

MONKEYPOX

Lessons learned



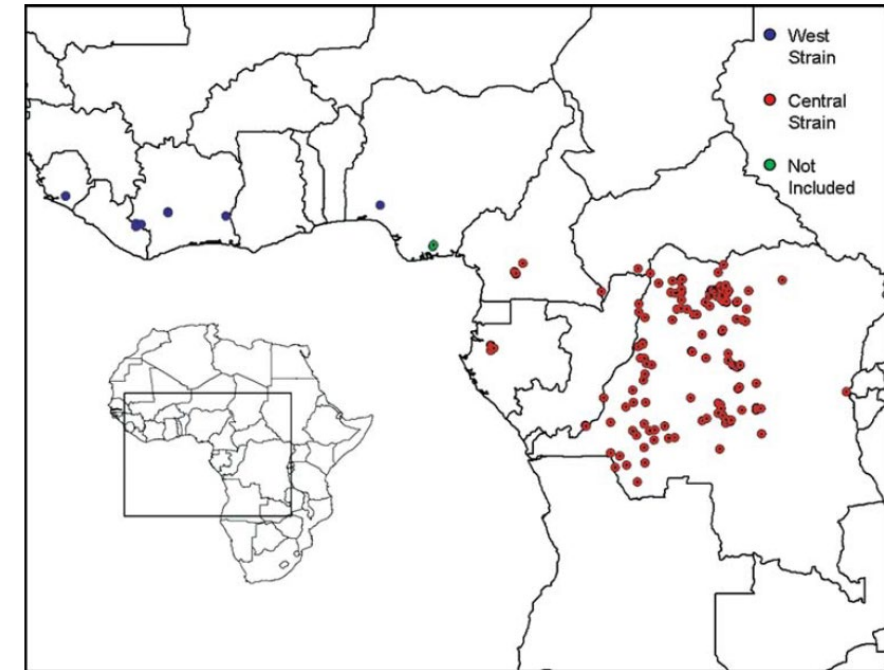
Emmanuel Nakouné-Yandoko
Institut Pasteur de Bangui
Central African Republic



Monkeypox

Monkeypox is a zoonotic orthopoxvirus that has a similar disease presentation as smallpox in humans with the additional distinguishing symptom of lymphadenopathy.

The recent apparent increase in human monkeypox cases across a wide geographical area, the potential for further spread and the lack of reliable surveillance, have raised the level of concern for this emerging zoonosis.

