This content was published before guidance to change “monkeypox” to “mpox” was delivered to CDC programs in December 2022.

MONKEYPOX

Monkeypox: history, preparedness efforts, and current emerging outbreak

November 10th, 2022

Christina L. Hutson, Ph.D., MS

Laboratory and Testing Task Force Lead

CDC 2022 Monkeypox Multinational Outbreak Response

Branch Chief

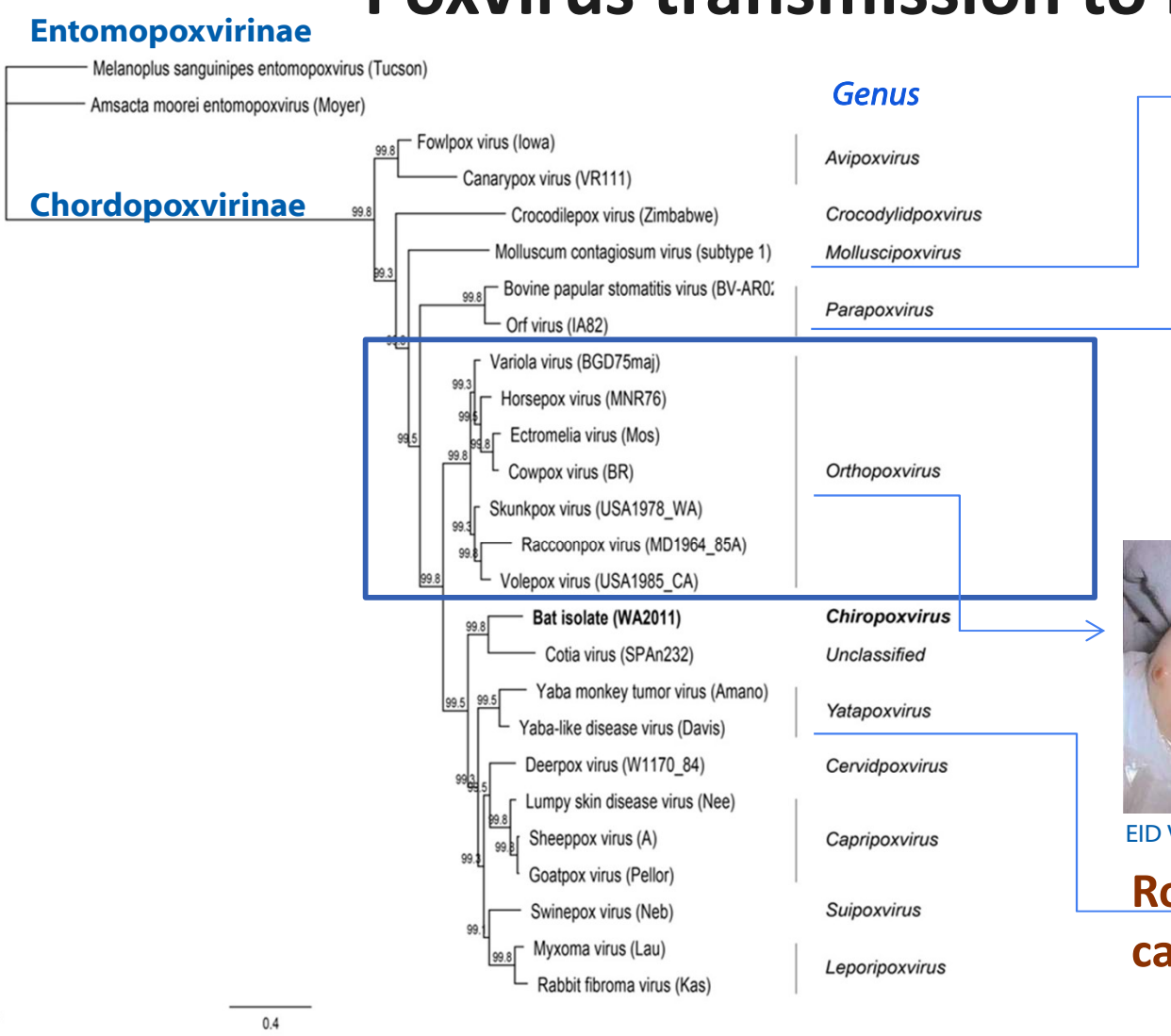
Poxvirus and Rabies Branch

MONKEYPOX

Outline

- Introduction to Orthopoxviruses
- Past preparedness activities
  - Medical countermeasures (diagnostic assays, anti-viral therapies, vaccines)
- Monkeypox outbreak 2022
  - Diagnostic testing
  - Sequencing efforts
  - Research activities

