



# GLOBAL FMD UPDATE: NEW APPROACHES TO MONITOR OUTBREAKS AND PREDICT THREATS?

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Department  
for Environment  
Food & Rural Affairs



FMD Reference Laboratory



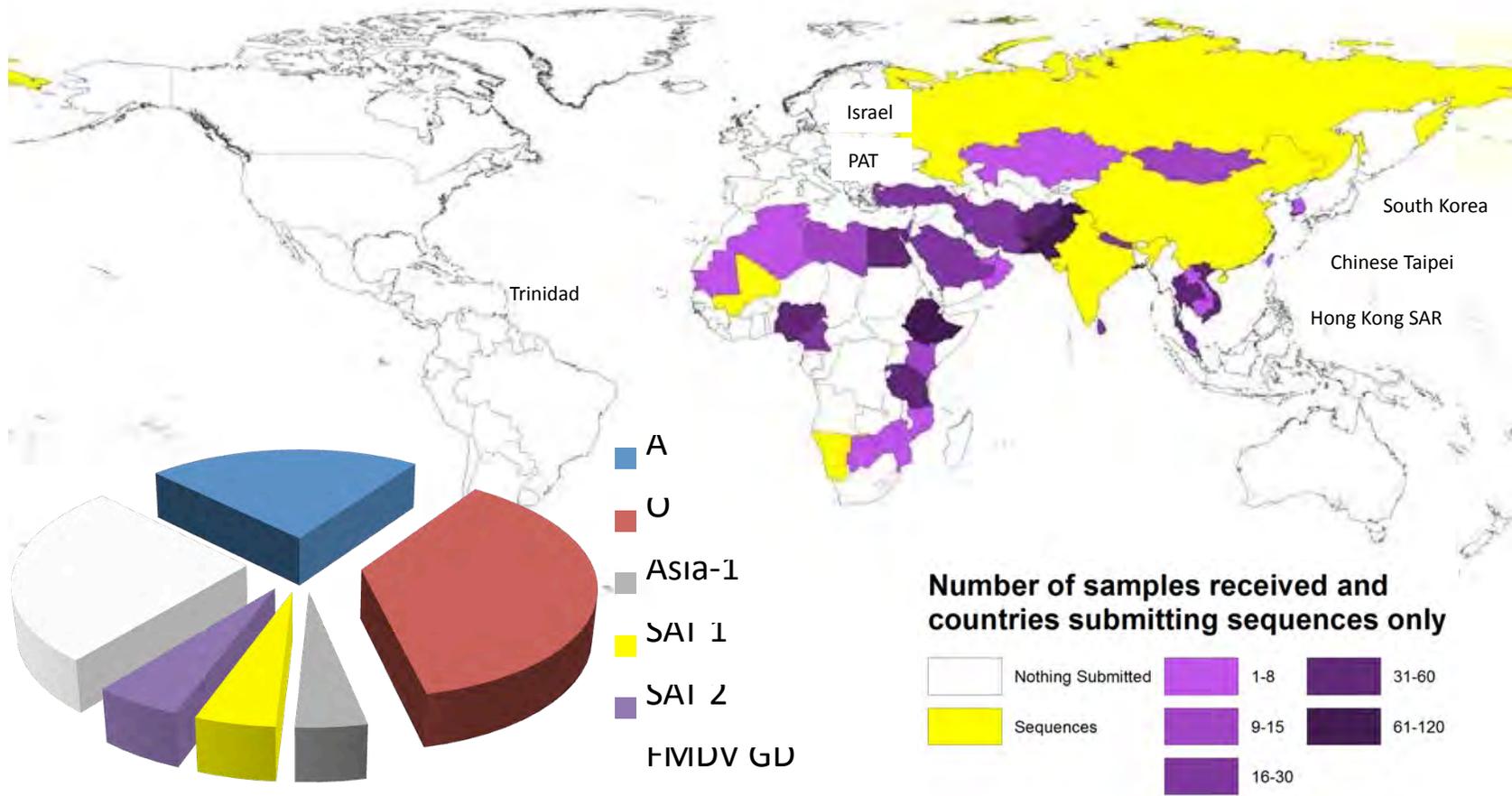
# BBSRC National Virology Centre: The Plowright Building

- Jan-Sept 2015: Occupied new high containment laboratory
- Transfer of QA accreditation
- Houses all work with “live” FMD and International Reference Laboratories for FMD, BT, PPR, ASF, AHS, Capripox



# Submissions to WRLFMD Pirbright

October 2013 – September 2015 (period of current LoA)



- Sequence exchange with China, Russia, India and BVI
- Reports for these samples can be found at: [www.wrlfmd.org](http://www.wrlfmd.org)

