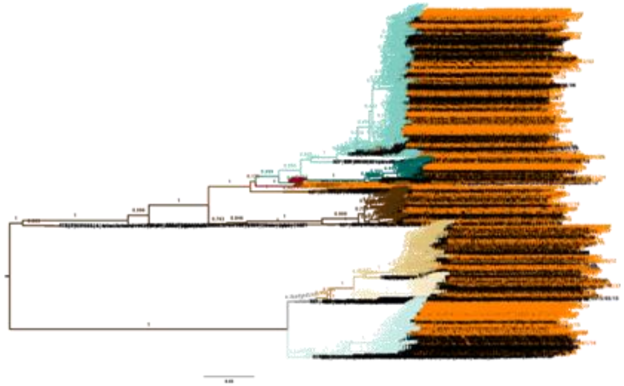
OFFLU Swine Influenza Virus technical meeting
27 – 28 February 2019
OIE Headquarters, Paris, France

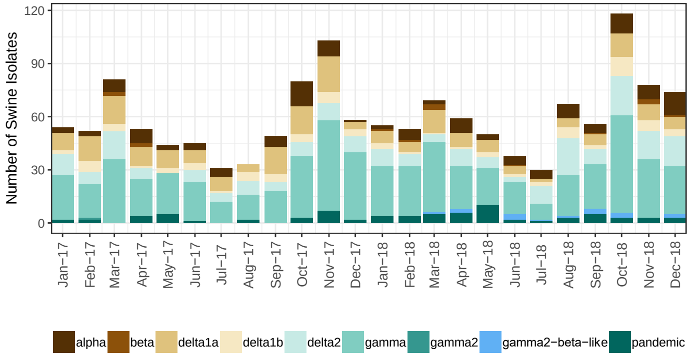
Amy Vincent
NADC Flu Crew
USDA-ARS

Genetic Diversity of Swine H1 and H3 HA Genes

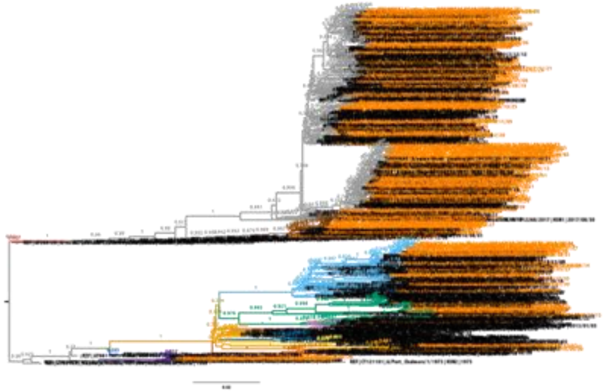
swine H1



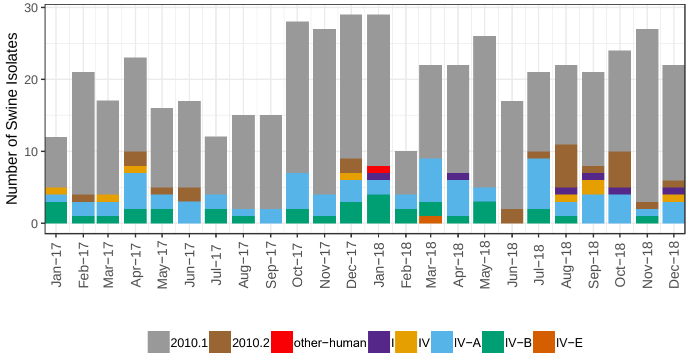
H1 phylogenetic−clades by month



swine H3



H3 phylogenetic−clades by month



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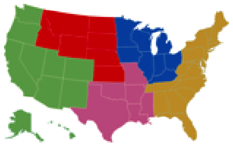
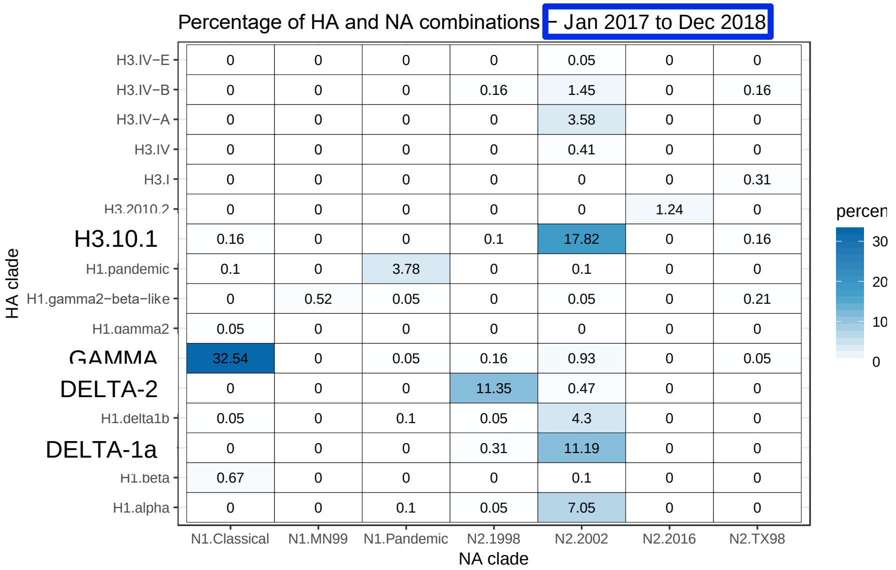
HA and NA Clade Combinations