Poxvirus transmission to humans



Person to person

www.cdc.gov

Cows, sheep, goats

NEJM 363;27 2010

EID Vol. 9, No. 11, 2003

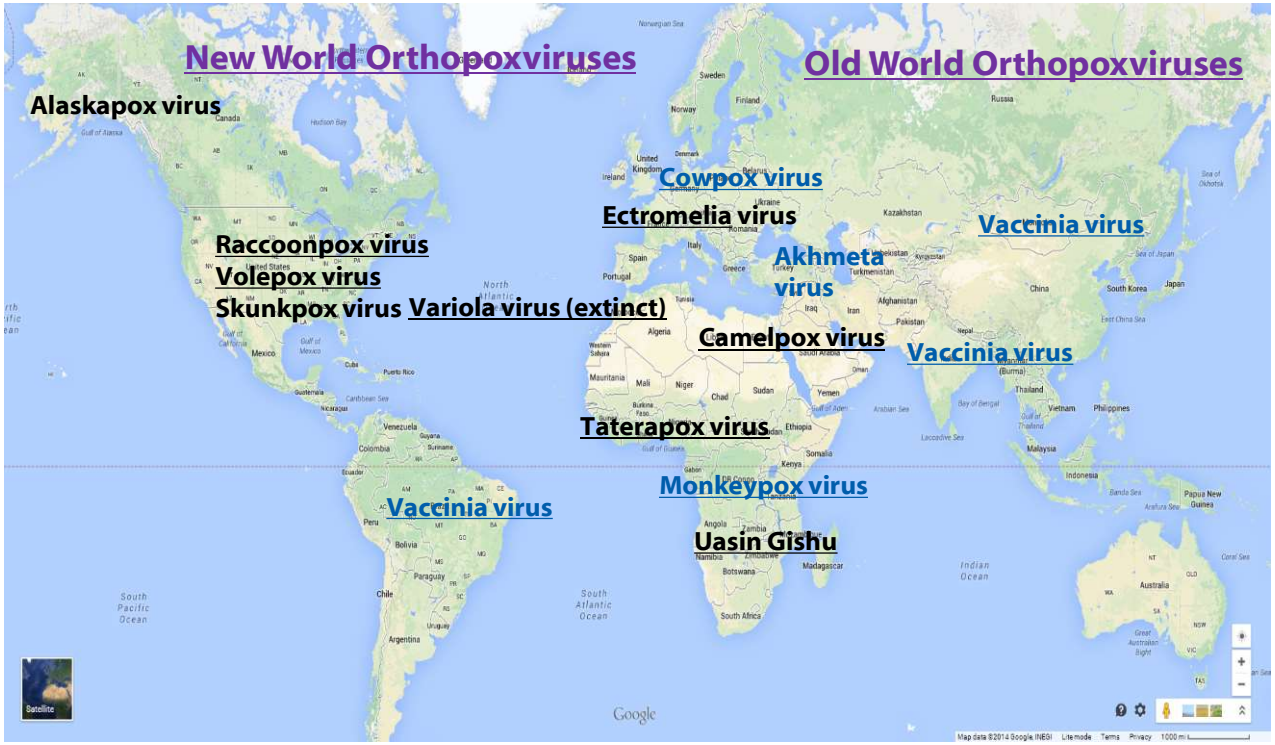
Primates, mosquitoes

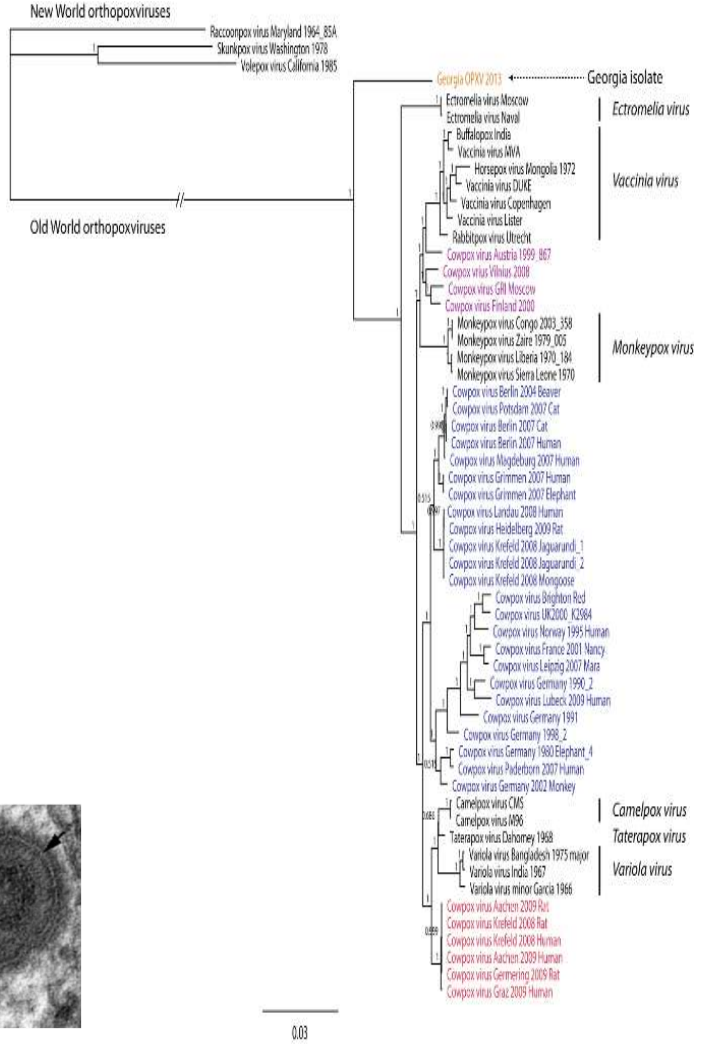
NEJM 2004; 350:361-366

Rodent reservoirs, cattle, pets

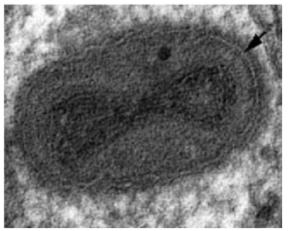
Restri

Orthopoxviruses around the world





- > 90% genetic similarity
- Serologically cross-reactive
  - Basis behind protective vaccination
- New isolates continue to be identified



