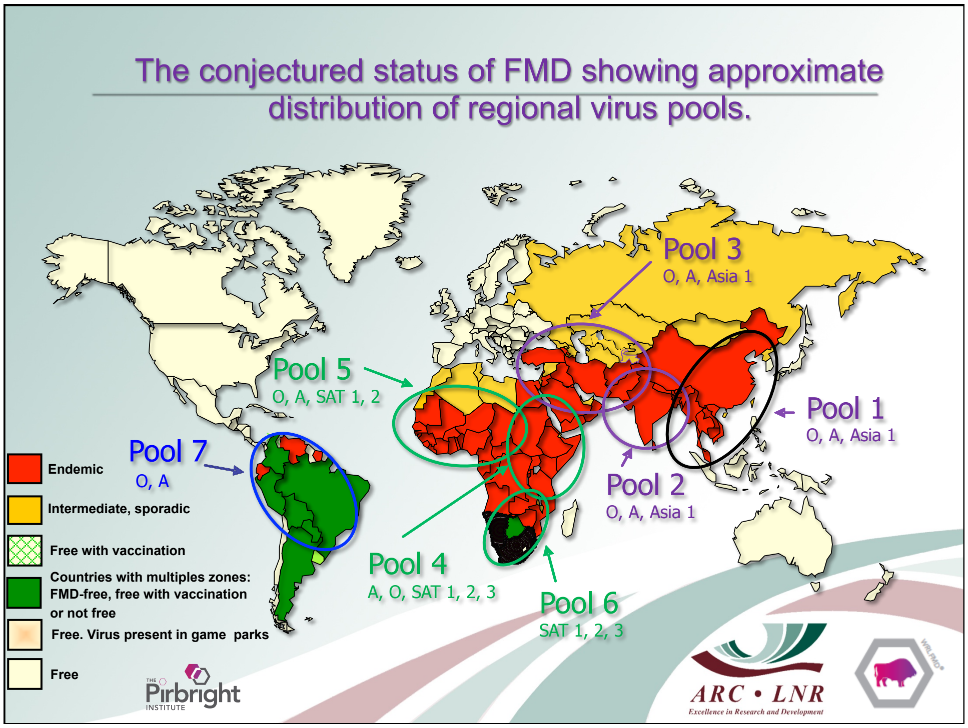
ARC • LNR
Excellence in Research and Development

A better understanding of the behaviour of different topotypes of Foot-and-Mouth Disease Viruses circulating in the domestic and wildlife populations.

Dwarka, RM, Maree, FF, Esterhuysen, JJ, Botha, B, Mtshali, N

ARC, Onderstepoort Veterinary Institute, Transboundary Animal Diseases Programme

---



The conjectured status of FMD showing approximate distribution of regional virus pools.

Pool 3
O, A, Asia 1

Pool 5
O, A, SAT 1, 2

Pool 1
O, A, Asia 1

Pool 7
O, A

Pool 2
O, A, Asia 1

Pool 4
A, O, SAT 1, 2, 3

Pool 6
SAT 1, 2, 3

- 🟥 **Endemic**
- 🟨 **Intermediate, sporadic**
- ▨ **Free with vaccination**
- 🟩 **Countries with multiples zones: FMD-free, free with vaccination or not free**
- 🟧 **Free. Virus present in game parks**
- □ **Free**

The Pirbright Institute

ARC • LNR
Excellence in Research and Development

Map of typed FMD outbreaks in Africa

Vosloo et al., 2002

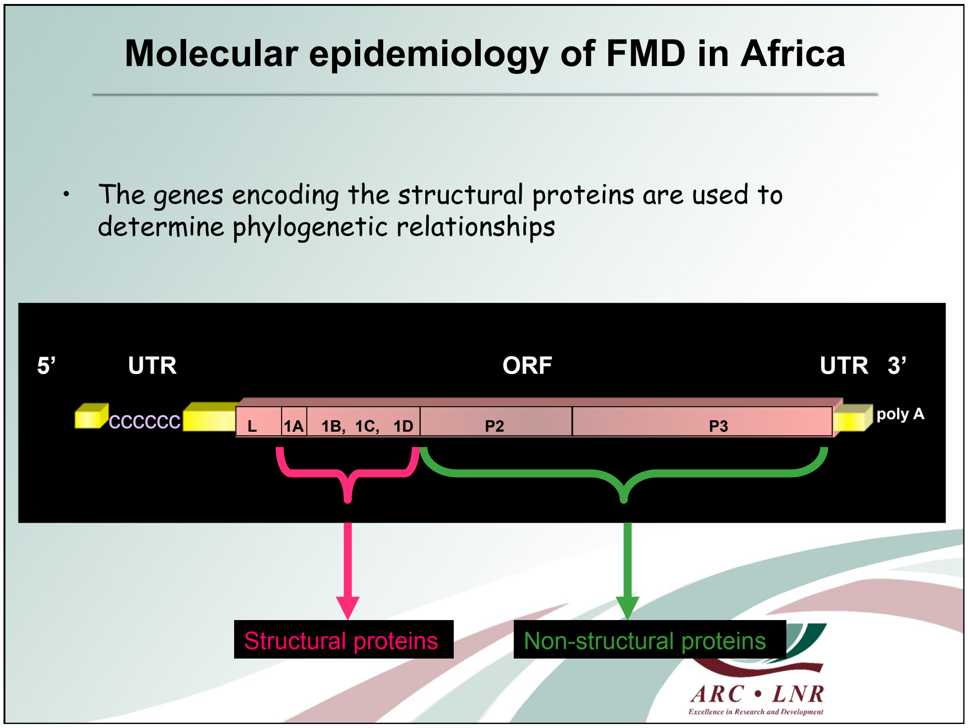
- In Africa, FMD is widespread throughout the continent
- Six of the seven serotypes occur on the continent
- Only serotype Asia 1 not recorded
- Different 'patterns' of disease occur

