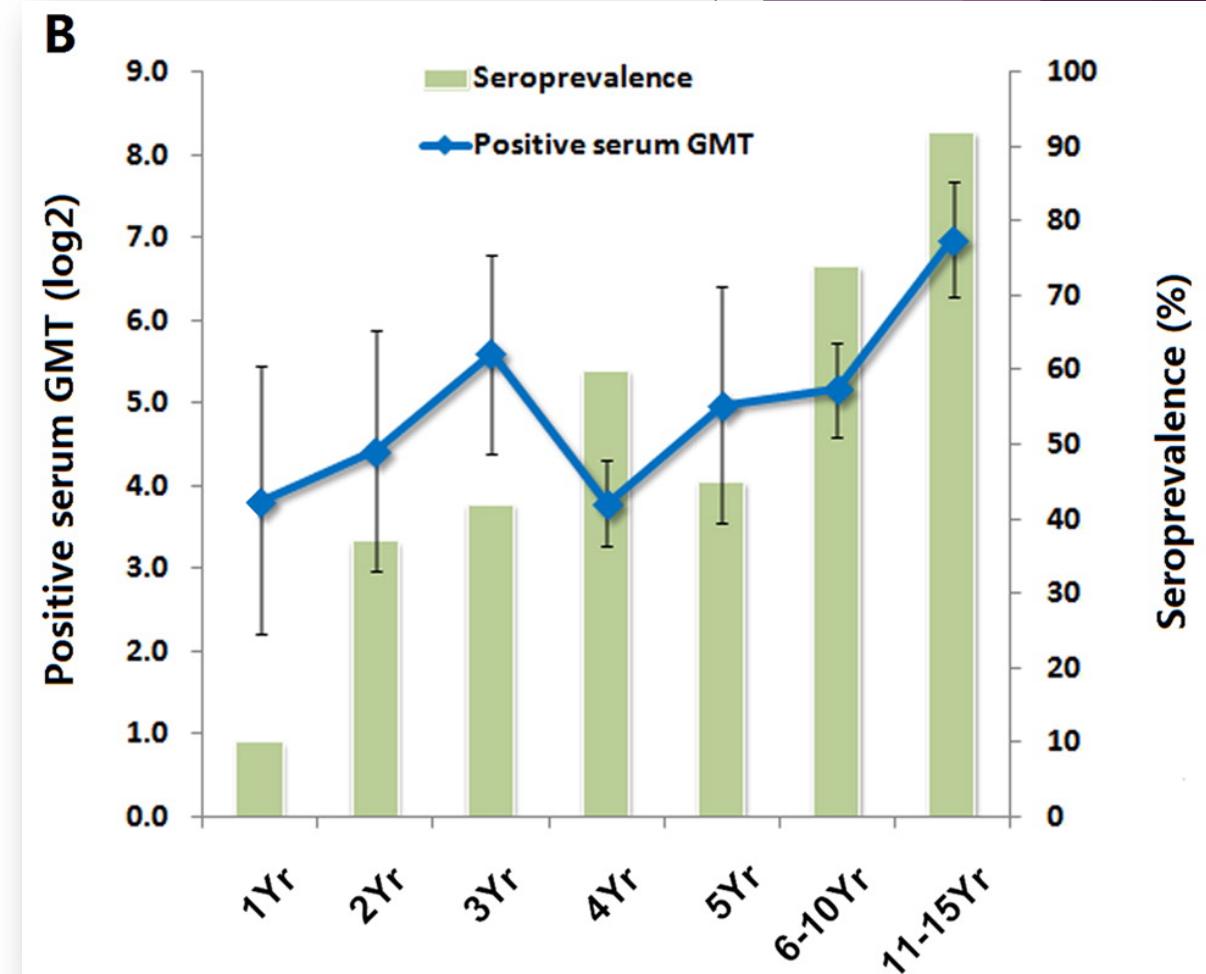
Is Antigen Evolution Important for D68?

