Review of current state of available vaccines for the control of PRRS

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PRRS: the disease

- Clinical signs

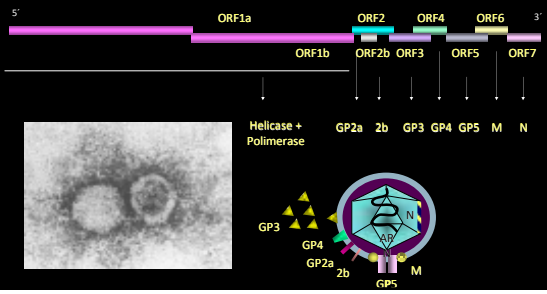
In the sow

Inespecific

In growing pigs

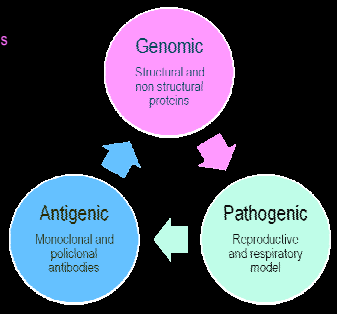
PRRS virus: main characteristics

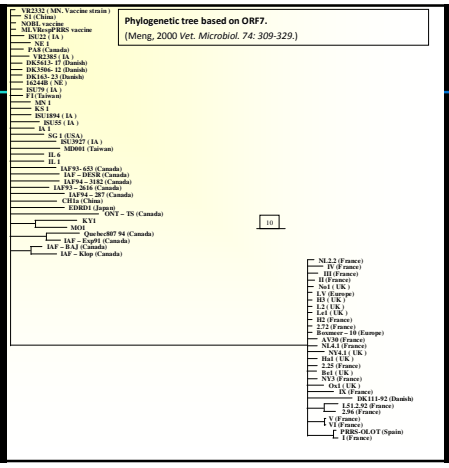
- Classification
  - *Arteriviridae* family
    - *Arterivirus* genus



PRRS virus: main characteristics

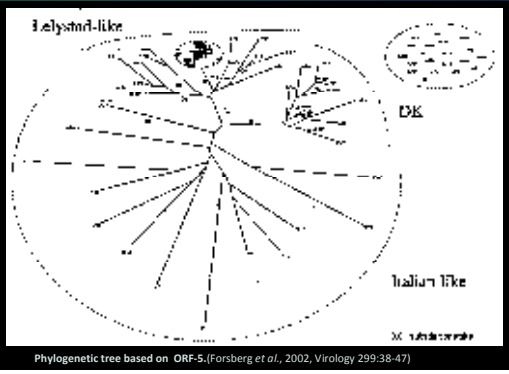
- Variability
  - Implications
    - Diagnosis
    - Control





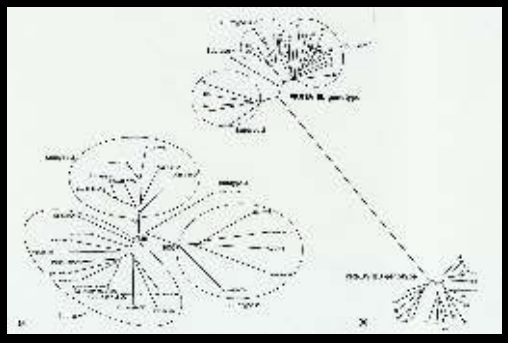
Phylogenetic tree based on ORF7.
(Meng, 2000 *Vet. Microbiol. 74: 309-329.*)

PRRSV variability



Phylogenetic tree based on ORF-5.(Forsberg *et al.*, 2002, Virology 299:38-47)

PRRSV variability



Phylogenetic tree of European-type PRRSV .(Stadejek et al., 2006, J Gen Virol, 87: 1835-1841)

Objective

- To review the state of the art in relation to PRRS vaccinology

Commercially available vaccines

Experimental vaccines

Future expectations

Licensed vaccines

- Types of vaccines currently available in Europe

- Inactivated:
  - Progressis
  - Suvaxyn PRRS
  - Ingelvac PRRS KV
  - Suipravac PRRS

- MLV:
  - Amervac PRRS
  - Pyrsvac 183
  - Porcilis PRRS
  - Ingelvac PRRS MLV

Inactivated vaccines

- Approved for use in reproductive herd

Main advantage:
THEY ARE VERY SAFE

But....
What about efficacy?

→ At least...
CONTROVERSIAL!!!