ARC • LNR
Excellence in Research and Development

Foot-and-mouth disease within pools 4, 5, 6 in Africa

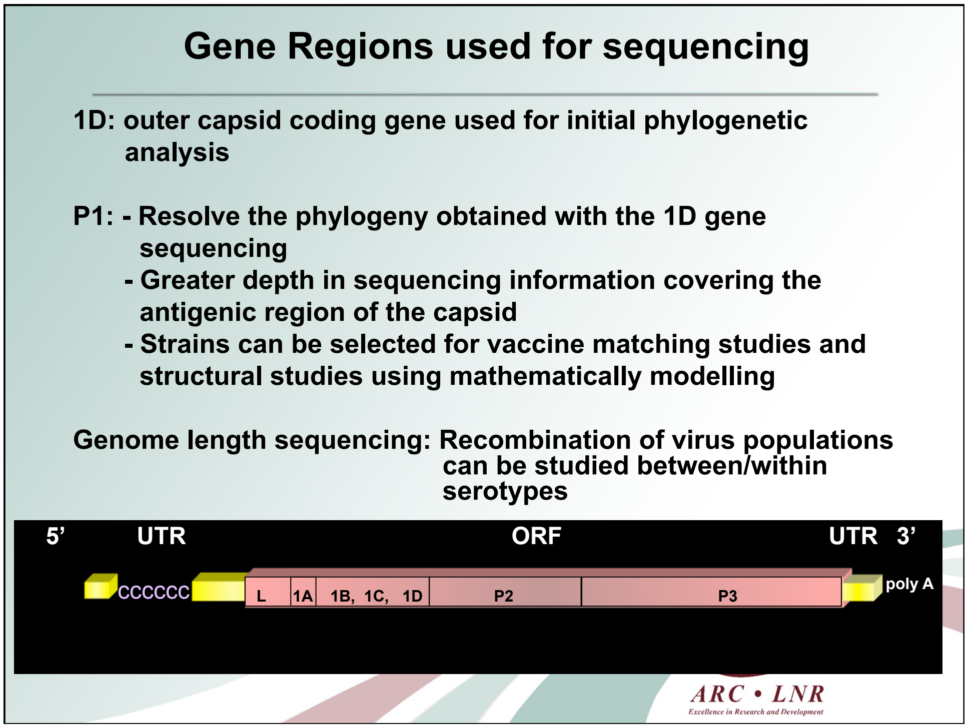
- FMD epidemiology is complex on the African continent
- Serotype distribution differs between geographic regions
- Wildlife are involved in certain regions
- Intratypic variants occur within serotypes

ARC • LNR
Excellence in Research and Development



Molecular epidemiology of FMD in Africa

- The genes encoding the structural proteins are used to determine phylogenetic relationships

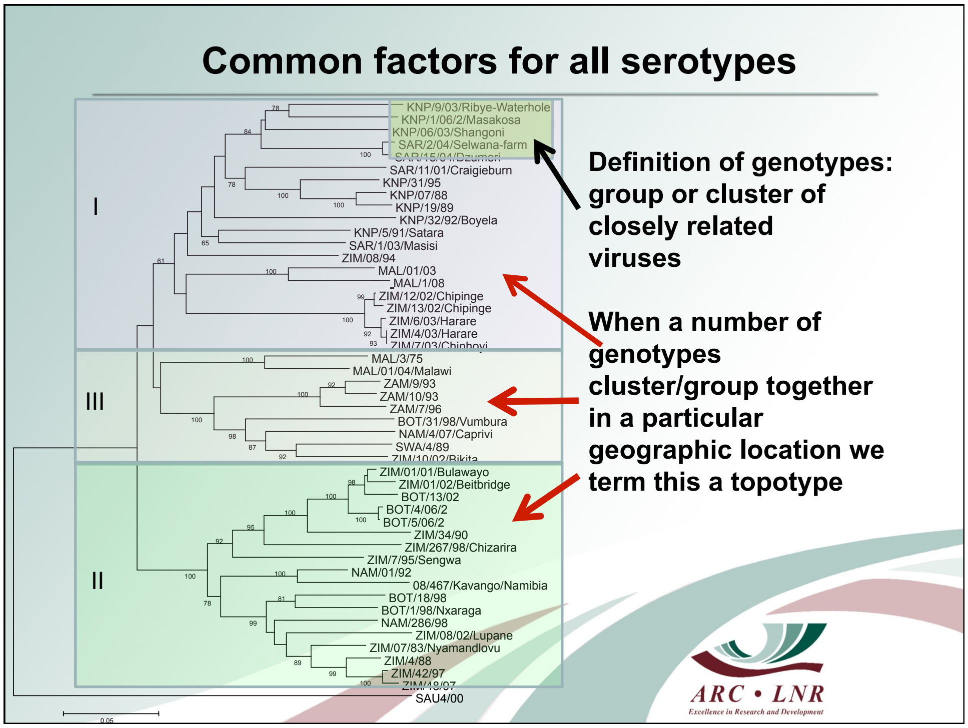


Gene Regions used for sequencing

1D: outer capsid coding gene used for initial phylogenetic analysis

P1: - Resolve the phylogeny obtained with the 1D gene sequencing
- Greater depth in sequencing information covering the antigenic region of the capsid
- Strains can be selected for vaccine matching studies and structural studies using mathematically modelling