- ▶ Childhood infection (naïve)



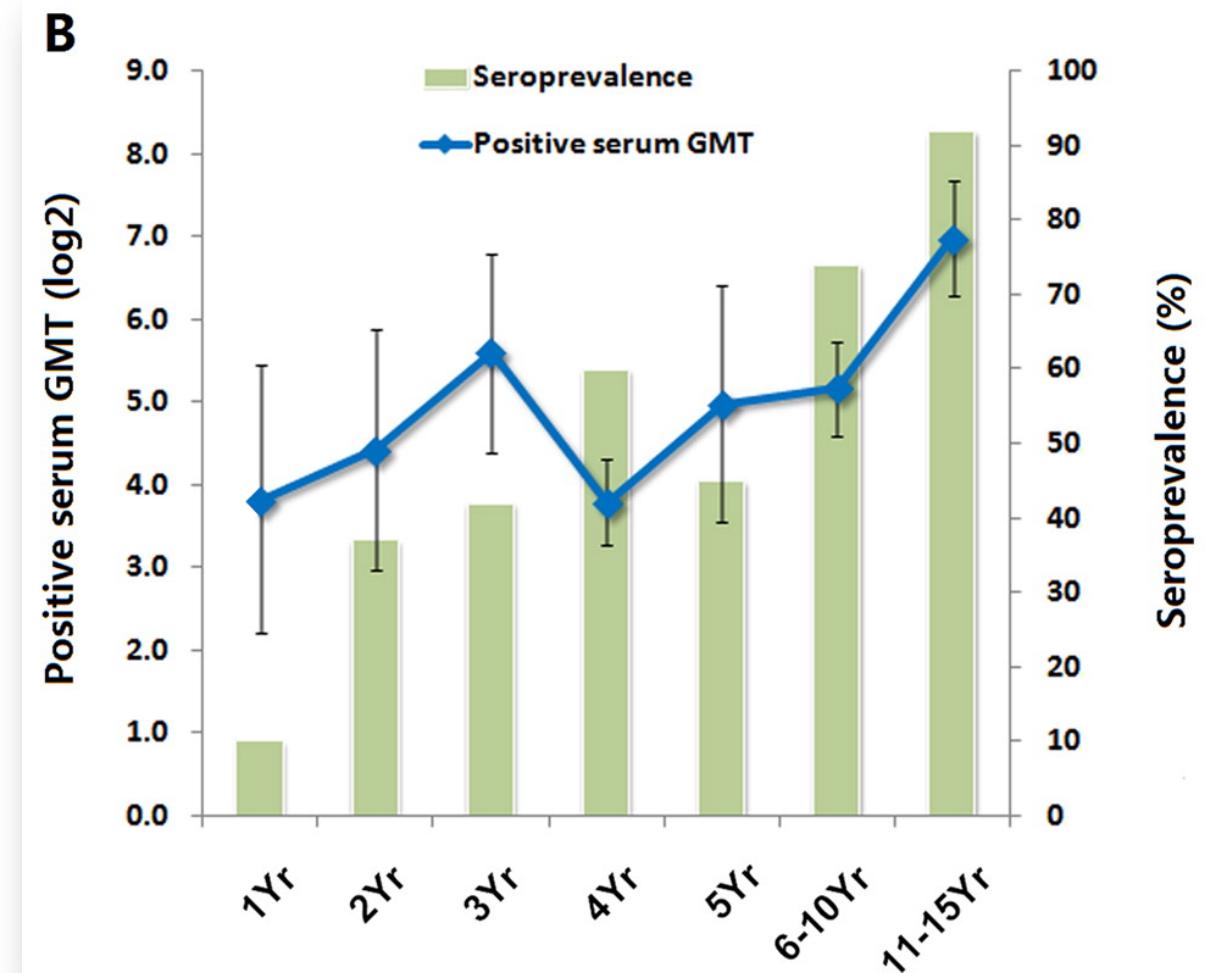
Is Antigen Evolution Important for D68?

- ▶ Childhood infection (naïve)
- ▶ Prevalent antibodies in adults
- ▶ Long-lived - 50 years



Is Antigen Evolution Important for D68?

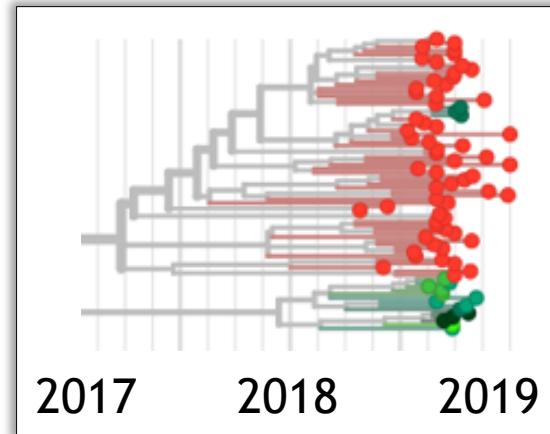
- ▶ Childhood infection (naïve)
- ▶ Prevalent antibodies in adults
- ▶ Long-lived - 50 years
- ▶ Does virus need to evolve to evade immune system?