Orthopoxvirus species	Geographic distribution	Reservoir host	Other naturally infected hosts
Eurasian (Old World)			
Camelpox	Africa, Asia	Camels	None
Cowpox	Europe, western Asia	Rodents	**Humans**, Cats, Cows, Zoo animals
Ectromelia	Europe	Rodents	None
Horsepox	Central Asia	Unknown	Horses
Monkeypox	Western, central Africa	Unknown	**Humans**, Monkeys
Taterapox	Western Africa	Gerbils	None
Uasin Gishu	Eastern Africa	Unknown	Horses
Vaccinia	Worldwide	Unknown	**Humans**, Rabbits, Cows, River buffaloes
Variola	Worldwide	**Humans only**	None
North American (New World)			
Raccoonpox	Eastern USA	Raccoons	Cats
Skunkpox	Western USA	Skunks	None
Volepox	Western USA	Voles	None

MONKEYPOX

Typical human Orthopoxvirus infections

- Febrile rash illness
- Systemic symptom include:
  - Soreness at site
  - Erythema
  - Malaise
  - Local lymphadenopathy
  - Fever
  - Flu-like symptoms

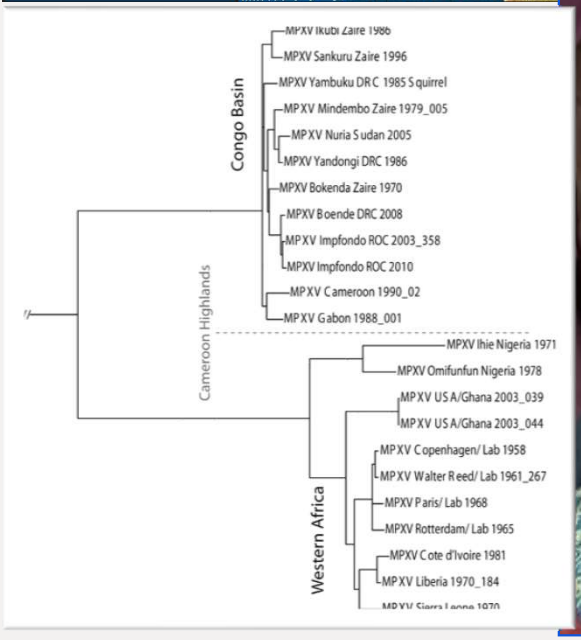
Human monkeypox; Reynolds et al. 2013

Vaccinia virus in Brazil; Trindade et al. 2009

Cowpox in rat and human; outbreak in Germany 2009; Campe et al. 2009

MONKEYPOX

- First described in monkeys (1958)
  - In humans in 1970
- Smallpox-like illness
  - Easily confused with varicella
- Two distinct clades of virus
  - Transmission, morbidity and mortality higher for Clade I (Congo Basin)
    - Mortality rate ~11%

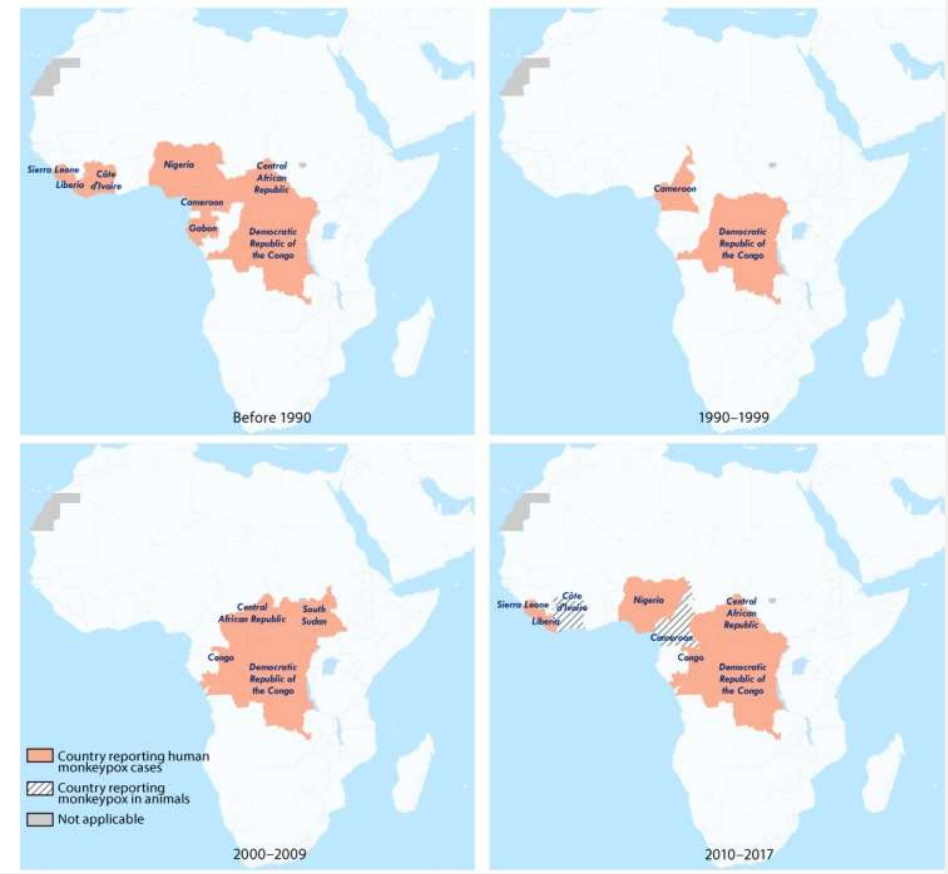


Damon, Roth, & Chowdhary 2006. NEJM 355(9):962-963
Rimoin *et al.* 2010. PNAS 107(7):16262-16267

MONKEYPOX

Monkeypox: a re-emerging disease?