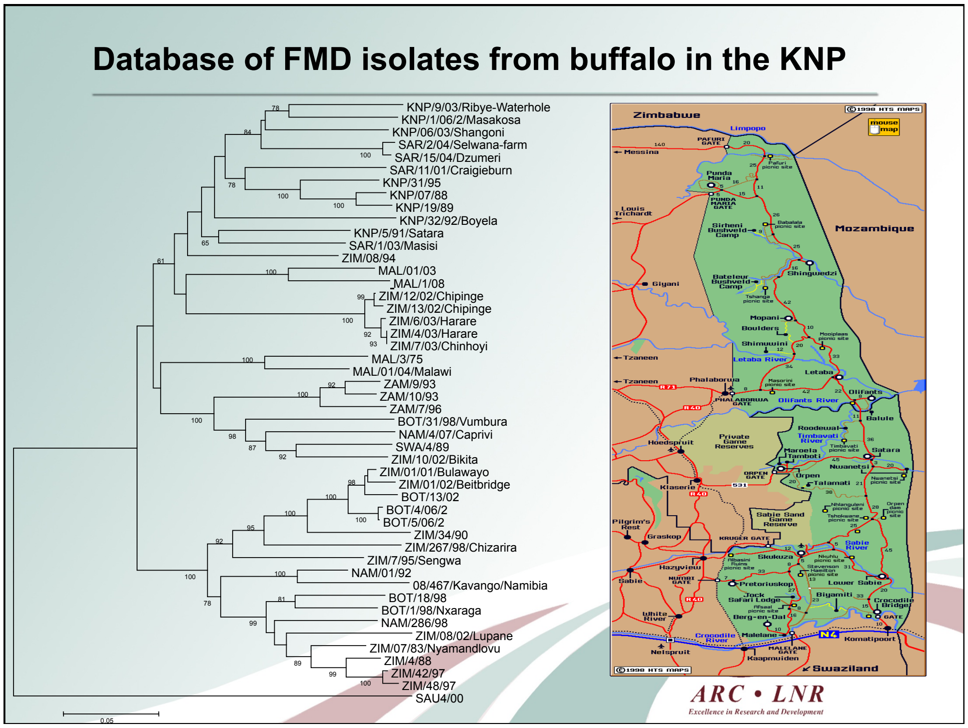
Genome length sequencing: Recombination of virus populations can be studied between/within serotypes



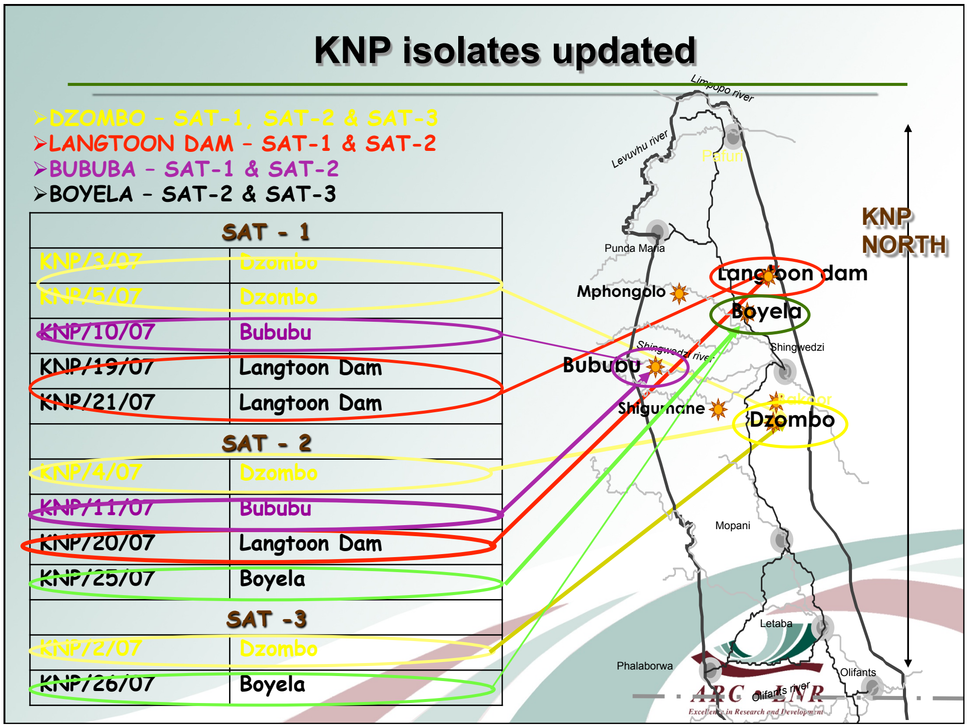
Common factors for all serotypes

Definition of genotypes: group or cluster of closely related viruses

When a number of genotypes cluster/group together in a particular geographic location we term this a topotype



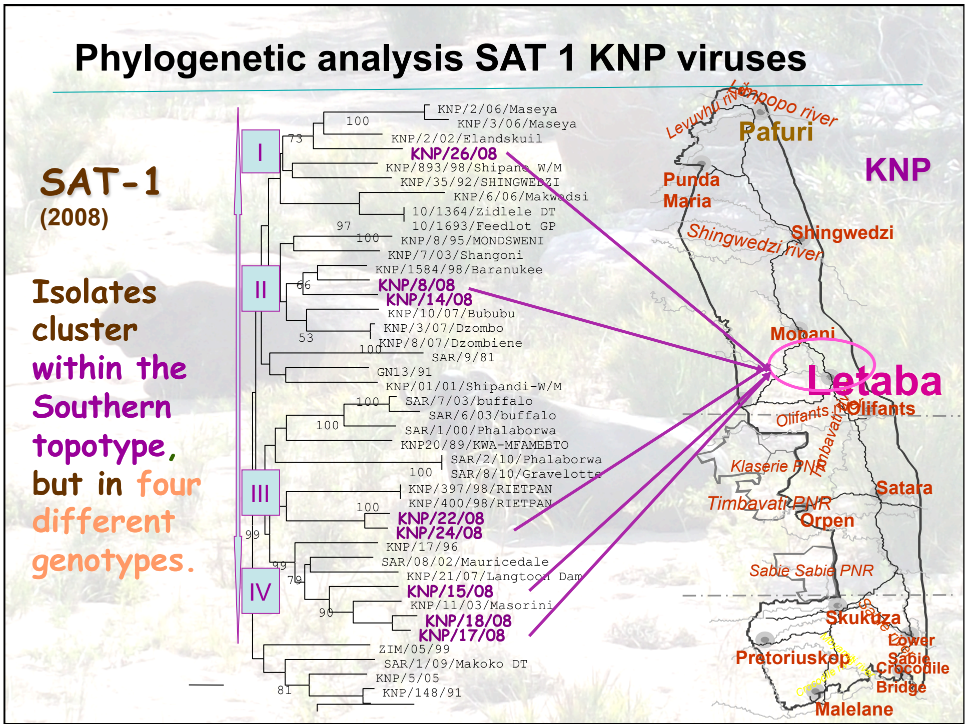
Database of FMD isolates from buffalo in the KNP



