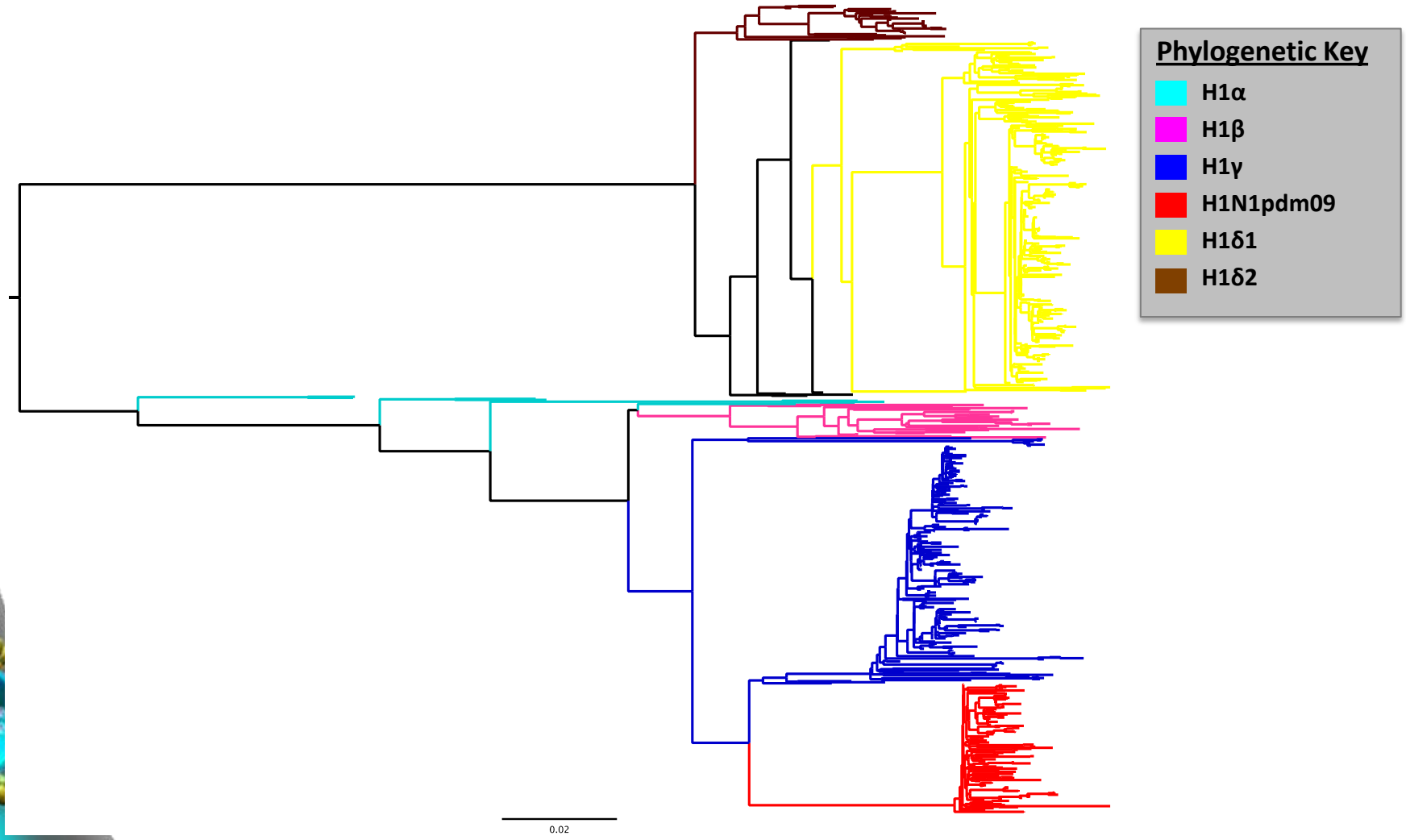
Influenza A virus research update from USDA National Animal Disease Center

Amy L. Vincent, DVM PhD
Research Veterinary Medical Officer
National Animal Disease Center
USDA-ARS