- Most experiments has been done using Suvaxyn PRRS

Inactivated vaccines

- Limited protection
  - Homologous protection (Plana – Durán *et al.*, 1997)

PRODUCTIVE RESULTS IN PREGNANT SOWS (4 experiments)

	Total born	Born alive	Born weak	Stillborns
Vaccinated	18	13	4	1
Unvaccinated	23	19	1	3

VIREMIA POST-CHALLENGE IN PREGNANT SOWS

	Time post-challenge						
	5 h	20 h	3 d	4 d	7 d	10 d	15 d
Vaccinated	0/5	9/9	7/7	7/7	7/7	7/7	5/9
Non-Vaccinated	0/5	3/3	3/3	3/3	3/3	3/3	4/5

Vaccinated	75	55	8	12
Unvaccinated	42	5	7	30

Inactivated vaccines

- Limited protection
  - Heterologous protection (Prieto *et al.*, 1997)

REPRODUCTIVE PERFORMANCE IN EARLY GESTATION

	Negative/Challenge	Immunized/Challenged	Negative controls
No. pregnant gilts	6	5	7
No. gilts repeating oestrus	1	2	0
No. litters infected	5	1	0
% of litters infected	83,3	20	0
Total corpora lutea (range)	120 (15-26)	93 (16-24)	144 (15-29)
Total embryos (range)	92 (7-22)	76 (10-20)	112 (6-24)
Total embryos/Total corpora lutea	0,77	0,82	0,78
Total live embryos (%)	77 (83,7)	44 (57,9)	101 (90,2)
No. live embryos infected	4	1	0
Total dead embryos (%)	15 (16,3)	32 (42,1)	11 (9,8)
No. dead embryos infected	3	0	0
% of embryos infected	7,6	1,3	0

Inactivated vaccines

- Limited protection
  - Heterologous protection (Scortti *et al.*, 2007)

REPRODUCTIVE PERFORMANCE OF PREGNANT GILTS

Group	N. of litters	Total born	Still born piglets: Total (%)	Still born piglets: Large mummies (%)	Born alive: Total (%)	Born alive: < 0.9 kg (%)	Lactation losses (%)	Weaned piglets (%)	Weaning weight
A	4	44[a]	2 (4.5)	0	42 (95.5)	3 (7.1)	6 (14.3)	36[a] (85.7)	4.8[a]
B	5	45/53 (84.9)	8 (14.3)	1/7[a] (87.5)	37/46[a] (100)	14/37[a] (100)	3/14[a] (92.9)	34/37[a] (100)	7.0[a] (100)
C	5	36/51 (70.6)	10 (16.7)	1/6[a] (42.9)	26/41[a] (80.6)	7/26[a] (85.2)	3/19[a] (66.4)	23/26[a] (90.9)	6.3[b] (76.2)

VIREMIA AND VIRAL SHEDDING POST-CHALLENGE IN PREGNANT SOWS

Group	Gilt number	Viremia: D0	Viremia: D3	Viremia: D6	Viremia: D9	Viremia: D12	Viremia: D21	Nasal Swabs: D0	Nasal Swabs: D3	Nasal Swabs: D6	Nasal Swabs: D9	Nasal Swabs: D12	Nasal Swabs: D21
A	5	-	+ (2.5)	(3.6)	(4.7)	(3.9)	-	-	7[a]	10[a]	21[a]	-	-
C	6	5	-	5+ (2.2)	(3.6)	(3.6)	(27.5)	-	31[b] (22.6)	(<1)	18 (67.7)	-	3.6[b]
Group B	7	-	-	+ (2.5)	(3.6)	-	-	-	-	+ (<1)	+ (<1)	-	-
	8	-	-	+ (2.5)	+ (2.6)	+(<1)	-	-	-	-	+ (<1)	-	-
	9	-	-	-	-	-	-	-	-	-	+ (<1)	-	-
	10	-	-	+ (3.6)	+ (3.6)	-	-	-	-	-	-	-	-
	11	-	-	+ (2.7)	+ (2.7)	-	-	-	-	+ (<1)	+ (<1)	-	Dead in lactation
Group C	12	-	-	+ (2.5)	-	-	-	-	-	+ (<1)	+ (<1)	-	-

TRANSPLACENTAL INFECTION

Group	Number of litters	Total born (%)	Still born piglets (%): Total	Still born piglets (%): Large mummies	Born alive[1]: D0	D4	D8	D15	D21	Dead in lactation	Weaned piglets
A	4	0/44	0/2[a]	0/0[a]	0/42[a]	-	-	-	0/35[a]	0/7[a]	0/35[a]
B	5	0	0	0	0	0	0	0	0	0	0
C	5	45/53 (84.9)	1/7[a] (14.3)	1/1[b] (87.5)	30/30[b] (100)	22/22[b] (100)	13/14[b] (92.9)	7/9[b] (77.8)	7/7[b] (100)	23/23[b] (100)	7/7[b] (100)
		36/51 (70.6)	1/6[a] (16.7)	6/14[b] (42.9)	25/31[a] (80.6)	23/27[a] (85.2)	19/22[a] (86.4)	20/22[b] (90.9)	16/21[b] (76.2)	9/10[b] (90.0)	20/21[b] (95.2)

