

A grayscale electron micrograph showing several large, roughly spherical virus particles with a textured surface. The particles are scattered across the field of view, with some appearing more prominent than others. The background is light gray with some faint, linear structures.

# **MONKEYPOX VIRUS SUB-SPECIES EVOLUTION**

Elliot Lefkowitz, University of Alabama at Birmingham

# Monkeypox virus Nomenclature

*Journal of General Virology* (2005), 86, 2661–2672

DOI 10.1099/vir.0.81215-0

## A tale of two clades: monkeypox viruses

**PLOS BIOLOGY**

PERSPECTIVE

### Urgent need for a non-discriminatory and non-stigmatizing nomenclature for monkeypox virus

#### **New nomenclature for mpox (monkeypox) and monkeypox virus clades**



In May, 2015, WHO recommended best practices for naming new infectious diseases to avoid offense or economic effect for any ethnic, regional, or

other groups.<sup>1</sup> Although mpox (formerly known as monkeypox) is not new, WHO has endorsed mpox as the new name for this re-emerging disease and backed the

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# What's In a Name?

Name	Poxvirus Example	Coronavirus Example	Who Creates?	Who Updates?
Disease	<ul style="list-style-type: none"> <li>• Monkeypox virus</li> <li>• <b>MPOX</b></li> </ul>	<ul style="list-style-type: none"> <li>• 2019-nCoV</li> <li>• hCoV-19</li> <li>• <b>COVID-19</b></li> </ul>	WHO	WHO
Virus	<b>Monkeypox virus</b>	<b>SARS-CoV-2</b>	Discoverer	Scientific community
Clade	<ul style="list-style-type: none"> <li>• West African; DRC, Congo Basin</li> <li>• 1, 2, 3</li> <li>• <b>I, IIa, IIb</b></li> </ul>	<b>Alpha, Beta, Gamma, Delta, Omicron...</b>	Scientific community (WHO-consulted)	Scientific community (WHO-consulted)
Species	<ul style="list-style-type: none"> <li>• <i>Monkeypox virus</i></li> <li>• <b><i>Orthopoxvirus monkeypox</i></b></li> </ul>	<ul style="list-style-type: none"> <li>• <i>Severe acute respiratory syndrome-related coronavirus</i></li> <li>• <b><i>Betacoronavirus pandemicum</i></b></li> </ul>	ICTV	ICTV