# Coordinating Global Networks

## OIE/FAO FMD Laboratory Network



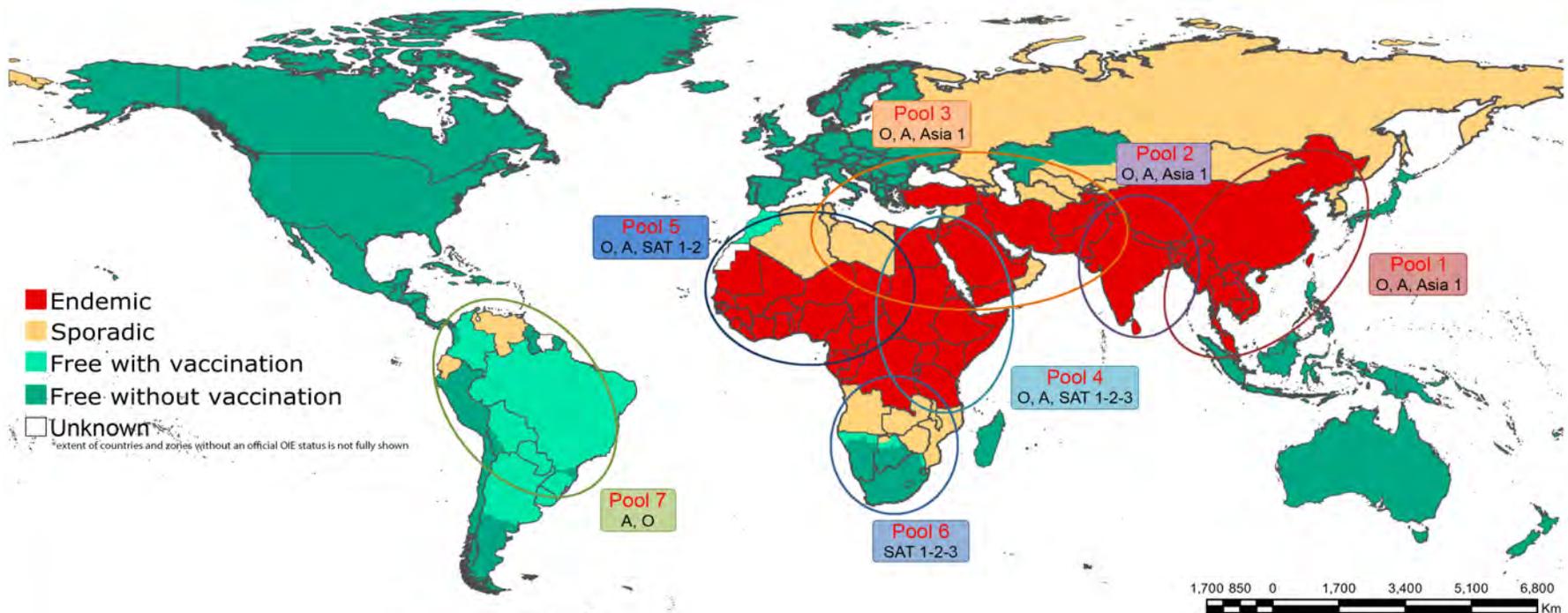
- OIE and FAO Reference Centres (+ affiliates)
- Annual meeting and report
- **Global surveillance and changing patterns in risk pathways**
- **Harmonised and improved lab capacity**



Brescia, Italy – November 2014

# FMD: Conjectured status

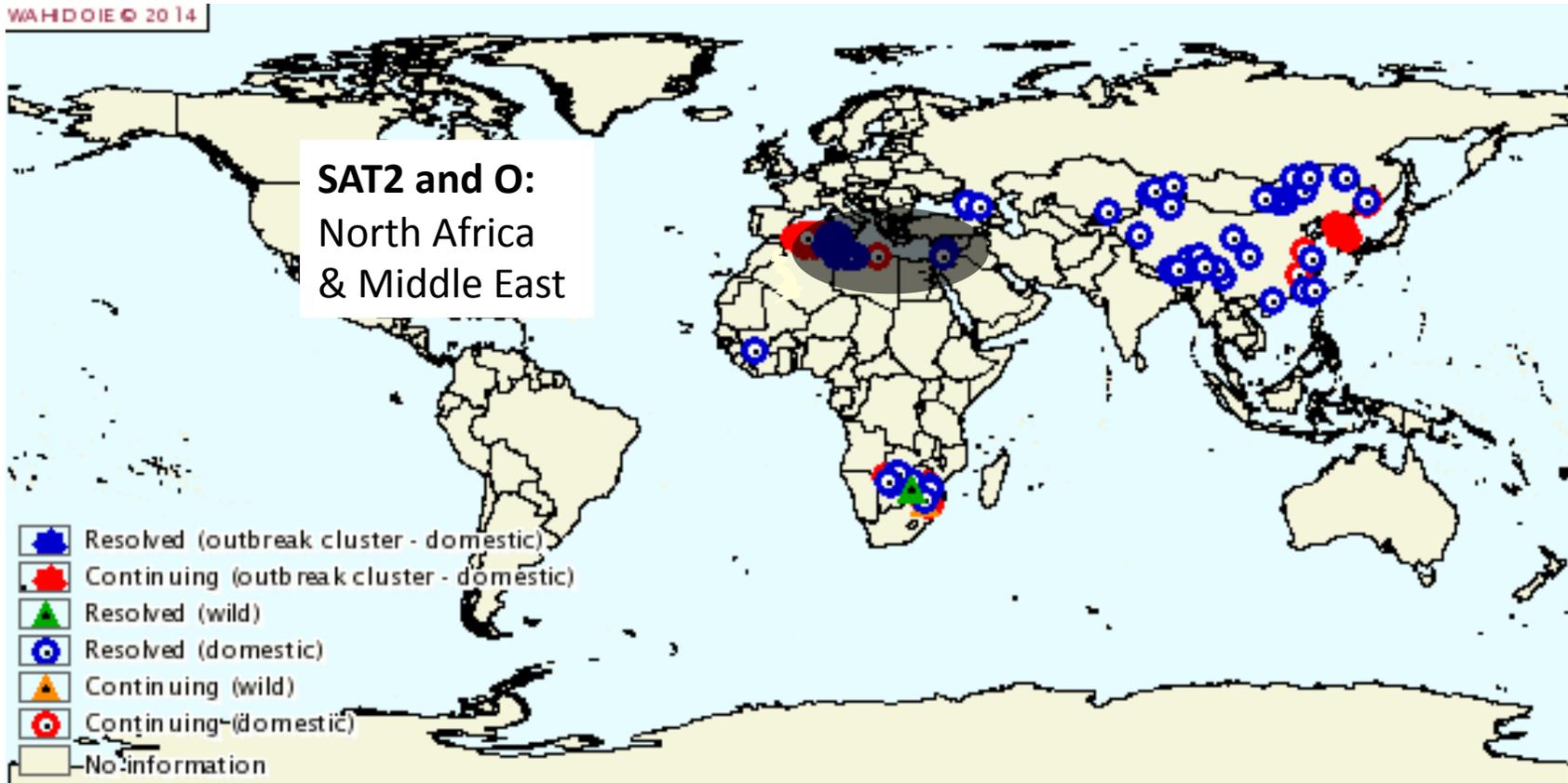
Seven endemic pools requiring tailored diagnostics and vaccines