Inactivated vaccines

- Limited protection
  - Heterologous protection (Nielsen *et al.*,1997)

VIREMIA AFTER CHALLENGE OF BOARS

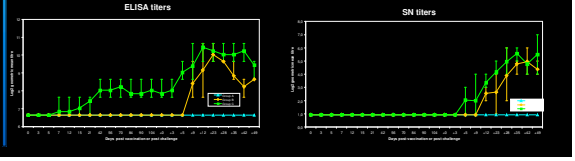
	Time post-challenge							
	4 days	7 days	10 days	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks
Unvaccinated	4/5	4/5	4/5	4/5	0/5	0/5	0/5	0/5
Vaccinated	5/5	4/5	5/5	2/5	2/5	0/5	0/5	0/5

VIRAL SHEDDING IN SEMEN AFTER CHALLENGE OF BOARS (bioassay)

	Time post-challenge						
	4 days	7 days	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks
Unvaccinated	ND	5	5	4	1	0	0
Vaccinated	ND	5	5	5	4	0	1

Inactivated vaccines

- Immune response to vaccination
  - No induction of neutralizing antibodies
    - Related to the lack of protection
  - Reported increase in SN antibodies after vaccination of infected pigs (PRRomiSe; Nilubol *et al.*, 2004)
  - Strong induction of cell-mediated immune response (Progressis; Piras *et al.*, 2005)



MLV vaccines

- Main concerns

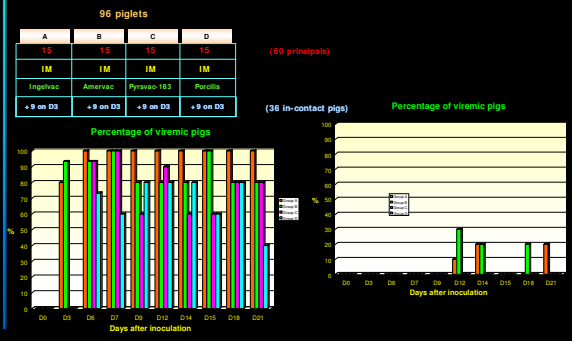
Safety

Efficacy

- Safety
  - Induction of long lasting viremia after vaccination
  - Viral shedding by different routes
  - Transmission to sentinel pigs
  - Transplacental transmission
  - Seminal shedding
  - Reversion to virulence

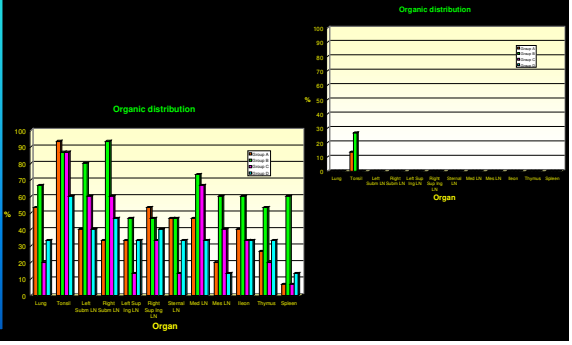
MLV vaccines

- Safety: viremia (Martínez-Lobo et al., 2008)



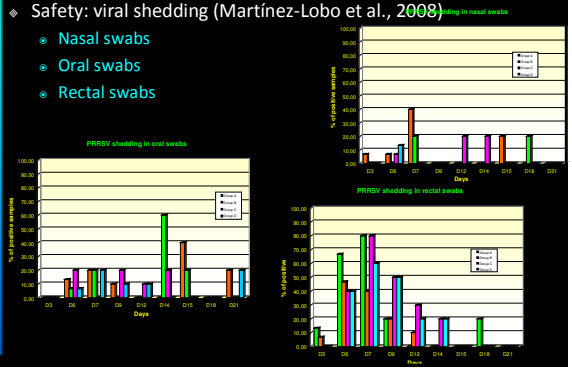
MLV vaccines

- Safety: organic distribution (Martínez-Lobo et al., 2008)



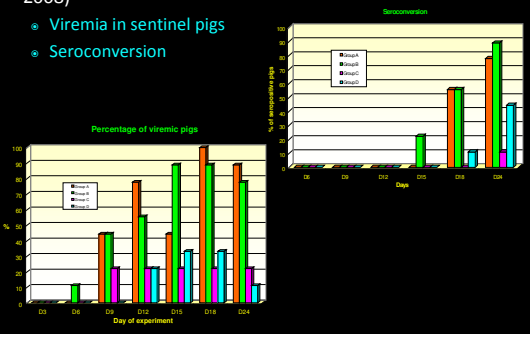
MLV vaccines

- Safety: viral shedding (Martínez-Lobo et al., 2008)
  - Nasal swabs
  - Oral swabs
  - Rectal swabs