KNP isolates updated

- ➢DZOMBO – SAT-1, SAT-2 & SAT-3
- ➢LANGTOON DAM – SAT-1 & SAT-2
- ➢BUBUBA – SAT-1 & SAT-2
- ➢BOYELA – SAT-2 & SAT-3

SAT - 1	
KNP/3/07	Dzombo
KNP/5/07	Dzombo
KNP/10/07	Bububu
KNP/19/07	Langtoon Dam
KNP/21/07	Langtoon Dam
SAT - 2	
KNP/4/07	Dzombo
KNP/11/07	Bububu
KNP/20/07	Langtoon Dam
KNP/25/07	Boyela
SAT -3	
KNP/2/07	Dzombo
KNP/26/07	Boyela

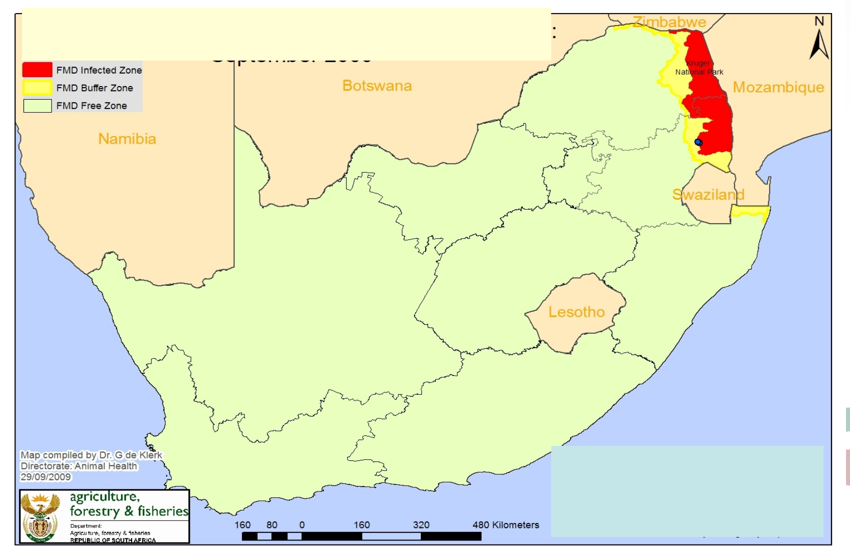


Phylogenetic analysis SAT 1 KNP viruses

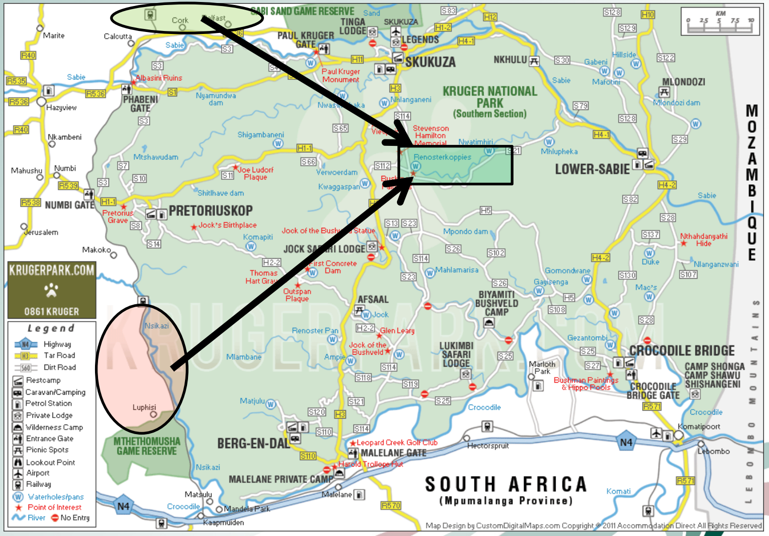
SAT-1
(2008)

Isolates cluster within the Southern topotype, but in four different genotypes.

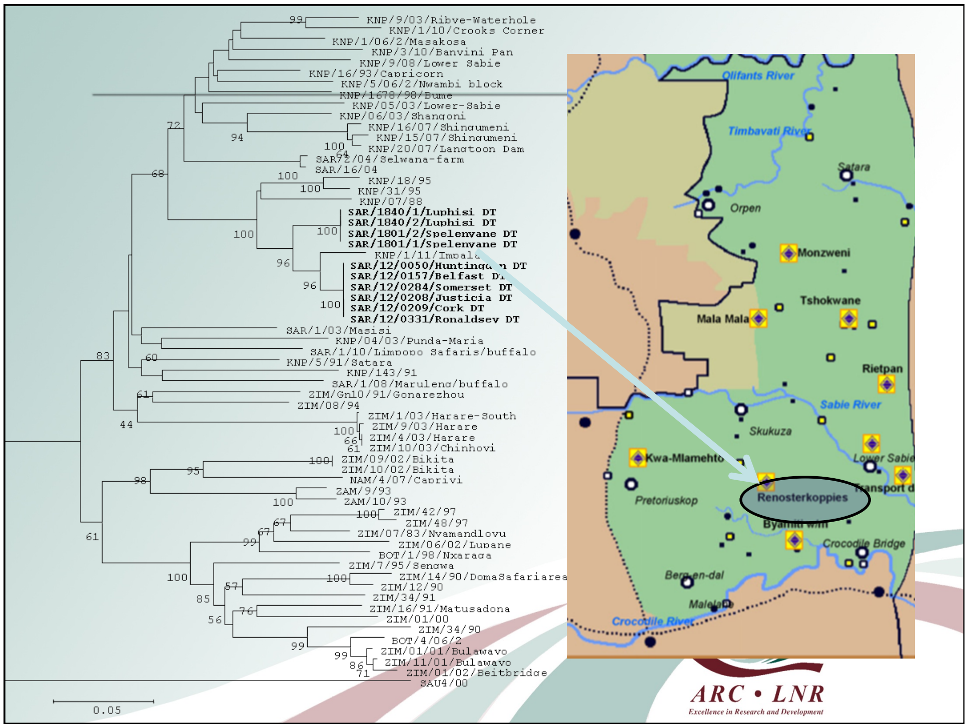
South Africa: Wildlife/ cattle interface

