New Avenues for Vaccine Development

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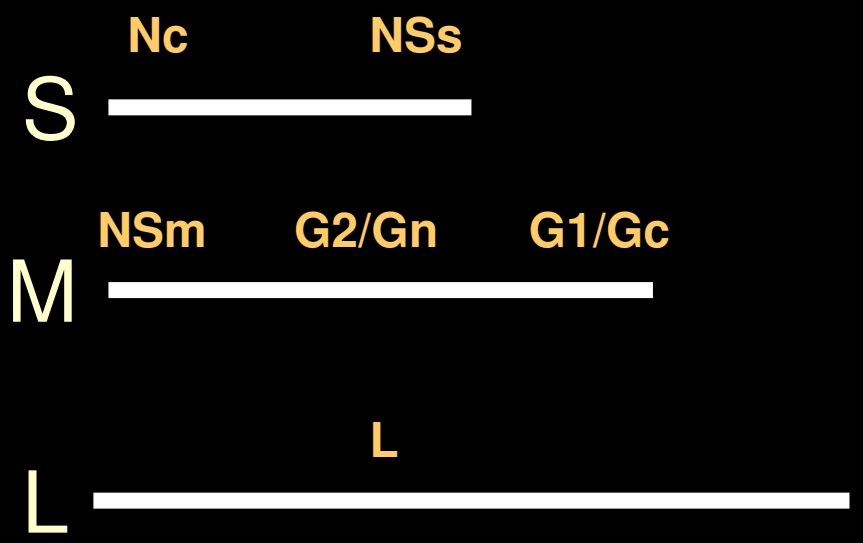
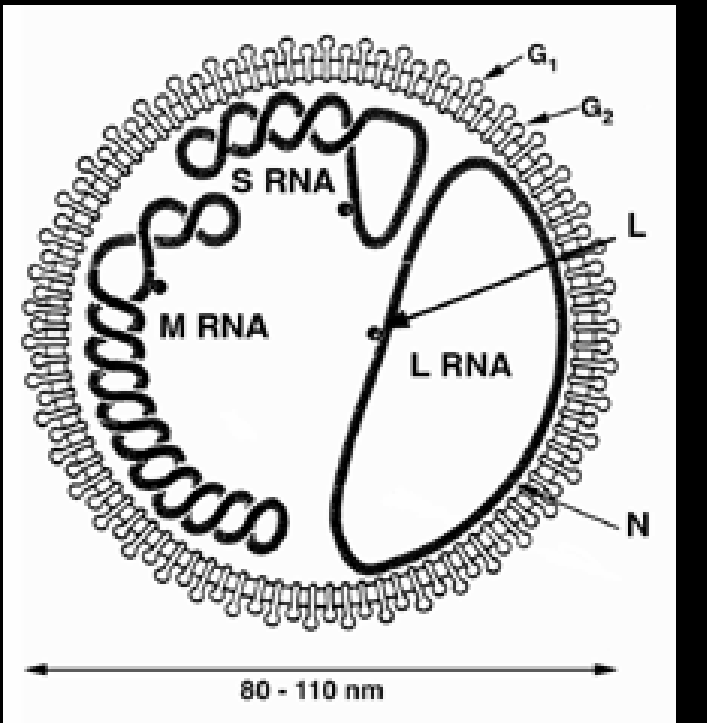
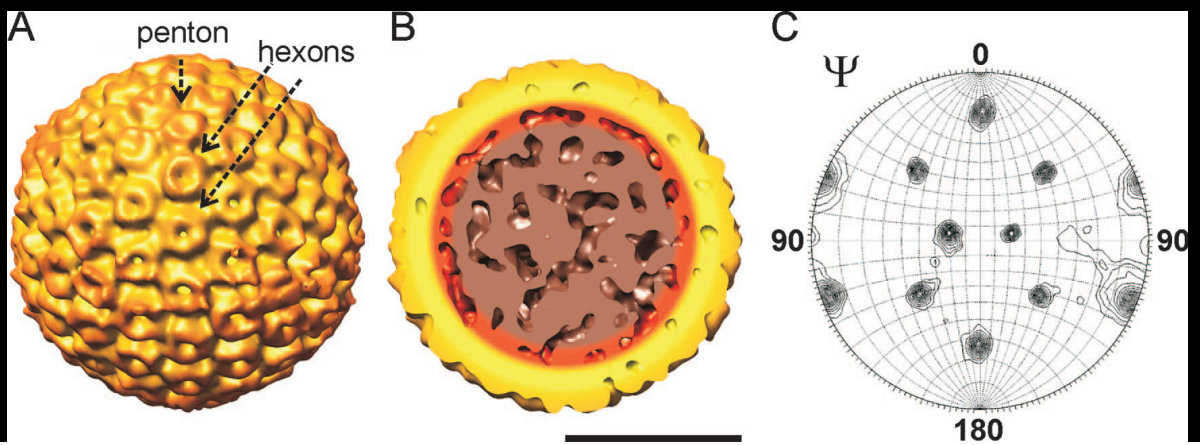
Virus structure and genomic layout