# Human Orthopoxvirus Disease

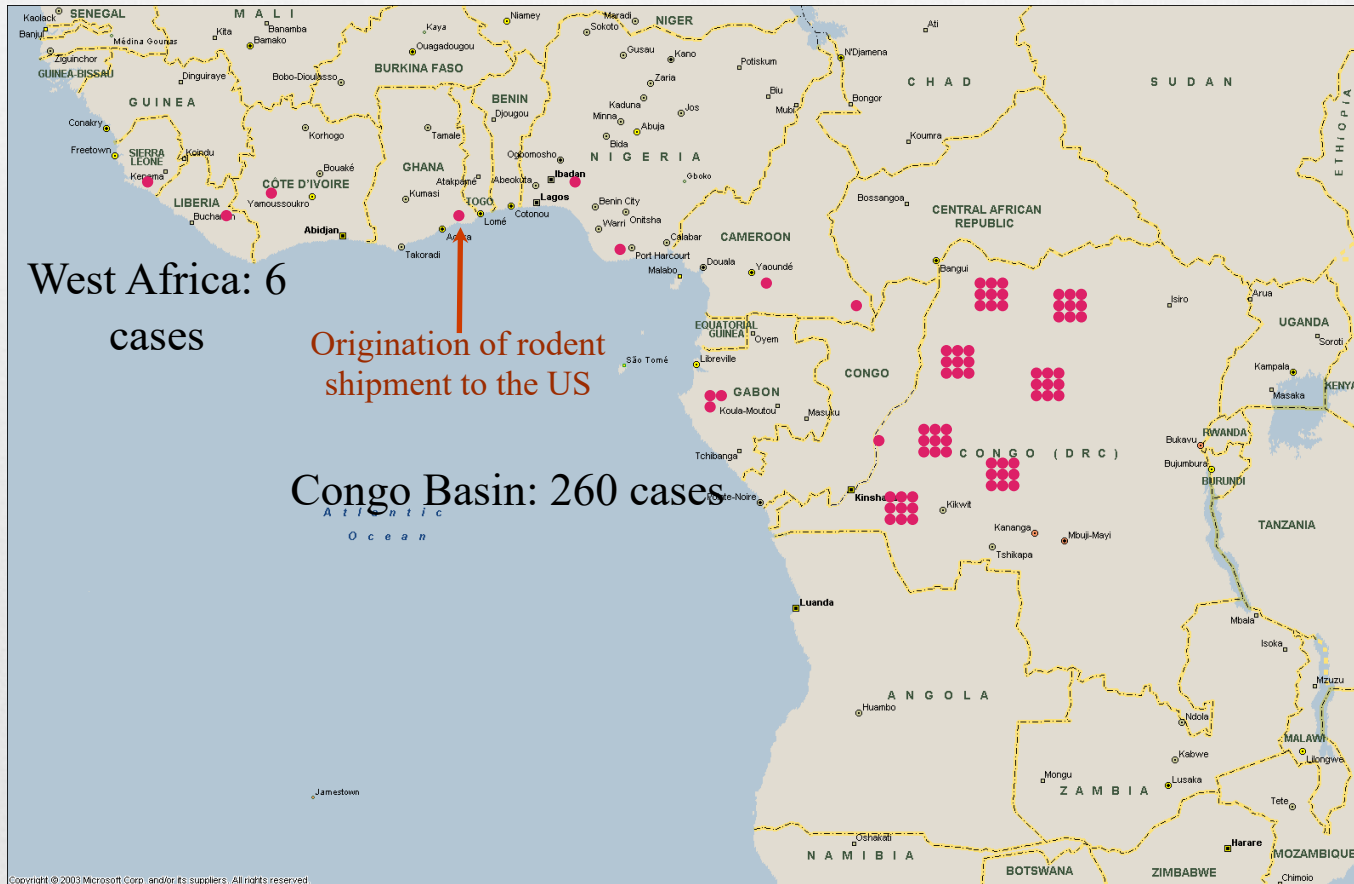
## SMALLPOX

- First identified: 1100 – 1500 BCE
- Host range: Exclusively human
- Symptoms: Rash, fever, aches, vomiting, hemorrhage
- Case fatality rate: 1-30%
  - Dependent on particular clade and vaccination status
- Human-human transmission rate
  - ~60% (30 - 90%)
- Extinct
  - Eradication (vaccination) campaign

## MPOX

- First identified: 1958 monkey colonies; 1970 human case
- Host range: Rodents, zoonotic transmission to primates and humans
- Symptoms: Rash, fever, aches, vomiting, lymphadenopathy
- Case fatality rate: 0 - 10%
  - Dependent on particular clade and vaccination status
- Human-human transmission rate:
  - ~10% (3 - 15%)
- Rodent reservoir
- Increasing incidence
  - Human encroachment on animal reservoir habitats
  - Waning vaccination status of population
  - Increased human-human transmission

# MPOX Cases in Africa 1970 - 1986



# U.S. Midwest MPOX Outbreak 2003

- ◆ April – June, 2003
- ◆ Infected rodents imported into the U.S. from West Africa
- ◆ Rodents housed with native prairie dogs
  - ◆ Infected prairie dogs transmitted virus to humans
  - ◆ Transmission due to respiratory and direct mucocutaneous exposure
- ◆ 72 confirmed or suspected human cases
  - ◆ No human fatalities
  - ◆ No human-human transmission

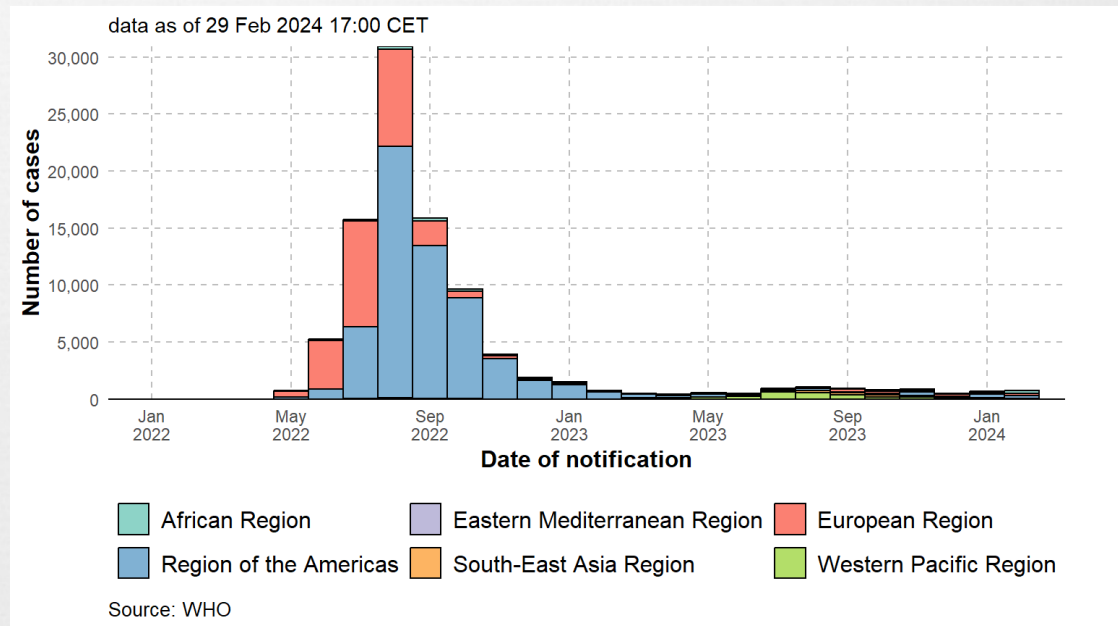
# World-wide MPOX Outbreak 2022 - Present

## ◆ Total

- ◆ Cases: 95,000
- ◆ Deaths: 181 (0.2%)
- ◆ Countries: 117

## ◆ February 2024

- ◆ Cases: 715
- ◆ Deaths: 2 (0.28%)
- ◆ Countries: 29



World Health Organization, 20 March 2024

[https://worldhealthorg.shinyapps.io/mpx\\_global/](https://worldhealthorg.shinyapps.io/mpx_global/)

A grayscale electron micrograph showing several large, roughly spherical virus particles with a textured surface. The particles are scattered across the field of view, with some appearing more prominent than others. The background is light and grainy.