Antigen evolution in EV-D68...

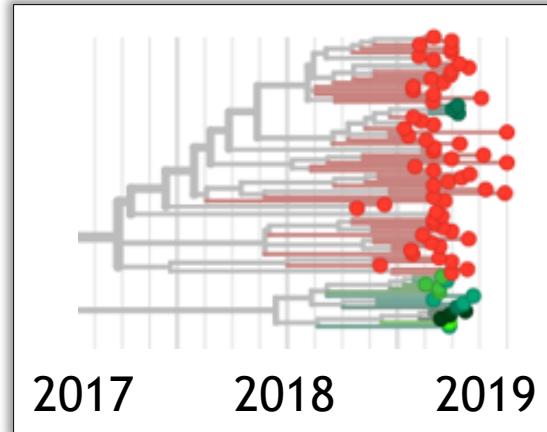
EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic
 - ▶ ‘Hidden’ divergence



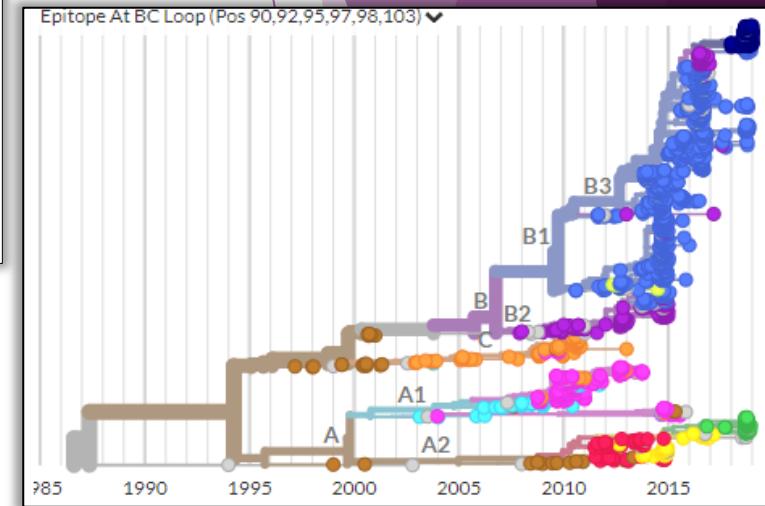
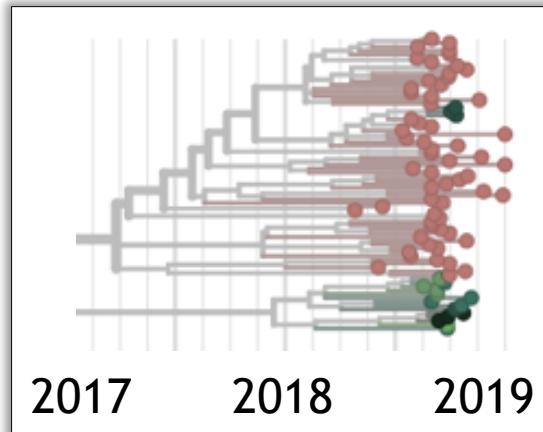
EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic
 - ▶ ‘Hidden’ divergence
 - ▶ *Adults: more travel, less doctors*



EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic
 - ▶ ‘Hidden’ divergence
 - ▶ *Adults: more travel, less doctors*
- ▶ Continuous antigenic evolution
 - ▶ Despite prevalent, long-lived antibodies