(Van Regenmortel et al., 2000)



(Freiberg et al., 2008)

Experimental vaccines:

(Clone 13) NSs-defective clone
(IFN antagonist)

MV P12 (ZH548) – mutagen-induced changes
(segments M & L)

R566 (Clone 13 + MV P12 – reassortment)
S segment Clone 13 and L & M of MV P12

- Safer, much less chance for reversion via reassortment with virulent strains in the field

Experimental vaccines - alternatives :

- Subunit
- DNA
- Reverse Genetics
- Virus-vectored

Experimental vaccines (continued) :

Subunit (Schmaljohn et al., 1989, Wallace et al., 2006)

- baculovirus : Gn & Gc - good protection in mice

- *E. coli* : tGn - good protection in mice
  NC - partial protection in mice

DNA (Spik et al., 2006; Wallace et al., 2006; Lorenzo et al., 2008)

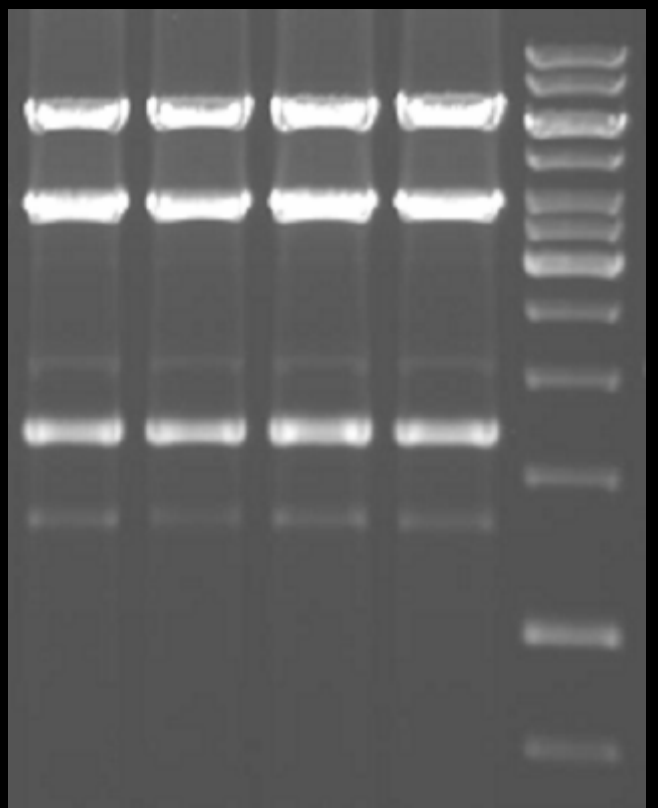
- GPs +NSm - poor antibody response & protection
- GPs -NSm - good antibody responses & protection
- NC - good and long-lasting antibodies (but, low neutralising)

Experimental vaccines (continued) :

Reverse genetics

(Gerrard et al., 2007; Bird et al., 2007; Won et al., 2007; Bird et al., 2008)

