Improving FMD vaccine potency by modification of vaccination protocols

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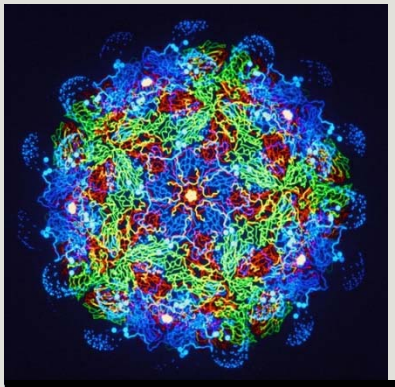
FMD Vaccines

- **Inactivated whole antigen formulated with adjuvants vaccines (only type commercially available)**
- Inactivated modified attenuated FMDV that may offer increased safety for production (i.e deleted viruses –leaderless, 3A, 3B)
- Live vector delivered subunit/peptide vaccines (**Adeno,** pox, pseudorabies, alpha-or other virus **encoding fractions or VLPs**)
- Recombinant subunit/fraction vaccines (peptides, **VLPs)**
- Next generation **live** attenuated marker vaccines (rationally mutated, or codon/codon pair deoptimized, with DIVA markers

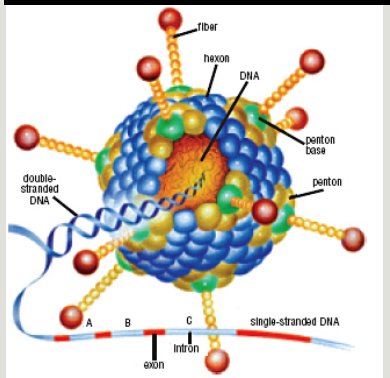
PIADC recent successes

Marker inactivated FMD-LL3B3D vaccine (ARS Rieder/ Rodriguez's labs in partnership with Zoetis)



Inactivated or live attenuated DIVA FMDV

Ad5-FMD vaccine (ARS-Grubman/de los Santos labs in partnership with DHS and GenVec Inc)



Human Replication Defective Adenovirus 5 -FMD VLPs

Highlights

PRODUCT PROFILE	FMD-LL3B3D INACTIVATED	Ad5-FMD
Prevents viral transmission	✓	✓
Early onset of immunity	✓	✓
Marked vaccine (DIVA capable)	✓	✓
Domestic production outside BSL3	**No**	✓
Long-term stability formulated product	**No**	✓
Readily deployable (ready to use)	**No**	✓
Compatible with “vaccinate to live” strategy	✓	✓
Provides cross-serotype protection	**No**	**No**

•However…need of cost effectiveness for applicability worldwide

Multiple approaches are being pursued to improve potency

- Increase potency and duration of immunity by adding NEW ADJUVANTS or changing vaccine formulation (molecular adjuvants, nanoparticles, etc) (*Diaz-San Segundo et al., 2014; Ren et al., 2012*).

- Increase potency of vector-delivered VLPs by modifying vector (new promoters, molecular adjuvants) (*Medina et al., 2015*).

- **Increase potency, and possibly duration of immunity, and prevent tissue damage -meat depreciation-, by changing the route of inoculation**

Intradermal delivery of inactivated FMD vaccine improves vaccine potency *in swine*

Advantages of intradermal (ID) inoculation:

- ✓ Skin contains numerous resident antigen presenting cells (APCs) such as, Langerhans cells and dermal DCs.

Vaccine 27 (2009) 1272–1278

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Intradermal vaccination of pigs against FMD with 1/10 dose results in comparable vaccine efficacy as intramuscular vaccination with a full dose

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IM vs ID- INDAL, Intervet

Intradermal delivery of inactivated FMD vaccine may improve vaccine potency but not change the breadth of coverage *in cattle*

Vaccine 30 (2012) 3106–3111

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

IM vs ID –Dermavac®

An alternate delivery system improves vaccine performance against foot-and-mouth disease virus (FMDV)

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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

No significant differences in the breadth of the foot-and-mouth disease serotype A vaccine induced antibody responses in cattle, using different adjuvants, mixed antigens and different routes of administration

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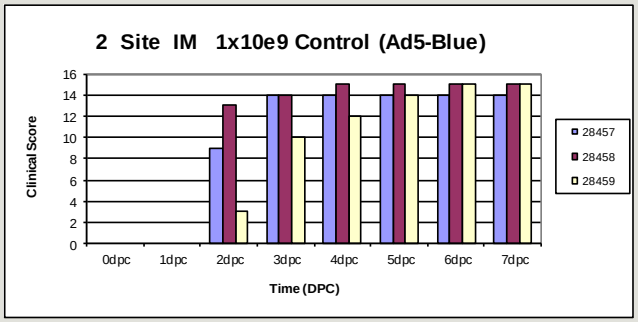
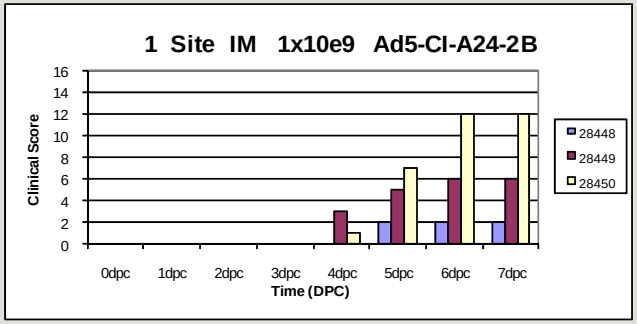
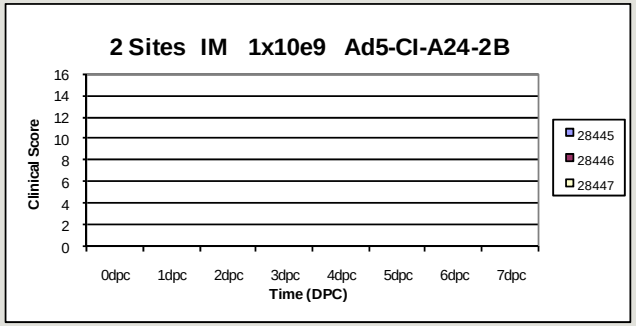
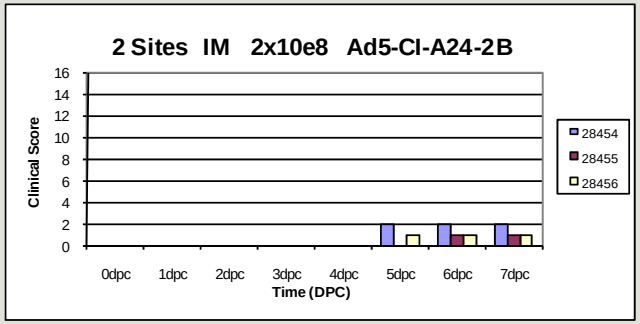
SC vs ID –INDAL, Intervet