Rolling 2 year window

Percentage of HA and NA combinations – Jan 2017 to Dec 2018

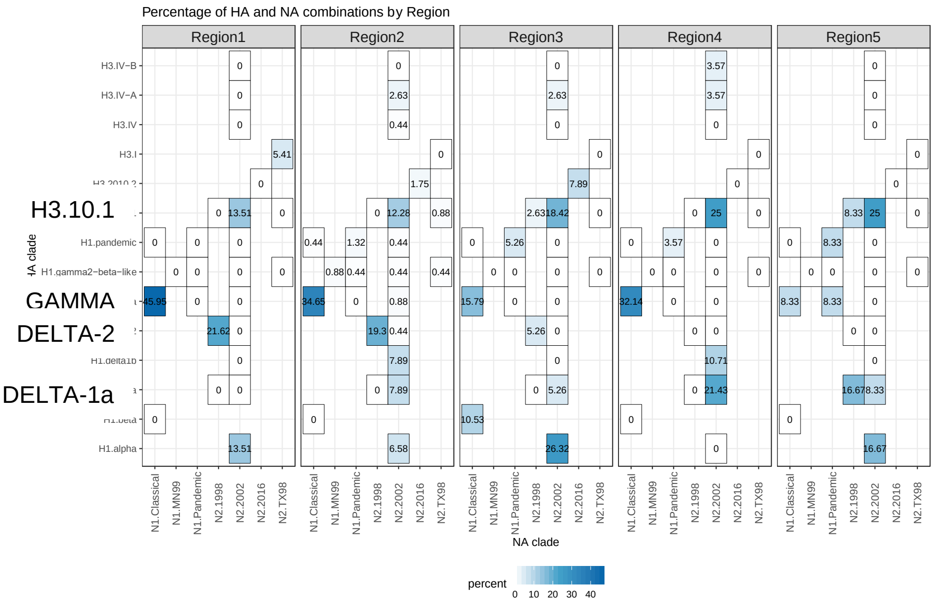


	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−E	0	0	0	0	0.05	0	0
H3.IV−B	0	0	0	0.16	1.45	0	0.16
H3.IV−A	0	0	0	0	3.58	0	0
H3.IV	0	0	0	0	0.41	0	0
H3.I	0	0	0	0	0	0	0.31
H3.2010.2	0	0	0	0	0	1.24	0
H3.10.1	0.16	0	0	0.1	17.82	0	0.16
H1.pandemic	0.1	0	3.78	0	0.1	0	0
H1.gamma2−beta−like	0	0.52	0.05	0	0.05	0	0.21
H1.gamma2	0.05	0	0	0	0	0	0
GAMMA	32.54	0	0.05	0.16	0.93	0	0.05
DELTA-2	0	0	0	11.35	0.47	0	0
H1.delta1b	0.05	0	0.1	0.05	4.3	0	0
DELTA-1a	0	0	0	0.31	11.19	0	0
H1.beta	0.67	0	0	0	0.1	0	0
H1.alpha	0	0	0.1	0.05	7.05	0	0

Total HA & NA combinations – 1,930

FY19 Quarter 1

Percentage of HA and NA combinations by Region



Region1

	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−B					0		
H3.IV−A					0		
H3.IV					0		
H3.I							5.41
H3.2010.2						0	
H3.10.1				0	13.51		0
H1.pandemic	0		0		0		
H1.gamma2−beta−like		0	0		0		0
GAMMA	45.95		0		0		
DELTA-2				21.62	0		
H1.delta1b					0		
DELTA-1a				0	0		
H1.beta	0						
H1.alpha					13.51		

Region2

	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−B					0		
H3.IV−A					2.63		
H3.IV					0.44		
H3.I							0
H3.2010.2						1.75	
H3.10.1				0	12.28		0.88
H1.pandemic	0.44		1.32		0.44		
H1.gamma2−beta−like		0.88	0.44		0.44		0.44
GAMMA	34.65		0		0.88		
DELTA-2				19.3	0.44		
H1.delta1b					7.89		
DELTA-1a				0	7.89		
H1.beta	0						
H1.alpha					6.58		

