



The value of *in vitro* antigen matching in predicting vaccine protection

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Which vaccine to use....

Tools to predict vaccine matching



- *In vitro* matching
 - Rapid and laboratory based
 - No need for live animals (once reagents are produced)
 - Variability
 - Difficult to predict protection with heterologous challenge
- *In vivo* matching
 - Gold standard
 - Inherently variable
 - Costly
 - High containment animal rooms
 - Ethical considerations
 - Time consuming

In vitro vaccine matching

- Compare field and vaccine viruses using VNT and/or ELISA
- The results are expressed as the relative homology (r_1) value

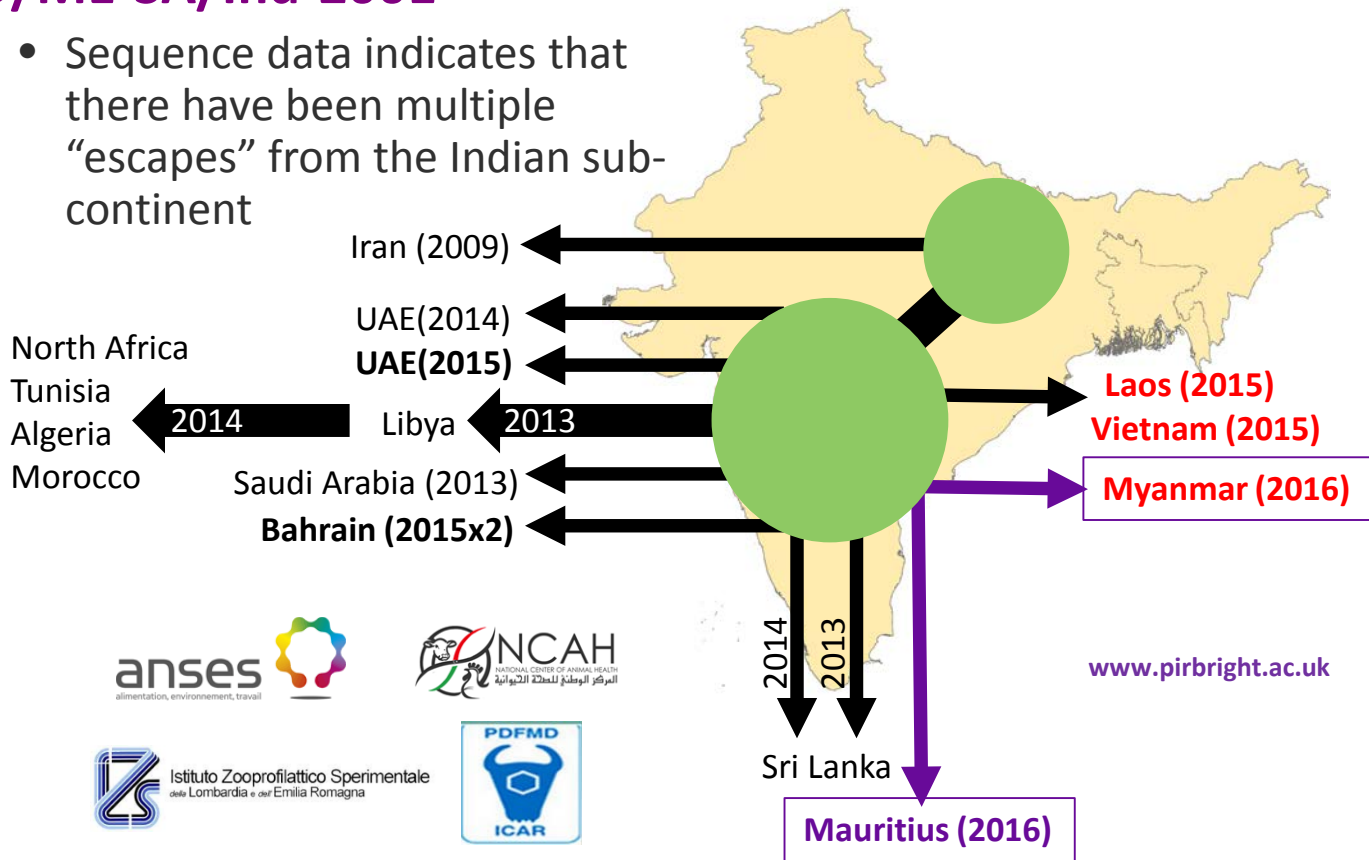
$$r_1 = \frac{\text{heterologous titre of vaccinal serum against field isolate}}{\text{homologous titre of vaccinal serum against vaccine strain}}$$