SC inoculation of Ad5-FMD at 2 sites improves vaccine potency *in swine*



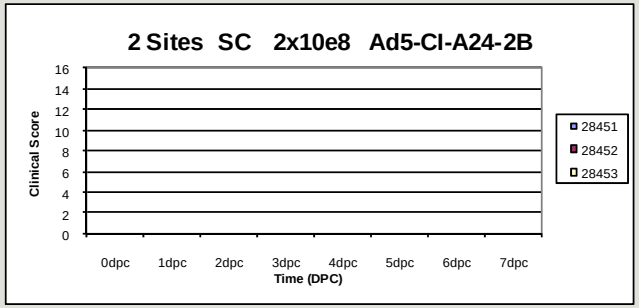




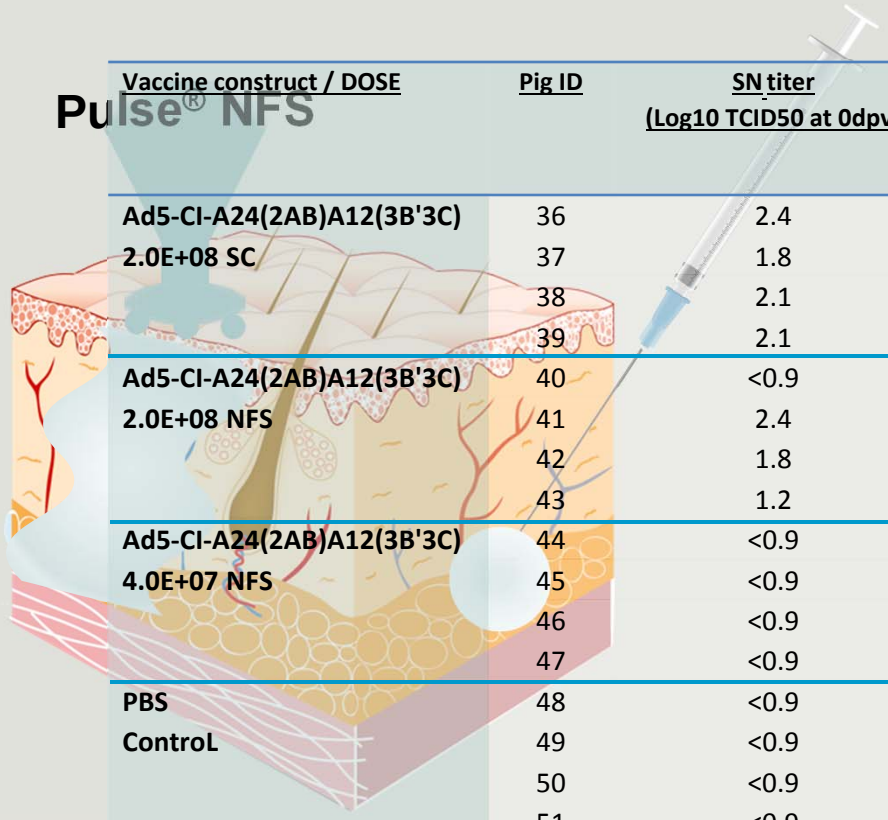


Vaccine dose can be reduced by 25x fold by SC inoculation at 2 sites as compared to IM inoculation at 1 site.

Grubman et al., 2012



SC and TRANSDERMAL vaccination with Ad5-FMD results in similar efficacy *in swine*



Vaccine construct / DOSE	Pig ID	SN titer (Log10 TCID50 at 0dpv)	Clinical Score[a] (number of lesions at 3, 4, 7dpc)	3ABC ELISA (21dpc)
Ad5-CI-A24(2AB)A12(3B'3C) 2.0E+08 SC	36	2.4	0/0/0	N
	37	1.8	0/0/0	N
	38	2.1	0/0/0	N
	39	2.1	0/0/0	N
Ad5-CI-A24(2AB)A12(3B'3C) 2.0E+08 NFS	40	<0.9	0/0/0	N
	41	2.4	0/0/0	N
	42	1.8	0/0/0	N
	43	1.2	0/0/0	N
Ad5-CI-A24(2AB)A12(3B'3C) 4.0E+07 NFS	44	<0.9	7/17/17	ND
	45	<0.9	0/7/15	P
	46	<0.9	0/0/15	p
	47	<0.9	6/16/17	P
PBS ControL	48	<0.9	0/4/15	P
	49	<0.9	4/17/17	P
	50	<0.9	10/17/17	P
	51	<0.9	15/17/17	P

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