New FMD-free zone (without vaccination) established in northern Kazakhstan

# Viruses on the move:

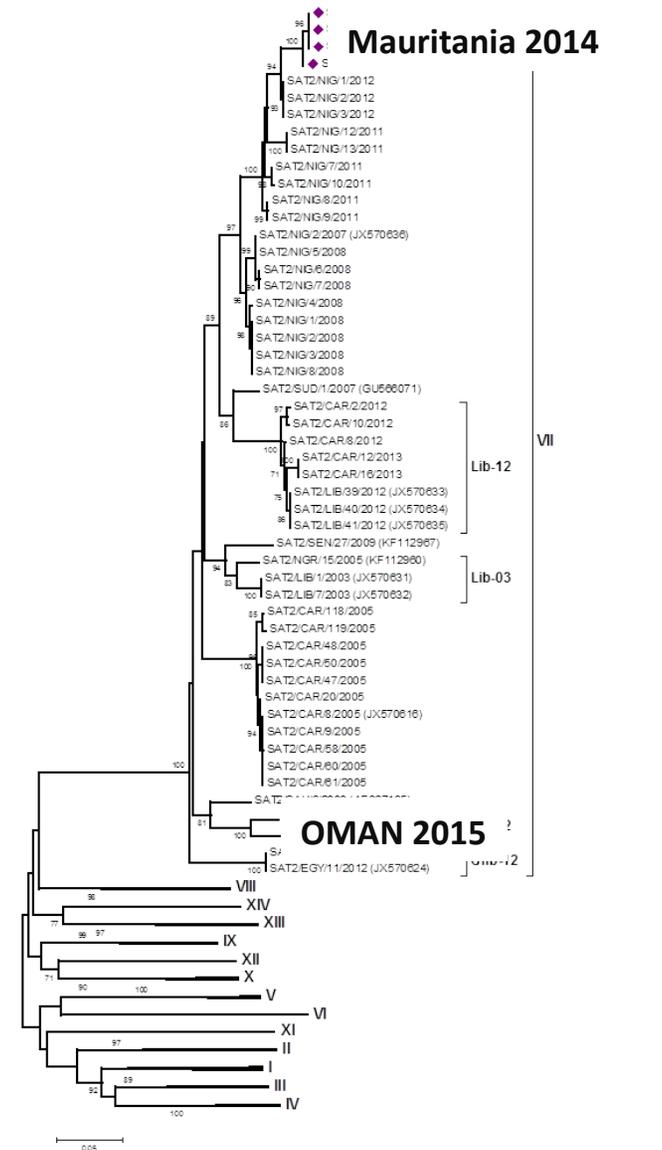
Changing epidemiological patterns



Outbreaks reported to the OIE (change of epidemiological status):  
<http://www.oie.int/wahid-prod/public.php?page=home>

# Recent outbreaks due to SAT 2 Mauritania and Oman

- New SAT 2 samples from field outbreaks
- VP1 sequencing: two different genetic groups within topotype VII
- Oman 2015:
  - Cattle
  - Genetically similar to FMD viruses from previous outbreaks in Egypt (Alx-12 sub-lineage)
- Mauritania 2014:
  - Cattle
  - Genetically most similar to FMD viruses from Nigeria





# Vaccine Potency Trial

O/ME-SA/Ind2001



- Funded via EU (from EU-RL) contribution
- Experiments hosted by CVI-Lelystad
- Adopted protocol according to European Pharmacopeia
- O-Manisa vaccination (at least 6PD<sub>50</sub>) with O/ALG/2014 challenge

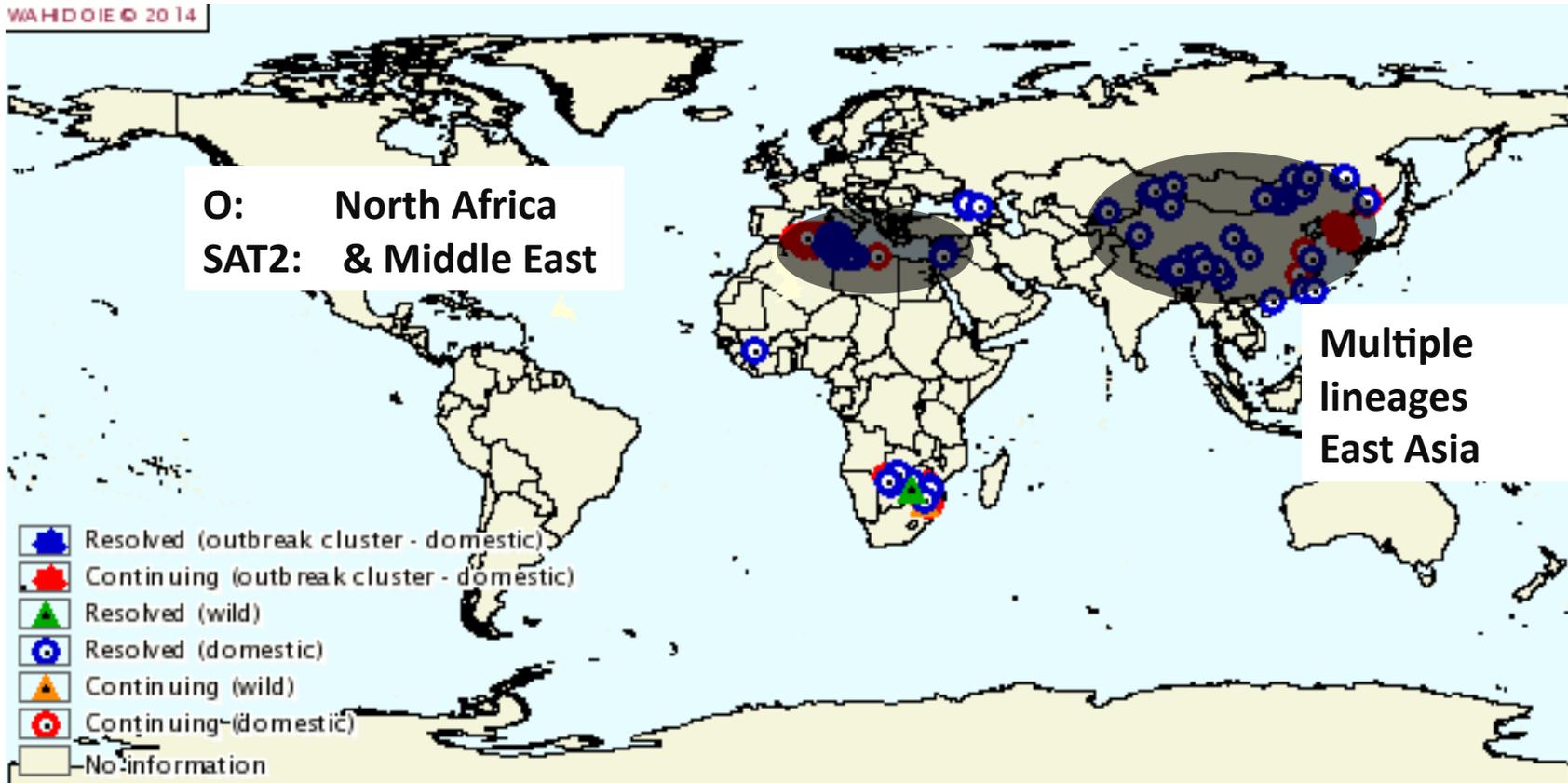
Vaccine Dose	Number Protected vs Vaccinated	Serological Results (O Manisa Log <sub>10</sub> VNT mean 21DPV)
Full	3/5	2.65
1/4	4/5	2.67
1/16	0/5	1.68
Unvaccinated*	0/2	0.9