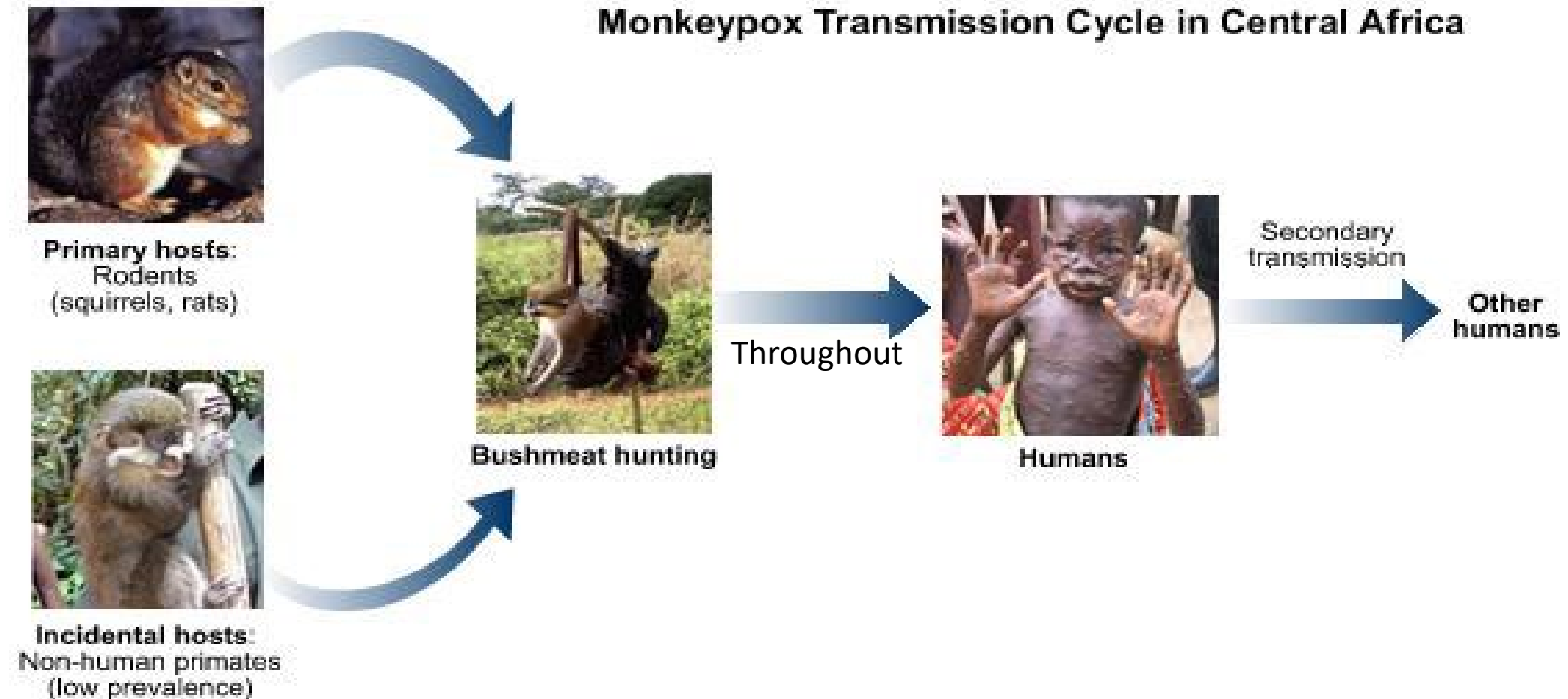


Levine et al. 2007

Monkeypox virus has 2 recognized clades: West African and Congo Basin. Differences in epidemiological and clinical features between viral isolates support the distinction between these 2 clades

Monkeypox

Monkeypox virus was first reported in 1959 as an outbreak of a pox-like disease in monkeys kept at a research institute in Copenhagen, Denmark

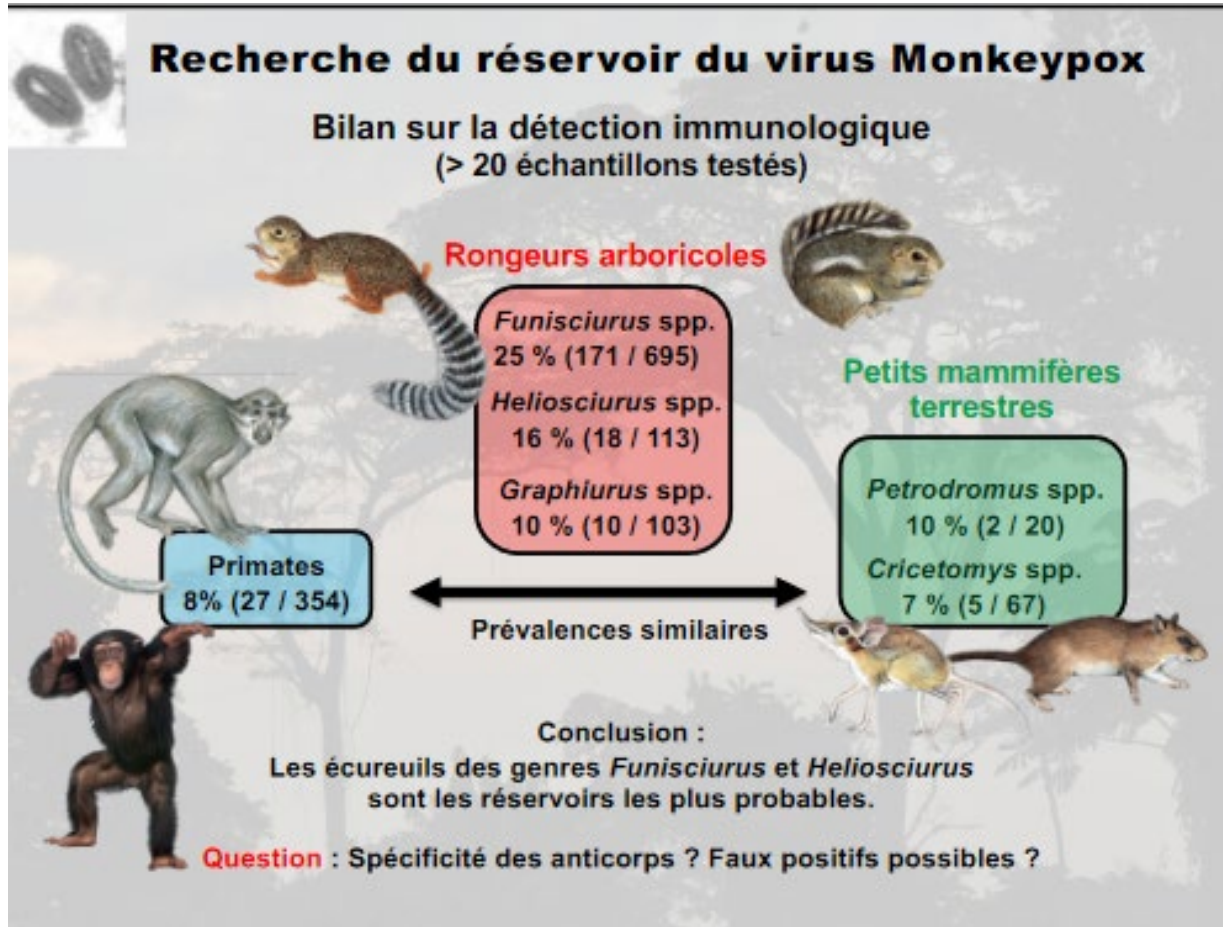


Although the reservoir host of MPXV has not been definitively identified, many mammalian species have been naturally infected with MPXV

Table 1. Natural monkeypox virus (MPXV)-infected animals.

