Foot and Mouth Disease Control, A vaccine perspective

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Countries in which FMD was reported to the OIE between 1990 and 2002

- Antigenic variation is common
- Multiple subtypes within each serotype
- Genetic variation in the capsid-coding region (P1)
- Databases of FMDV epidemiology & sequences
  - http://www.wrlfmd.org/
  - http://www.iah-virus.org/

Current FMDV vaccines

- **Safety:**
  - Vaccine production requires adaptation and growth of large amounts of virus requiring high containment facilities for manufacture

- **Efficacy**
  - Short duration of Immunity (6 months)
  - Narrow coverage; Poor cross protection for serotypes and subtypes
  - Window of susceptibility to natural infection post vaccination
  - Vaccinated animals can be persistent carries following natural exposure
  - cannot Differentiate Infected from Vaccinated Animals (DIVA)
Characteristics of an “Ideal” FMDV vaccine

• Effective, rapid and long-lasting protection with one inoculation
  – Long duration of immunity
• Prevents virus transmission
• Allow differentiation of infected from vaccinated animals (DIVA)
• Safe: produced without the need for virulent FMDV
  – No need for adaptation of field strains to cell culture
• Prevent development of carrier state
• Broad antigenic coverage
• Stable antigen – long shelf life
Novel Ad5-FMD Vaccine

• Developed by ARS scientists under leadership of Dr. Marvin Grubman
Ad5-A24 Prevention of FMDV virus shedding and transmission; Protection from disease

Grubman et al. 2010 Future Virol 5:51-54
FMDV Genome

Grubman et al. 2010
FMDV vaccines

• Human Adenovirus 5: replication defective Ad5 used as vector to deliver FMDV capsid proteins - DIVA vaccine

• Can be manufactured at BSL-2, no high containment facility required

• Unknown duration of immunity
FMDV vaccines

Research objectives

1. Evaluate duration of protection for up to 1 year following a single vaccination

2. Evaluate the route of administration (needle-free vaccination)

3. Accelerate the development of vaccine technology for FMDV by characterizing host response to vaccination, focusing on the CD8 T cell response
Ad5-A24 delivered vaccines

Ad5-A24-P1-3Cpro
(B cell vaccine)

P1

3C

3C\textsuperscript{pro} found to be required for Development of virus neutralizing antibodies and protection following challenge

Grubman et al. 2010 Future Virol 5:51-54
Pulse Needle Free Vaccination Device
Adaptive immune responses

- Naïve B cell
- Naïve T helper cell
- Dendritic cell
- Virus infected cell
- Activated macrophage
- Plasma cell
- Memory B cell
- Antibodies

Cell Types:
- CD4
- CD8 Killer T Cells

Phases:
- B cell expansion
- T cell expansion
- CD4
- CD8 T cell expansion

Virus interaction:
- Virus

Ad5-A24 delivered vaccines

Ad5-A24-P1
(T cell vaccine)

P1

3C cleavage

P1
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Protection from intradermal/lingual FMDV-A24 challenge in steers vaccinated with Ad5-A24

- IM 80%
- SQ 60%
- TD 100%
- Naïve 0
Characteristics of an “Ideal” FMDV vaccine

✓ Effective, rapid and long-lasting protection with one inoculation
  – Long duration of immunity ?? 6 months
✓ Prevents virus transmission ??
✓ Allows differentiation of infected from vaccinated animals (DIVA)
✓ Safe: produced without the need for virulent FMDV
  – No need for adaptation of field strains to cell culture
• Prevent development of carrier state
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Alternative Vaccine constructs

Ad5-A24-P1

Ad5-A24 Bov-Ii-P1

Ad5-A24-P1-2AB

Bovine Invariant Chain

P1

Steffensen et al. 2012 PLoS One

Moraes et al. 2011 Vaccine
Acknowledgements

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• Dr. Tatjana Sitt
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• Mary Kenney

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• AFRI-NIFA pre-doctoral fellowship (MP)
B cell vaccine

Release of empty viral capsids

Uptake by APCs

CTL vaccine

Peptide

MHC class I

MHC class II

B-cell
Foot & mouth disease virus (FMDV)

- Positive strand RNA virus, *Picornaviridae* family, genus *Aphthovirus*
- Infects cloven hoofed animals; cattle, sheep, goats and swine
- Fever, salivation, vesicular lesions on the tongue, feet, snout, teats and lameness, viremia lasts 3-4 days
- 7 major serotypes, many subtypes
- Countries with FMDV cannot export animals or animal products
FMDV vaccines

Vaccination against foot-and-mouth disease virus confers complete clinical protection in 7 days and partial protection in 4 days: Use in emergency outbreak response

William T. Golde, Juan M. Pacheco, Hernando Duque, Timothy Doel, Barry Penfold, Geoffrey S. Ferman, Douglas R. Gregg, Luis L. Rodriguez

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b Department of Pathobiology and Veterinary Sciences, University of Connecticut, Storrs, CT, USA
c Merial Animal Health Ltd., Pirbright, Surrey, UK
Vaccination against foot-and-mouth disease virus confers complete clinical protection in 7 days and partial protection in 4 days: Use in emergency outbreak response

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Available online at www.sciencedirect.com

Vaccine 23 (2005) 5775–5782

Killed virus

Rapid protection of cattle from direct challenge with foot-and-mouth disease virus (FMDV) by a single inoculation with an adenovirus-vectored FMDV subunit vaccine

Juan M. Pacheco, Mario C.S. Brum, Mauro P. Moraes, William T. Golde, Marvin J. Grubman

Available online at www.sciencedirect.com


Ad5 FMDV
Food and Mouth Disease Virus Vaccine: Duration of Immunity to Ad5-A24

Construction of replication-defective human adenovirus 5 (Ad5) vector containing FMDV capsid proteins

3C\textsuperscript{pro} found to be required for Development of virus neutralizing antibodies and protection following challenge
Food and Mouth Disease Virus Vaccine: Duration of Immunity to Ad5-A24

Objectives:

To determine serum virus neutralization titers and protection from challenge at time points up to 1 year following vaccination with Ad5-A24

To determine Ad5-A24 vaccine performance using a needleless transdermal injection system

Cohort 1 – 6 month post single vaccination challenge
  Needle Intramuscular n=5
  Needle subcutaneous n=5
  Needle-free transdermal n=5
  Naïve n=3
Discovery of CTL specificities for FMDV

The role of cellular immunity in protection is controversial

- clearance of virus in persistent infections
- reduction of shedding during early (acute) phase of infection