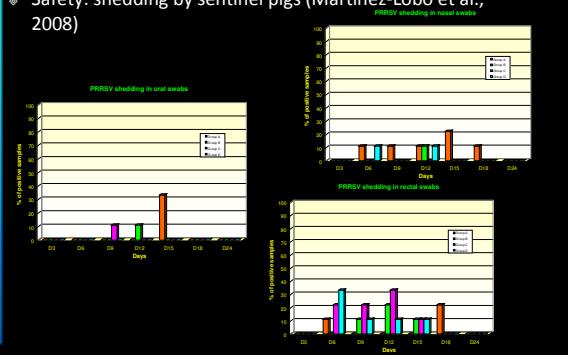
MLV vaccines

- Safety: transmission to sentinel pigs (Martínez-Lobo et al., 2008)
  - Viremia in sentinel pigs
  - Seroconversion



MLV vaccines

- Safety: shedding by sentinel pigs (Martínez-Lobo et al., 2008)



MLV vaccines

- Safety: transplacental transmission (Scortti *et al*., 2006)

VIREMIA AFTER EXPOSURE ON DAY 90 OF GESTATION

Group Virus strain	Gilt	Post-inoculation days 0	3	5	9	12	21	28
B Virulent Strain	5	– / –a	2.5 / –	2.6 / –	2.5 / –	– / –	– / –	– / –
	6	– / –	2.5 / –	3.5 / –	3.9 / –	3.5 / –	2.2 / –	– / –
	7	– / –	2.2 / –	2.9 / –	4.2 / –	– / –	– / –	– / –
	8	– / –	2.5 / –	<1 / –	– / –	– / –	– / –	– / –
C VP046 Bis	9	– / –	– / 2.6	– / 2	– / –	– / –	– / –	– / –
	10	– / –	– / 2.3	– / 3	– / –	– / –	– / –	– / –
	11	– / –	– / –	– / 2.3	– / –	– / –	– / –	– / –
	12	– / –	– / 2.4	– / 2	– / –	– / –	– / –	– / –
D All-183	13	– / –	– / 3.4	– / 3.6	– / –	– / –	– / –	– / –
	14	– / –	– / –	– / –	– / –	– / –	– / –	– / –
	15	– / –	– / –	– / –	– / –	– / –	– / –	– / –
	16	– / –	– / 2.3	– / 3	– / –	– / –	– / –	– / –

MLV vaccines

- Safety: transplacental transmission(Scortti *et al*., 2006)

PRRSV POSITIVE SAMPLES OF PIGLETS BORN TO EXPOSED GILTS (using PAM cultures)

Group	Virus strain	Gilt	Total Born	Dead Born	Serum samples of live born D0[a]	D4	D8	D15	D21	Pre-weaning deaths [b]	Necropsy at weaning [b]
B	Virulent Strain	5	7	-	7/7c	6/6	6/6	5/5	1/1	6/6	1/1
		6	12	1/2	3/10	1/9	3/9	4/9	2/3	4/7	3/3
		7	14	3/4	10/10	10/10	10/10	8/10	9/10	-	9/10
		8	13	1/1	4/12	11/11	11/11	11/11	10/10	2/2	10/10
C	VP046 Bis	9	11	-	2/11	0/10	0/10	0/10	0/10	0/1	0/10
		10	9	-	0/9	0/8	0/7	0/7	0/7	0/2	0/7
		11	14	-	0/14	0/13	0/13	0/13	0/13	0/1	0/13
		12	9	3/4	0/5	0/4	0/4	0/4	0/4	0/1	0/4
D	All-183	13	9	-	0/9	0/8	0/8	0/7	0/7	0/2	0/7
		14	9	-	0/9	0/9	0/9	0/9	0/9	-	0/9
		15	15	-	2/15	0/12	0/12	0/12	0/12	2/3	0/12
		16	11	-	1/11	2/11	0/11	4/11	7/11	-	7/11

*: pre-colostral serum from pigs born alive
b: serum, tissue samples and/or lung lavage.
c: number of positive pigs/number of pigs examined

MLV vaccines

- Safety: transplacental transmission(Scortti *et al*., 2006)

PRRSV POSITIVE SAMPLES OF PIGLETS BORN TO EXPOSED GILTS (using MARC 145)