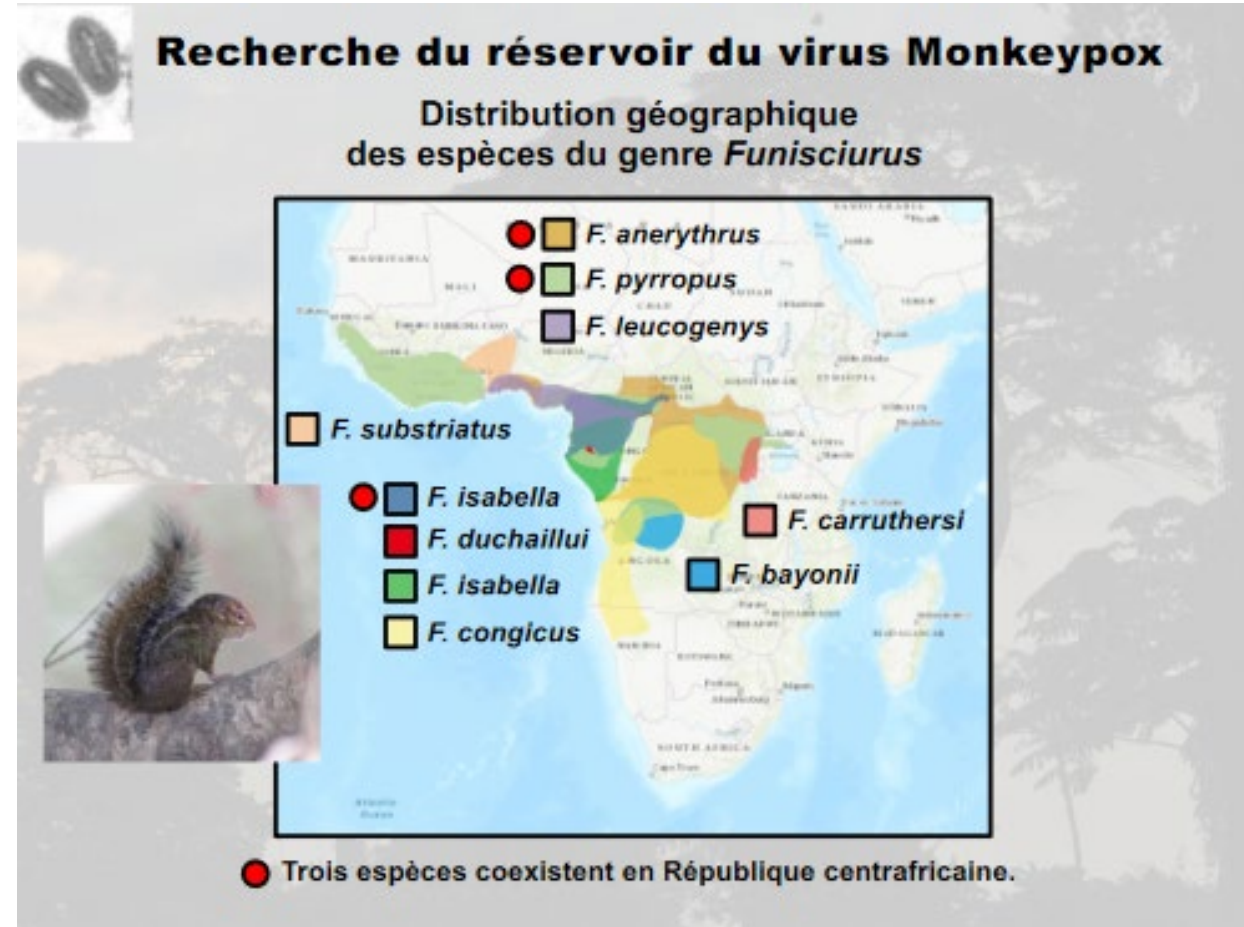
	Geographic Location/Countries	Method of Detection	References
Sooty mangabey monkey (<i>Cercocebus atys</i>)	Côte d'Ivoire	PCR	[66,84]
Gambian-pouched rat (<i>Cricetomys gambianus</i>)	Africa	PCR and viral isolation	[85–89]
Rhesus macaques (<i>Macaca mulatta</i>)	Copenhagen	Serological test	[15,90–94]
Cynomolgus Macaque (<i>Macaca fascicularis</i>)	Singapore/Copenhagen	Viral isolation	[49,92,95,96]
Asian Monkeys (<i>M. fascicularis</i>)	Copenhagen	Viral isolation	[97–100]
Southern opossum (<i>Didelphis marsupialis</i>)	South America	PCR and viral isolation	[88,89,98,99]
Sun squirrel (<i>Heliosciurus</i> sp.)	Zaire	Antibody detection test	[62,88,89,98,101,102]
African hedgehogs (<i>Atelerix</i> sp.)	Africa	PCR, antibody detection test, and viral isolation	[81]
Jerboas (<i>Jaculus</i> sp.)	Illinois, USA	PCR, antibody detection test, and viral isolation	[49,81]
Woodchucks (<i>Marmota monax</i>)	USA	PCR and viral isolation	[98,100]
Shot-tailed opossum (<i>Monodelphis domestica</i>)	USA	PCR and viral isolation	[98,100]
Porcupines (<i>Atherurus africanus</i>)	Zaire	PCR and viral isolation	[58,61,78,89]
Giant anteaters (<i>Myrmecophaga tridactyla</i>)	Rotterdam	Viral isolation	[103]
Prairie dogs (<i>Cynomys</i> spp.)	USA	PCR and viral isolation	[33,81,99,104–106]
Elephant shrew (<i>Petrodromus tetradactylus</i>)	DR Congo	Serological test	[99,107]
Domestic pig (<i>Sus scrofa</i>)	DR Congo	Serological test	[99,108]
Rope squirrel (<i>Funisciurus</i> sp.)	Zaire	PCR and viral isolation	[55,87,88,104,107–109]
African dormice (<i>Graphiurus</i> spp.)	USA	PCR and viral isolation	[55,104,109]