- Estimated heterologous potency ~3 PD<sub>50</sub>



# Viruses on the move:

Changing epidemiological patterns



Outbreaks reported to the OIE (change of epidemiological status):

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# Pool 1: Endemic countries

Characterisation of different FMD virus lineages

2009-2015: based on data from the OIE/FAO Lab Network

Country	O				A		Asia-1
	SEA / Mya-98	CATHAY	ME-SA / PanAsia	ME-SA / PanAsia-2	ASIA / Sea-97	ASIA/Ind	
Cambodia	2014		2013		2014		2005 2006
Laos	2013		2012		2015		
Malaysia	2014			2006	2013		
Myanmar	2009					2010	
Thailand	2015	2012	2011		2015		
Vietnam	2015	2008	2014		2015		

Is this the true picture of FMD in SEA?

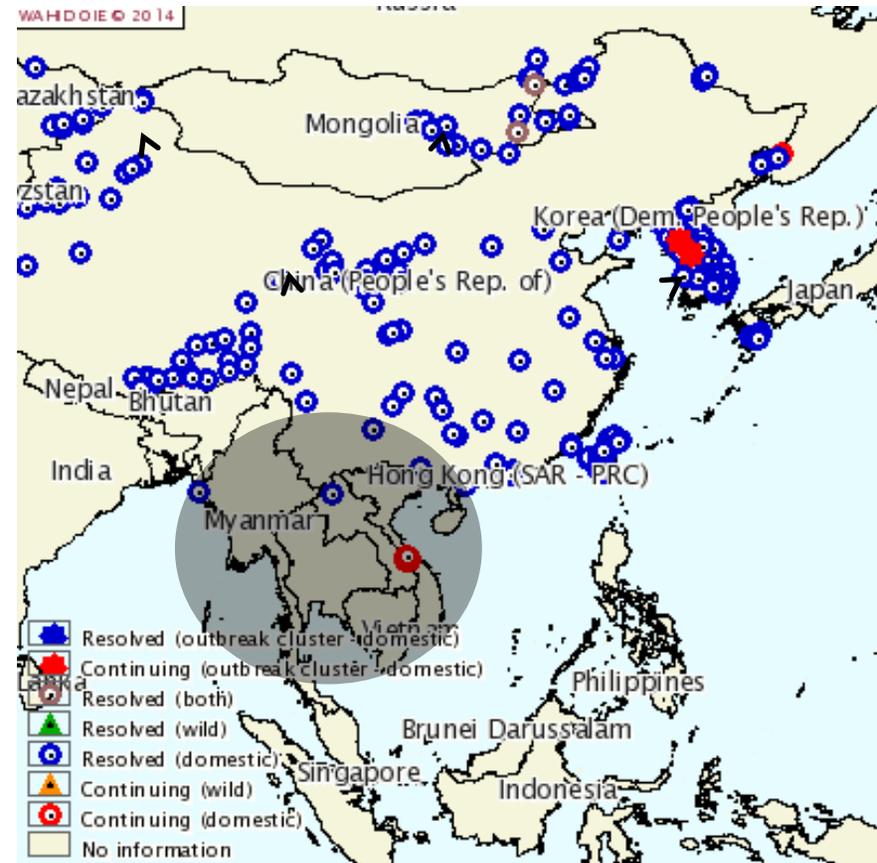
..... or does under-sampling bias our understanding of the epidemiology of the disease?

# East Asia: outbreaks due to exotic FMDVs

FMD outbreaks since 2008

Spread of three FMD virus lineages from Southeast Asia:

- **O/ME-SA/PanAsia**  
China, Russia, Mongolia, Kazakhstan
- **O/SEA/Mya-98**  
China, Japan, South Korea, North Korea, Russia, **Mongolia 2015**, Taiwan
- **A/ASIA/Sea-97**  
South Korea, China, Kazakhstan, Mongolia, Russia, **Taiwan (2015)**