Group	Virus strain	Gilt	Total Born	Dead Born	Serum samples of live born D0 a	D4	D8	D15	D21	Pre-weaning deaths [b]	Necropsy at weaning [b]
C	VP046 Bis	9	11	-	3/11 c	1/10	0/10	0/10	0/10	0/1	0/10
		10	9	-	1/9	0/8	0/7	0/7	0/7	1/2	0/7
		11	14	-	0/14	0/13	0/13	0/13	0/13	0/1	0/13
		12	9	4/4	1/5	0/4	0/4	0/4	0/4	1/1	0/4
D	All-183	13	9	-	0/9	0/8	0/8	0/7	0/7	0/2	0/7
		14	9	-	0/9	0/9	0/9	0/9	0/9	-	0/9
		15	15	-	4/15	2/12	0/12	0/12	0/12	3/3	0/12
		16	11	-	2/11	2/11	2/11	3/11	3/11	-	6/11

*: pre-colostral serum from pigs born alive
b: serum, tissue samples and/or lung lavage.
c: number of positive pigs/number of pigs examined

MLV vaccines

- Safety: transplacental transmission(Scortti *et al.*, 2006)

REPRODUCTIVE PERFORMANCE OF GILTS EXPOSED TO VACCINE STRAINS DURING GESTATION

		Number of pigs and fetuses					Survival 21 days	Mean pig weight (kg)	
Group	Virus Strain	Total	Late-term death	Stillborn	Born alive	Born Weak		Day 0	Day 21
A	None	39	0	0	39[A] (100)[B]	0 (0)	37[a] (94.9)	1.28[a] ±0.20[C]	5.26[a] ±0.79
B	Virulent	46	2	5	39[a] (84.8)	4 (10.2)	24[b] (61.5)	1.28[a] ±0.27	3.63[c] ±1.10
C	VP-046BIS	43	0	4	39[a] (90.7)	2 (5.2)	34[a] (87.2)	1.27[a] ±0.28	5.22[a] ±1.11
D	All-183	44	0	0	44[c] (100)	9 (20.4)	39[a] (88.6)	1.11[b] ±0.28	4.63[b] ±0.96

[A] Different superscripts within each column indicate significantly different values ($P<0.05$)
[B] Percentage
[C] Standard deviation

MLV vaccines

- Safety: seminal shedding (Christopher-Hennings *et al.*, 1997)
  - Viremia in boars after vaccination
    - Shedding of PRRSV in semen for variable periods of time post-vaccination

MLV vaccines

- Reversion to virulence
  - Danish case (Bøtner *et al.*, 1997)
    - Acute PRRS-like symptoms in sow herds after introduction of a MLV vaccine in the country
      - In unvaccinated sows
      - In unvaccinated herds
    - Some isolates seem to derivate of the vaccine strain based on the nucleotide sequence data
    - Virulence experimentally proven for an isolate with 99,6% identity to the vaccine strain (Nielsen *et al.*, 2002)
  - Isolation of field strains closely related to different vaccine strains in the recent years in several countries

MLV vaccines

- Efficacy
  - Big problem in the field
    - Changes in acclimatization strategies
- Generally, good homologous protection

  But....

  what happens with heterologous protection?
- Variable results
  - Different degrees of partial protection

Strong dependence of similarity between vaccine strain and challenge strain

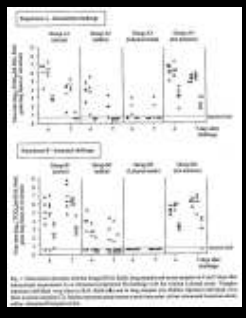
MLV vaccines

Very distant isolates

- Efficacy
  - Poor protection between American and European types
    - van Woensel *et al.* (1998)
      - American-type vaccine does not protect against three European isolates
      - European-type vaccine induces at least some degree of protection against other European isolates

MLV vaccines

- Efficacy
  - Poor protection between American and European types
    - Labarque *et al.* (2003)

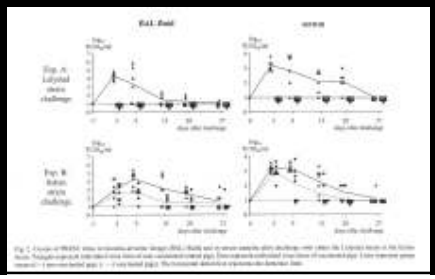


Very distant isolates

MLV vaccines

- Efficacy
  - Variable protection within European subtype
    - Labarque *et al.* (2004)

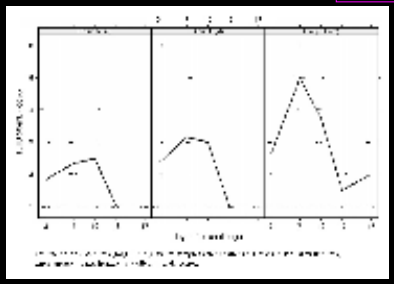
Closer isolates: same group, different cluster



