In vivo testing of vaccines in SEA

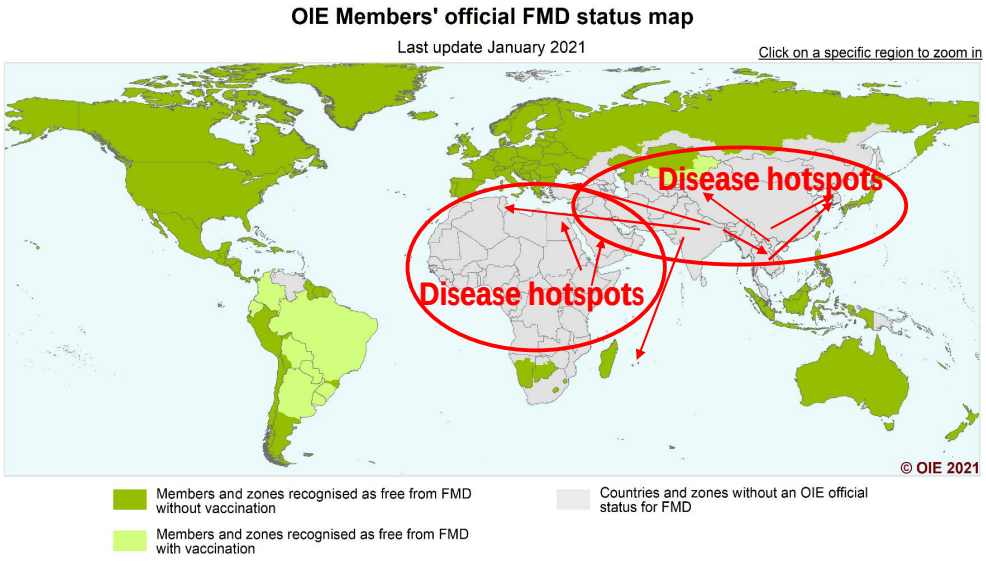
How well do antigen matching correlate with protection?

Wilna Vosloo | 25 March 2021

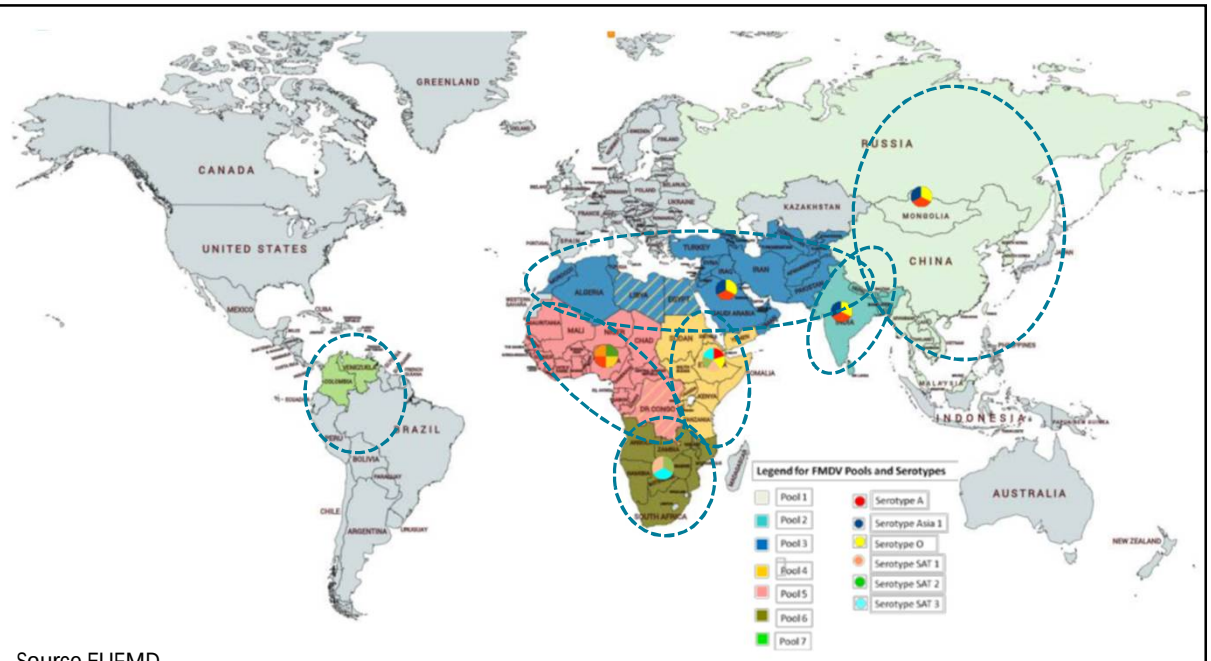
Australia's National Science Agency

1

Changing patterns and threats



2



Source EUFMD

3

Preparedness

- 'Trans-pool' movements warrant continuous monitoring and improved surveillance globally
  - O/ME-SA/Ind 2001 strains (d and e sub-lineages) west and east from South Asia
  - A/Asia/G-VII from South Asia westwards
  - O/SEA/Mya-98 (emerged in SEA – spread east and north)
- Knowledge on circulating strains assist with preparedness
  - Update vaccines?
  - Update diagnostic assays?