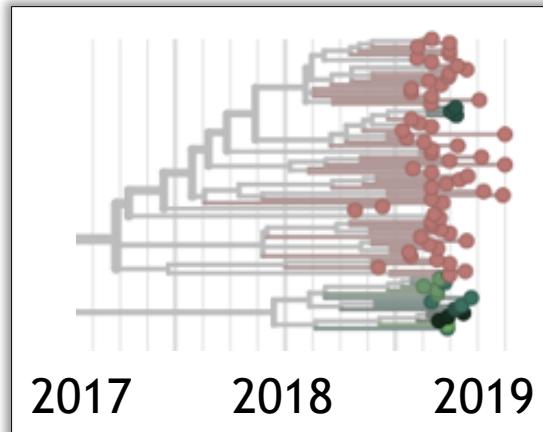


EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic

- ▶ ‘Hidden’ divergence

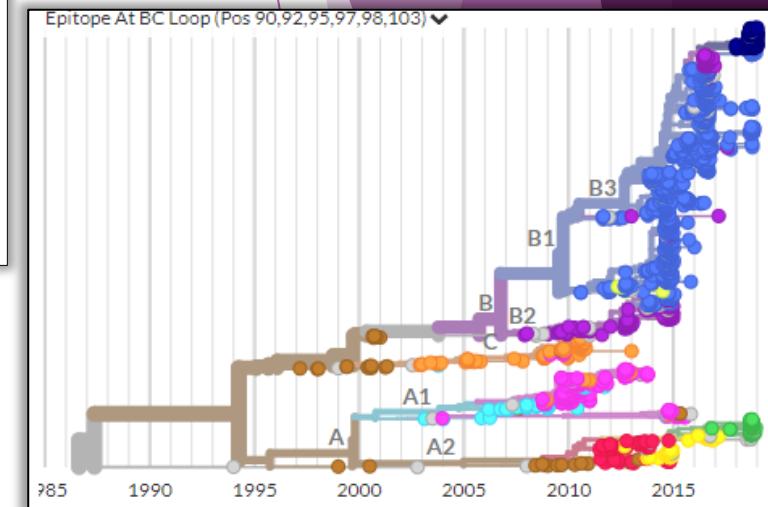
- ▶ *Adults: more travel, less doctors*



- ▶ Continuous antigenic evolution

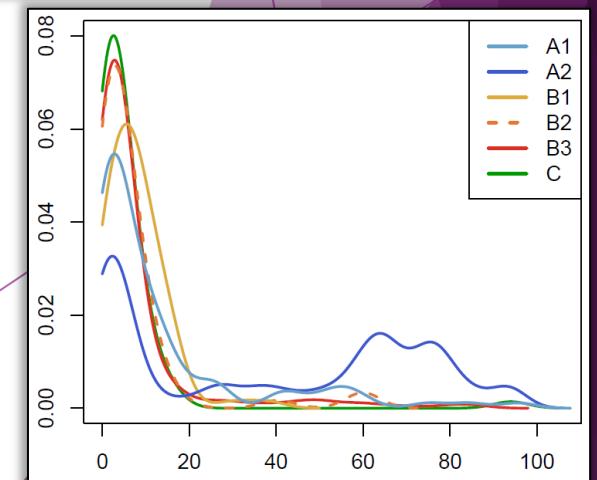
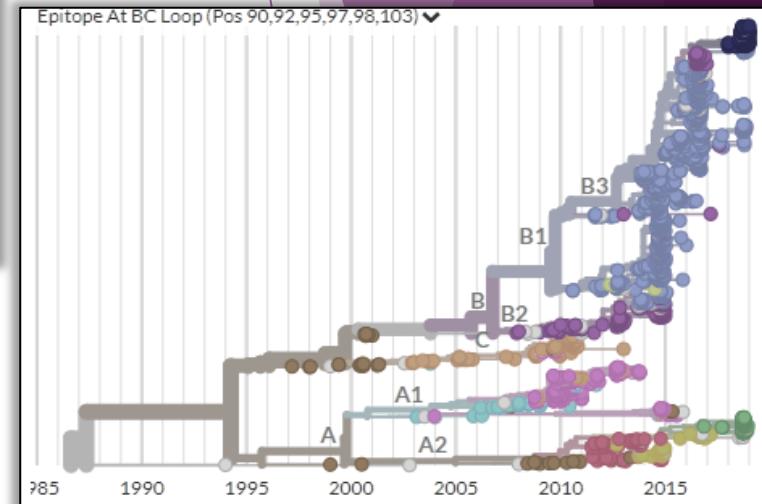
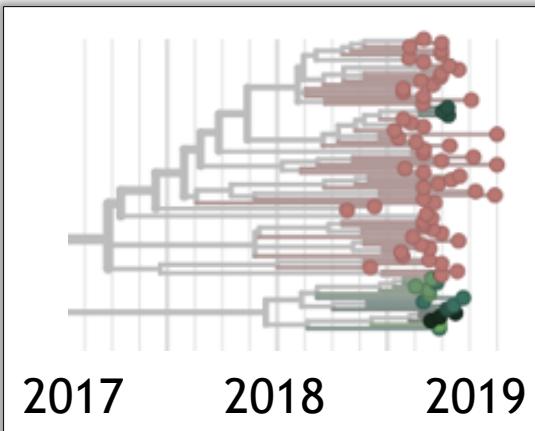
- ▶ Despite prevalent, long-lived antibodies