- Increased monkeypox case reports
- Exportations:
  - US 2003, 2020, 2021
  - UK 2018, 2019, 2021
  - Israel 2018
  - Singapore 2019
  - > 92 countries 2022

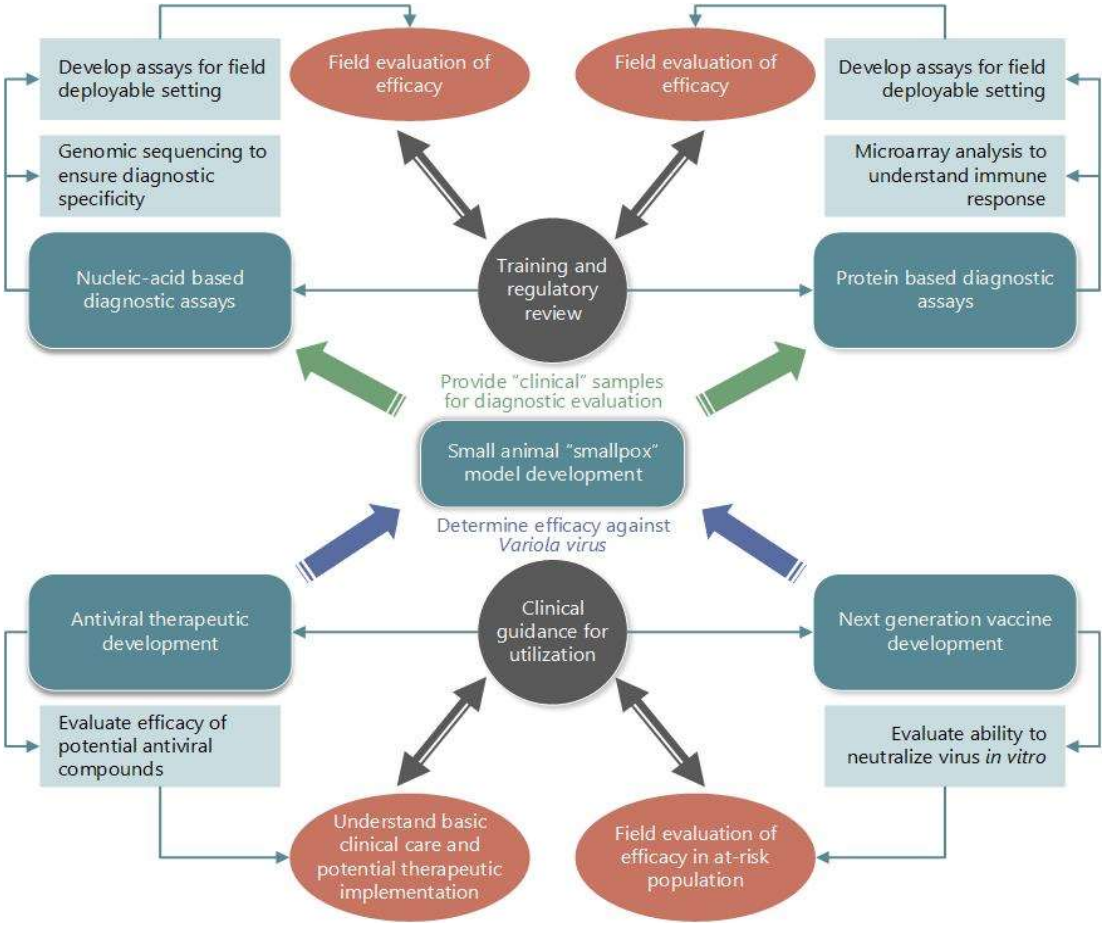


Durski, KN *et. al* MMWR. 2018 Mar 16; 67(10):306-310.

Preparedness activities

United States Smallpox Research Agenda

- Critical support for smallpox vaccine utilization (1999)
  - Diagnostic assays
  - Clinical guidance
  - Training of healthcare professionals
- Development of potential medical countermeasures (2009)
  - Regulatory review of diagnostics
  - Validation of potential medical countermeasures against smallpox
    - Anti-viral therapies
    - Vaccines



http://www.nationalacademies.org/hmd/Reports/1999/Assessment-of-Future-Scientific-Needs-for-Live-Variola-Virus.aspx

MONKEYPOX

OPXV diagnostic testing

- Laboratory Response Network
  - Integrated network of laboratories
    - State and local public health
    - Federal (United States)
    - Military
    - International
  - Respond to bioterrorism and other public health emergencies

Laboratory Information | CDC

- FDA cleared tests prepositioned within the LRN
  - Non-variola orthopoxvirus tests
  - Variola specific tests