*Monkeypox virus* the species vs.  
**Monkeypox virus** the sub-species



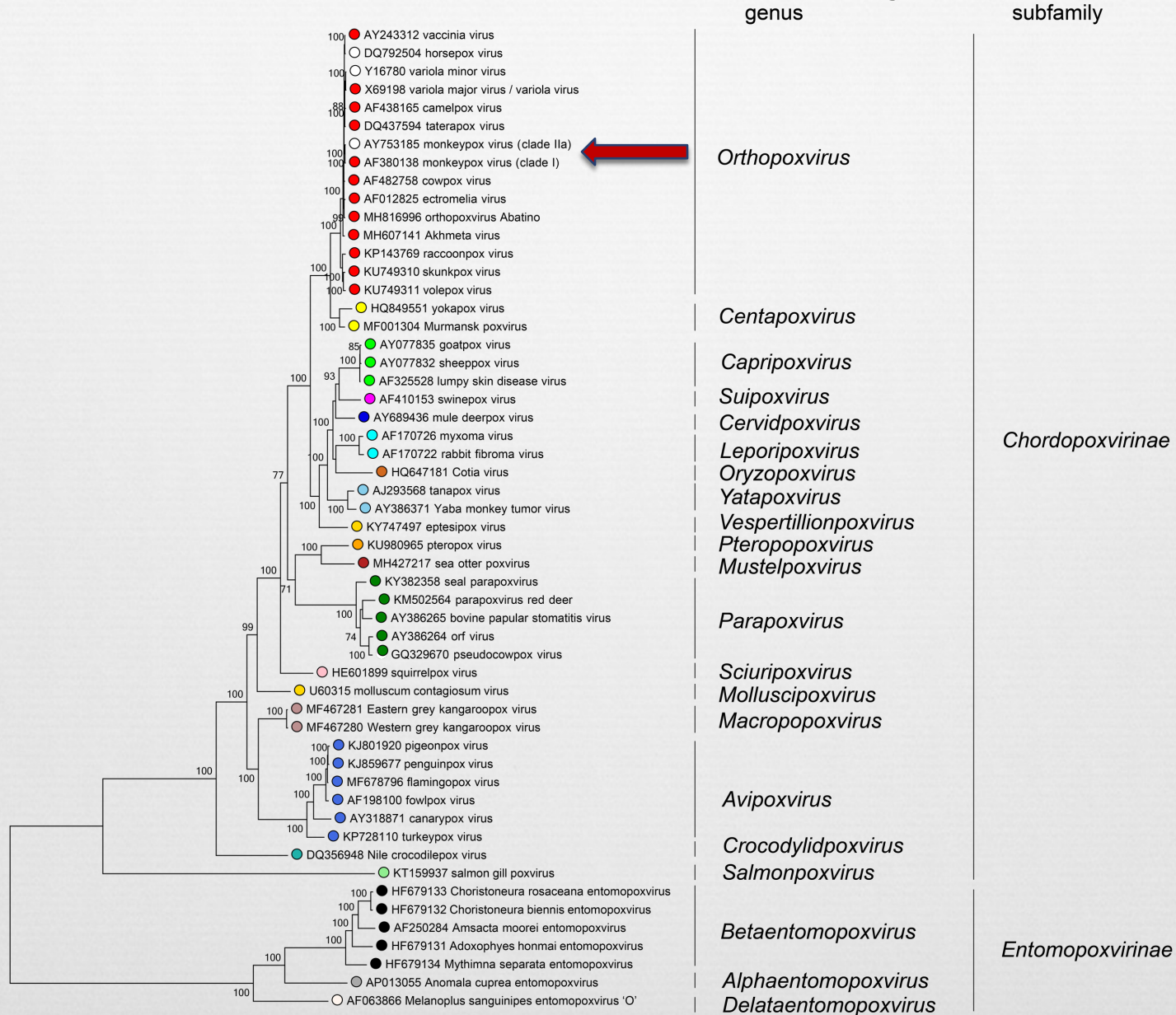


# Demarcation Criteria *Poxviridae*:

## Subfamily:Genera:Species

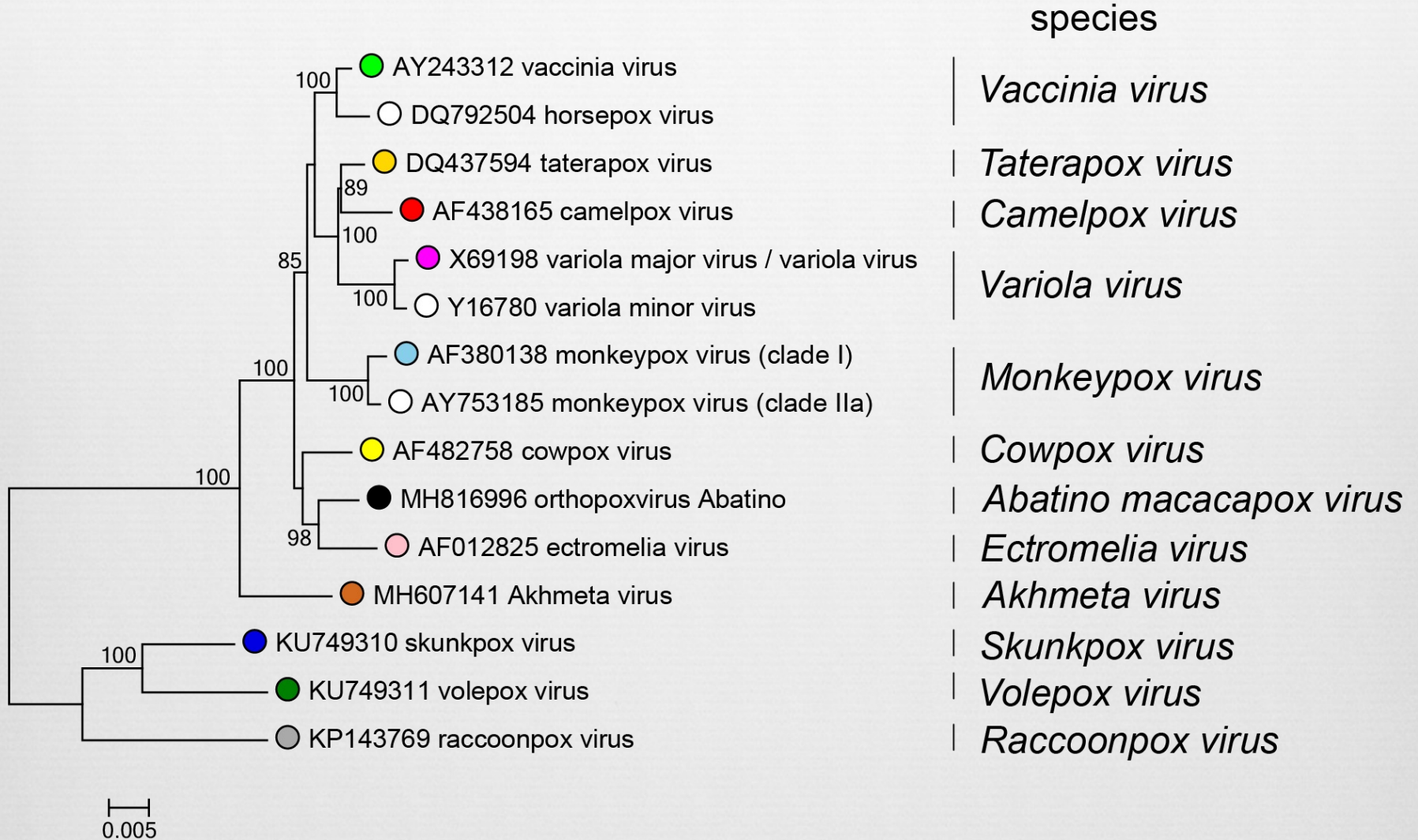
- ◆ Phenotypic
  - ◆ Natural host range (Subfamily)
  - ◆ Growth characteristics and host range in cell culture
    - ◆ Morphology of pocks; Plaque characteristics
  - ◆ Disease characteristics.
    - ◆ Morbidity, mortality, etc.
  - ◆ Serological criteria
    - ◆ Plaque neutralization tests, cross-protection in animals
  