- ▶ *In flu: ↑ children infected == ↓ antigen evolution*



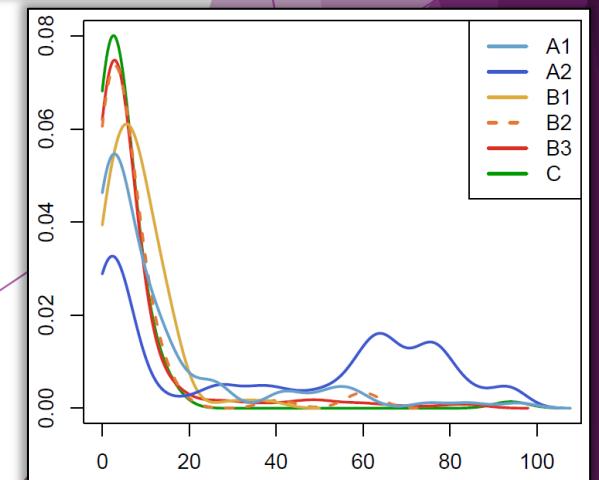
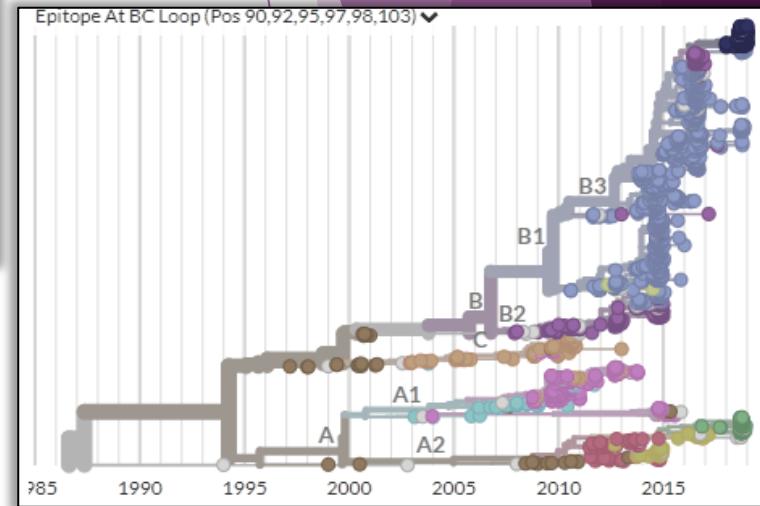
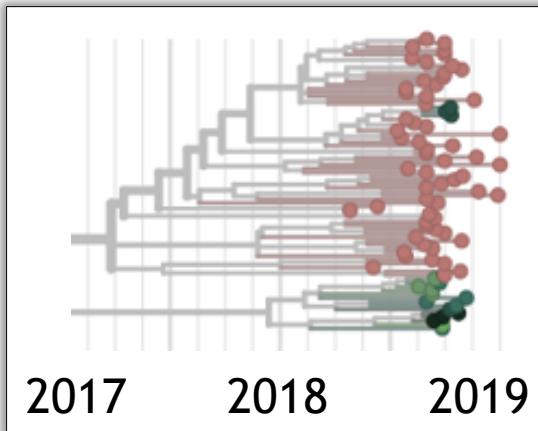
EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic
 - ▶ ‘Hidden’ divergence
 - ▶ *Adults: more travel, less doctors*
- ▶ Continuous antigenic evolution
 - ▶ Despite prevalent, long-lived antibodies
 - ▶ *In flu: ↑ children infected == ↓ antigen evolution*
- ▶ A2 clade associated with older people
 - ▶ Prevalence or sampling?



EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic
 - ▶ ‘Hidden’ divergence
 - ▶ *Adults: more travel, less doctors*
- ▶ Continuous antigenic evolution
 - ▶ Despite prevalent, long-lived antibodies
 - ▶ *In flu: ↑ children infected == ↓ antigen evolution*
- ▶ A2 clade associated with older people
 - ▶ Prevalence or sampling?
 - ▶ *Has antigen evolution in A2 led to ↑ adults?*

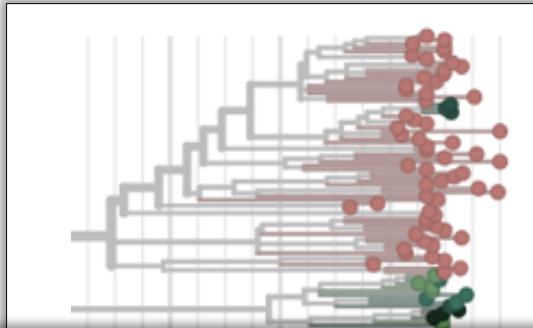


EV-D68 Driven by Re-Infection of Adults?