MONKEYPOX

Testing for Suspect MPX Cases

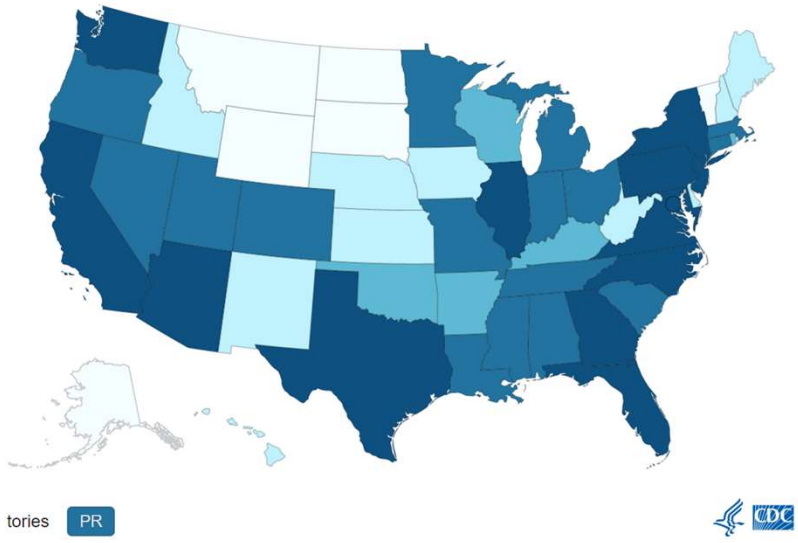
- US Laboratory Response Network (LRN) labs (10,000 tests/week)
  - LRN labs (located within the state public health labs) were perform CDC's FDA cleared non-variola Orthopoxvirus (NVO)-specific PCR test
  - Laboratories send samples to CDC for MPX-specific PCR and sequencing
    - CDC has Clade I, Clade II and Generic MPXV tests
- Commercial laboratory testing is now available (70,000 additional tests/week)
  - 40,000 testing capacity per week using CDC NVO test
  - 30,000 tests of commercial MPOX-specific laboratory test
- Current testing capacity is at least 80,000 tests per week

MONKEYPOX

28, 797 Total confirmed November 9th, 2022 monkeypox/orthopoxvirus cases in US

- https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html

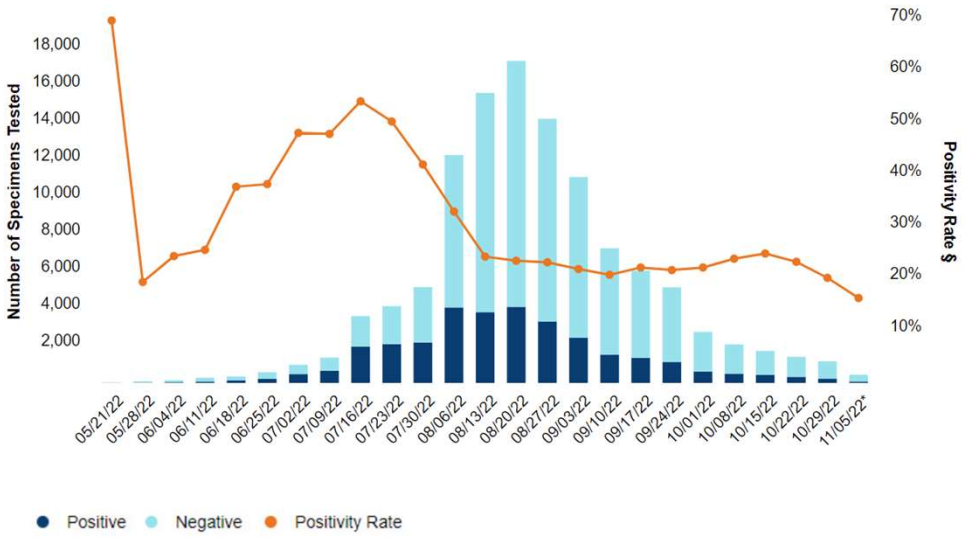
California	5512
New York	4132
Florida	2768
Texas	2760
Georgia	1929
Illinois	1397
Pennsylva	848
New Jerse	754
Maryland	722
North Car	659



MONKEYPOX

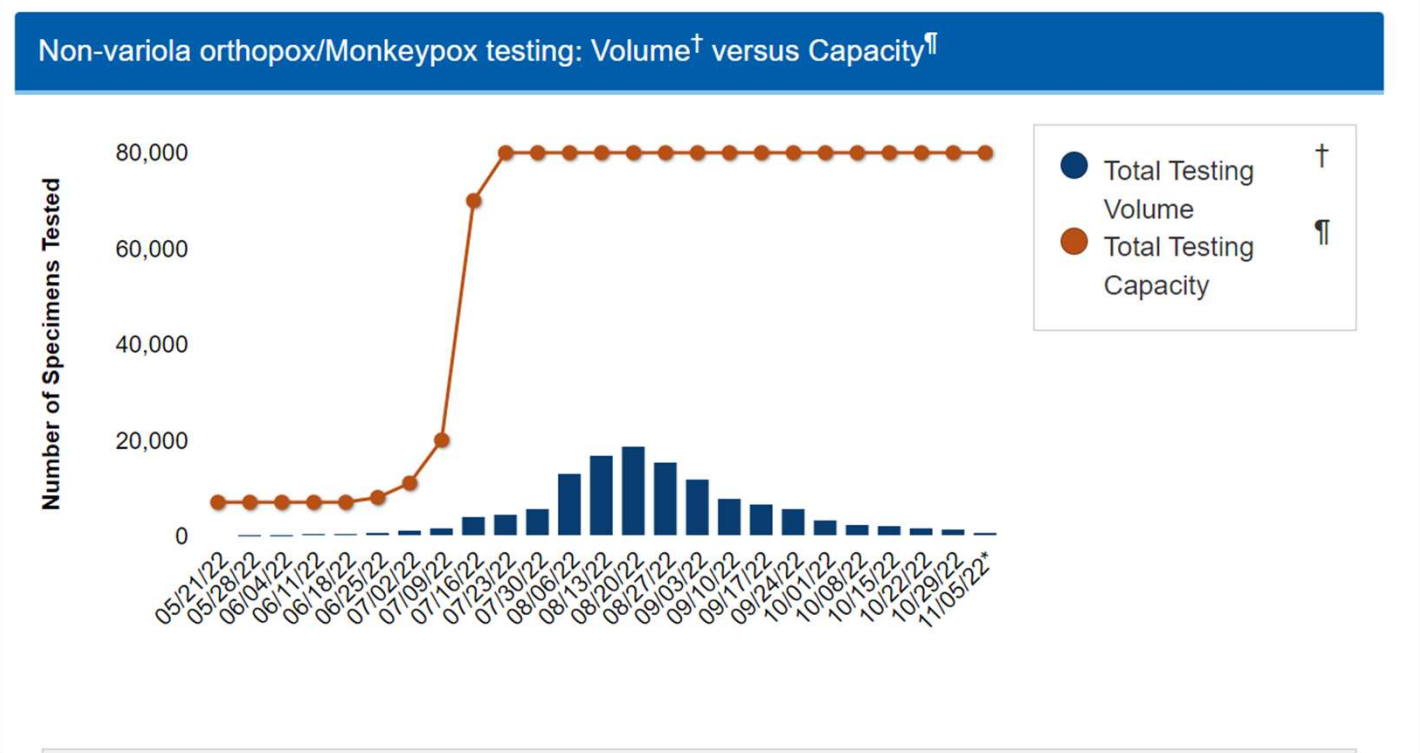
Total Specimens Tested	Cumulative Positivity Rate	Capacity¶ Available
123,809	27.5%	98.4%