- An r_1 value >0.3 (by VNT) is considered homologous

r_1 value (ELISA)	Relative homology	Predicted vaccine efficacy
< 0.20	Heterologous (distantly related)	Unlikely to be protective
$0.20 - 0.39$	Intermediate	Might be suitable if a closer vaccine match can't be found
> 0.39	Homologous (closely related)	Likely to be protective

O/ME-SA/Ind-2001

- Sequence data indicates that there have been multiple “escapes” from the Indian sub-continent



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O1 Manisa BVS

VIT 4/2010
VIT 15/2011
CAM 4/2012
LAO 11/2012
TAI 28/2013
TAI 30/2013
TAI 36/2013
TAI 42-2/2014
TAI 145/2014
TAI 154/2014
TAI 11/2015
TAI 19/2015

VIT 14/2010
CAM 1/2012
LAO 10/2012
LAO 13/2012
TAI 29/2012
TAI 33/2013
TAI 44/2013
TAI 94/1/2014
TAI 148/2014
TAI 164/2014
TAI 17/2015
LAO 3/2015

23.76%

16.83%

VIT 12/2010
VIT 16/2010
VIT 6/2011
VIT 31/2011
LAO 19/2012
VIT 7/2012
TAI 36/2013
TAI 125/2014

VIT 13/2010
VIT 4/2011
VIT 14/2011
LAO 11/2012
LAO 20/2012
VIT/8/2012
TAI 42-2/2014
TAI 164/2014
TAI 19/2015

VIT 9/2008
VIT 3/2011
VIT 17/2011
VIT 25/2011
VIT 28/2011
VIT 32/2011
CAM 1/2012
LAO 14/2012
LAO 21/2012
VIT 9/2012
VIT 21/2012
TAI 30/2013
TAI 38/2013
TAI 51/2013
VIT 16/2013
TAI 49/1/2014
TAI 125/2014
TAI 154/2014
LAO 2/2015
TAI 13/1/2015

VIT 6/2010
VIT 8/2011
VIT 22/2011
VIT 26/2011
VIT 29/2011
VIT 34/2011
CAM 4/2012
LAO 18/2012
TAI 29/2012
VIT 11/2012
TAI 2/2013
TAI 33/2013
TAI 44/2013
VIT 12/2013
VIT 40/2013
TAI 69/1/2014
TAI 145/2014
TAI 146/2014
LAO 3/2015
TAI 15/1/2015

VIT 10/2010
VIT 2013/2011
VIT 23/2011
VIT 27/2011
VIT 30/2011
VIT 35/2011
LAO 12/2012
LAO 20/2012
VIT 2/2012
VIT 14/2012
TAI 27/2013
TAI 35/2013
TAI 49-1/2013
VIT 14/2013
TAI 42/3/2014
TAI 123/1/2014
TAI 148/2/2014
VIT 13/2014
TAI 10/1/2015
TAI 17/2015

59.41%

O-3039 BVS

VIT 4/2010	VIT 10/2010	VIT 12/2010
VIT 13/2010	VIT 14/2010	VIT 16/2010
VIT 3/2011	VIT 6/2011	VIT 8/2011
VIT 14/2011	VIT 17/2011	VIT 26/2011
VIT 28/2011	VIT 31/2011	VIT 32/2011
VIT 34/2011	LAO 10/2012	LAO 11/2012
LAO 12/2012	LAO 13/2012	LAO 14/2012
LAO 18/2012	LAO 20/2012	LAO 21/2012
TAI 29/2012	VIT 9/2012	TAI 27/2013
TAI 28/2013	TAI 30/2013	TAI 33/2013
TAI 36/2013	TAI 44/2013	VIT 40/2013
TAI 42-2/2014	TAI 94/1/2014	TAI 125/2014
TAI 145/2014	TAI 148/2014	TAI 154/2014
TAI 164/2014	LAO 3/2015	TAI 11/2015