- ▶ Highly mixed epidemic

- ▶ ‘Hidden’ divergence

- ▶ *Adults: more travel, less doctors*



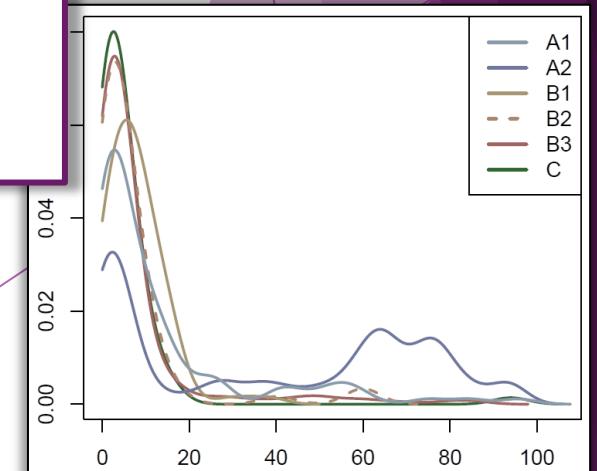
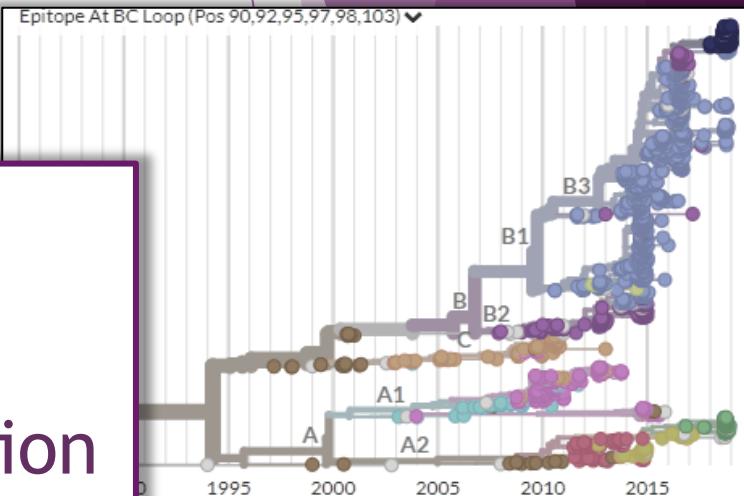
- ▶ Continuous an

- Unprecedented dataset size
 - Intuitive interaction & exploration
 - Updatable & repeatable

- ▶ A2 clade associated with older people

- ▶ Prevalence or sampling?

- ▶ *Has antigen evolution in A2 led to ↑ adults?*





nextstrain

Relevant

- ▶ Real-time - powerful - time-trees in minutes
- ▶ Updatable & repeatable

Flexible

Communicable



nextstrain

Relevant

- ▶ Real-time - powerful - time-trees in minutes
- ▶ Updatable & repeatable

Flexible

- ▶ Composable & compatible
- ▶ Many analyses → one tool
- ▶ Locally run

Communicable



nextstrain

Relevant

- ▶ Real-time - powerful - time-trees in minutes
- ▶ Updatable & repeatable

Flexible

- ▶ Composable & compatible
- ▶ Many analyses → one tool
- ▶ Locally run

Communicable

- ▶ Easily sharable on Github - or not
- ▶ Intuitive & customizable
- ▶ Encourage exploration

Have a look!

Intra- and interpatient evolution of enterovirus D68 analyzed by whole-genome deep sequencing

Robert Dyrdak, Monika Mastafa, Emma B. Hodcroft,  Richard A. Neher,  Jan Albert

doi: <https://doi.org/10.1101/420836>

- ▶ See the previous EV-D68 paper:

tinyurl.com/entero-d68-ve

- ▶ See the data:

nextstrain.org/enterovirus/d68



nextstrain



nextstrain

Relevant • Flexible • Communicable
analyses *tool* *results*



Dr. Emma Hodcroft
University of Basel

open-source • powerful
intuitive • run locally
sharable • customizable

Explore the EV-D68 data!
nextstrain.org/enterovirus/d68