Monkeypox : animal reservoir



tree-dwelling rodents

small land mammals



Squirrels of the genera *Funesciurus* and *Heliosciurus* are the most likely reservoirs

AFRIPOX Project

A One Health approach of monkeypox in the Central African Republic

ZOOLOGY

Animal reservoir and intermediate hosts
identification – proliferation - contacts

ECOLOGY

Environnement, ecotopes,
ecological changes

ZOOLOGY

ECOLOGY

VIROLOGY

Molecular field diagnostic test
Sequencing & phylogeny
Serological test

VIROLOGY

ANTHROPOLOGY

ANTHROPOLOGY

illness, changing ecologies,
wildlife

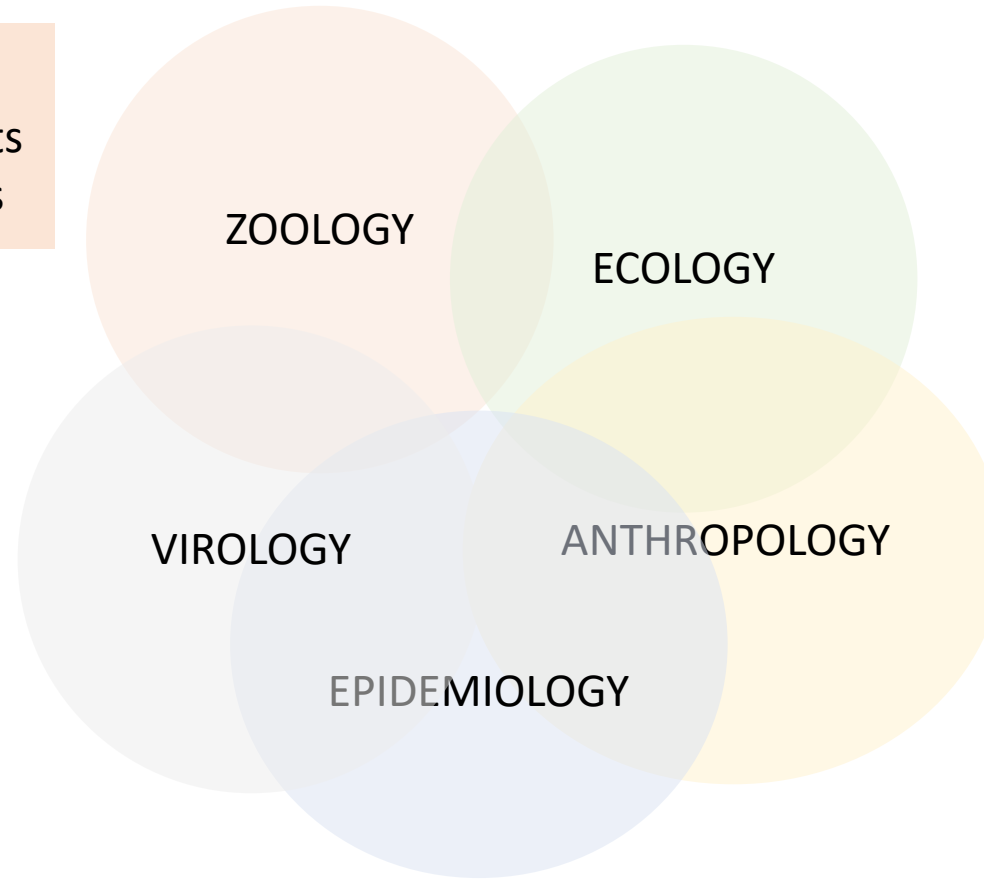
EPIDEMIIOLOGY

EPIDEMIIOLOGY

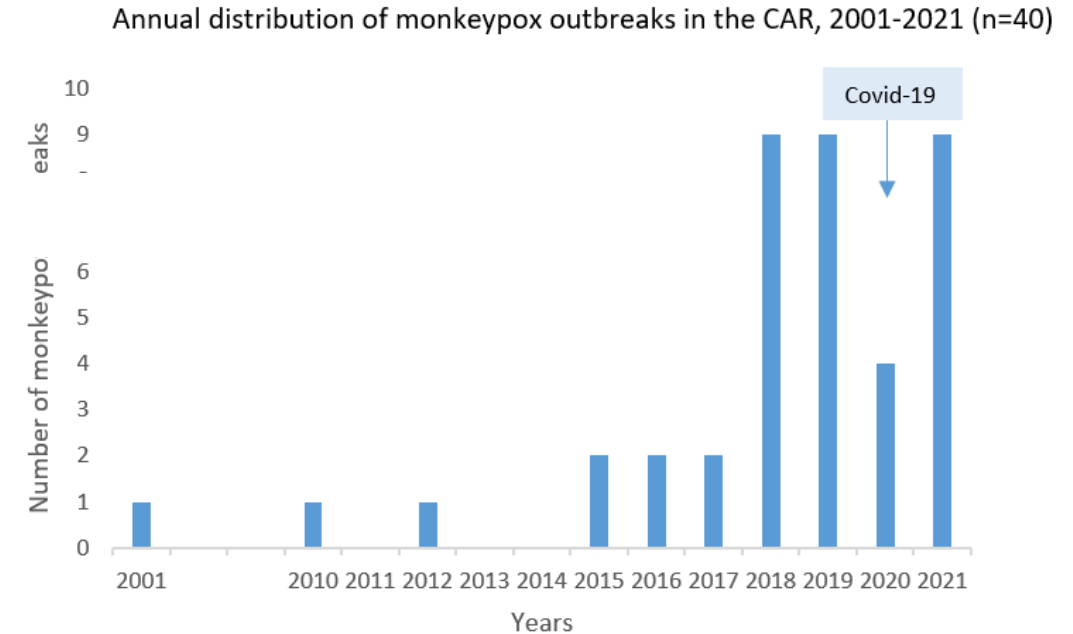
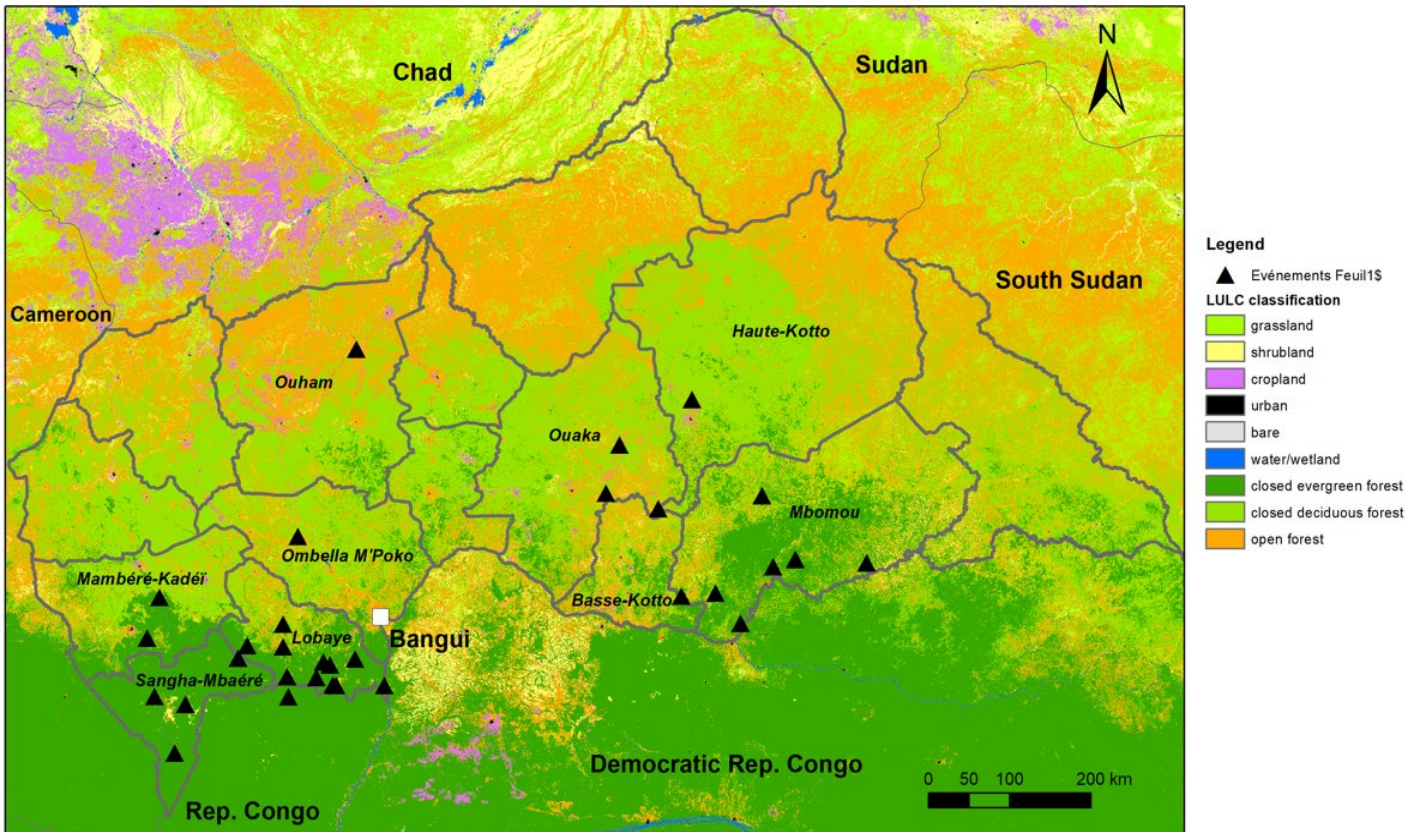
Surveillance, outbreak investigation,
modeling, transmission, natural history