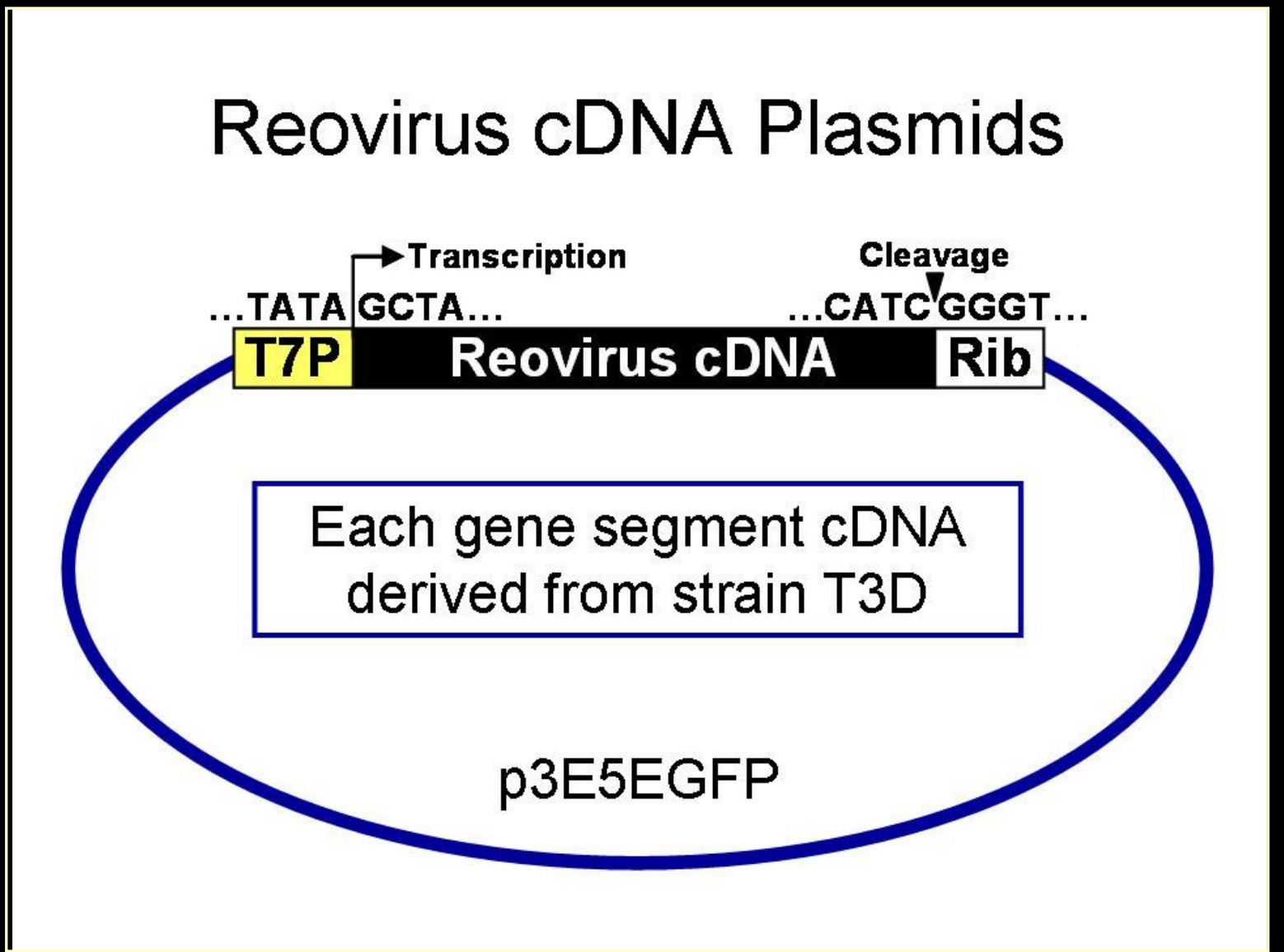
RVFV genome



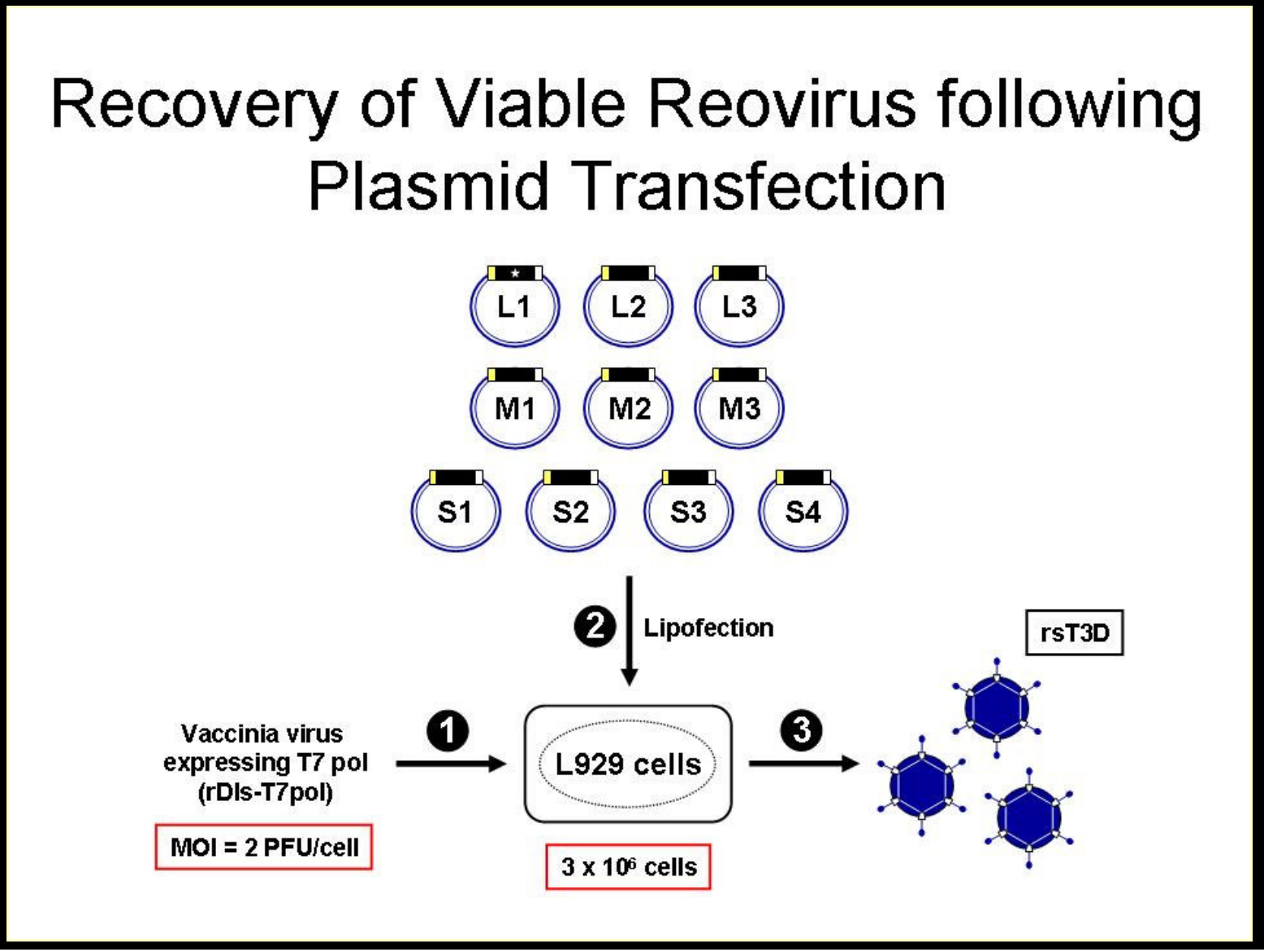
(Dr Christiaan Potgieter)