Region3

	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−B					0		
H3.IV−A					2.63		
H3.IV					0		
H3.I							0
H3.2010.2						7.89	
H3.10.1				2.63	18.42		0
H1.pandemic	0		5.26		0		
H1.gamma2−beta−like		0	0		0		0
GAMMA	15.79		0		0		
DELTA-2				5.26	0		
H1.delta1b					0		
DELTA-1a				0	5.26		
H1.beta	10.53						
H1.alpha					26.32		

Region4

	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−B					3.57		
H3.IV−A					3.57		
H3.IV					0		
H3.I							0
H3.2010.2						0	
H3.10.1				0	25		0
H1.pandemic	0		3.57		0		
H1.gamma2−beta−like		0	0		0		0
GAMMA	32.14		0		0		
DELTA-2				0	0		
H1.delta1b					10.71		
DELTA-1a				0	21.43		
H1.beta	0						
H1.alpha					0		

Region5

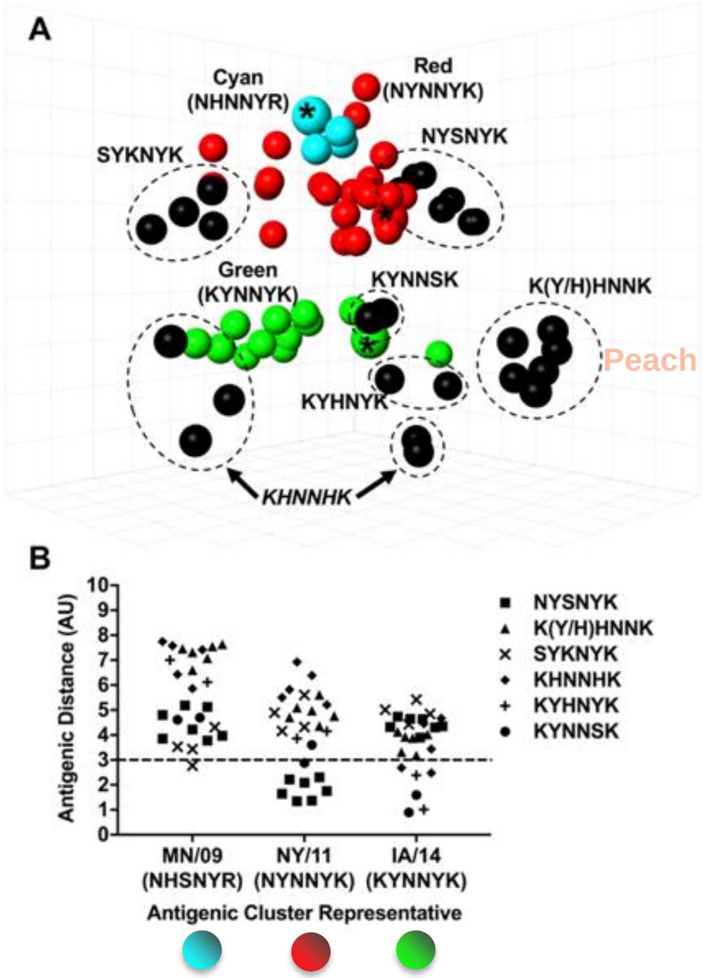
	N1.Classical	N1.MN99	N1.Pandemic	N2.1998	N2.2002	N2.2016	N2.TX98
H3.IV−B					0		
H3.IV−A					0		
H3.IV					0		
H3.I							0
H3.2010.2						0	
H3.10.1				8.33	25		0
H1.pandemic	0		8.33		0		
H1.gamma2−beta−like		0	0		0		0
GAMMA	8.33		8.33		0		
DELTA-2				0	0		
H1.delta1b					0		
DELTA-1a				16.67	8.33		
H1.beta	0						
H1.alpha					16.67		