CLINICAL RESEARCH

with University of Oxford:
clinical trial of tecovirimat



EPIDEMIOLOGY



40 outbreaks, size range: 1 to 13 (1 to 25)
99 confirmed cases, (160 with suspected cases)
Case-fatality rate: 12/160 (7.5%)

Landuse/Landcover data source: Copernicus 2019 Global 100m Landcover

Buchhorn, M. ; Lesiv, M. ; Tsendbazar, N. - E. ; Herold, M. ; Bertels, L. ; Smets, B. Copernicus Global Land Cover Layers — Collection 2. Remote Sensing 2020, 12, Volume 108, 1044. DOI 10.3390/rs12061044

Besombes C. et al. Emerg Infect Dis. 2022 Dec;28(12):2435-2445
National Monkeypox Surveillance, Central African Republic, 2001-2021.

VIROLOGY – diagnostic tools

Molecular field diagnostics

- Monoplex (RT-LAMP) and multiplex (RT-LAMP QUASR) rapid tests Integrated test cartridges (Withings) (MPX lineage, VZV)
- Detection by isothermal amplification / RPA strip technology

Serological diagnostic tests

- Multiplex test based on a library of more than 7891 viral peptides representative of the proteome of human pathogenic OPXV (MPXV, VACV, CPXV, VARV) (PhiP-Seq)
- Multiplex assay based on a combination of a selection of 10 MPXV proteins and peptides (MMIA)



VIROLOGY - sequencing

- Use of capture probes for long DNA fragments
- Microfluidic technology and droplet generation for targeted enrichment of droplets containing viral genome fragments
- Direct Illumina sequencing, or direct and real-time MinION sequencing on samples

www.nature.com/scientificreports/

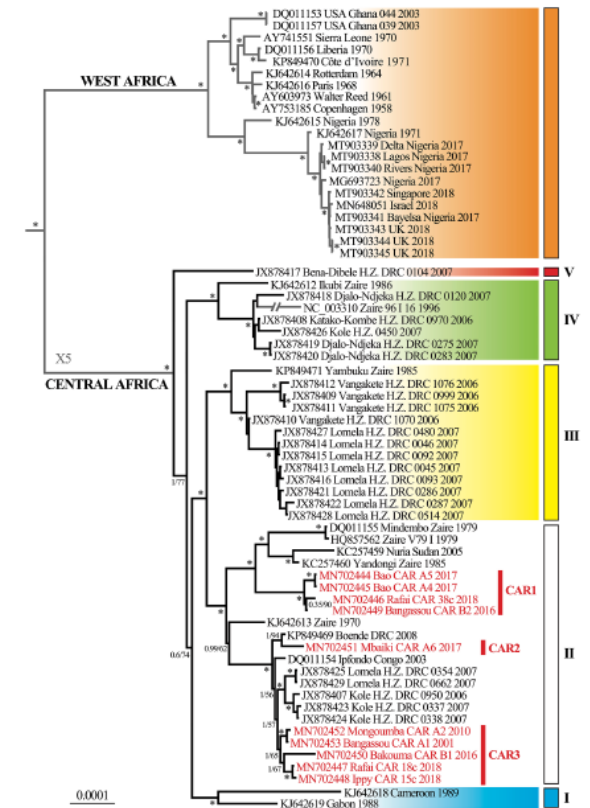
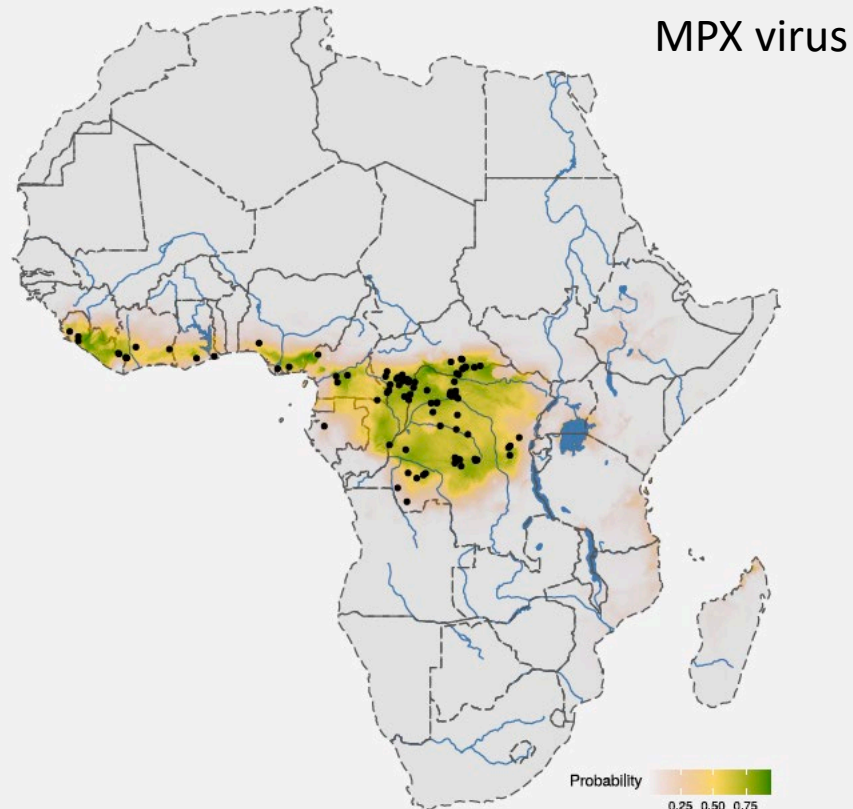