RVFV genomes amplified and sequenced using Roche' GS technology (ARC-OVI)

The Terry Dermody reverse genetics strategy for reovirus



The Terry Dermody reverse genetics strategy for reovirus (continued)



Experimental vaccines (continued) :

Reverse genetics (Bird et al., 2008)

Deleted NSs gene alone or with NSm (EGFP-tagged)

- fully protected rats
- good DIVA properties (lack of NSm antibodies)

Experimental vaccines (continued) :

Virus-vectored:

Sindbis-replicon vectored (Heise et al., 2009)

(Express GP genes : 100% protection in mice, good Nab levels in sheep)

Pox-vectored: VV (Collett et al., 1987) &

LSDV (Wallace & Viljoen, 2005; Wallace et al., 2006)

Advantages of LSDV-vectored vaccines :

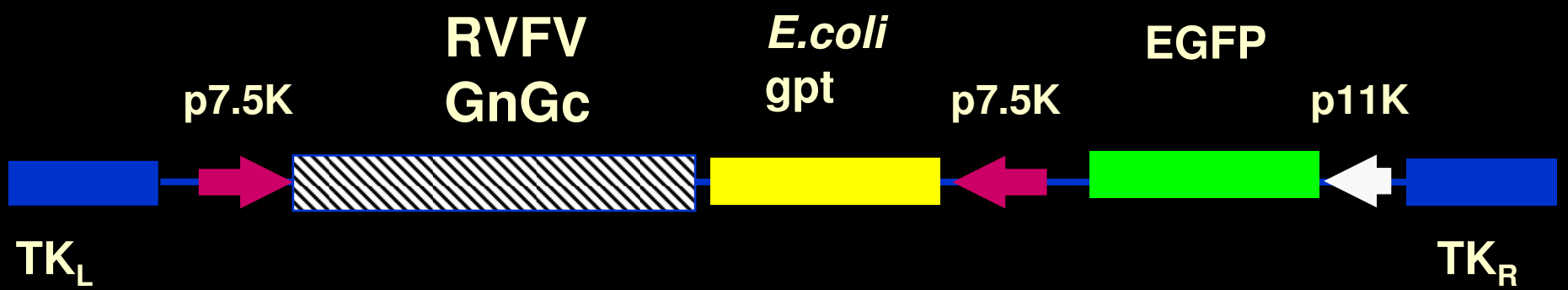
Vector: live, attenuated, stable, immunity

