FMD Vaccine Strain Selection

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Conclusions

• Vaccine match is one component of vaccine efficacy
• Vaccine quality may compensate for imperfect match
• Predicting vaccine match is a key surveillance task
• Inter-regional co-operation is highly desirable
• May be scope to simplify vaccine strain usage?
• Research can speed up laboratory vaccine matching tests and make them more reliable
• Measuring vaccine match in the field is challenging
• Highly cross-reactive vaccines are still some way off?
Importance of vaccine strain selection

- Antigenic change due to mutation and recombination
- Some serotypes more antigenically diverse
- Field evidence of importance
  - Major disease outbreaks in properly vaccinated animals?
  - Reduced efficacy of vaccination?
    - A Arg 2001 strain cases in A24 vaccinated cattle in S America
    - A Iran 05 strain cases in A Iran 96 vaccinated cattle in Middle East
    - SAT 2 outbreaks in Botswana
    - O 2009 outbreaks in Ecuador in O Campos vaccinated cattle
    - O PanAsia2 in the Middle East
    - O Mya 98 strain outbreaks outside SEA in 2010/11
    - Asia 1 in Turkey in 2011/12
- Experimental evidence of cross-protection and its lack
Protection 'Windows' Conferred by Homologous and Heterologous FMD Vaccines

Adapted from Pay, 1994
High potency vaccines induce protection against heterologous challenge with foot-and-mouth disease virus

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**KEYWORDS**
Foot-and-mouth disease virus; Protection by vaccines; Serology

**Summary** In a series of three homologous and eight heterologous challenge experiments, it was shown that high potency vaccines against foot-and-mouth disease (FMD) serotype A can induce protection even against heterologous challenge infection with viruses that give low $r$-values with the vaccine strains.

The challenge virus specific neutralizing antibody response on the day of challenge (21 days post vaccination) generally correlated with protection.

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Vaccine strain selection in practice

- **Field work**
  - to investigate outbreaks and collect samples
- **Lab work**
  - to determine the serotype, strain and vaccine match
- **Vaccine producer**
  - to produce and supply the vaccine
- **Livestock industry / competent authority**
  - to determine the vaccination policy and purchase vaccine for use / banks
- **Overall decision making process and international dimension**
International cooperation

Pools 1-3

- same 3 serotypes
- need more cooperation and early warning
- might be scope for common vaccine strains
Research goals

• Simplify and speed up matching process and make results more reliable and informative

• Better field indicators of vaccine effectiveness

• More broadly reactive vaccines
Prospects for better vaccine matching

• Lab-based matching
  - Difficulties with current arrangements
  - Cartographic methods
  - Identify critical epitopes - dominance and variability
  - Sequence based alternatives to serology

• Field measurements of vaccine effect
  - Post-vaccination serology
  - Vaccine effectiveness
Antigenic Cartography

A. Ludi- FMDV Serotype A

Purple - Africa
Green - Euro/S. America
Blue - Asia

Institute for Animal Health
Anna Ludi, PhD Student, IAH-Cambridge
Correlation between serological cross-reactivity and amino acid changes with multiple virus pairs

72 type O viruses
5 antisera

EURO-SA
CATHAY
MIDDLE EAST/ASIA
FMDV Type O - epitope predictions

Epitopes of known antigenic sites - RED
Epitopes identified by structural predictions – PURPLE, or if already known – YELLOW
Epitopes predicted by comparing pairwise sequences and serology – BLUE
Epitopes predicted by both of above two - ORANGE
Epitopes predicted by reactivity of O1 Kaufbeuren serum – GREEN
Vaccine antisera tested by VNT against O₁Kaufbeuren virus mar mutants

- 57 cattle sera
  - O₁BFS
  - O₁Lausanne
  - O₁Kaufbeuren

- 33 pig sera
  - O₁BFS

- 20 sheep sera
  - O₁BFS

Compare titre reductions to those against O₁Kaufbeuren
Prospects for broader cross-protection

- Concepts from influenza and HIV
  - Viral surface acts as an immune decoy
  - Prominent but flexible and variable surface structures attract antibodies
  - Virus critical features are conserved but poorly accessible to antibodies
- Identify conserved and protective epitopes
- Develop into vaccines
- Will this work for FMDV?
Practical solutions

- Improve monitoring in the field and target surveillance
- More sharing of matching reagents, viruses and vaccines
- Regional vaccine strains
- Careful standardisation of vaccine matching serology
Research opportunities

- Further development of cartographic and sequence based matching methods
- Better understanding of epitope conservation and dominance and effects this has on humoral immunity
- Basis for antibody induced protection *in vivo*
- Recombinant vaccine platforms that facilitate rapid introduction of new antigenic motifs or presentation of conserved epitopes
- Prospective field studies to look at vaccine effectiveness directly including influence of vaccine match
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