OIE: WAHID

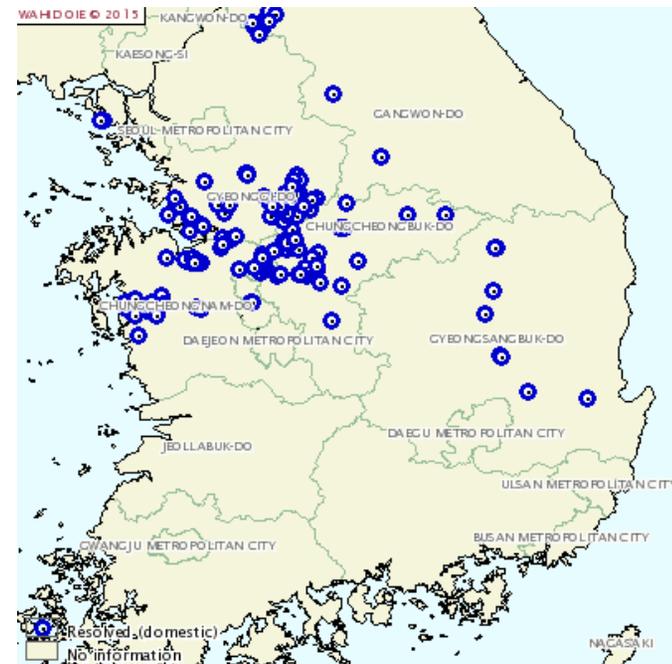
# South Korea

## FMD outbreaks in 2014/15 (all serotype O)

- July 2014
  - 3 outbreaks
- December 2014
  - 185 reported outbreaks
  - Mainly pigs affected
  - West and central parts of the country
  - Reported as “resolved” to OIE on 22/5/2015
- Clinical cases in pigs in spite of a vaccination campaign



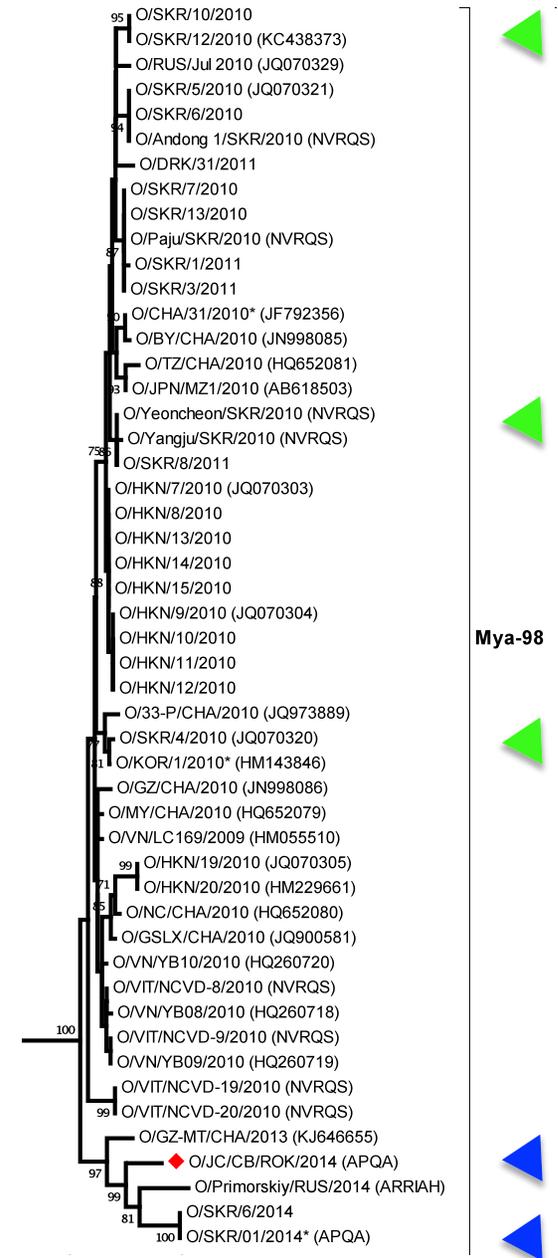
<http://koreajoongangdaily.joins.com/news/article/article.aspx?aid=2999365&clcc=rss%7Cnews%7Cjoongangdaily>



# FMD Outbreaks in South Korea

## Relationships from VP1 sequences

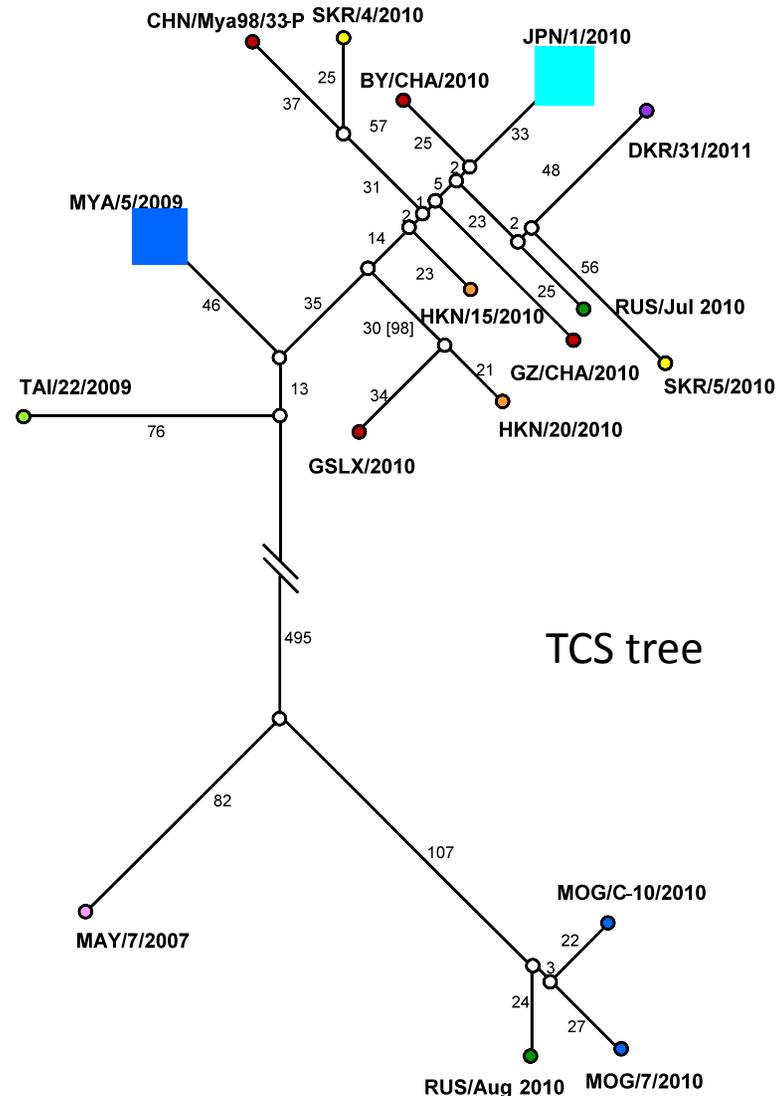
- Virus sequencing undertaken at QIA and WRLFMD
- New outbreaks (within the O/SEA/Mya-98 lineage)
- Sequence data indicate multiple introductions into South Korea
  - 2 in 2014? 
  - 3+ in 2010? 
- Do these data provide an indication of the severity of “infectious pressure” from other countries in the region?