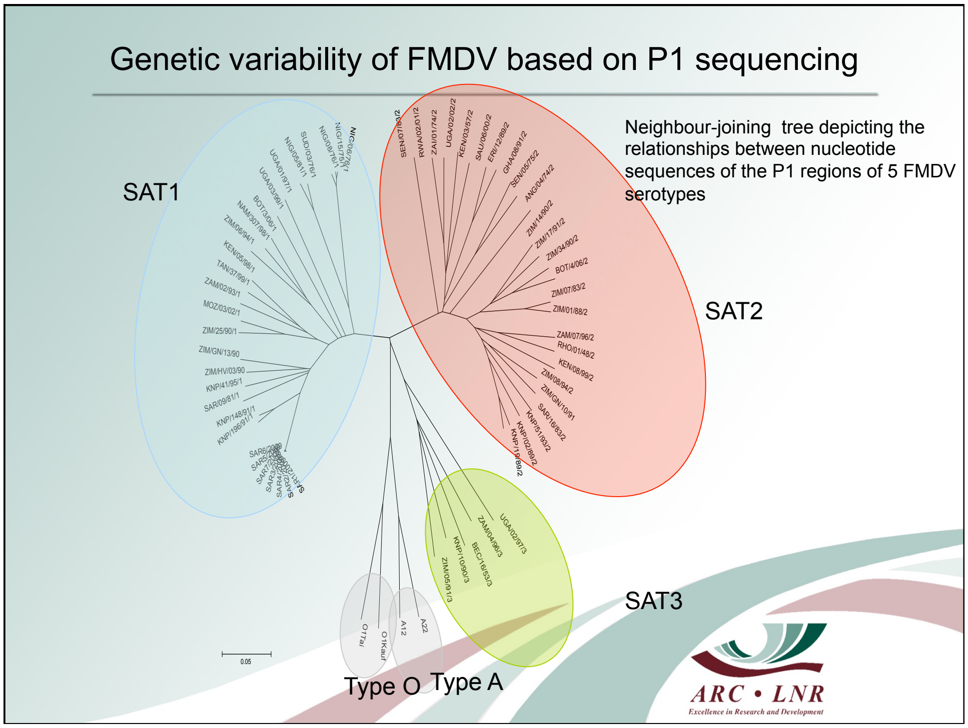


ARC • LNR
Excellence in Research and Development



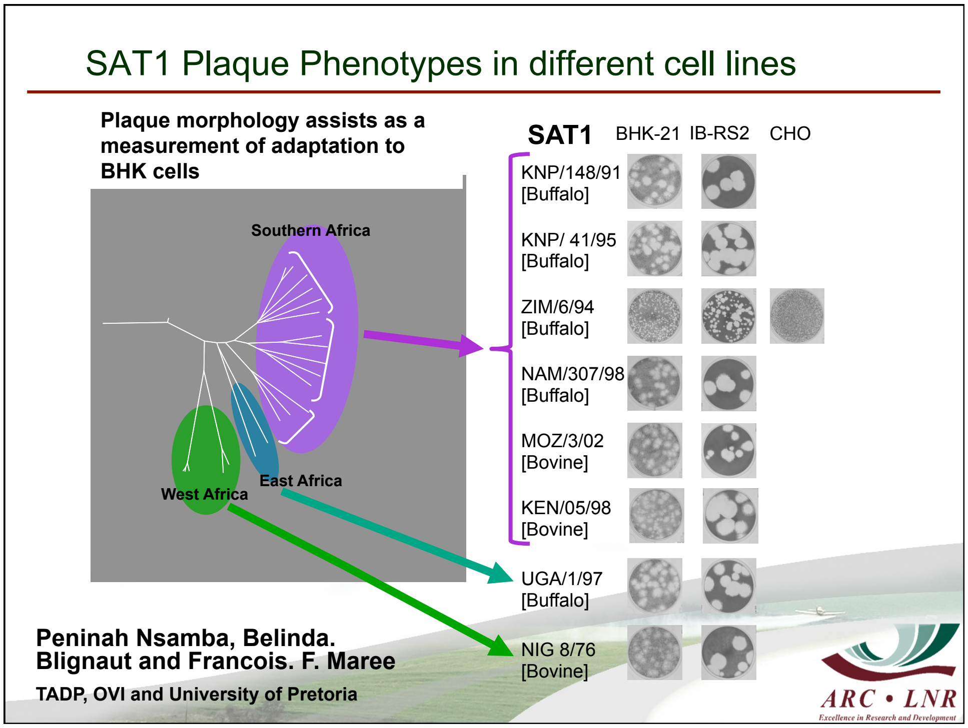
ARC • LNR
Excellence in Research and Development





Genetic variability of FMDV based on P1 sequencing

Neighbour-joining tree depicting the relationships between nucleotide sequences of the P1 regions of 5 FMDV serotypes



SAT1 Plaque Phenotypes in different cell lines

Plaque morphology assists as a measurement of adaptation to BHK cells

SAT1 BHK-21 IB-RS2 CHO

KNP/148/91 [Buffalo]

KNP/ 41/95 [Buffalo]

ZIM/6/94 [Buffalo]

NAM/307/98 [Buffalo]

MOZ/3/02 [Bovine]