MLV vaccines

- Efficacy
  - Variable protection within European subtype
    - Martelli *et al.* (2007)

Closer isolates: same group, different cluster



MLV vaccines

- Efficacy
  - Variable protection within European subtype
    - Scortti *et al.* (2006)

Closer isolates: same group, different cluster

VIREMIA OF PREGNANT GILTS AFTER CHALLENGE

Group	Gilt number	Sera D0	Sera D3	Sera D5	Sera D9	Sera D12	Sera D21	Nasal Swabs D0	Nasal Swabs D3	Nasal Swabs D5	Nasal Swabs D9	Nasal Swabs D12	Nasal Swabs D21
	5	-	+ (2.5)	+ (3.6)	+ (4.7)	+ (3.9)	-	-	-	-	-	-	-
	6	-	+ (2.2)	+ (3.5)	+ (3.6)	-	-	-	+ (<1)	+ (<1)	-	-	-
Group B	7	-	+ (2.5)	+ (3.6)	-	-	-	-	+ (<1)	+ (<1)	-	-	-
	8	-	+ (2.5)	+ (2.6)	+(<1)	-	-	-	-	+ (<1)	-	-	-
	9	-	-	-	+ (<1)	-	-	-	-	+ (<1)	-	-	-
	10	-	+ (1.4)	+ (3.2)	-	-	-	-	-	-	-	-	-
	11	-	-	-	-	-	-	-	-	-	-	-	-
	12	-	-	-	-	-	-	-	-	-	-	-	-
Group C	13	-	+ (3.4)	+ (3.1)	-	-	-	-	+ (<1)	-	-	-	-
	14	-	+ (2.6)	-	-	-	-	-	+ (<1)	-	-	-	-
	15	-	-	-	-	-	-	-	-	-	-	-	-
	16	-	-	+ (2.6)	-	-	-	-	-	-	-	-	-
	17	-	-	-	-	-	-	-	-	-	-	-	-
	18	-	+ (2.6)	-	-	-	-	-	-	-	-	-	-
Group D	19	-	+ (2.9)	-	-	-	-	-	-	-	-	-	-
	20	-	-	-	-	-	-	-	-	-	-	-	-
	21	-	-	-	-	-	-	-	-	-	-	-	-

MLV vaccines

- Efficacy
  - Variable protection within European subtype
    - Scortti *et al.* (2006)

Closer isolates: same group, different cluster

REPRODUCTIVE PERFORMANCE

Group	No. of litters	Total born	Stillborn piglets Total (%)	Late-term dead fetuses (%)	Born alive Total (%)	Born alive < 0.9 kg (%)	Lactation losses (%)	Weaned piglets (%)	Weaning weight
A	4	44	2	0	42	3	6	36	4.8
			(4,5)	(0)	(95,5)	(7,1)	(14,3)	(85,7)	
B	5	53	23	16	30	6	23	7	3.3
			(43,4)	(30,2)	(56,6)	(20)	(76,7)	(23,2)	
C	7	77	6	4	71	6	10	61	4.9
			(7,8)	(5,2)	(92,2)	(8,5)	(14,1)	(85,9)	
D	5	56	3	2	53	3	11	42	4.8
			(5,4)	(3,6)	(94,6)	(5,7)	(20,8)	(79,2)	

TRANSPLACENTAL INFECTION

Group	Number of litters	Total born (%)	Stillborn piglets (%) Total	Normal	Large mummies	Born alive D0	D4	D8	D15	D21	Death during lactation	Weaned piglets
A	4	0/44 (0)	2	0/2 (0)	0/0 (0)	0/42 (0)	-	-	-	0/35 (0)	0/7 (0)	0/35 (0)
B	5	45/53 (84.9)	23	1/7 (14.3)	14/16 (87.5)	30/30 (100)	22/22 (100)	13/14 (92.9)	7/9 (77.8)	7/7 (100)	23/23 (100)	7/7 (100)
C	7	8/77 (10.4)	6	0/2 (0)	3/4 (75.0)	5/71 (7.0)	1/65 (1.5)	1/64 (1.6)	0/62 (0)	0/61 (0)	2/10 (20)	3/61 (3.3)
D	5	3/56 (2.1)	3	0/1 (0)	1/2 (50)	1/53 (2.0)	7/44 (15.9)	6/42 (14.3)	6/42 (14.3)	6/42 (14.3)	1/11 (36.4)	1/42 (2.3)

MLV vaccines

- Efficacy
  - Variable protection within European subtype
    - Prieto *et al.* (2008)