Figure 2. Phylogeny of monkeypox viruses (MPXV) based on complete genomes. The Bayesian tree was

(Berthet et al, Scientific Reports, 2021)

ZOOLOGY – Ecological niche



Curaudeau *et al.*, in prep

Ecological Niche Modelling with MaxEnt in R

African squirrels as a potential reservoir of Monkeypox virus

Squirrels



Funisciurus anerythrus



Funisciurus bayoni



Heliosciurus rufobrachium

1. MMPXV isolated from two African squirrels
 - *Funisciurus anerythrus* (Khodakevich *et al.*, 1986)
 - *Funisciurus bayonii* (Mariën *et al.*, in review)
 2. MPXV DNA in African squirrel museum specimens (Tiee *et al.*, 2018)
 - Five species of *Funisciurus* including two new species
 3. Anti-OPXV antibodies in African squirrels (Khodakevich *et al.*, 1988)
 - *Funisciurus*
 - *Heliosciurus*
- **African squirrels are good candidates for the reservoir of Monkeypox virus**
- **Focus on African squirrels**

ZOOLOGY – Field work



Animal samples: 250

2019 Toma outbreak

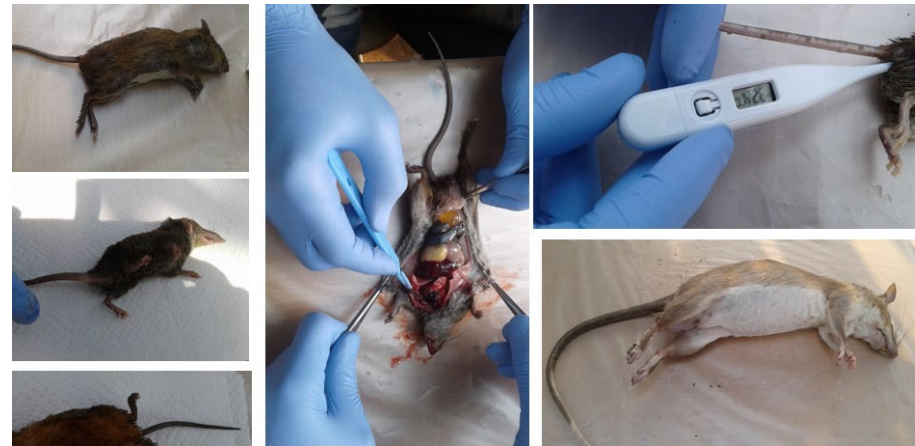
2021 Moloukou outbreak

2021 Grima outbreak

Rodents, duikers, squirrels,
bats, pangolins

PCR

Serological assay



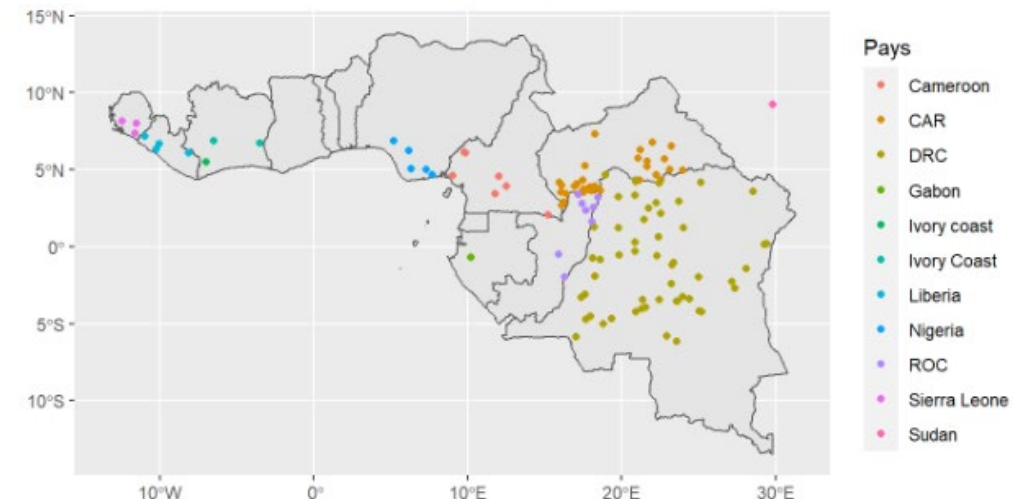
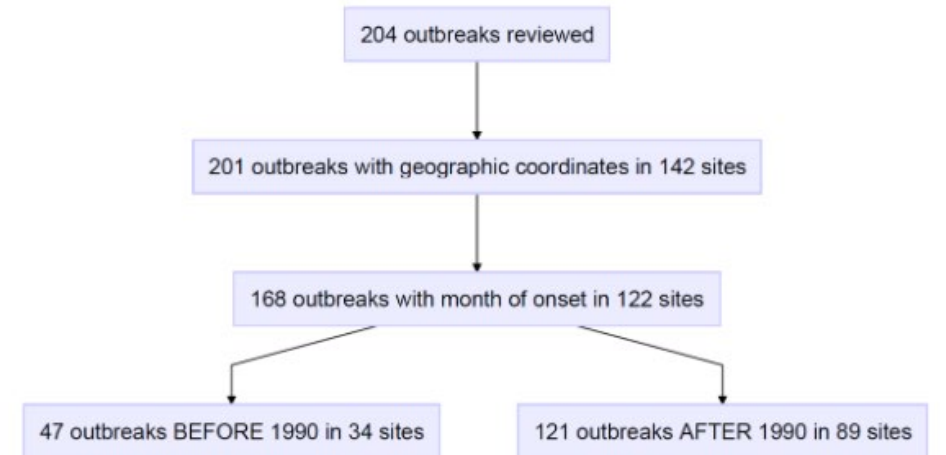
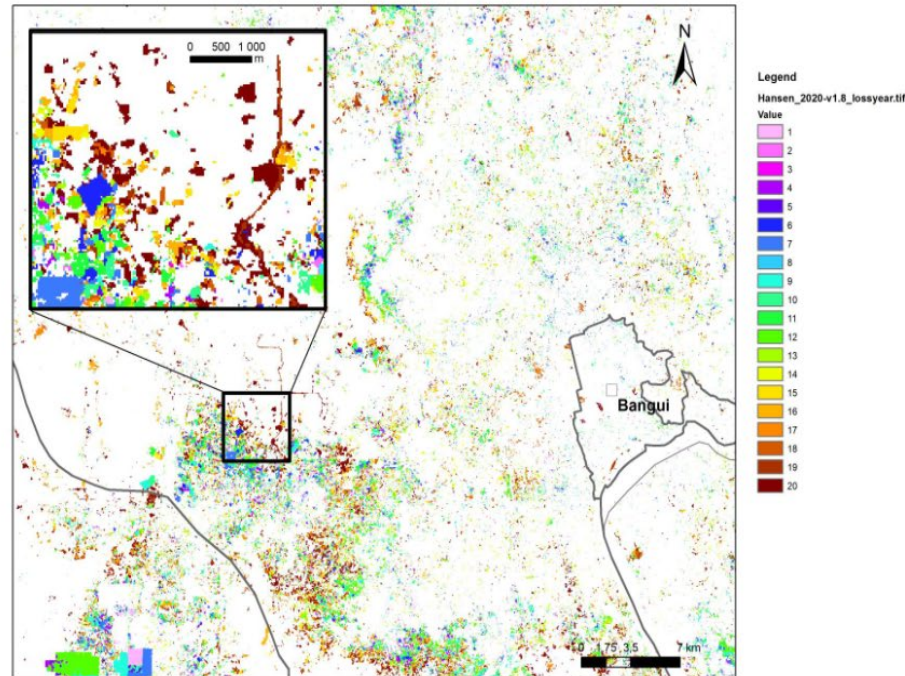
ECOLOGY

Environmental atlas

Climate profile

Human activities

DEFORESTATION