# Full genome sequences

Use to define relationships between outbreaks

- Greater resolution to distinguish between FMD outbreaks
- Approach can be used to substantiate the idea for multiple introductions of FMD into South Korea
- Important information of genetic determinates outside of VP1
- Could be routinely used to improve our understanding of FMD epidemiology in SEA



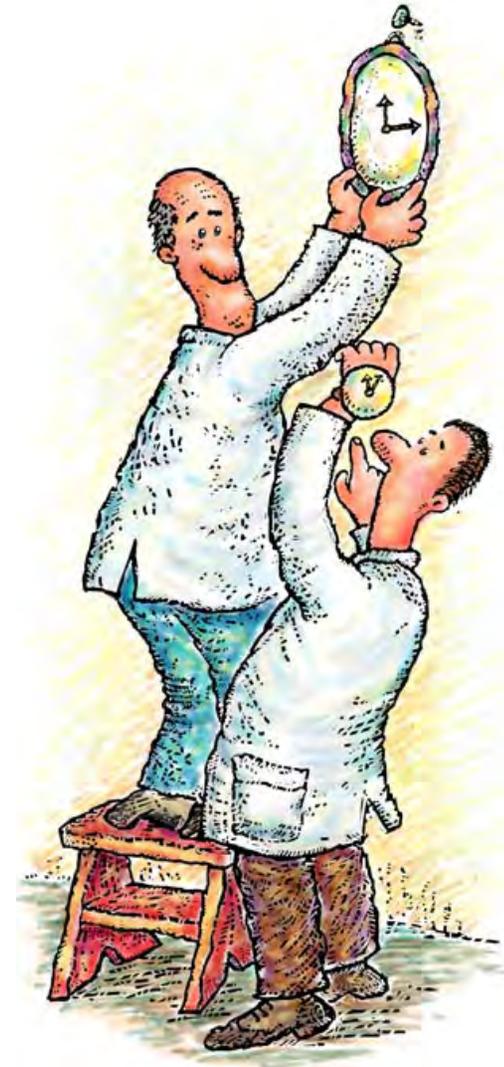
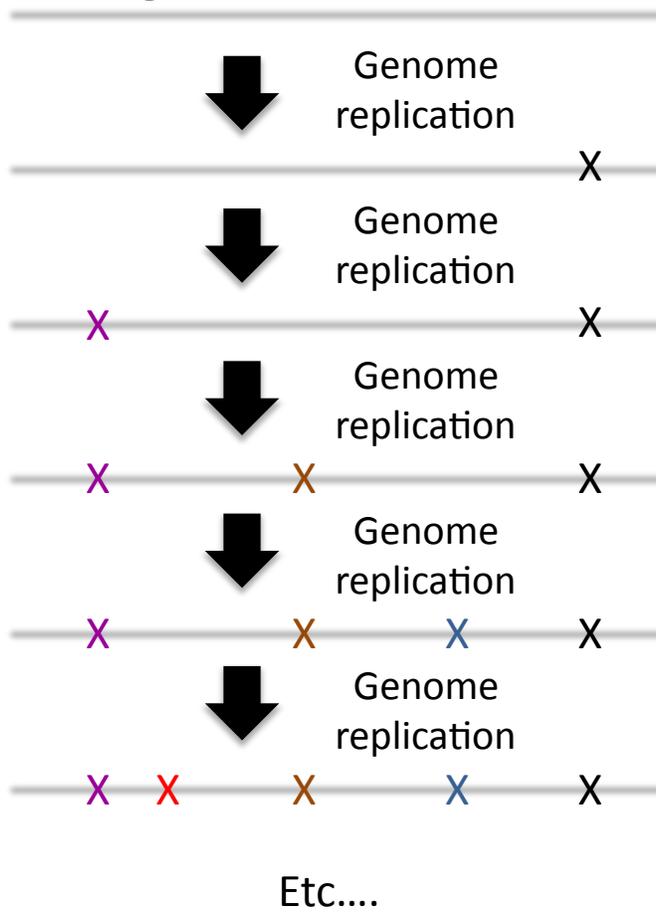
## Some key questions

- What are the regional patterns of FMDV movements
  - contribution of animals/products/people?
- How frequently do FMD viruses enter a country / district / zone?
- Are specific viruses maintained within countries / districts / zones?
- How much FMD is circulating in a region?
- What is the TRUE unbiased prevalence of the different viral lineages?
- Are efforts to control FMD having a positive impact upon burden of disease? – (in the different regional roadmaps)

# Molecular clocks

Are these a predictable indicator of FMDV replication in hosts?