4

Standards for vaccines

- r_1-values (>0.3 based on VNT accepted as protection)
- Homologous virus challenge to test vaccines
  - Protective dose test (one PD_{50} – the dose of vaccine that will protect 50% of the animals)
    - Animals vaccinated with different doses of vaccine (full, ¼ and 1/16 dose)
      - 3 PD_{50}/dose: routine vaccination
      - 6 PD_{50}/dose: emergency vaccination
  - Protection against podal generalisation (PPG) test
    - Potency measured as % of animals protected after a single dose
      - 75% acceptable

5

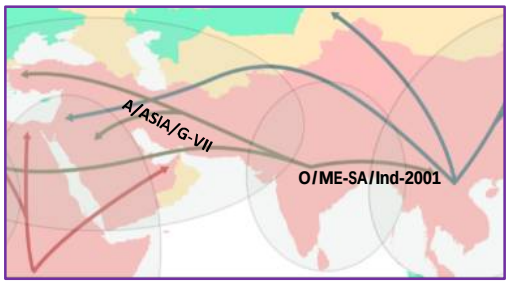
Current status of vaccines

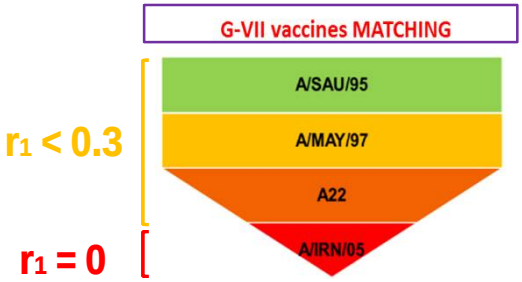
- There are limited numbers of commercial vaccine strains (some are restricted to geographical regions)
- FMDV is constantly evolving and changing
- Rapid antigenic drift noticed in the past 30 years
- Laboratory vaccine matching is not reliable in predicting heterologous protection (limited studies so far)
- Live animal challenge is still the 'gold standard'

6

Potential threats

- A/ASIA/G-VII – South Asia (Pool 2)
- Vaccines used in the field → poor protection
- *In vitro* vaccine matching data:
  - A/ASIA/G-VII field viruses matched poorly with used in Eurasia and SEA
- New emerging strain problem for
  - Endemic countries
  - FMDV free countries
    - Vaccine banks





7

Testing current vaccine strains against A/ASIA/GVII

- Calculated geometric mean r1-values
  - A22/IRQ - 0.1 (95% CI <0.04, 0.3>)
  - A/MAY/97 - 0.2 (95% CI <0.1,0.4>)
  - A/IRN/05 - 0
  - A/SAU/95 - 0.2 (95% CI <0.1; 0.4>)

8

Previous work

- PGP with commercial polyvalent vaccine (A/SAU/95 and A/IRN/05)
  - 56.3% protection*
- Tested A/MAY/97 and A22/IRQ monovalent vaccines (>6PD_{50}/dose)
  - 7 animals - A/MAY/97
  - 7 animals - A22/IRQ
- A/MAY/97 vaccine:
  - 72% protection ~ 3 PD_{50}/dose
  - Reduced virus shedding in mouth swabs
  - Good correlation VN-titre and protection (p=0.008)

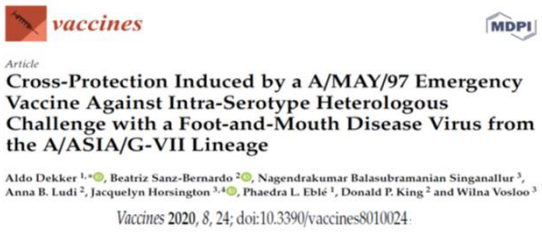
Vaccine	Podal generalization	Protected
A/MAY/97	2/7 (28.5%)	5/7 (71.5%)
A22	5/7 (71.5%)	2/7 (28.5%)