- ◆ Genotypic
  - ◆ Gene content
  - ◆ Genome organization
  - ◆ Amino acid sequence identity of commonly shared genes.
    - ◆ hemagglutinin or A-type inclusion protein
  - ◆ Nucleotide sequence identity, conserved, core region of orthopoxvirus genomes
    - ◆ Different species <96% - 98%
    - ◆ Isolate >98%
  - ◆ **Phylogenetic analysis**

# Poxviridae Family



0.2

# Orthopoxvirus Genus



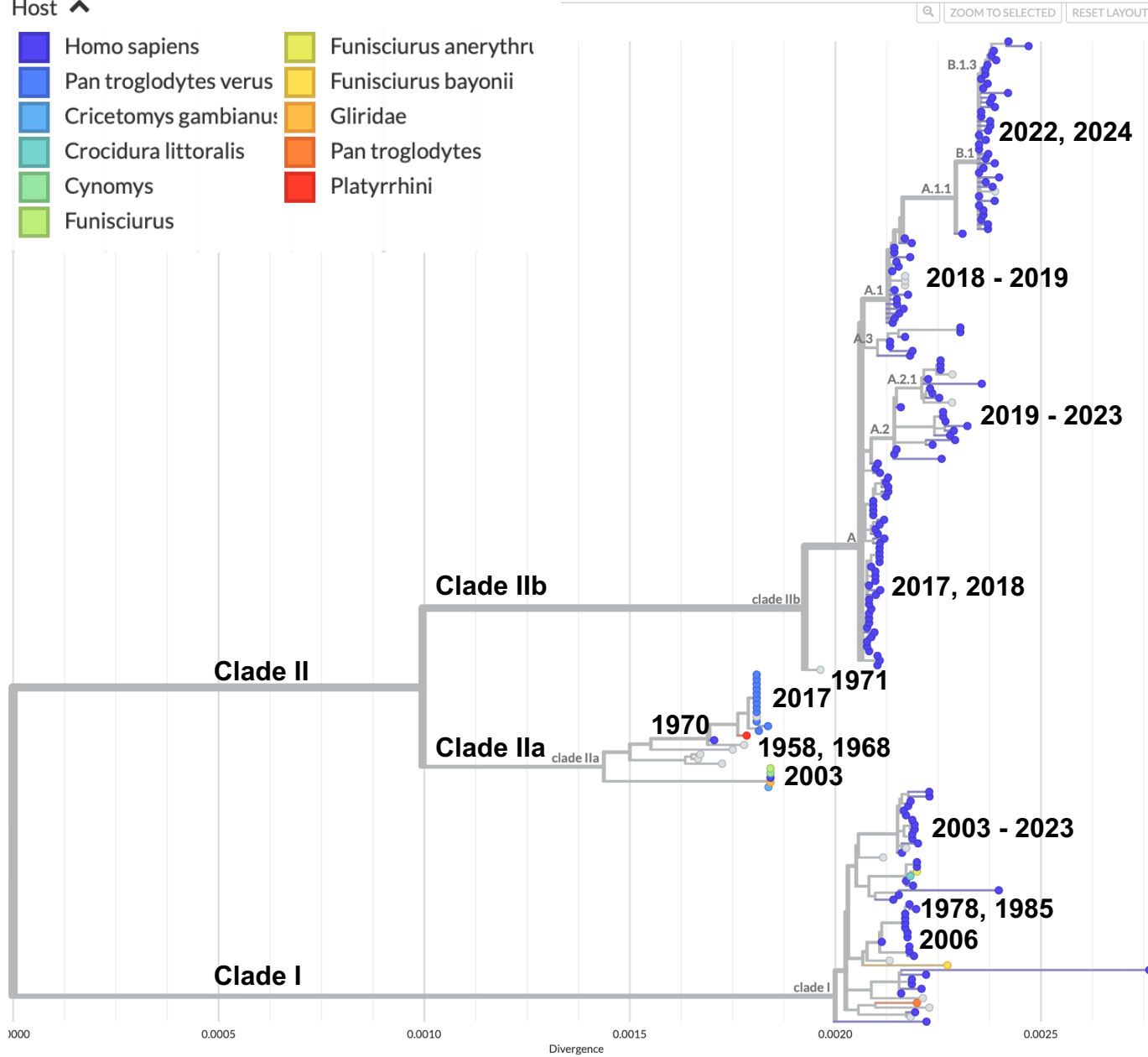
# Genomic epidemiology of mpox viruses across clades