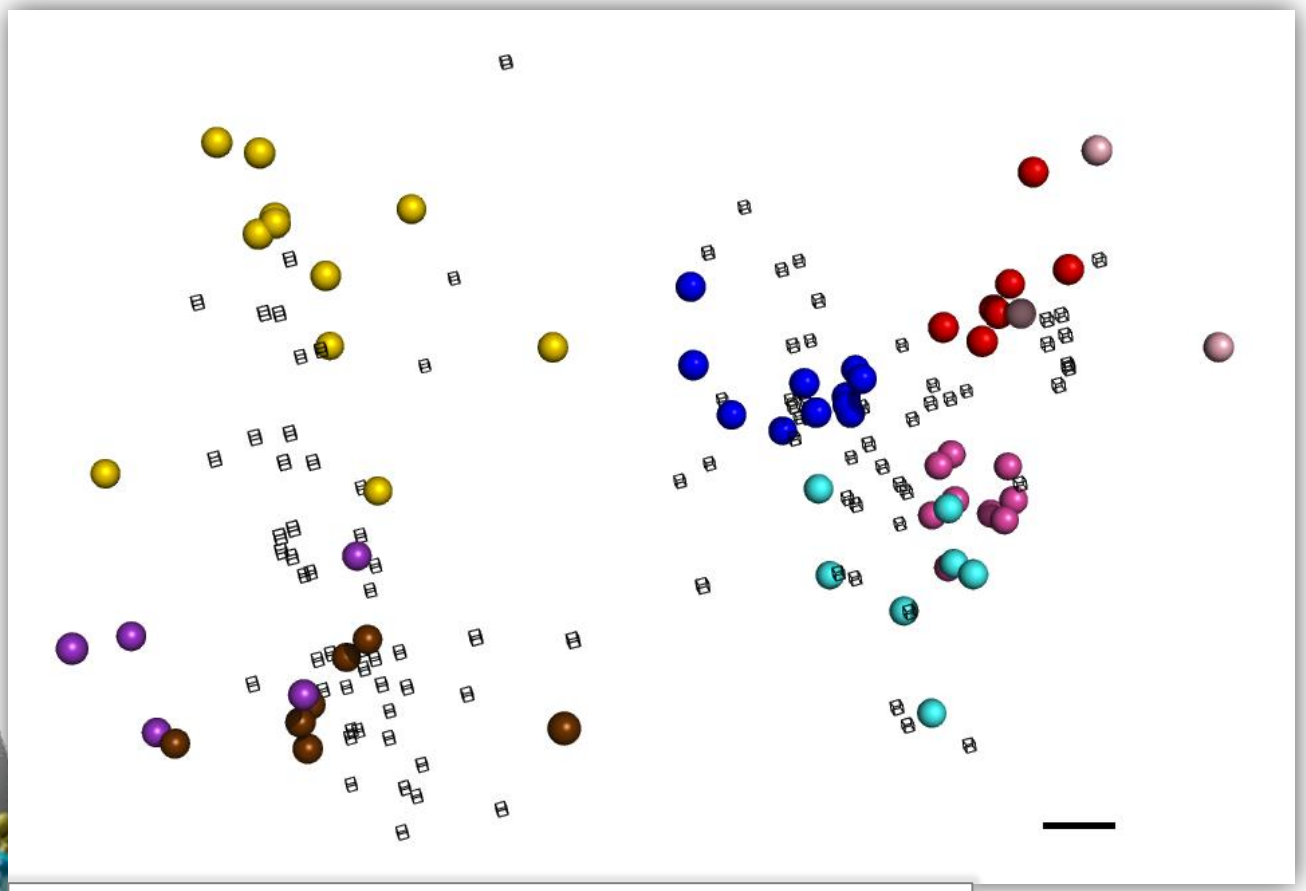
Pravina Kitikoon
Tavis Anderson
USDA-NADC Team
USDA-NVSL
USDA-NAHLN Laboratories
USDA-NSU
US Swine Producers and Veterinarians