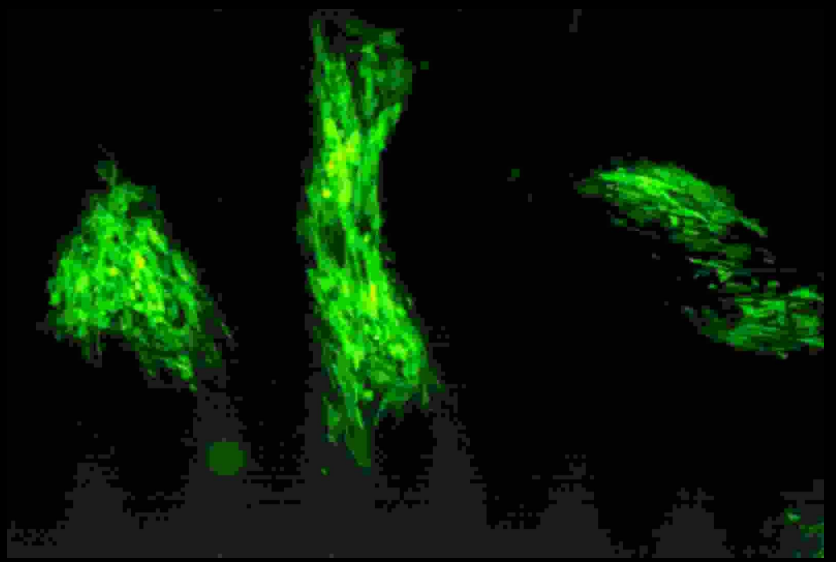
Dual potential: LSDV, SPV, GPV

Marker vaccine - DIVA

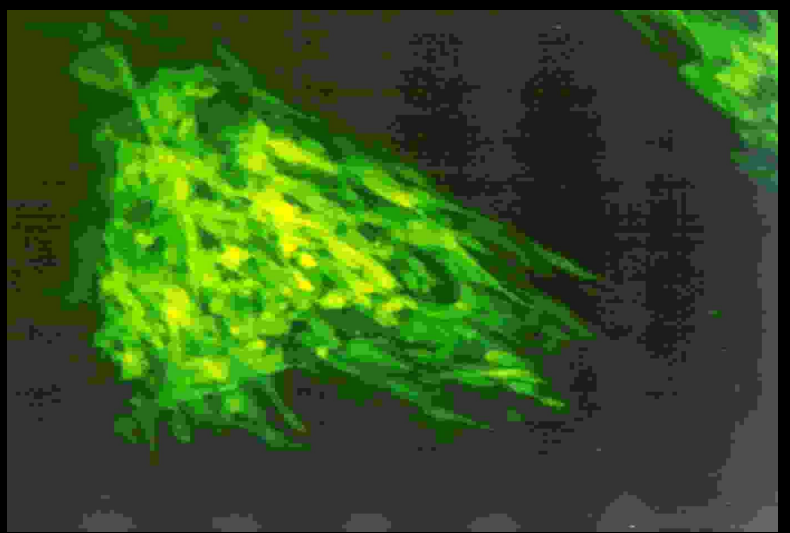
Potential human vaccine? (e.g. rLSDV-RVFV)