Closer isolates: same group, same cluster

VIREMIA IN VACCINATED PIGS

Group	Pig number	Sera D0	Sera D3	Sera D6	Sera D9	Sera D14	Sera D24	Nasal Swabs D0	Nasal Swabs D3	Nasal Swabs D6	Nasal Swabs D9	Nasal Swabs D14	Nasal Swabs D24
A	1	-	+ (2.3)	-	-	-	-	-	-	+ (<1.6)	-	-	-
(Vaccinated)	2	-	-	+ (2.5)	-	-	-	-	-	-	-	-	-
	3	-	-	+ (2.6)	-	-	-	-	+ (2.3)	-	-	-	-
	4	-	+ (2.5)	+ (3.6)	+ (2.6)	-	-	-	-	-	-	-	-
	5	-	+ (2.6)	+ (3.5)	-	-	-	-	-	+ (<1.6)	-	-	-
B	6	-	+ (2.6)	+ (2.5)	+ (2.6)	+ (2.5)	+ (2.0)	-	-	-	-	-	-
(Unvaccinated)	7	-	+ (2.5)	+ (2.0)	+ (2.5)	+ (2.3)	-	-	-	-	-	-	-
	8	-	+ (3.5)	+ (3.5)	+ (2.3)	+ (2.0)	-	-	-	-	-	-	-
	9	-	+ (2.6)	+ (1.6)	+ (2.0)	+ (<1.6)	-	-	+ (2.5)	-	-	-	-
	10	-	+ (2.5)	+ (2.5)	+ (2.3)	+ (1.5)	-	-	-	-	-	-	-

* Negative results are indicated by a "-". Positive results are presented as infectivity titers (log 10 $TCID_{50}$/mL of sample)

ORGANIC DISTRIBUTION AFTER CHALLENGE

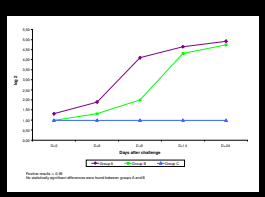
Group	Pig number	Tissues collected at necropsy: Lung	Tonsil	Ileum	Thymus	Subm. LN	Mes. LN	Med. LN	Sup Iliac LN
A	1	-	-	-	-	-	+ (<2.0)	-	-
(Vaccinated)	2	-	-	-	-	-	+ (2.6)	-	-
	3	-	-	+ (3.5)	-	+ (<2.0)	-	-	+ (2.0)
	4	-	-	-	-	-	-	-	-
	5	-	+ (<2.0)	-	-	-	-	-	-
B	6	+ (2.0)	+ (<2.0)	-	-	+ (2.5)	+ (2.3)	+ (2.3)	+ (2.5)
(Unvaccinated)	7	-	+ (<2.0)	-	-	-	-	-	-
	8	+ (<2.0)	+ (2.5)	-	-	+ (<2.0)	+ (2.6)	+ (2.3)	+ (<2.0)
	9	-	+ (2.5)	-	-	-	-	-	-
	10	+ (2.2)	+ (2.6)	-	-	+ (2.2)	+ (2.3)	+ (2.0)	+ (<2.0)

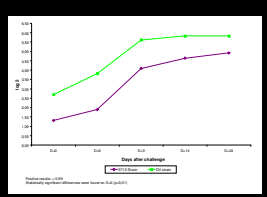
* Negative results are indicated by a "-". Positive results are presented as infectivity titers (log 10 $TCID_{50}$/g of sample)

Causes of vaccine failure

- Possible causes of lack of efficacy (Prieto et al., 2008)

Antigenic variability → **Effects on efficacy of NA**





Ability of genomic similarity to predict antigenic similarity????

Theory of serogroups for vaccine design

- SN assays
  - (Martínez-Lobo et al., 2008)

Sera	Strains																	
	Germ	Dutch	2-sp	3-sp	4-sp	6-sp	7-sp	12-sp	16-sp	20-sp	22-sp	24b-sp	26-sp	27-sp	28-sp	29-sp	30-sp	31-sp	32-sp
German	6	3	3	1	4	2	2	0	1	3	1	1	1	3	3	0	1	0	1
Dutch	1	5	3	1	7	0	3	1	1	4	1	3	3	2	2	2	1	1	1
2-sp	5	-	5	2	4	0	2	1	1	7	0	3	2	3	3	3	3	2	1
3-sp	2	4	6	6	7	4	3	5	2	7	6	2	4	4	2	6	4	2	2
6-sp	3	2	7	4	7	5	4	4	3	7	4	3	4	3	2	6	4	7	2
12-sp	0	0	3	2	3	1	3	6	2	4	2	2	1	2	1	2	2	5	2
16-sp	2	3	3	0	2	0	2	2	5	3	3	-	2	3	2	2	1	2	0
20-sp	-	2	4	0	3	1	3	2	1	7	1	3	3	3	1	2	3	3	1
22-sp	2	3	2	1	5	0	0	1	0	0	7	-	1	2	0	0	1	0	-
27-sp	5	1	4	0	2	0	2	0	0	3	2	2	2	6	4	0	2	0	1
28-sp	0	-	2	0	3	1	1	0	1	3	2	7	-	2	7	0	2	1	1