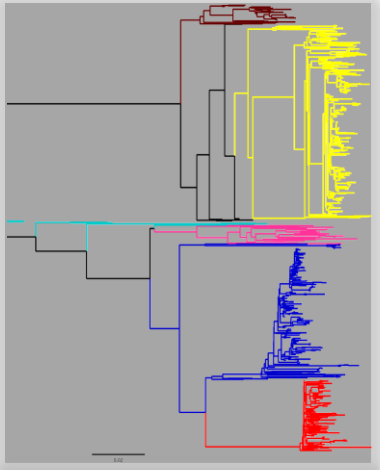
USA H1 Tree



Tavis Anderson

USA H1 cartography





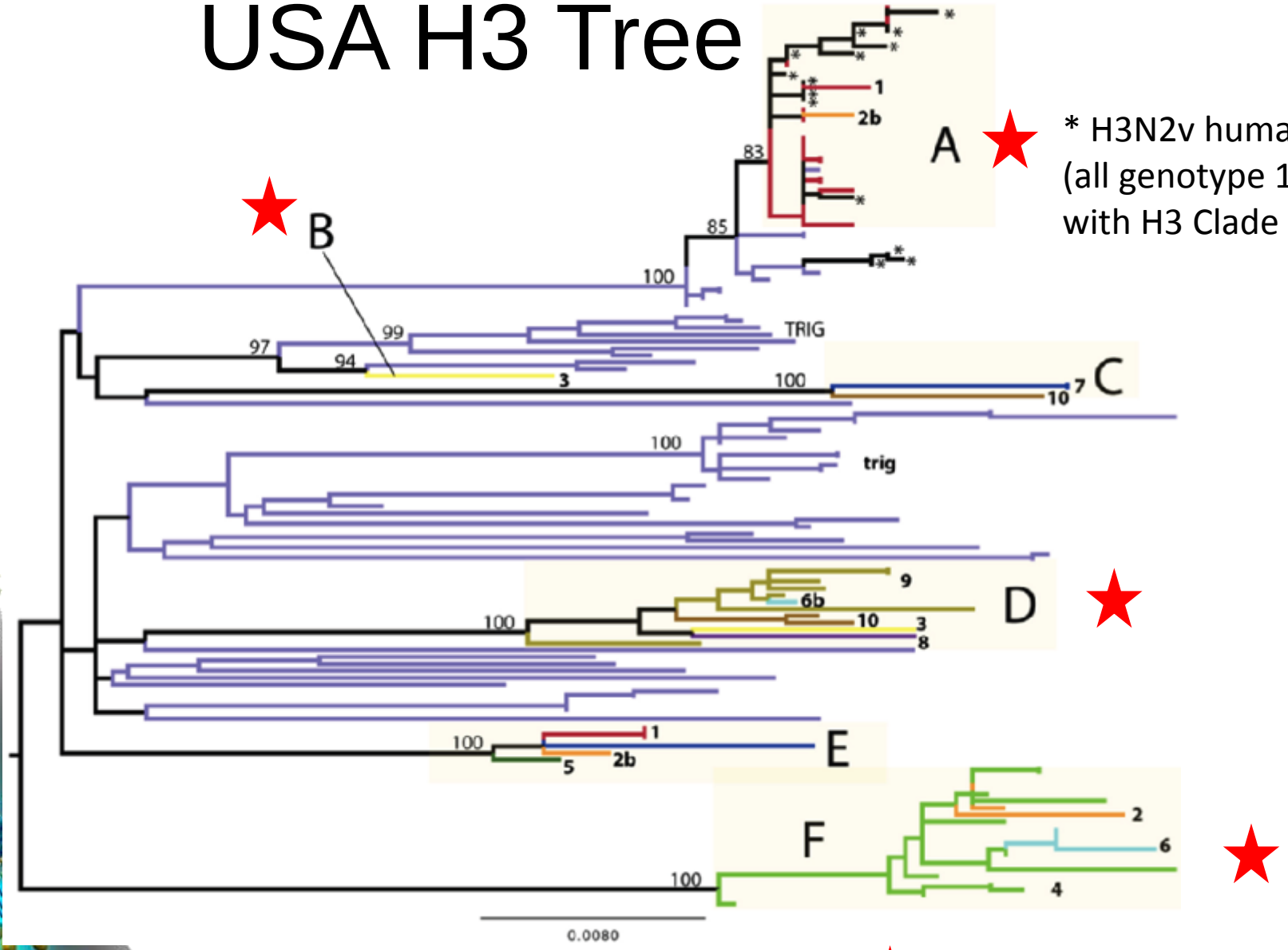
Virus Key

- Alpha
- Beta
- Gamma
- Swine pdm
- Human pdm
- Delta-1
- Delta-2
- Human H1

- 36 new viruses to generate swine anti-sera (x2)
  - 5 human strains
- 60 viruses tested against new antisera
- 29 viruses in previous H1 serum panel (x2)

