


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

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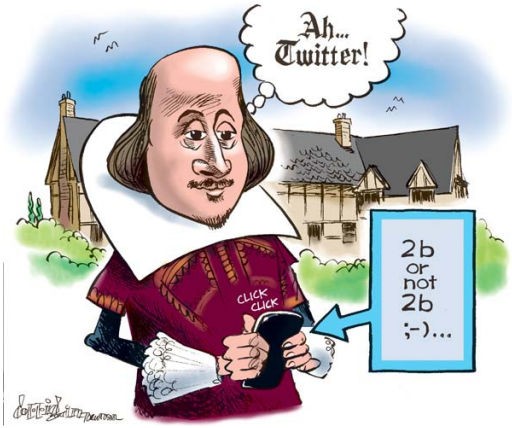
To vaccinate or not……

- Options for disease control during an outbreak – impact on return to freedom without vaccination (OIE)
  - Stamp out all infected animals
    - 3 month waiting period
  - Vaccinate and remove all the vaccinated animals
    - 3 month waiting period
  - Vaccinate and keep the vaccinates
    - 6 month waiting period



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

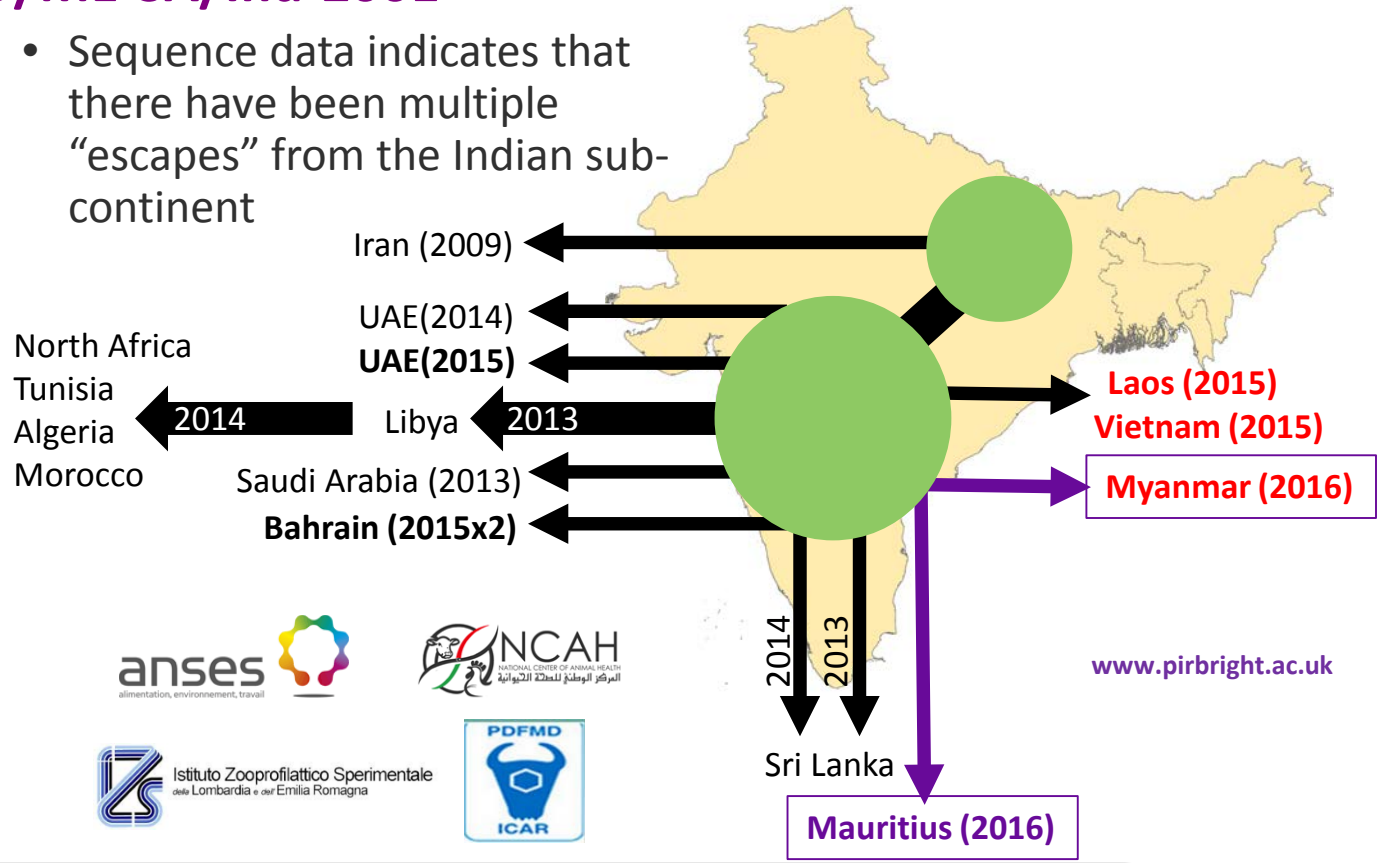
$$r_1 = \frac{heterologous\ titre\ of\ vaccinal\ serum\ against\ field\ isolate}{homologous\ titre\ of\ vaccinal\ serum\ against\ vaccine\ strain}$$

- 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



O1 Manisa BVS

23.76%

16.83%

59.41%

O-3039 BVS

41.90%

21.90%

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

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