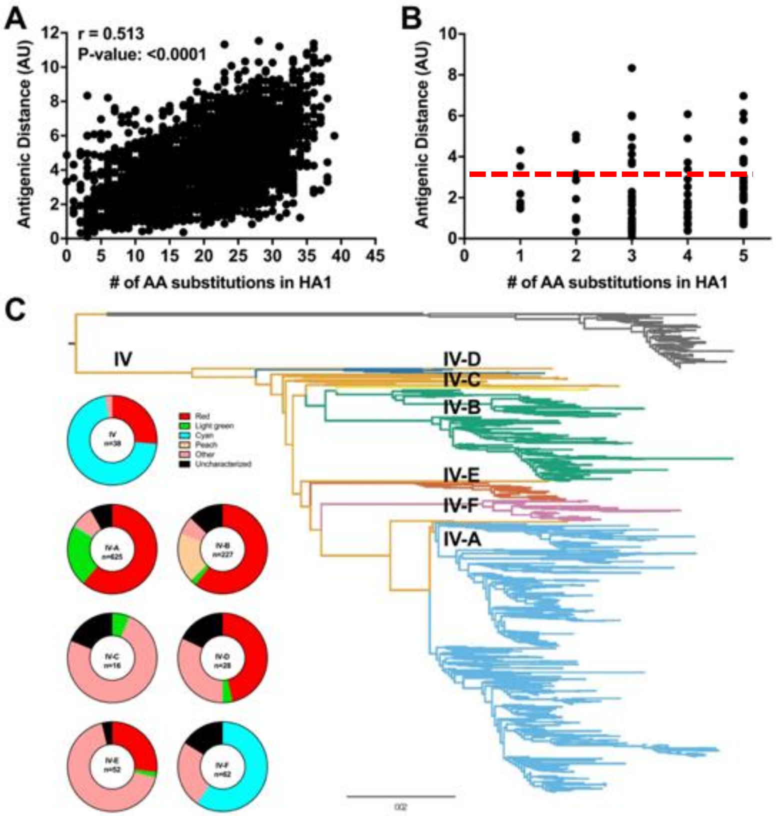
Total HA & NA combinations – 343

- **Gamma (1A.3.3.3) - 33%**
- H3.10.1 - 18%
- Delta-2 (1B.2.1) – 11%
- Delta-1a (1B.2.2.1) – 11%

Jennifer Chang

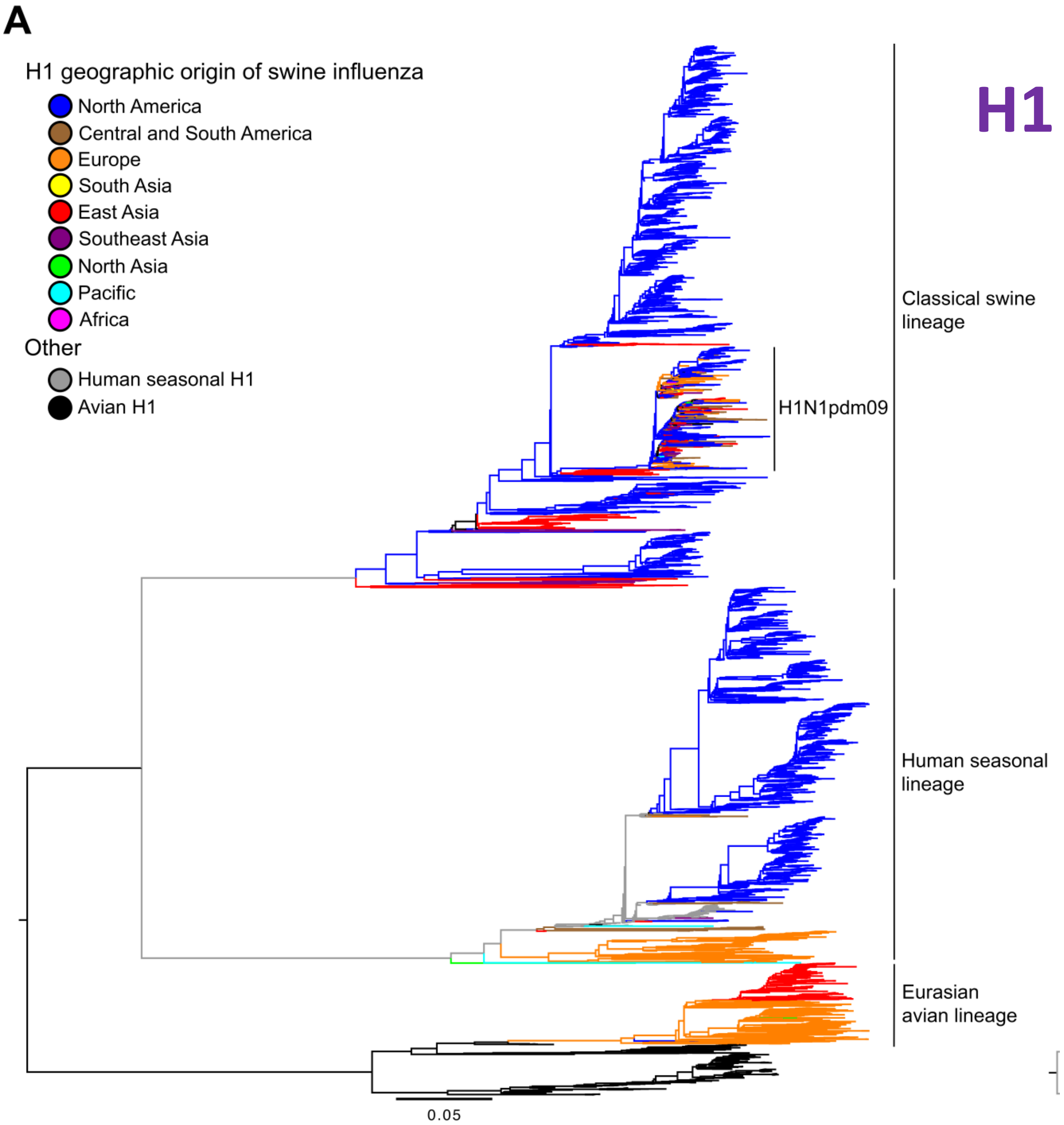
Antigenic drift is not fully controlled by motif