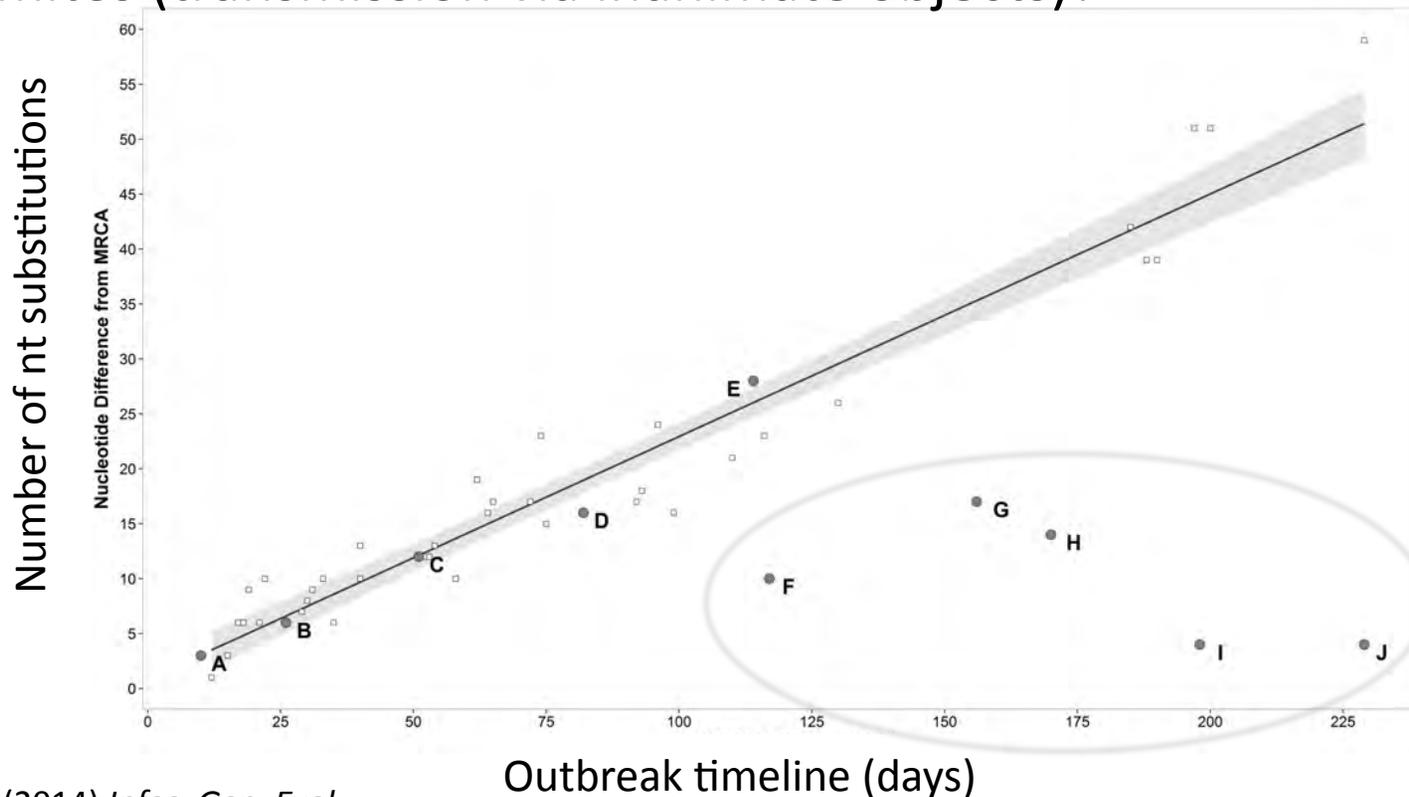
FMDV genome (Error rate  $10^{-2}$ - $10^{-4}$  replication event)



# Evolutionary rates

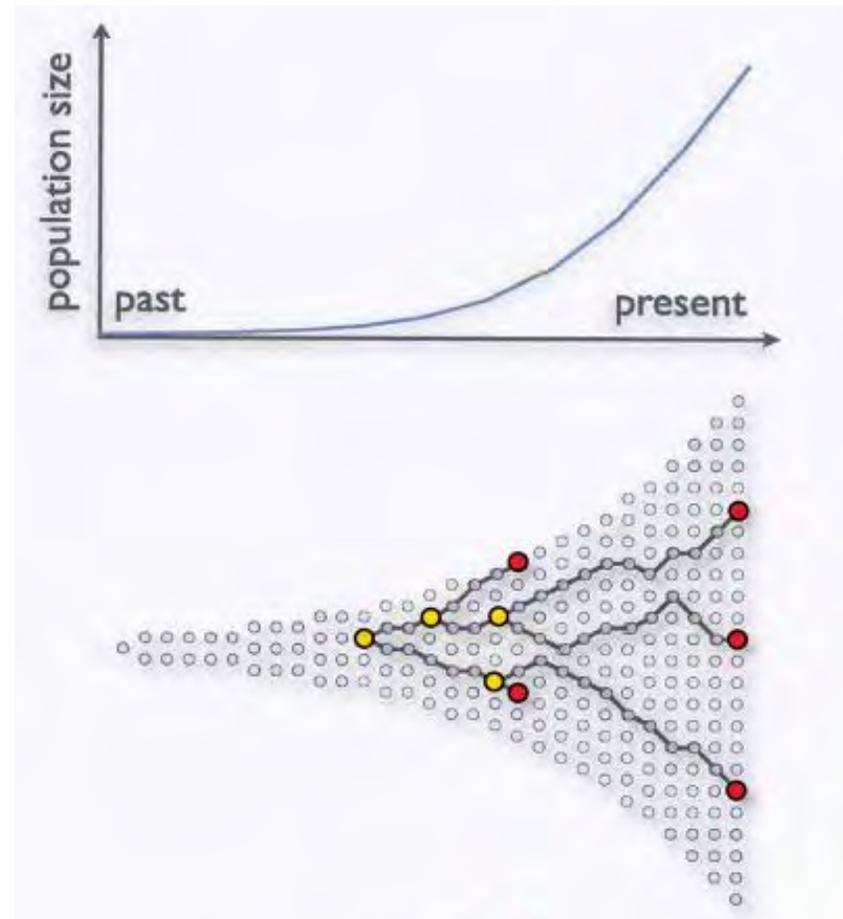
## Understanding transmission events

- Retrospective analysis of the 1968-9 epidemic in the UK
- Remarkably consistent substitution rate
  - $\sim 2 \times 10^{-5}$  nt substitutions/site/day
- Evolutionary standstill for some viruses indicative of role of fomites (transmission via inanimate objects)?