Non-variola orthopox/Monkeypox testing from public health and select commercial laboratories †



Source: Non-Variola Orthopoxvirus and Monkeypox Virus Laboratory Testing Data | Monkeypox | Poxvirus | CDC

MONKEYPOX



Source: Non-Variola Orthopoxvirus and Monkeypox Virus Laboratory Testing Data | Monkeypox | Poxvirus | CDC

MONKEYPOX

2022 Monkeypox virus sequencing update

- All publicly available MPXV genomes from the 2022 Monkeypox outbreak to date belong to Clade IIb (formerly West African) MPXV

- Genomes published during the 2022 monkeypox outbreak share a common ancestor with MPXV from Nigeria; however, sequences from surrounding countries are limited and most of our understanding of these relationships comes from viruses linked to or identified in Nigeria

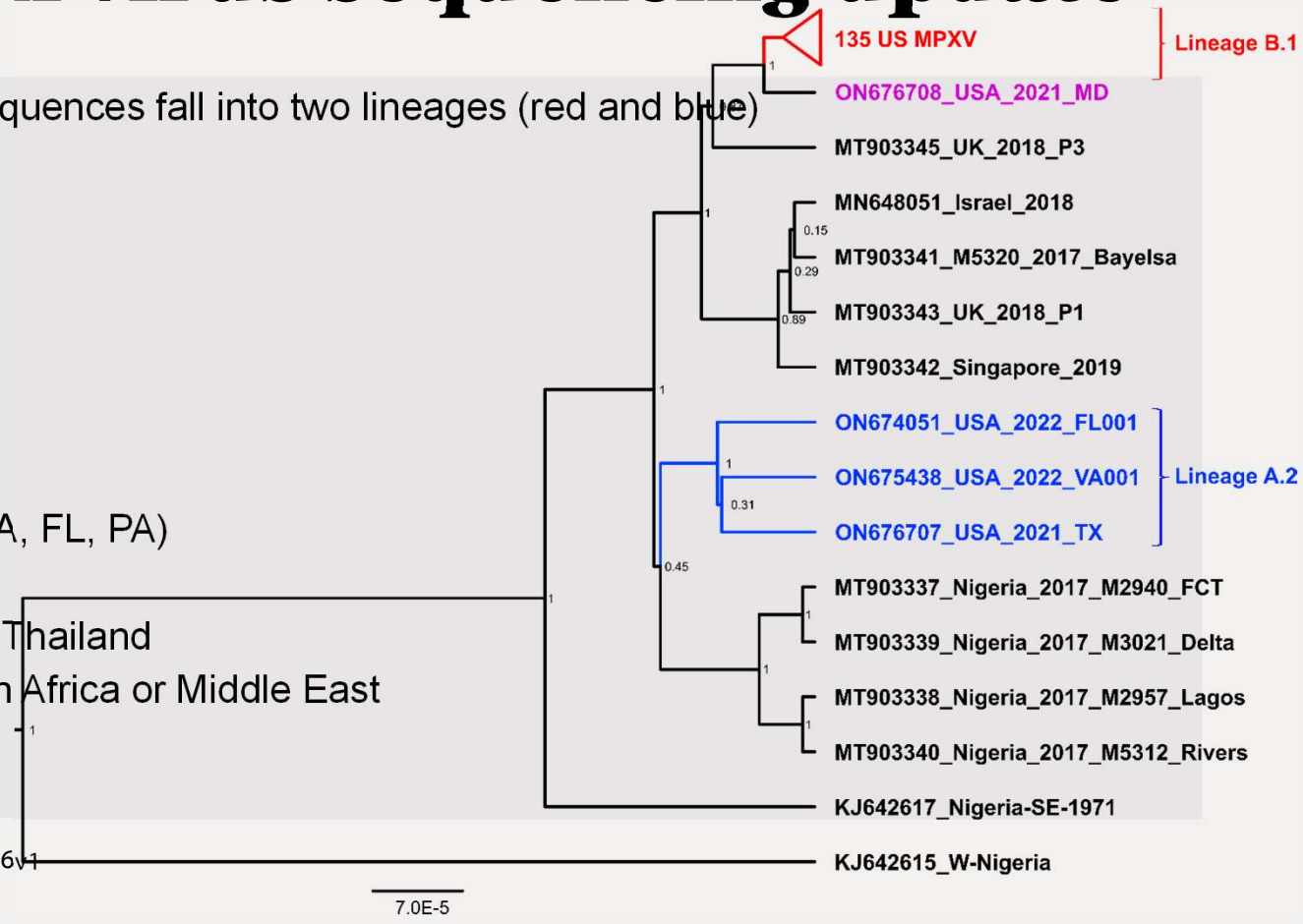
MONKEYPOX

U.S. Monkeypox virus sequencing update