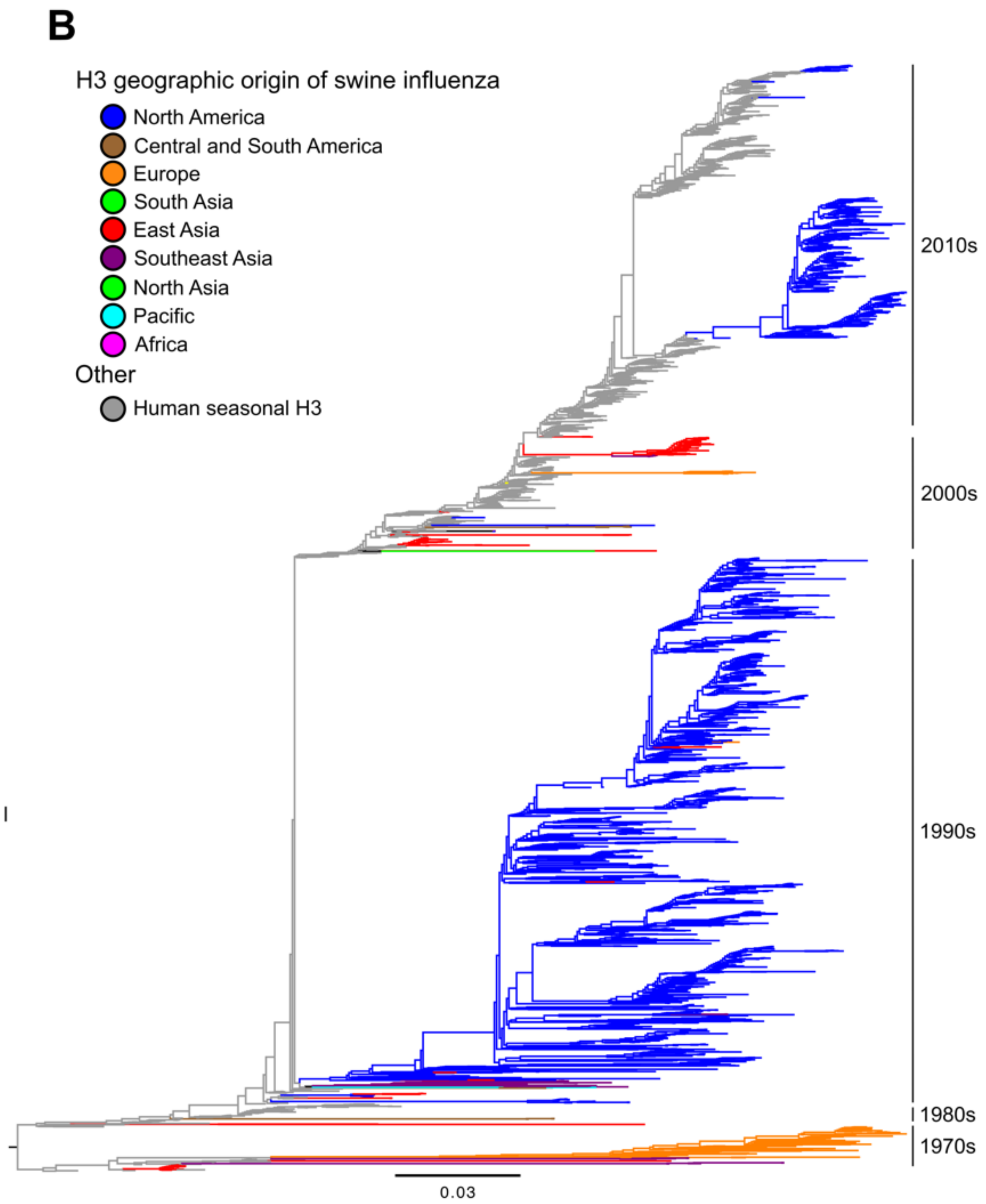


Bolton et al., Influenza Other Respir Viruses 2018

H1 Global Update



Tavis Anderson



H3 Global Nomenclature

By Decade

- H3.1970
- H3.1980
- H3.1990
- H3.2000
- H3.2010
  - H3.2010.1
  - H3.2010.2

Etc.