Built with [nextstrain/mpox](#). Maintained by [Nextstrain team](#). Data updated 2024-04-02. Enabled by data from [GenBank](#).

Showing 210 of 210 genomes.

Host

- |                       |                       |
|-----------------------|-----------------------|
| Homo sapiens          | Funisciurus anerythri |
| Pan troglodytes verus | Funisciurus bayonii   |
| Cricetomys gambianus  | Gliridae              |
| Crocidura littoralis  | Pan troglodytes       |
| Cynomys               | Platyrrhini           |
| Funisciurus           |                       |



# Variability of MPOX Infections

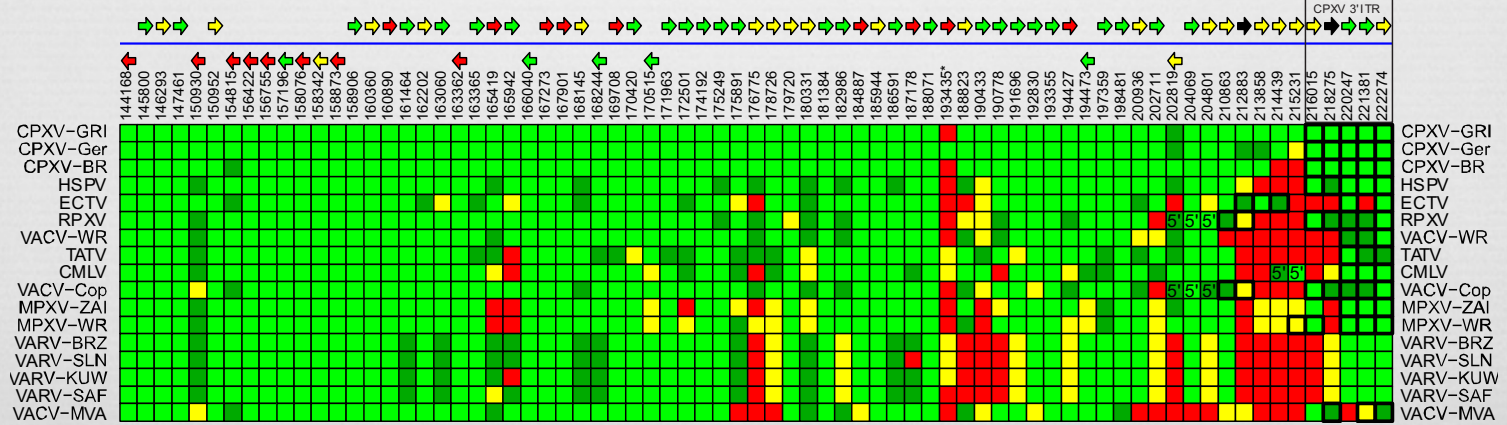
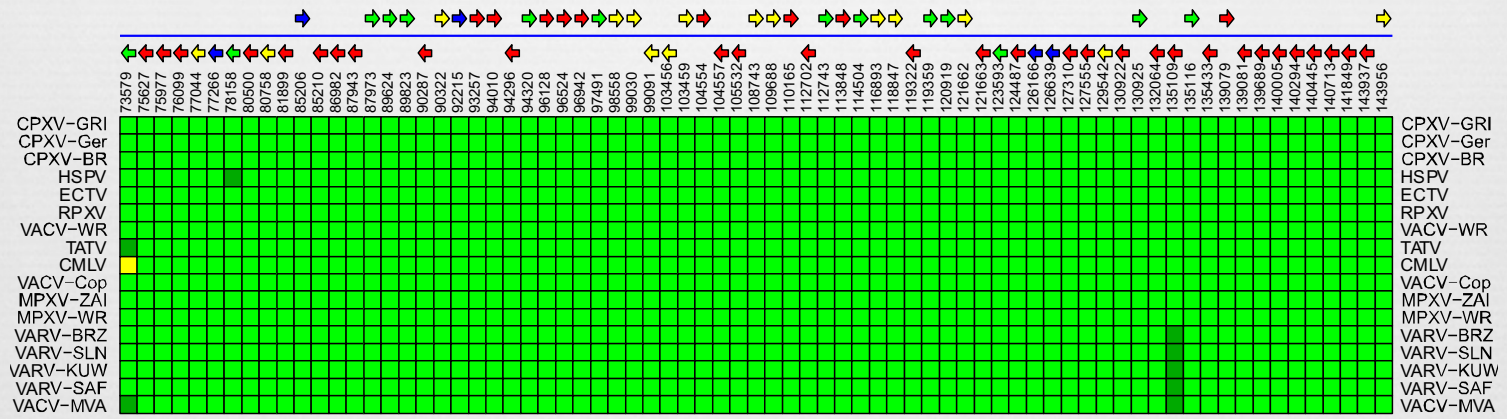
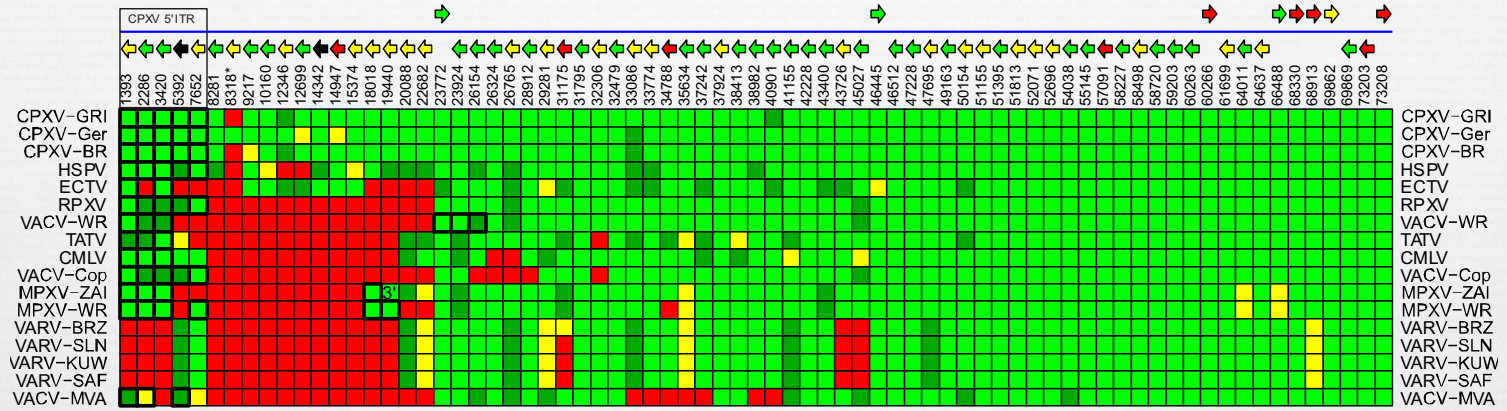
## Clade I vs. II