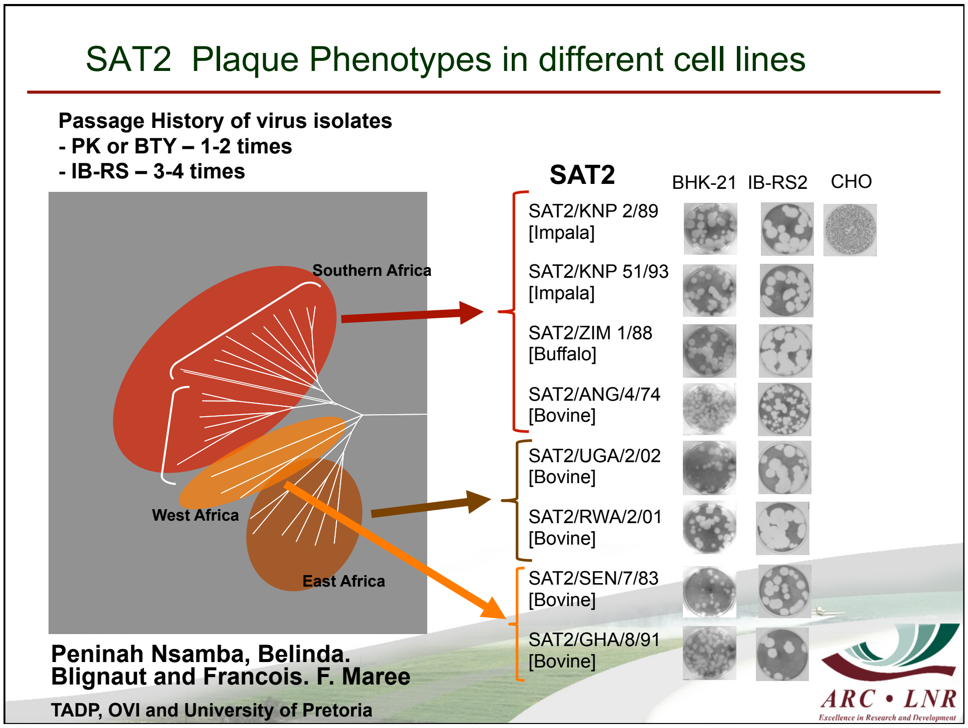
KEN/05/98 [Bovine]

UGA/1/97 [Buffalo]

NIG 8/76 [Bovine]

Peninah Nsamba, Belinda. Blignaut and Francois. F. Maree

TADP, OVI and University of Pretoria



SAT2 Plaque Phenotypes in different cell lines

Passage History of virus isolates
- PK or BTY – 1-2 times
- IB-RS – 3-4 times

SAT2 BHK-21 IB-RS2 CHO

SAT2/KNP 2/89 [Impala]

SAT2/KNP 51/93 [Impala]

SAT2/ZIM 1/88 [Buffalo]

SAT2/ANG/4/74 [Bovine]

SAT2/UGA/2/02 [Bovine]

SAT2/RWA/2/01 [Bovine]

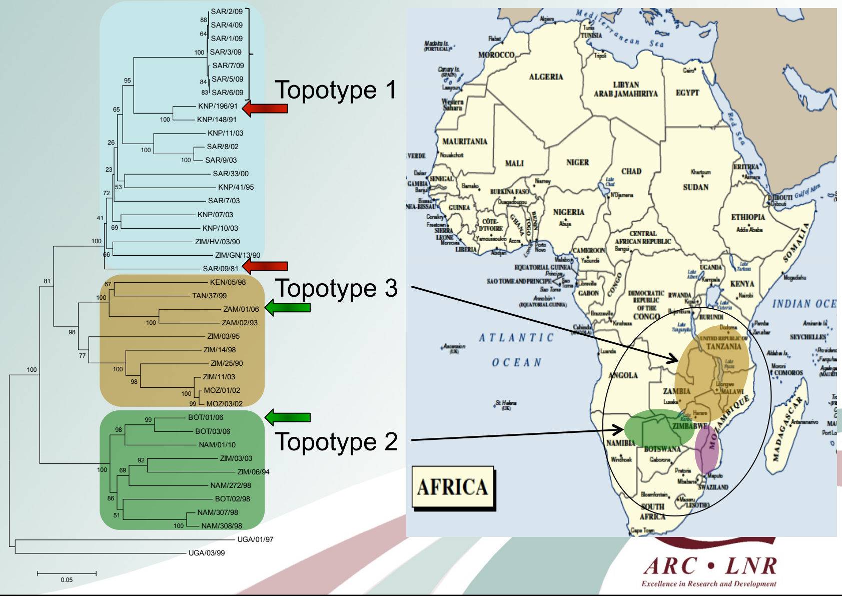
SAT2/SEN/7/83 [Bovine]

SAT2/GHA/8/91 [Bovine]

Peninah Nsamba, Belinda. Blignaut and Francois. F. Maree

TADP, OVI and University of Pretoria

Vaccine matching studies



Topotype 1

Topotype 3

Topotype 2

Pool 6

Antigenic variation (r values)

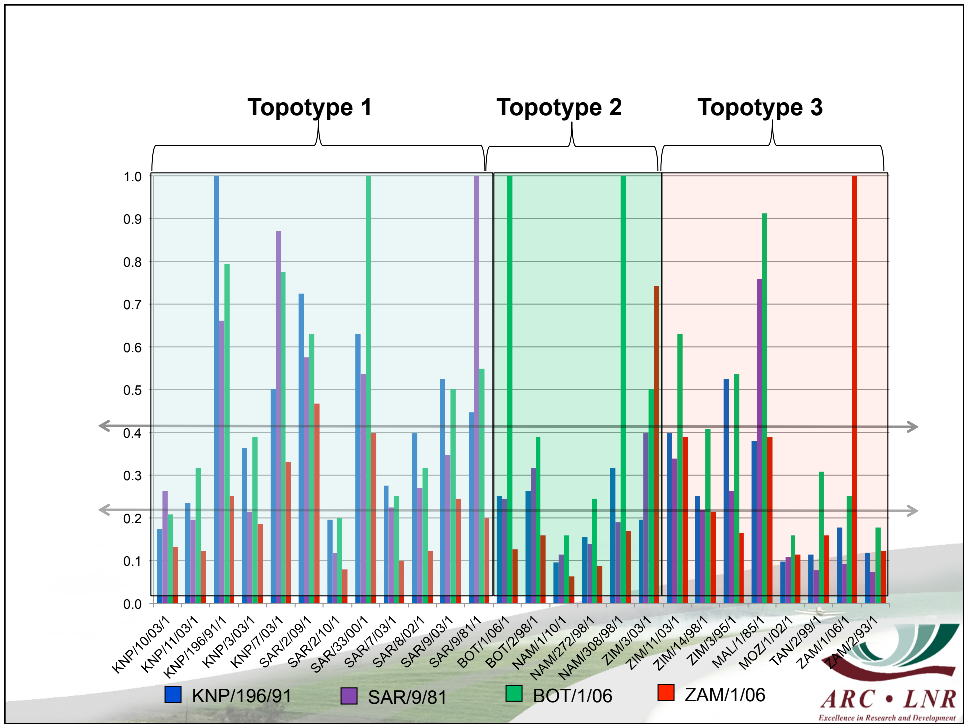
- **r-value = heterologous neutralising titer / homologous titer**