Put your sequences in GenBank! Please! (or send to Tavis)

Tavis.Anderson@ars.usda.gov

IAV vaccine studies in swine

RP-HA provided partial protection between H3 red and green Ag clusters

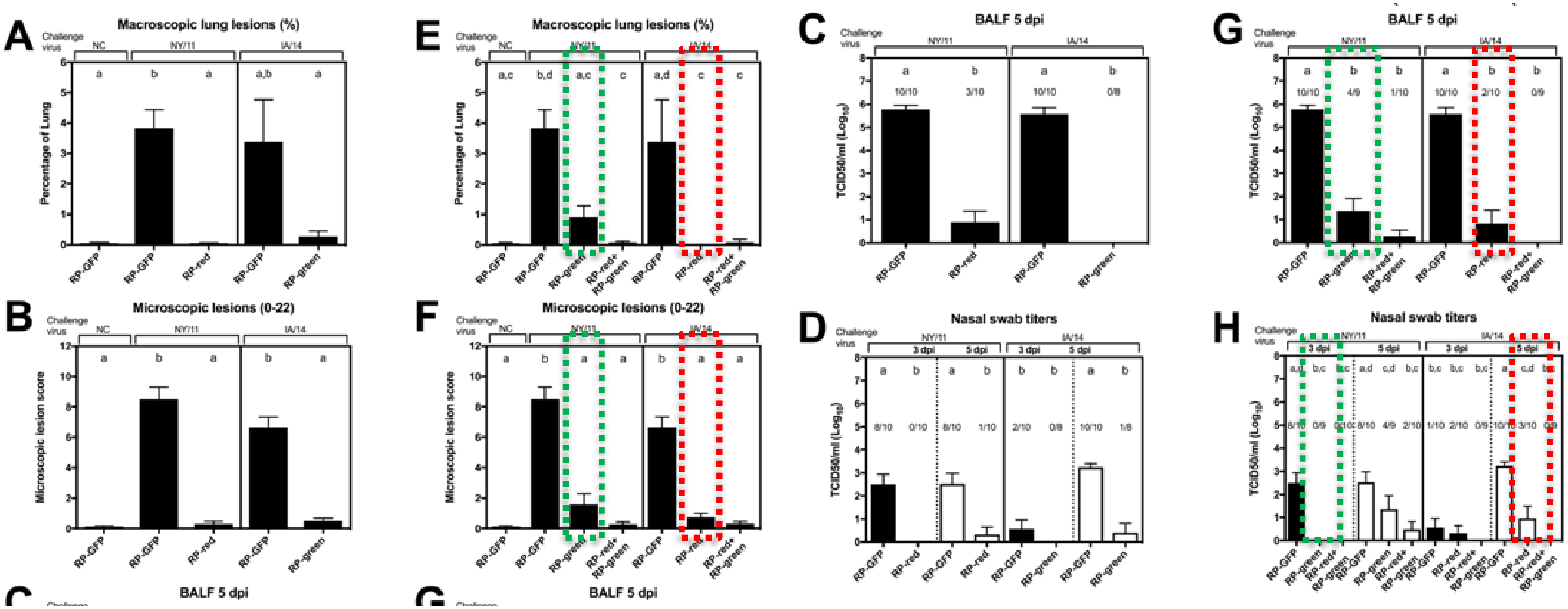
Table 1. Animal study design.

Groups	Vaccine	Challenge virus (antigenic cluster)
RP-GFP->NC	RP-GFP	No challenge
RP-GFP->NY/11 RP-red->NY/11 RP-green->NY/11 RP-red+RP-green->NY/11	RP-GFP **RP-red** **RP-green** **RP-red** + **RP-green**	NY/11 (red) NY/11 (red) NY/11 (red) NY/11 (red)
RP-GFP->IA/14 RP-red->IA/14 RP-green->IA/14 RP-red+RP-green->IA/14	RP-GFP **RP-red** **RP-green** **RP-red** + **RP-green**	IA/14 (green) IA/14 (green) IA/14 (green) IA/14 (green)

NC, non-challenged.