- ◆ Clade I
  - ◆ Congo basin
    - ◆ Pre 2022, >90% of reported cases
      - ◆ Case fatality rate : 1-5% to >10%
    - ◆ Zoonotic outbreaks
      - ◆ Human-human transmission (limited)
  
- ◆ Clade II
  - ◆ West African
    - ◆ CFR (pre-2022): 0-4%
    - ◆ Zoonotic outbreaks
      - ◆ Human-human transmission: none (very limited)
    - ◆ Source of 2003 US Midwest outbreak virus (Clade IIa)
  - ◆ World-wide outbreak 2022 (Clade II.b B.1)
    - ◆ CFR: 0.2%
    - ◆ Human-human transmission
      - ◆ STD, Male (96%); MSM (84%)

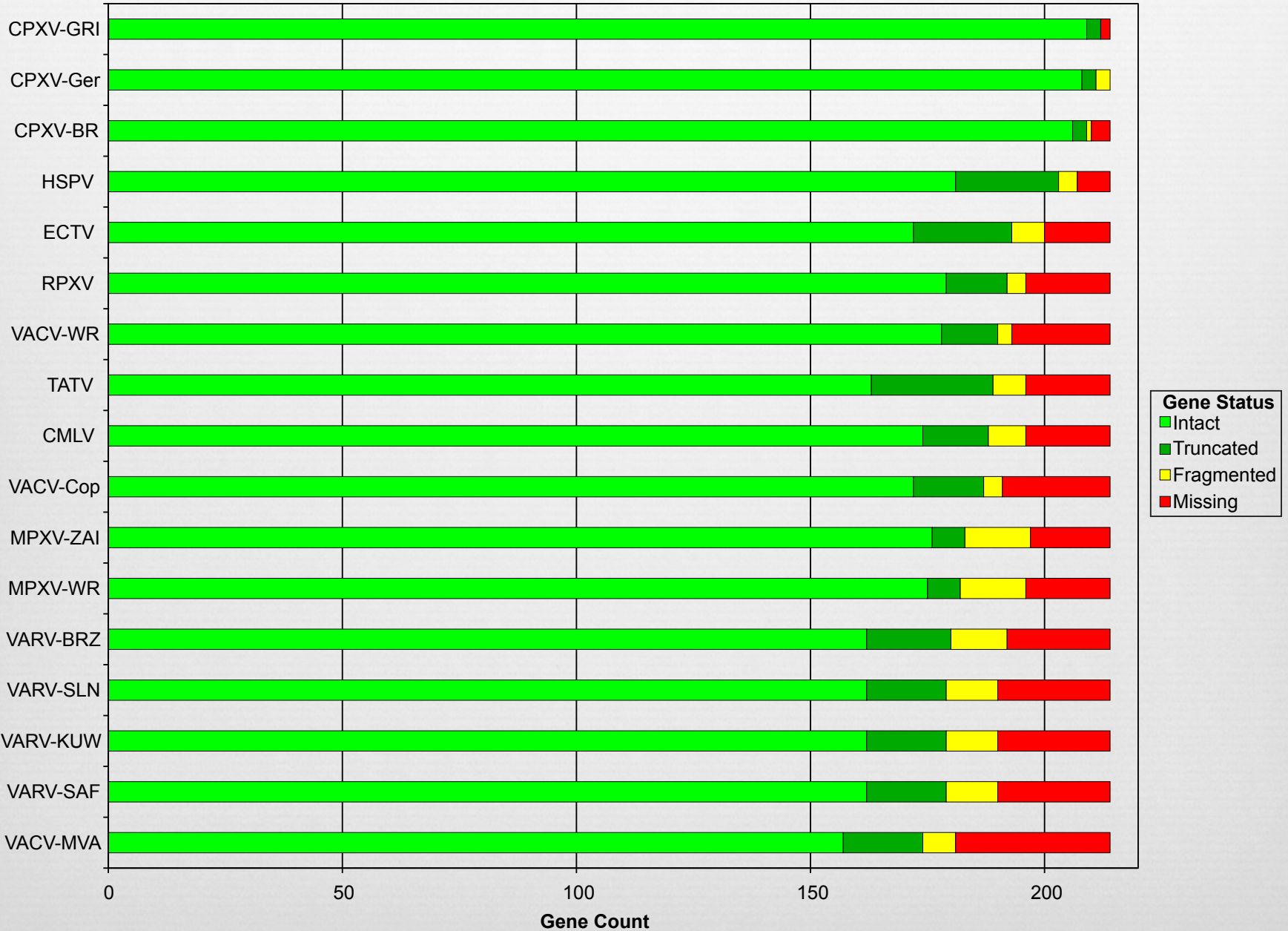
The background of the slide is a grayscale electron micrograph showing several large, roughly spherical particles with a granular internal structure, characteristic of orthopoxviruses. The particles are scattered across the field of view, with some appearing more prominent than others. The overall texture is grainy and high-contrast, typical of electron microscopy.