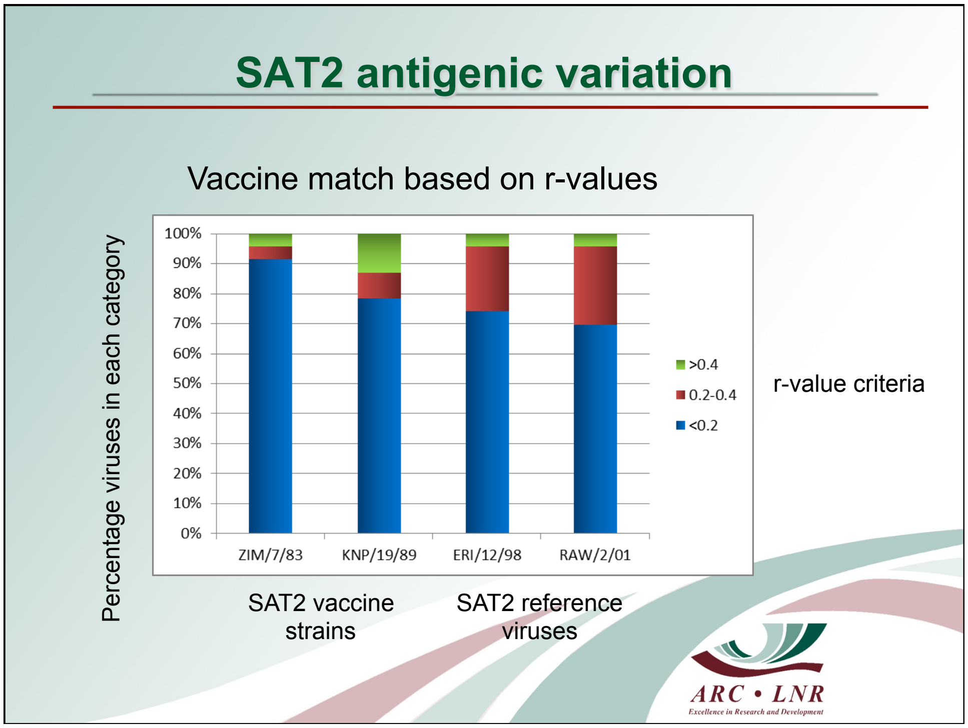
- **r-value range:**

0.4-1.0: good cross-protection against outbreak strain

0.2-0.4: reasonable cross-protection; a potent vaccine will still protect against outbreak virus