ANTHROPOLOGY

- **Anthropological investigation** of monkeypox illness, diagnosis & treatment pathways, care: formal health care workers, traditional healers, former patients
- **Participatory investigation of « local epidemiologies »** (local understandings of origins, emergence, transmission)
- **Ethnohistorical** study of local ecological (forest, wildlife) & social changes implied in monkeypox emergence in the CAR since 1970
- **Ethnoecology:** local conceptions and observations of wildlife; current practices with wildlife



OUTLOOK

- Train staff to strengthen national surveillance and patient management
- Support countries in the sub-region to develop cross-border surveillance
- Participate in clinical trials to evaluate the effectiveness of Tecovirimat
- Adaptation of the therapeutic trial and vaccination protocol
- Extend the compassionate use of Tecovirimat[®] to southeastern CAR.

Collaborators

Camille Besombes
Romulus Breban
Laura Schaeffer
Arnaud Fontanet

Nicolas Berthet (IP Paris & IP Shanghai)
Lingjing Mao (IP Shanghai)
Jessica Vanhomwegen
Valérie Caro
Christophe Batejat
Jean-Claude Manuguerra

Cassandra Von Platen

Antoine Gessain

Romain Duda
Tamara Giles-Vernick



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Manon Curaudeau
Alexandre Hassanin

Jordi Landier
Pascal Handschumacher
Jean Gaudart