Lumpy skin disease virus-vectored RVFV experimental vaccine



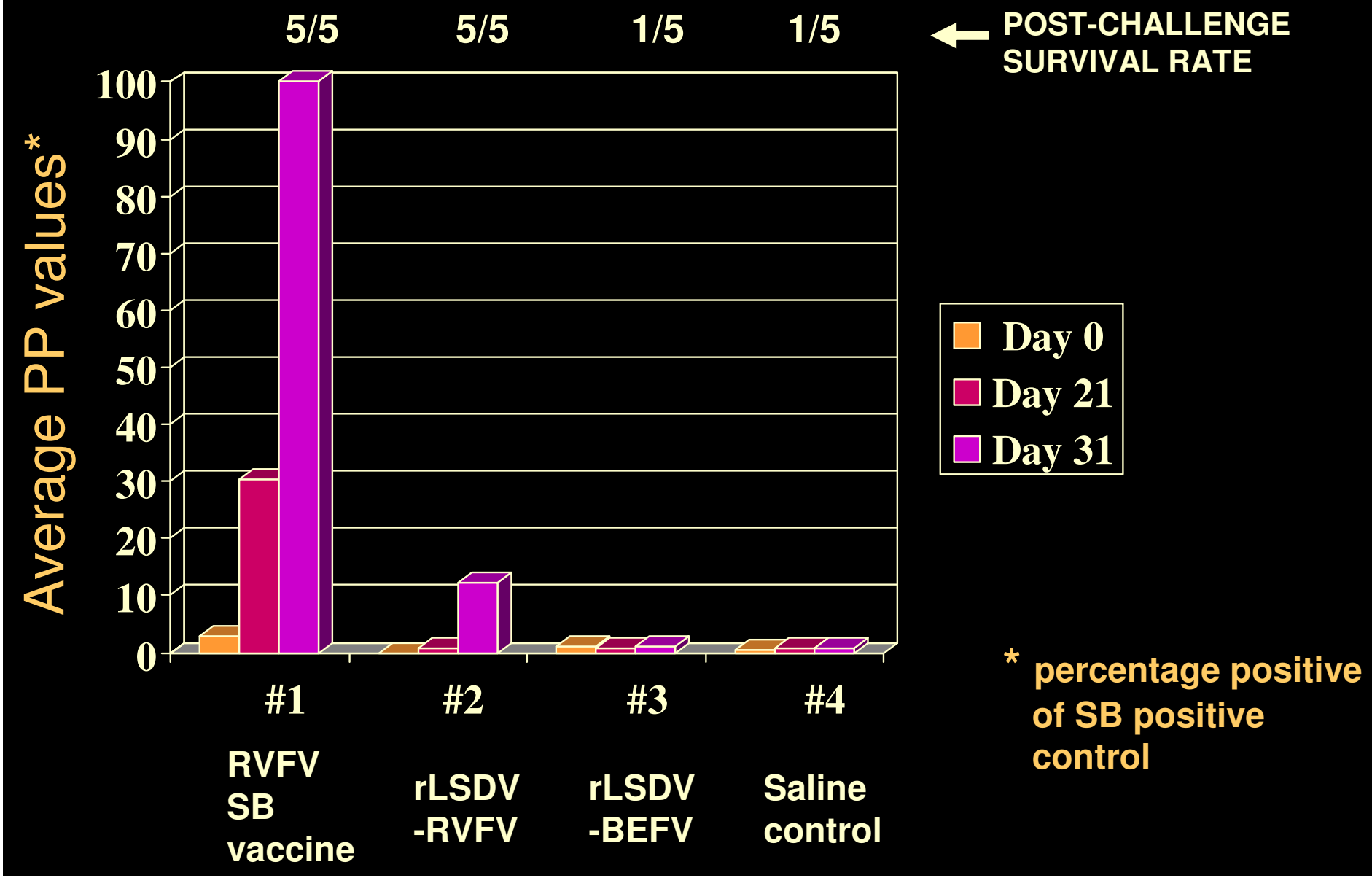


X 40

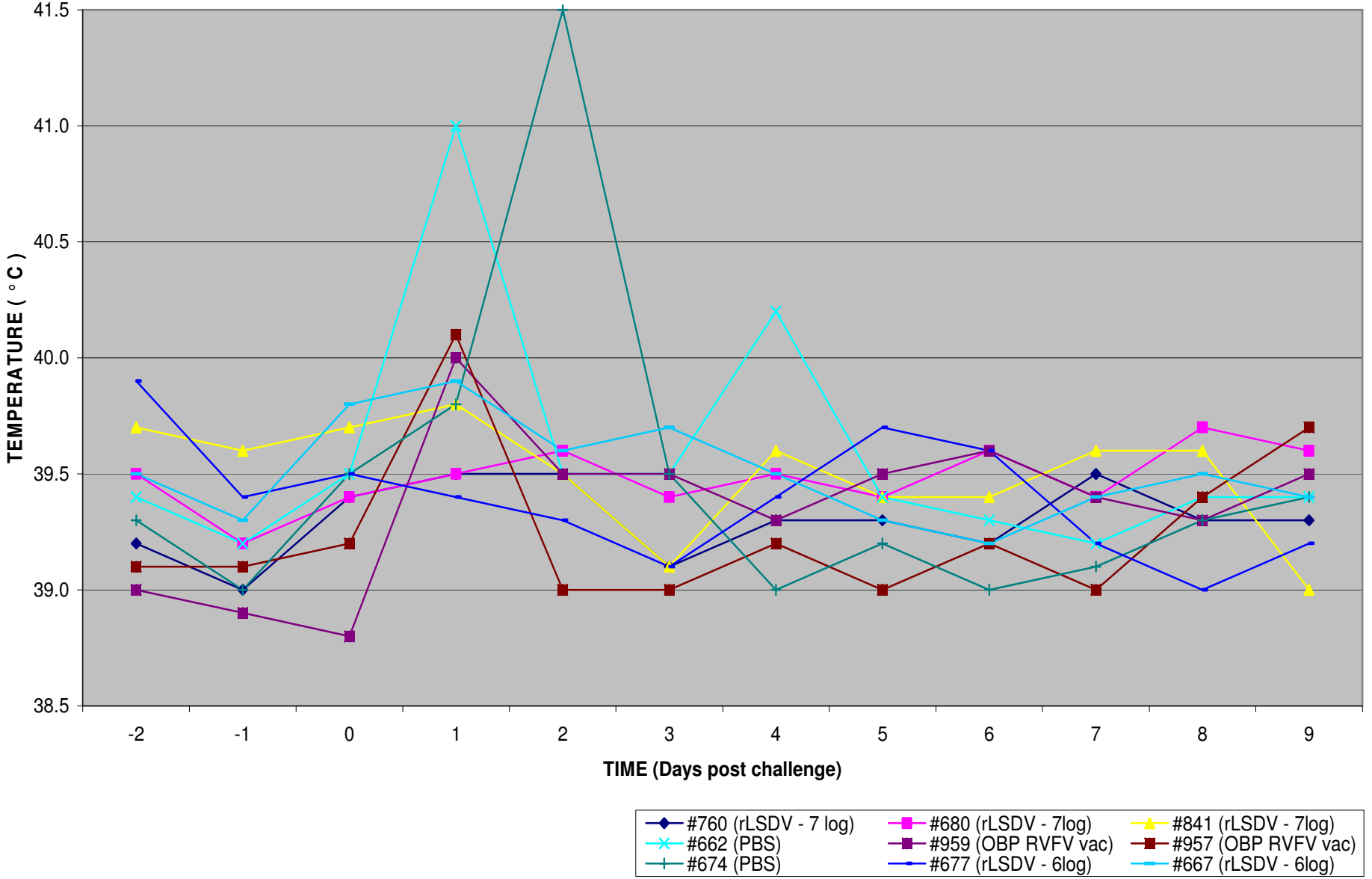


X 100

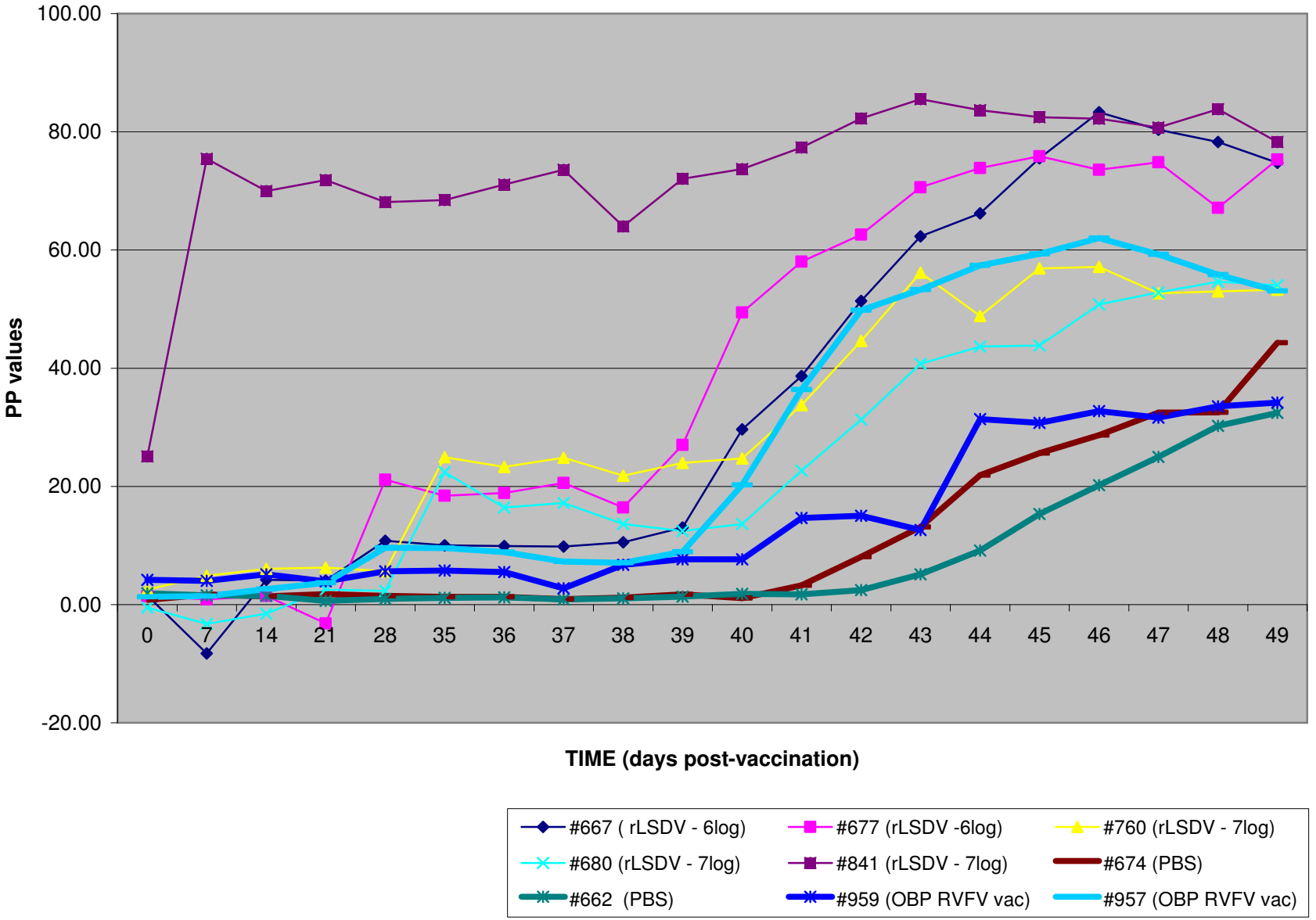
RVFV IgG ELISA and mouse challenge studies



rLSDV-RVFV challenge trial in sheep – Temperature reactions



rLSDV-RVFV challenge trial in sheep – RVFV-specific antibodies



Current work :

- Removal of selection marker genes (GALVmed funded)
- Removal of putative immunomodulatory genes (ourselves and CIRAD)
- Planning combined animal trials

Conclusion :

- Many different types of new “vaccines” and delivery systems (e.g. plants, VEE, canarypox)
- New technologies (e.g. nanoparticles)
- New generation adjuvants
- Likely that more than one will require full development due to differing needs (e.g. governmental policies etc.)