0-0.2: poor/no cross-protection





SAT2 antigenic variation

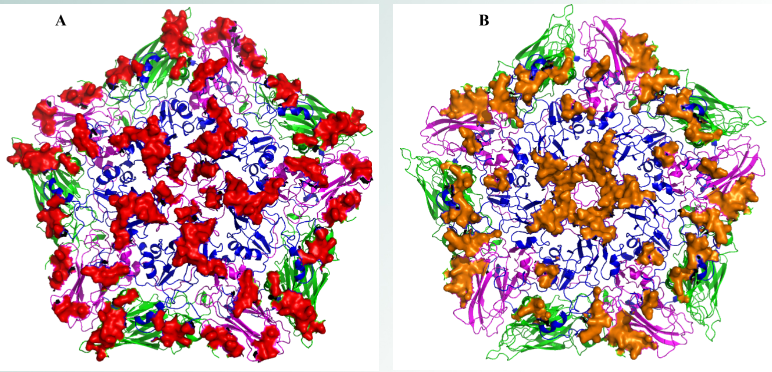
Vaccine match based on r-values

r-value criteria

SAT2 vaccine strains

SAT2 reference viruses

Structural models of FMDV

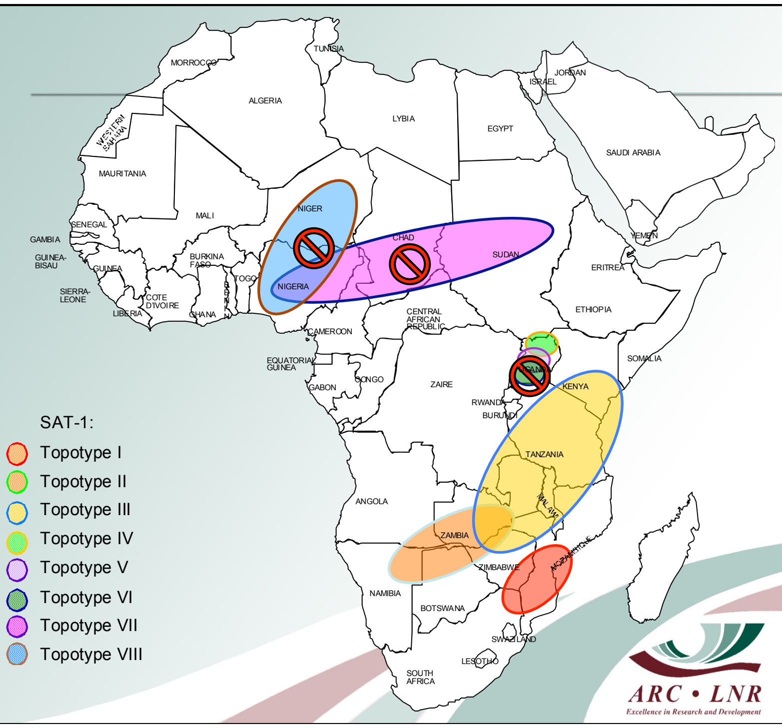


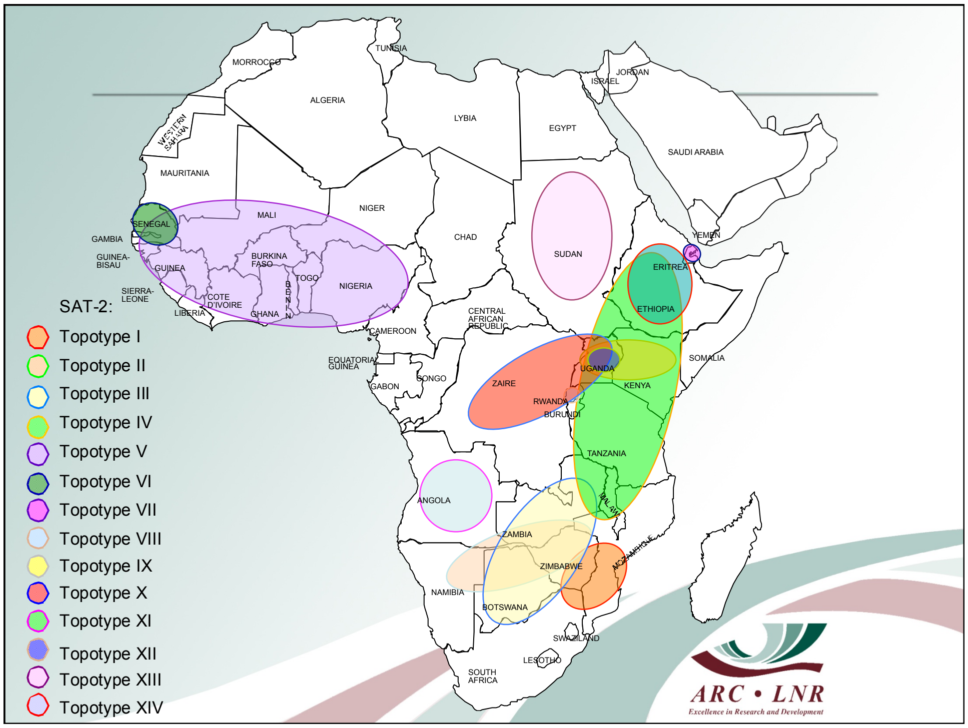
SAT1/SAR/9/81

SAT2/ZIM/7/83

Capsid structures of SAT 1 and SAT 2.
Variation in surface exposed regions.
Study of correlation between the field isolates and vaccines

Fig. 2: Maree et al.





SAT-2:

- Topotype I
- Topotype II
- Topotype III
- Topotype IV
- Topotype V
- Topotype VI
- Topotype VII
- Topotype VIII
- Topotype IX
- Topotype X
- Topotype XI
- Topotype XII
- Topotype XIII
- Topotype XIV

ARC • LNR
Excellence in Research and Development

Regional Activities SADC TADs Project

Buffalo/cattle sampling in SADC countries during 2010-2012:

- Malawi
- Tanzania
- Zambia
- Mozambique
- Angola

ARC • LNR
Excellence in Research and Development

Concluding remarks

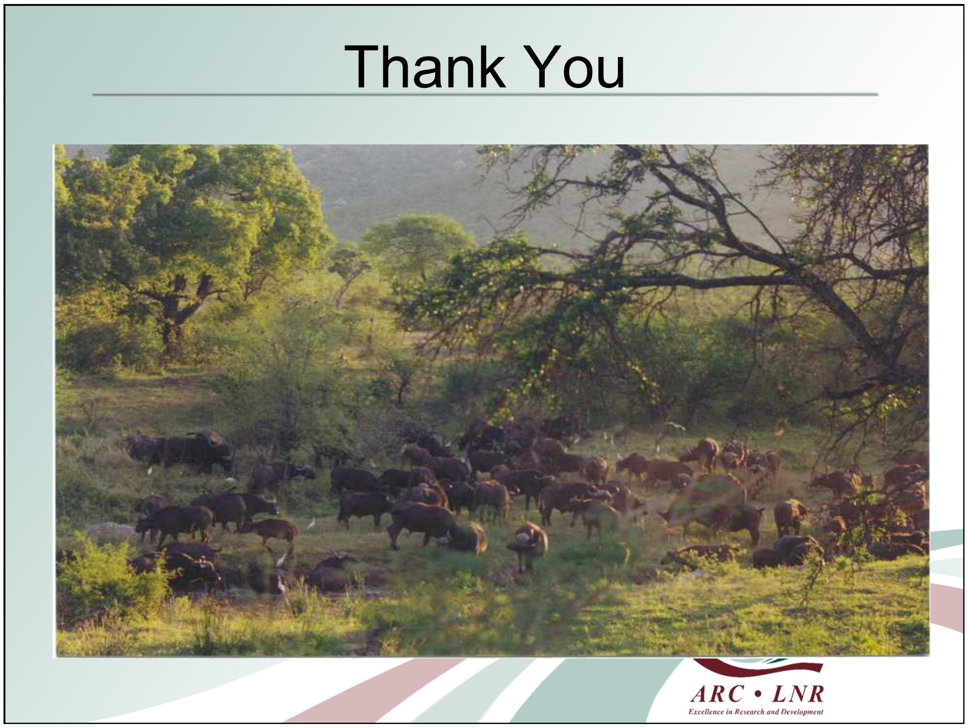
- A comprehensive database of FMD viruses and sequences from SADC countries enables a better understanding on the evolution of the virus.
- When a FMD virus database is represented by diverse topotypes, it enables diagnosticians to better understand and trace the possible origins of outbreak strains.
- Understanding the possible source of an outbreak could play a role in the immediate control strategy for that region. It also enables scientists to assess if a particular topotype is dominant in a region, which could have an impact on vaccine strain selection for that area.

ARC • LNR
Excellence in Research and Development

Concluding remarks

- If vaccination is applied as a control measure, a topotype rich database of viruses will enable better vaccine matching studies to be performed to evaluate the most appropriate vaccine strain.
- Scientists can study the relationships between FMD viruses from different topotypes and perform vaccine matching studies across topotypes,
- However, for a holistic regional control strategy, concerted collaborative efforts between governments, industry, farmers and research institutions are central to effectively mitigating the risk posed by a disease such as FMD.

ARC • LNR
Excellence in Research and Development



Thank You

ARC • LNR

Excellence in Research and Development