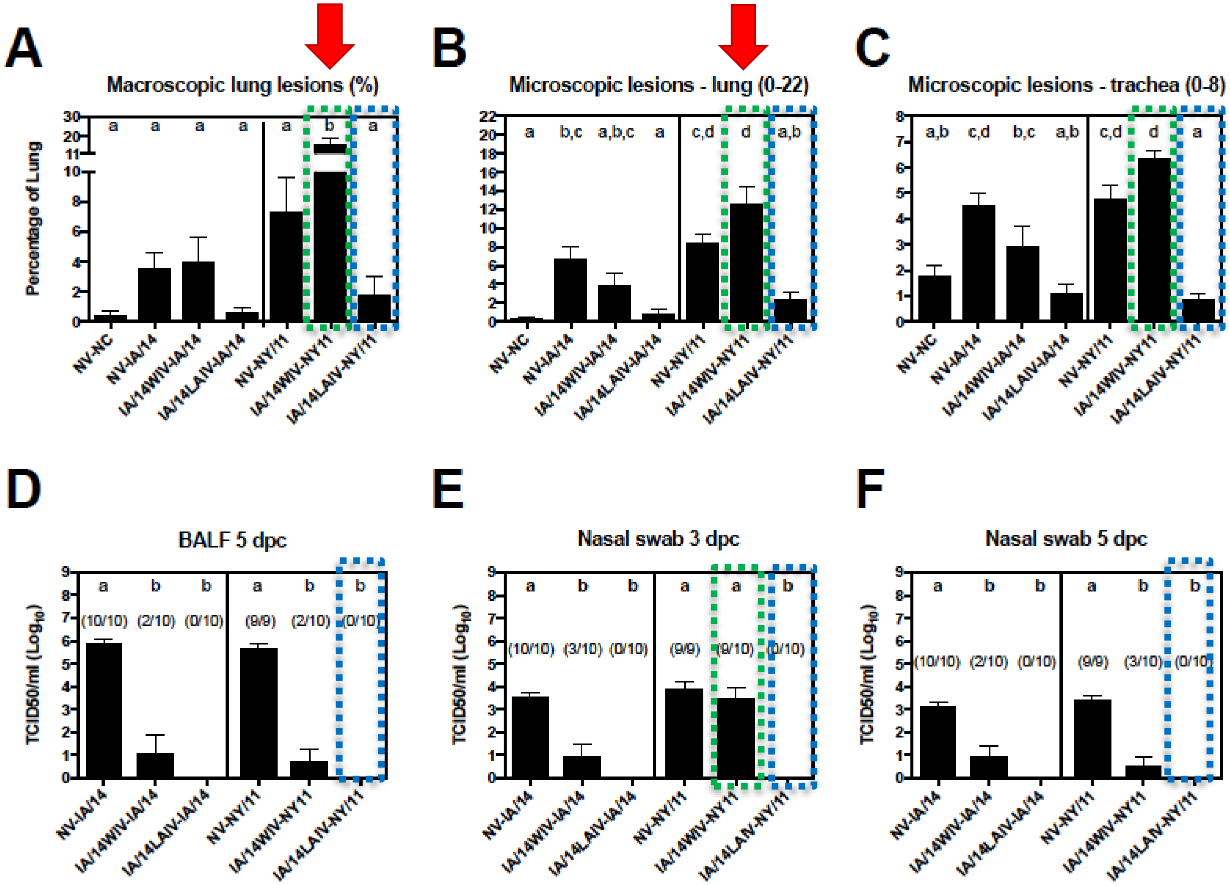
Abente et al., Vaccine 2019

RP-HA provided partial protection between red and green Ag clusters



Abente et al., Vaccine 2019

Green WIV led to VAERD with Red challenge, LAIV was protective

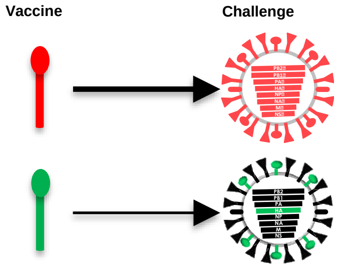


Abente et al., JVI 2018

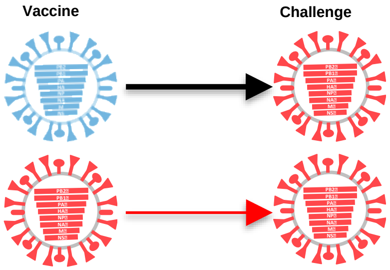
Vaccine Platform Studies with

Antigenically Mismatched H3 Viruses

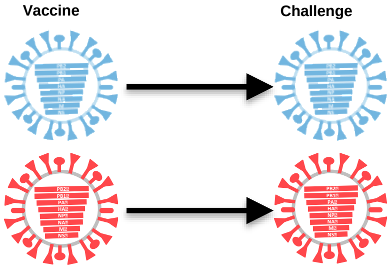
	HA RNA vaccine (alphavirus vectored)	Whole inactivated virus (WIV; adjuvanted)	Live-attenuated influenza virus (att mutations in PB1 and PB2)
			
Advantages	-Induces cellular immunity -Robust expression -Rapid production	-High homologous HI titers	-Induces cellular immunity -Cross-protection against heterologous challenge
Disadvantages	-Limited to a subset of proteins	-Inefficient protection against heterologous challenge -Possibility of vaccine associated enhanced disease (VAERD)	-Possibility of reversion or reassortment



Efficient protection observed against challenge with an antigenically distinct virus