# Applications: estimating what we do not see?

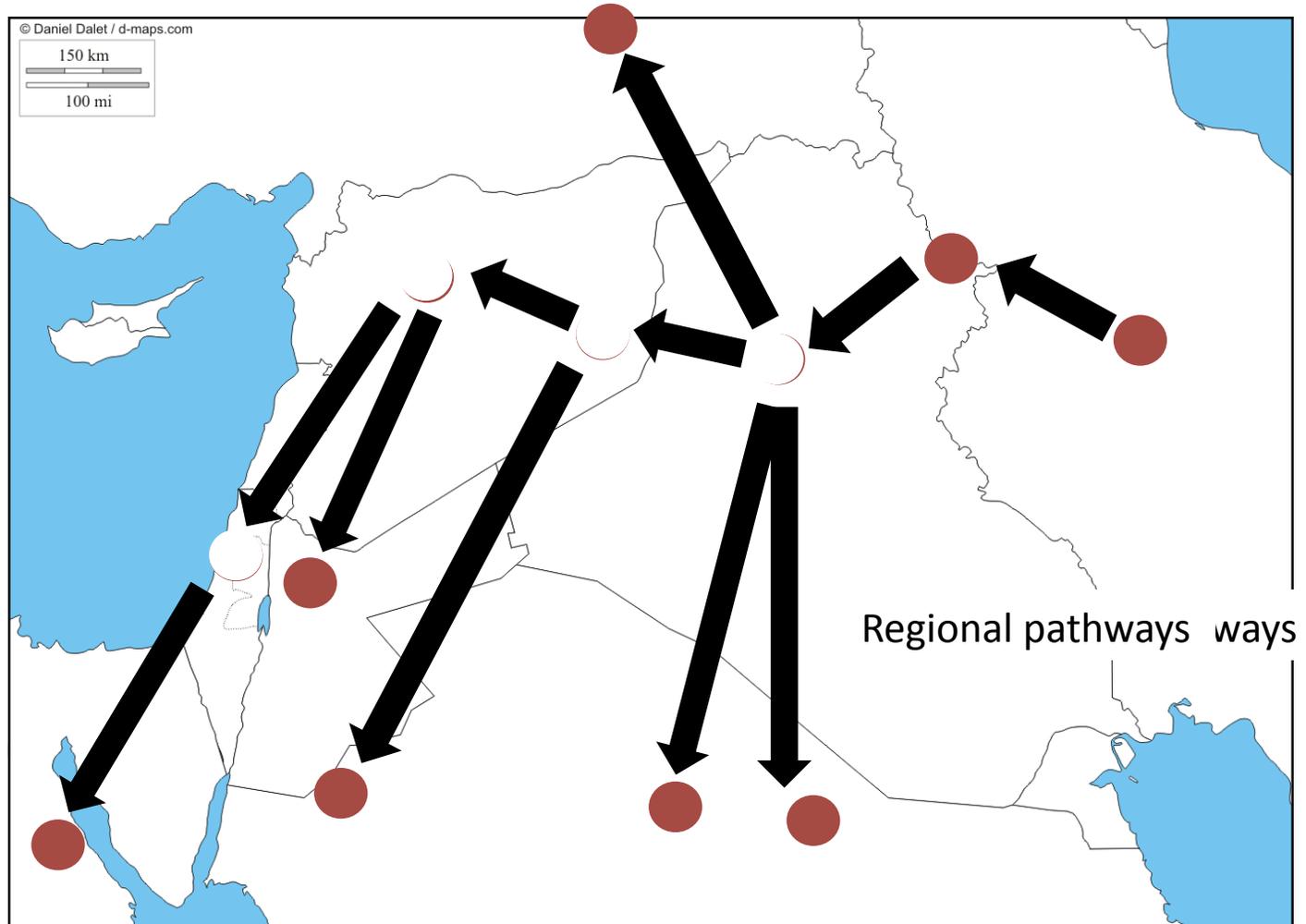
- Assuming:
  - polymerase error rates are *clock-like* and can be estimated
- Can we use the differences in sequences to model the extent of un-sampled sequences (“dark matter”) between samples received for analysis?
- At the regional scale – can this be used as a proxy for FMD prevalence?
  - Calibrated with real data



Andrew Rambaut, University of Edinburgh

# “dark” matter (un-sampled sequences)

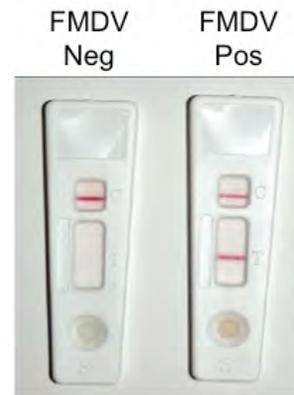
Transmission to another animal



# Improved sampling of field outbreaks

New tools for field sampling and transport?

- Rapid detection of FMDV antigen in the field
- FMDV can be detected by real-time RT-PCR using nucleic acid recovered from positive LFDs
- RNA is stable > 1 month
- Possible to generate larger RT-PCR amplicons
  - Strain characterisation
  - “live” virus recovery by electroporation into BHK cells
- Use of LFDs to ship FMDV positive material to Ref. Labs?



Paulo-Fupi Raphael  
in Tanzania (2013)



[www.pirbright.ac.uk](http://www.pirbright.ac.uk)

# Talk summary

- Epidemiology of FMD is very dynamic
  - Sampling of field outbreaks is critical
  - New patterns in Asia and North Africa
  - Multiple FMDV lineages may have different epidemiological features
- Opportunities to utilize FMDV sequence data in creative ways to understand:
  - What are the regional patterns of FMDV movements?
  - How much FMD is circulating in the region?
  - What is the TRUE unbiased prevalence of the different viral lineages?
  - Are efforts to control FMD having a positive impact upon burden of disease? – (SEACFMD roadmap)

# Acknowledgements

- Support for the WRLFMD and research projects
- Collaborating FMD Reference Laboratories and field teams
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- Partners within the OIE/FAO FMD Lab Network



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