TAI 17/2015

TAI 19/2015

41.90%

VIT 6/2010	VIT 4/2011
VIT 15/2011	VIT 22/2011
VIT 23/2011	VIT 25/2011
VIT 27/2011	VIT 30/2011
VIT 35/2011	LAO 11/2012
VIT 2/2012	VIT 8/2012
VIT 14/2012	VIT 21/2012
TAI 36/2013	TAI 49-1/2013
VIT 14/2013	VIT 16/2013
TAI 42-2/2014	TAI 125/2014
TAI 164/2014	VIT 13/2014

TAI 19/2015

21.90%

VIT/9/2008	VIT/13/2011	VIT/29/2011
CAM 1/2012	CAM 4/2012	LAO 10/2012
LAO 14/2012	LAO 18/2012	LAO 19/2012
LAO 20/2012	LAO 21/2012	TAI 29/2012
VIT/7/2012	VIT/11/2012	TAI 2/2013
TAI 27/2013	TAI 33/2013	TAI 35/2013
TAI 38/2013	TAI 44/2013	TAI 51/2013
VIT/12/2013	TAI 42/3/2014	TAI 49/1/2014
TAI 69/1/2014	TAI 123/1/2014	TAI 145/2014
TAI 154/2014	TAI 148/2/2014	TAI 146/2014
VIT 27/2014	TAI 10/1/2015	TAI 11/2015
TAI 13/1/2015	TAI 15/1/2015	TAI 17/2015

LAO 2/2015

LAO 3/2015

36.19%

Serotype O vaccines against O/Ind/2001d lineage

Vaccine	O-3039		O-3030 / O1 Manisa	
Species	Cattle			
Challenge dpv	7	21	7	21
Route	IDL	IDL	IDL	IDL
Challenge virus	O/ALG/2014		O/ALG/2014	
Protection %	60	100	80	100
r-values	<0.19			

Summary of serotype A vaccine testing

Vaccine	A May 97						A22 Iraq						A May 97 + A22 Iraq	
Species	Pigs		Cattle		Pigs		Cattle		Sheep	Pigs		Pigs		
Challenge (dpv)	4	7	7	21	7	21	7	21	4	7	21	7	21	
Route	HB	HB	IDL	IDL	HB	HB	IDL	IDL	INP	HB	HB	HB	HB	
Challenge virus	VIT/2005		VIT/2012		TAI/2014		VIT/2012		VIT/12	TAI/2014		TAI/2014		
Protection %	100	75	80	100	0	20	60	100	83	0	20	0	80	
r-values	0.51		0.17		0.10		0.16			0.05		0.05		

Bivalent serotype A vaccine in pigs

Vaccine	A22 Iraq		A May 97		A May 97 + A22 Iraq	
Species	Pigs		Pigs		Pigs	
Challenge dpv	7	21	7	21	7	21
Route	HB	HB	HB	HB	HB	HB
Challenge virus	TAI/2014		TAI/2014		TAI/2014	
Protection %	0	20	0	20	0	80
r_1 -values	0.05		0.10			

Summary of serotype Asia-1 vaccine testing

Vaccine	Asia1 Shamir		
Species	Sheep		
Challenge dpv	4	7	21
Route	INP		
Challenge virus	Asia-1/PAK/2014		
Protection %	80	100	100
r_1 -values	0.18		

Factors that impact on *in vivo* results

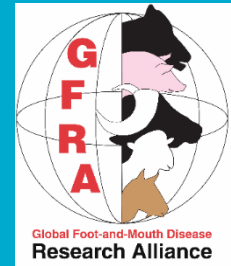
- Study design, number of animals (impact on statistical analysis)
- Facility design
- Challenge route (direct inoculation versus natural infection)
 - Impact on carriers and NSP testing
- Breed and condition of animals
- Extrapolation to real farming systems challenging



Stenfeldt *et al.*, 2015

Vaccine efficacy studies in cattle, pigs and sheep - Conclusions and recommendations

- A poor match *in vitro* does not always equate to no protection *in vivo* with high potency vaccines
 - Highlights the importance of combined approaches (e.g. sequencing, monitoring) when determining which vaccine will be most effective
 - Consider combinations of strains?
- High-potency vaccines for emergency use during an outbreak will slow spread (reduced virus excretion) and fully/partially protect cattle and sheep, but pigs to a lesser extent
 - New approaches to pig vaccination are required
 - Time of challenge post vaccination will be important



Thank you

Health and Biosecurity (AAHL)

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