- 2022 U.S. monkeypox virus sequences fall into two lineages (red and blue)

- Lineage B.1 (red)
  - Most U.S. sequences
  - Most global sequences

- Lineage A.2
  - Three 2022 U.S. cases (VA, FL, PA)
  - One 2021 case (TX)
  - Also reported in India and Thailand
  - Most had travel to Western Africa or Middle East

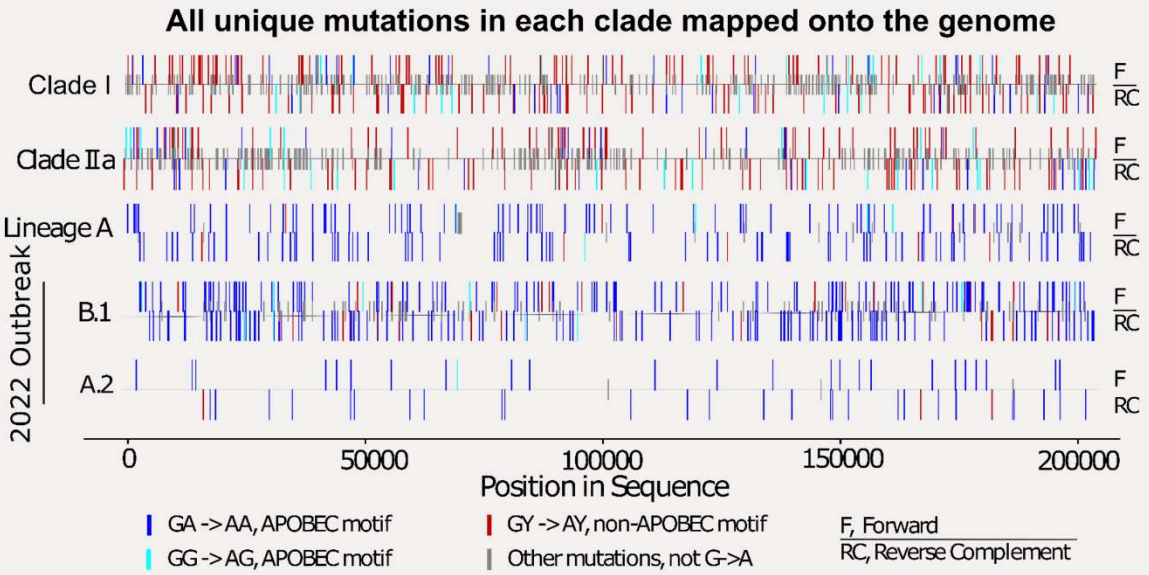


https://www.biorxiv.org/content/10.1101/2022.06.10.495526v1

MONKEYPOX

Increased mutations observed in 2022 MPXV, evidence of host protein ABOBEC3 activity

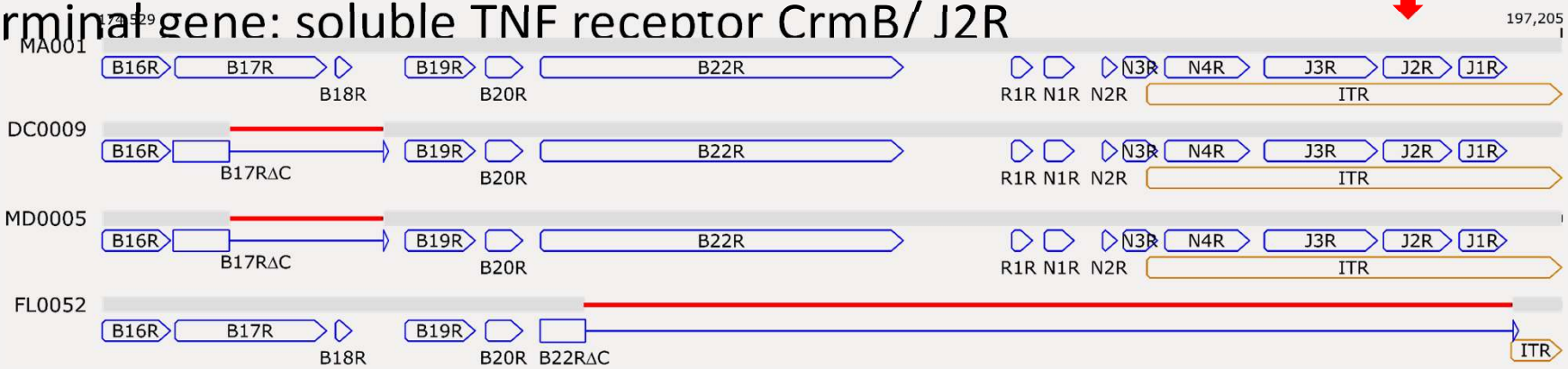
- Many of the observed mutations in the 2022 outbreak MPXV sequences are GA-to-AA
- This is indicative of Apolipoprotein B mRNA Editing Catalytic Polypeptide-like3 (APOBEC3) deaminase activity
- APOBEC3 proteins are part of vertebrate innate immune system that restrict the replication of viruses through cytosine-to-uracil deaminase activity