FIN!

Acknowledgements:

Dr Bjorn Reininghaus – for photo in opening slide

Dr Christiaan Potgieter – slides and helpful discussions

ARC-OVI Directorate – funding for attendance at this meeting

POX-VECTORED VACCINES?

Use of a poxvirus (e.g. LSDV) as a vehicle for the expression of immunogenic proteins of a pathogen in specific target animals to confer protection against the pathogen.

LSDV expressing the F and HA genes of RPV – dual protection

(Romero et al., 2003)

Important considerations :

- Efficacy (saftey in animals/humans, recombinantion/revertence)
- Type and duration of immunity
- DIVA (marker vaccine)
- Geographical region (indigenous vs exotic)

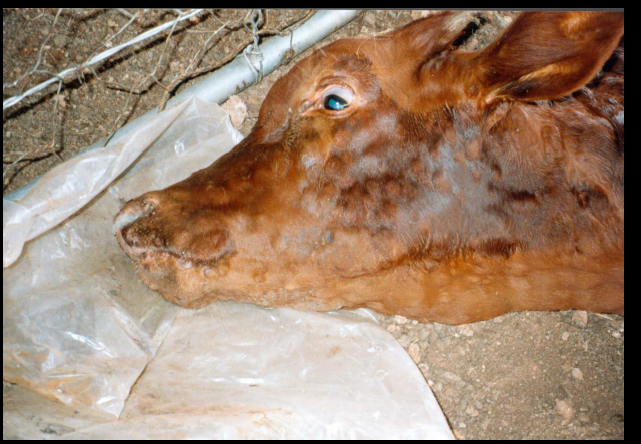
3.2 million cattle with LSD in Egypt in 2006.