Seroneutralization antibody titers are expressed as log 2
"0" means neutralization with undiluted sera
"-" means no neutralization

There are no antigenic groups

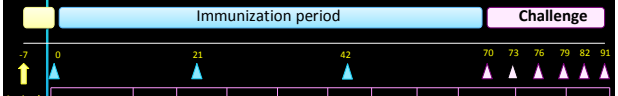
- Today
  - 30 hyperimmune sera
  - 60 PRRSV isolates

There are strains with high neutralizing activity against a variety of isolates

Capacity of those strains to induce better heterologous protection?

Correlation between *in vitro* SN and *in vivo* protection

- Strain with high neutralizing activity *in vitro*
  - Experimental design



Group	1	2	3	4	5	6	7	8	9	10
Strain	EU-17	AM-7	EU-2	EU-18	SP-14	SP-11	SP-17	EU-1	SP-1	SP-2
Genotype	Italy EU	USA	Holand EU	Italy EU	Spain EU	Spain EU	Spain EU	Germany EU	Spain EU	Spain EU
Cross-neutralization titers	-	1/16	1/16	1/32	1/32	1/64	1/128	>1/128	>1/128	1/64

  - General results
  - Next step

Experimental vaccines

- Other aproaches
  - Baculovirus expression of proteins (Plana- Durán *et al*., 1997; Kreutz & Mengeling, 1997; Wang *et al*., 2007)
  - DNA immunization (Pirzadeh & Dea, 1998; Kwang *et al*., 1999; Xue *et al*., 2004; Barfoed *et al*., 2004; Rompato *et al*., 2006; Jiang *et al*., 2006)
  - Recombinant *Mycobacterium bovis* BCG (Bastos *et al*., 2002, 2004)
  - Semliki Forest virus expression system (Jung *et al*., 2002)
  - *E. coli* expression (Fernández *et al*., 2003)
  - Recombinant adenovirus (Gagnon *et al*., 2003; Jiang *et al*., 2006, 2008)
  - Defective PRRSV (wan Welch *et al*., 2004)
  - *S. typhimurium* delivering eukaryotic vectors (Jiang *et al*., 2004)

Experimental vaccines

- Other approaches
  - Recombinant PRV (Tian *et al*, 2005; Qiu *et al*., 2005; Álvarez *et al*., 2004; Jiang *et al*., 2007; Diéz-Fuertes *et al*., unpublished)
  - Recombinant Fowlpox (Guoshun *et al*., 2007)
  - Recombinant vaccinia (Suárez, unpublished; Zheng *et al*., 2007)
  - Modifications of GP5 protein to improve expression (Kheyar *et al*., 2005; Fang *et al*., 2006; Jiang *et al*., 2007)
  - Plasmid co-expressing swine ubiquitin and GP5 (Hou *et al*., 2008)
  - DIVA vaccines (de Lima *et al*., 2008)

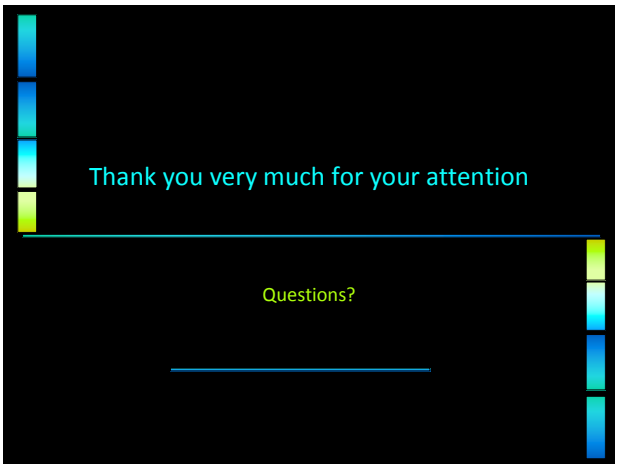
But....
What about efficacy?

Experimental vaccines

- Some of them claim to achieve protection in pigs!!!
  - Too optimistic?
- Main problems
  - Expression
    - Especially in the case of GP5
  - Induction of a detectable immune response
    - In many cases only priming of the immune system
  - Induction of an undesired immune response
    - Non-protective antibodies that exacerbate disease
      - ADE?
  - If some were able to induce a good immune response.....
    - What about variability and cross-protection?

Future expectations

- Needs
  - To improve the range of protection of available vaccines
    - Universal vaccine
  - To improve safety
  - To obtain DIVA vaccines
    - Important for the eradication of the disease


Thank you very much for your attention
Questions?