MONKEYPOX

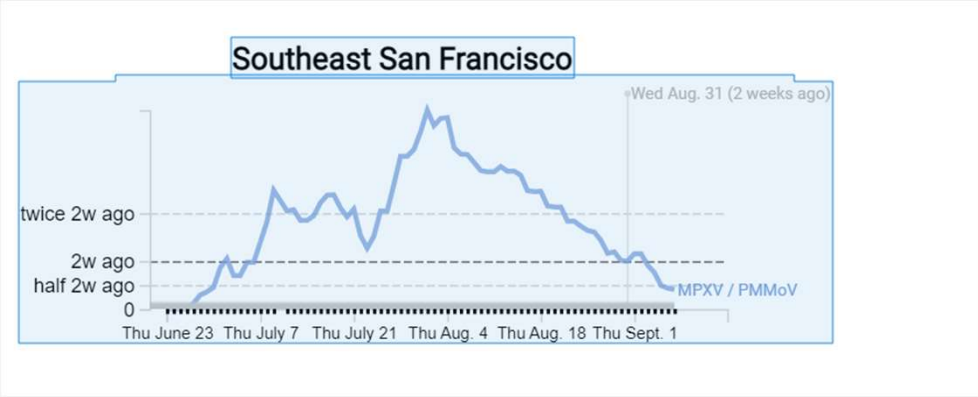
Preliminary finding: evidence of large deletions in 2022 MPXV

- ~3% of MPXV genomes contain evidence of deletions
- Deletions have potential to impact diagnosis and efficacy of therapeutics
- Deletions are more common in the terminal regions of the genome, where non-essential genes are located
- MPXV Clade II (West African)-specific, MPXV generic assays target a terminal gene: soluble TNF receptor CrmB/ J2R



MONKEYPOX

Research Efforts *



- Transmission to animals
  - Domestic animals
  - Escape to wildlife
- Wastewater detection
  - Research – WastewaterSCAN
  - CDC efforts
- Testing sensitivity of isolates with changes in the TPOXX target (F13L (VP37))
  - Culture of viral isolates for sensitivity testing
  - FDA- TPOXX works by inhibiting a viral protein, called VP37, that all orthopoxviruses (including monkeypox) share.
  - Small changes to the VP37 protein could have a large impact on the antiviral activity

MONKEYPOX

Research Efforts *

- Prevalence of monkeypox prior to first confirmed case
  - Serologic retrospective studies
  - PCR testing of banked specimens
- Prevalence of undetected monkeypox within higher risk populations
  - Serologic prospective studies
  - PCR testing of banked specimens

Specimens for detection prior to rash onset

- District of Columbia Department of Forensic Sciences Public Health Laboratory Division and CDC collaborative study
- Objectives
  - To determine if MPX DNA can be detected in specimens prior to lesion/rash presence among persons at elevated risk of MPX exposure (i.e., persons presenting for PEP or PEP++).
  - To assess the immune response against JYNNEOS from the US population after at least one dose of vaccine.
- Visit 1:
  - 529 throat swabs tested
  - 166 rectal swabs tested
  - 334 blood
    - Testing whole blood by PCR
    - 327 samples from the Day 0 timepoint tested with IgG
  - 841 completed survey
- Visit 2-specimen testing is complete
  - Analysis ongoing

MONKEYPOX

Conclusions

- Largest monkeypox outbreak outside African continent currently ongoing
  - >28,000 cases in US; >78,000 globally in 110 countries
    - US has had 11 deaths
  - High transmission between men who have sex with men (MSM)
- Multiple medical countermeasures developed through US Smallpox Research Agenda are beneficial for detection and treatment of monkeypox
  - Characterized diagnostic assay within Laboratory Response Network
    - Expansion to commercial laboratories
  - Two anti-viral therapies (TPOXX® and Tembexa®) approved by US Food and Drug Administration
  - Smallpox and monkeypox vaccine [IMVAMUNE® (JYNNEOS ®)] approved by US Food and Drug Administration

MONKEYPOX

Acknowledgements

CDC:

The Monkeypox Outbreak Response

- The Laboratory and Testing Task Force
- The Epidemiology Task Force

The Poxvirus and Rabies Branch

CDC DRC:

Joelle Kabamba, MD, MPH

District of Columbia Department of Forensic Sciences Public Health Laboratory Division

- National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA
- Leidos Inc., Reston, VA 20190, USA
- Los Alamos National Laboratory
- Massachusetts Department of Public Health
- Maryland Department of Health
- Minnesota Department of Health
- Florida Department of health
- Washington DC department of health
- Maryland department of health
- Rhode Island department of health
- Dallas County Health and Human Services Public Health Laboratory
- Florida Department of Health Bureau of Public Health Laboratories-Jacksonville
- Florida Department of Health in Broward County
- Virginia Department of General Services
- Virginia Department of Health
- Utah Department of Health and Human Services
- Sacramento County Public Health
- Leidos Inc., Reston, VA 20190, USA

Questions?

1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348   www.cdc.gov