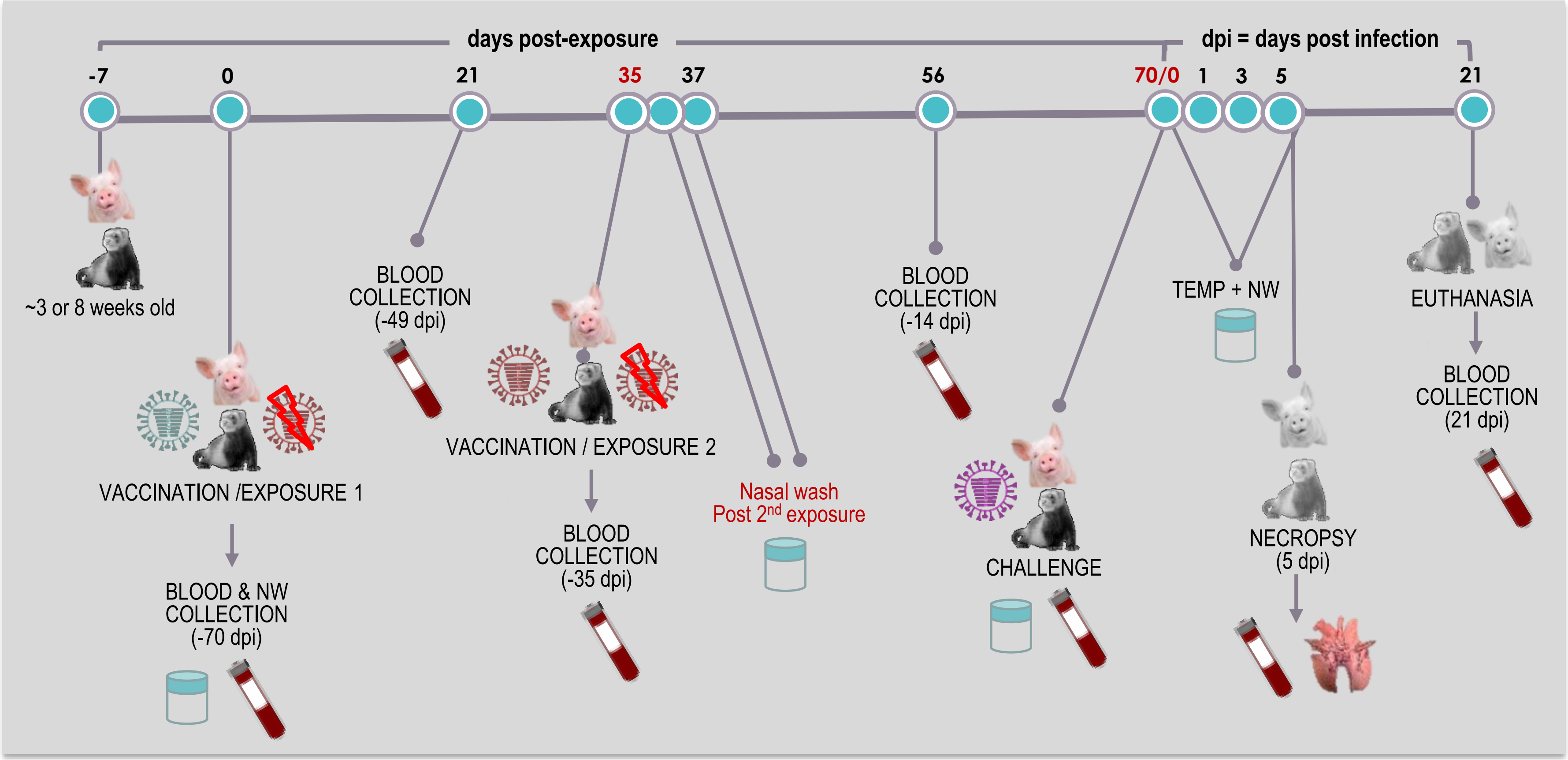


Minimal protection observed against challenge with an antigenically distinct virus; enhanced lung pathology observed in one mismatch - **VAERD**



Complete protection observed against challenge with an antigenically distinct virus

Swine & Ferret Comparative Study



days post-exposure

dpi = days post infection

~3 or 8 weeks old

VACCINATION /EXPOSURE 1

BLOOD & NW COLLECTION (-70 dpi)

BLOOD COLLECTION (-49 dpi)

VACCINATION / EXPOSURE 2

BLOOD COLLECTION (-35 dpi)

Nasal wash Post 2nd exposure

BLOOD COLLECTION (-14 dpi)

CHALLENGE

TEMP + NW

NECROPSY (5 dpi)

EUTHANASIA

BLOOD COLLECTION (21 dpi)

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http://influenza.cvm.iastate.edu

https://www.fludb.org/