# **Orthopoxviruses: Mechanisms of Variation**

# Orthopoxvirus Gene Conservation

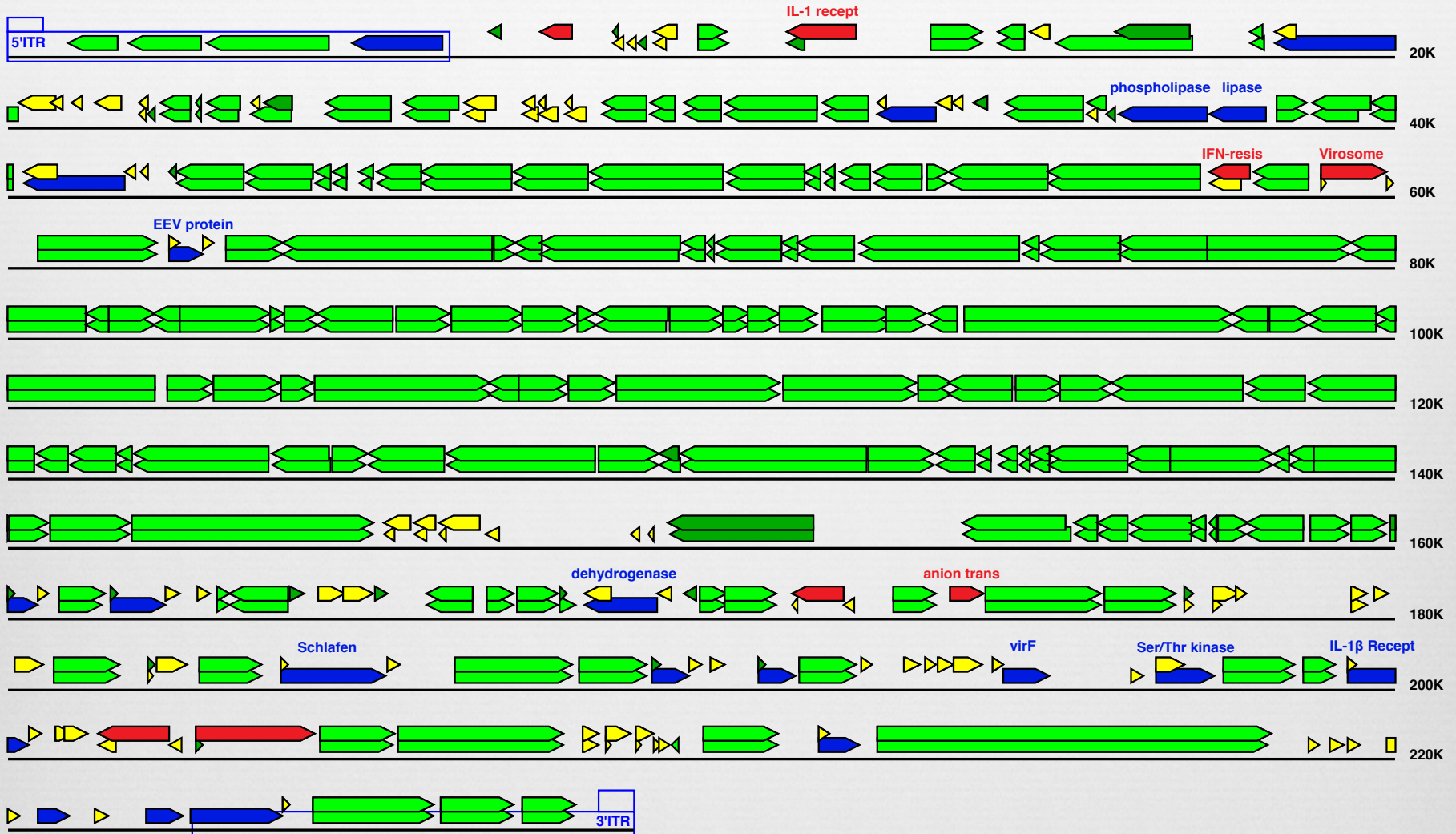


# Orthopoxvirus Gene Content





# Variola:Monkeypox



Variola: 8 unique genes  
Monkeypox: 20 unique genes  
Cowpox: 0 unique genes

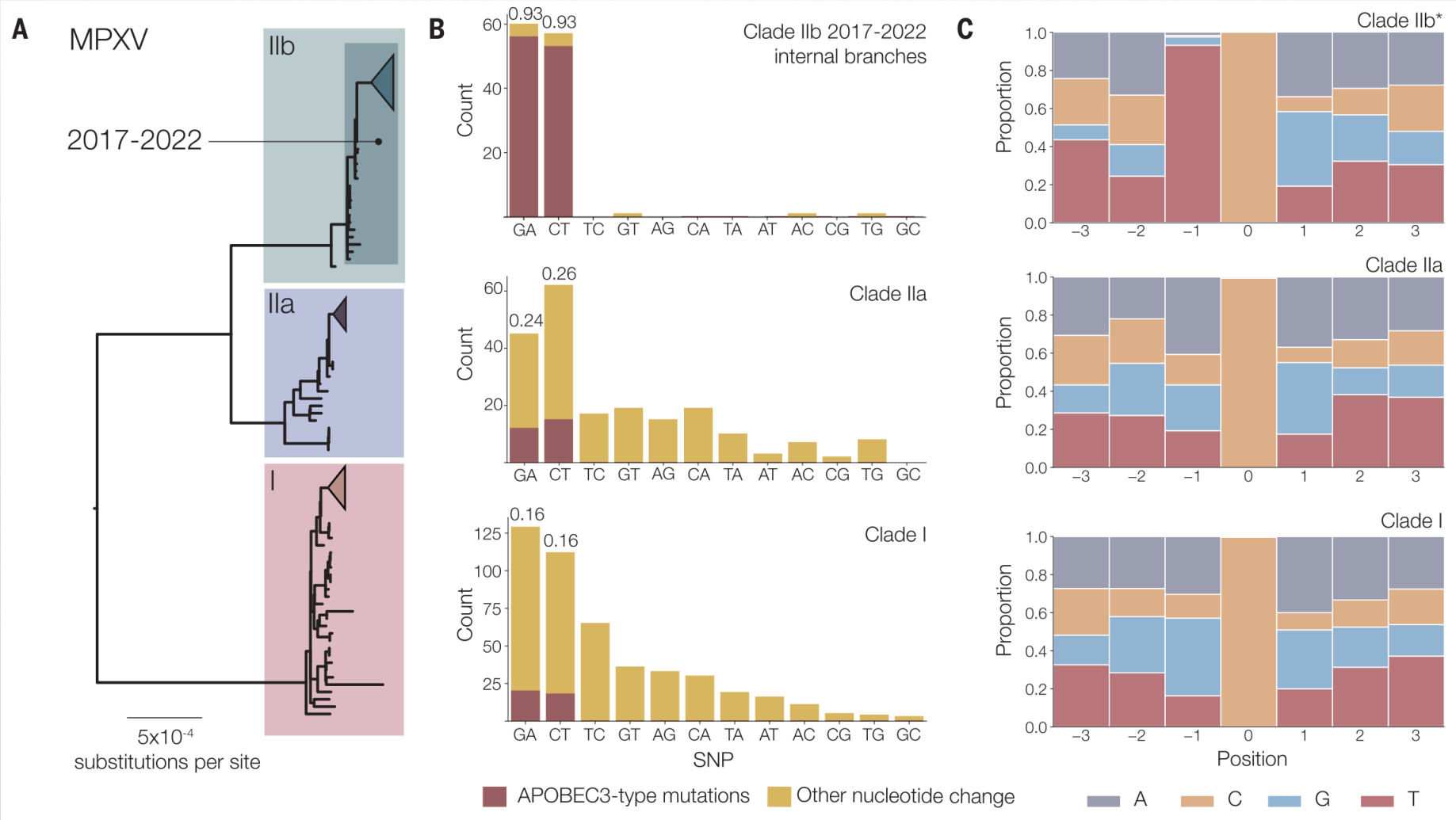
# Monkeypox – Clade I:II



Clade I: 3 unique genes

Clade II: 0 unique genes

# Specific enrichment of APOBEC3-type mutations in MPXV samples collected since 2017



Science

AAAS

# Evolution of Monkeypox virus

- ◆ Host dependent
  - ◆ Long periods of variation in an unknown reservoir host
  - ◆ Periodic zoonoses into alternative hosts
    - ◆ Primate species; Humans
  - ◆ More extended transmission in human hosts
    - ◆ Clade IIb
- ◆ Mechanisms of genotypic variation
  - ◆ SNPs, small indels
  - ◆ APOBEC3-driven mutagenesis
- ◆ Extent of phenotypic variation
  - ◆ Clade I and II: CFR, transmission differences (?)
  - ◆ Within Clade II: Limited to none (?)

# Thanks To

## ◆ UAB Alumni

- ◆ Eneida Hatcher
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- ◆ Curtis Hendrickson
- ◆ Login Mims
- ◆ Steve Powell

## ◆ ICTV

- ◆ Executive Committee
- ◆ SG Members

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- ◆ Chris Upton
- ◆ CDC Team