*Waters et al. 2018

9

Potency test with A/MAY/97

- Vaccine: A/MAY/97
- Challenge: A/ASIA/G-VII
- Results
  - 6.5 PD_{50}/dose (heterologous)
  - Reduced virus shedding
  - Good correlation VN-titre and protection
- Conclusion
  - Good quality, high potent vaccines can protect against heterologous challenge


vaccines

MDPI

Article

Cross-Protection Induced by a A/MAY/97 Emergency Vaccine Against Intra-Serotype Heterologous Challenge with a Foot-and-Mouth Disease Virus from the A/ASIA/G-VII Lineage

Aldo Dekker [1,*], Beatriz Sanz-Bernardo [2], Nagendrakumar Balasubramanian Singanallur [3], Anna B. Ludi [2], Jacquelyn Horsington [3,4], Phaedra L. Eblé [1], Donald P. King [2] and Wilna Vosloo [3]

Vaccines 2020, 8, 24; doi:10.3390/vaccines8010024

10

Broadly protective vaccine strains

- Vaccines O1 Campos and O/Primorsky (>6PD$_{50}$)

Vaccine strain	Topotype/lineage	r_1-value	% nt difference VP1
O1 Campos	EURO-SA	0.33-0.83	25
O/Primorsky	ME-SA/Mya-98	0.41-0.73	3

- Challenge O/SKR/2014 (O/ME-SA/Mya-98 lineage) in pigs
- Protection in SPF pigs (14 and 28 pdv) and protective titres at different times post weaning in the field
- Importance of testing vaccines locally

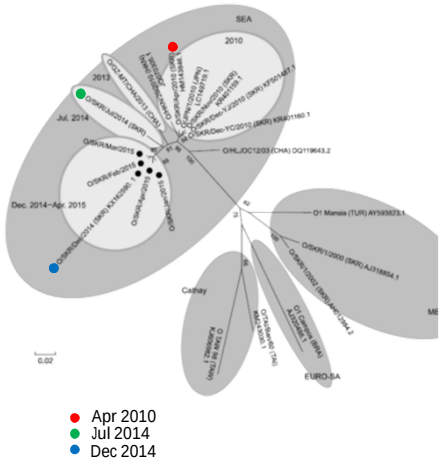
Choi et al. 2021, Galdo Novo et al. 2018

11

Combinations of strains to broaden immunity

- Serotype O outbreaks in South Korea caused by O/SEA/Mya98 lineage
- Three different introductions with diversification
- O1 Manisa may not be sufficient – combined with O3039

Virus/Vaccine	O1 Manisa	O 3039
O/SKR/Dec/2014	0.1-0.3 (non matching)	0.42-0.73 (matching)



J-H Park et al, 2018

12

Combinations of strains to broaden immunity

Challenge virus	Species	O1 Manisa + O 3039	O3039
O/SKR/Dec/2014	Pigs	100% protection 14 & 28 dpv	50% protection 28 dpv
O/ALG/3/2014 (O/Ind/2001)	Cattle	80% protection 7 dpv; 100% protection 21 dpv	60% protection 7 dpv; 100% protection 21 dpv

J-H Park et al, 2018; Singanallur et al, in prep

13

Combinations of strains to broaden immunity

- A22/IRQ and A/MAY/97 challenged with A/ASIA/SEA-97 virus in pigs

Vaccine	Protection 21 dpv	r_1-values
A/MAY/97	20%	~0.3
A/22/IRQ	20%	~0.3
A/MAY/97 + A/22/IRQ	80%	

The increased antigen payload or the synergetic effects of cross-protection of two antigens in bivalent vaccine might affect the protective efficacy

14

Summary

- High potency vaccines provide sufficient heterologous protection even when r_1-values predict poor protection
  - Experimental studies use small numbers of animals
  - Challenge is via IDL route – unnatural route
- Genetic comparisons do not always correlate with expected r_1-values and vaccine efficacy
- Benefits of vaccination even if clinical protection is not perfect
  - Decreases duration and level of virus excretion
- Vaccination does not prevent persistent infection
- More research needed regarding relationship between the heterologous and homologous potency of a vaccine

15

FMD READY PROJECT

Thank you

Nagendra Singanallur, Petrus Jansen van Vuren, Jacquelyn Horsington, Jong-Hyeon Park, Yanmin Li, Zengjun Lu, Charles Nfon, Don King, Anna Ludi, Phaedra Eblé, Aldo Dekker

Australia's National Science Agency

- Australian Centre for Disease Preparedness
- Animal, Plant and Fisheries Quarantine and Inspection Agency, South Korea
- Lanzhou Veterinary Research Institute, China
- National Centre for Foreign Animal Diseases, Canada
- The Pirbright Institute, UK
- Wageningen Bioveterinary Research, The Netherlands

16