400 000 deaths.

A solution:

- LSDV – developed as vaccine vector
- SA OBP vaccine strain proven track-record.
- Good results in animal trials (e.g. rLSDV-RVFV)

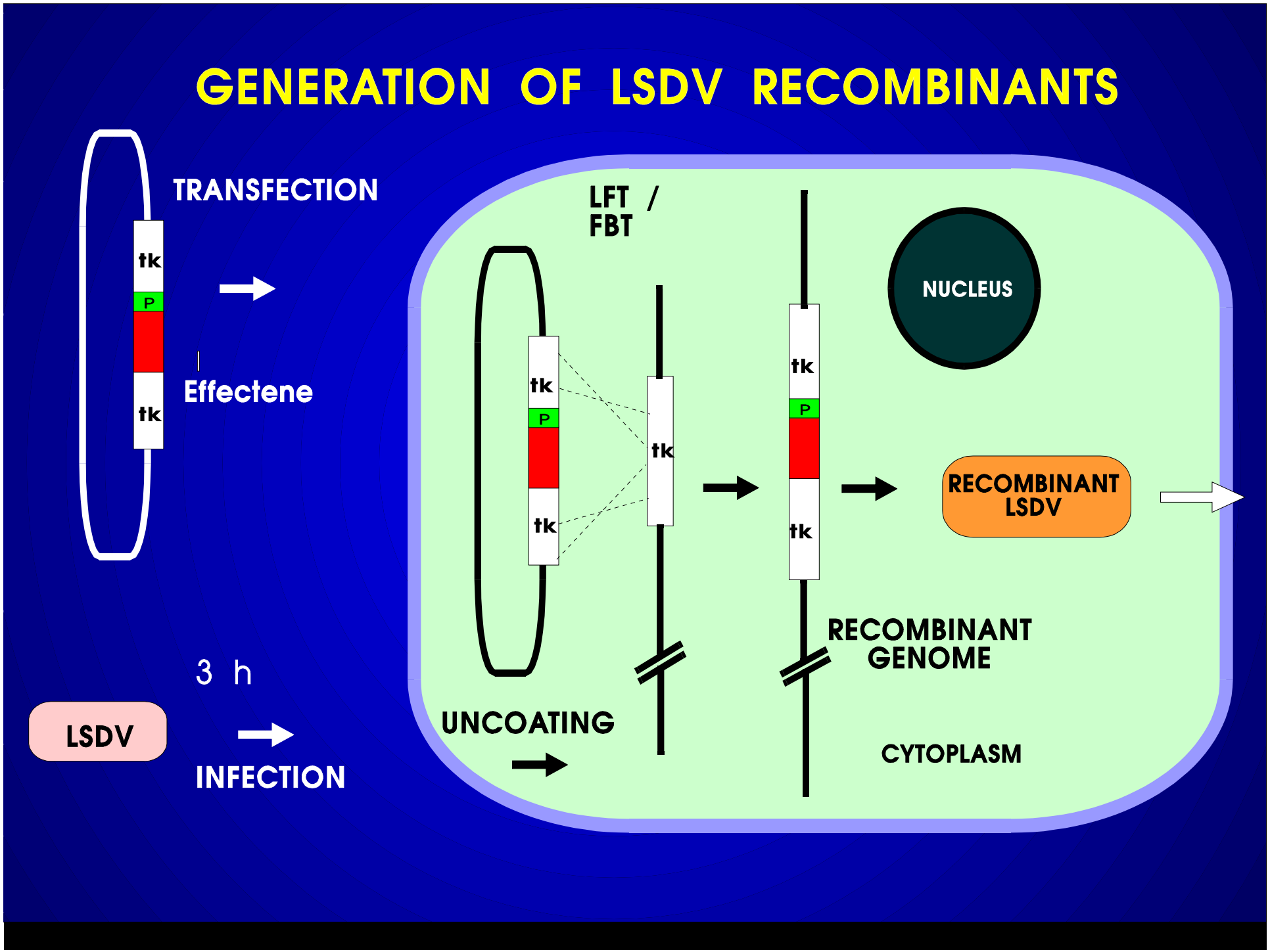
Construct description:



- LSDV SA OBP vaccine
- Vaccinia virus p7.5K promoter
- Positive selectable marker gene: gpt
- Visual marker gene: EGFP

Next stage:

- Remove of putative immunomodulatory genes (for improving immune responses – antibody levels, duration etc.)


GENERATION OF LSDV RECOMBINANTS
TRANSFECTION
tk
P
tk
Effectene
3 h
LSDV
INFECTION
LFT / FBT
tk
P
tk
tk
UNCOATING
NUCLEUS
tk
P
tk
RECOMBINANT GENOME
RECOMBINANT LSDV
CYTOPLASM

RVFV genomic layout