Pravina Kitikoon and Nicola Lewis

USA H3 Tree

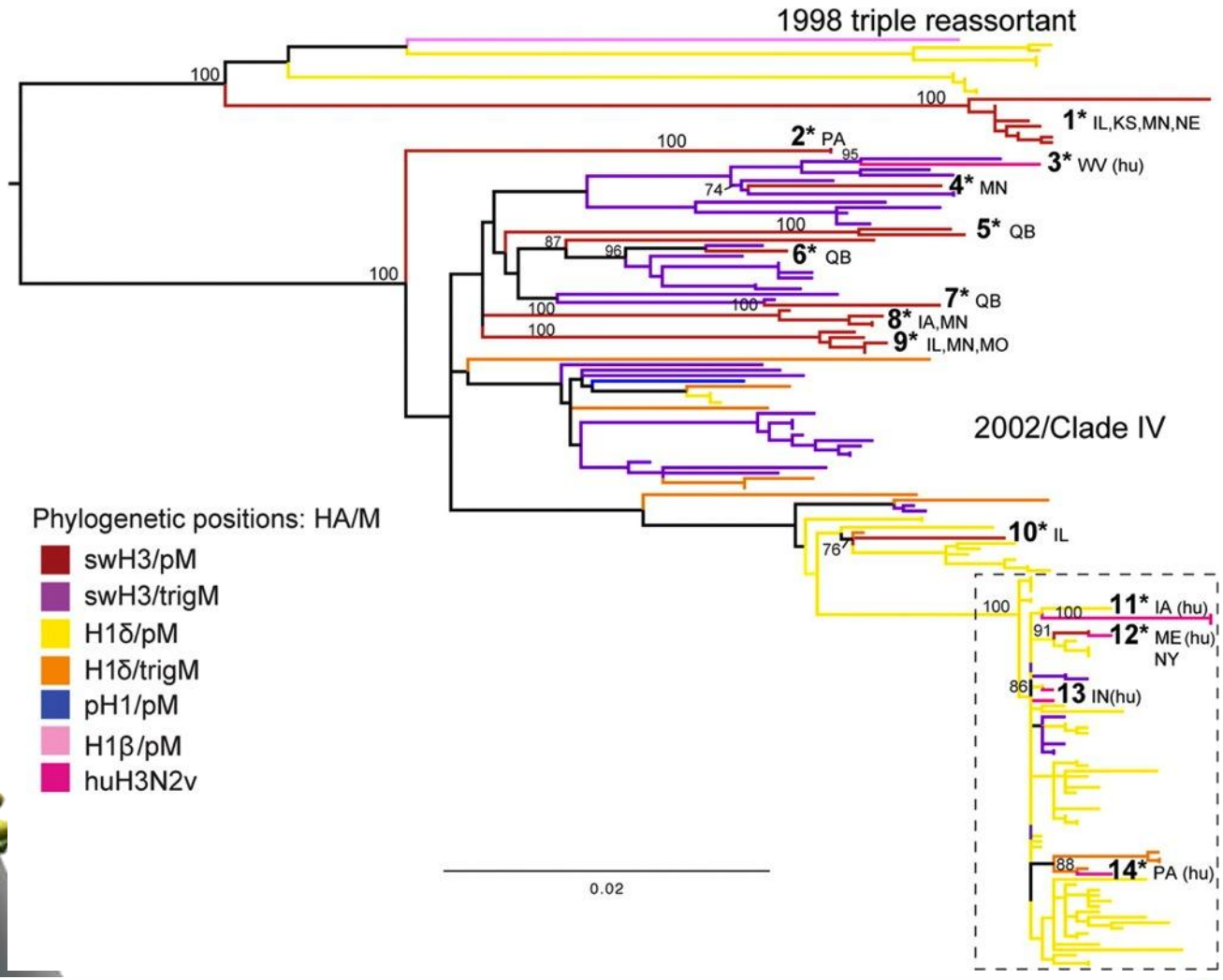


* H3N2v human (all genotype 1 with H3 Clade A)

Kitikoon et al., J Gen Virol accepted

Expanding forward into 2013

USA N2 Tree



2012 human H3N2v N2 among predominantly δ1-H1N2 2002-N2 genes

Nelson M I et al. J. Virol. 2012;86:8872-8878 Journal of Virology

Genotype patterns of contemporary reassorted H3N2 (rH3N2p) virus in U.S. swine

Genotype	PB2	PB1	PA	HA	NP	NA	M	NS	# of isolates
1				A, E		2002			23
2				A, E, F		1998			5*
3				B, D		2002			2
4				F		1998			14*
5				E		2002			1
6				D, F		1998			5*
7				C, E		2002			3
8				D		1998			1
9				D		2002			7
10				C, D		2002			3
TRIG				A		2002			55

North American H3 and N2 human lineage

TRIG avian lineage

Pandemic H1N1 origin

TRIG swine lineage

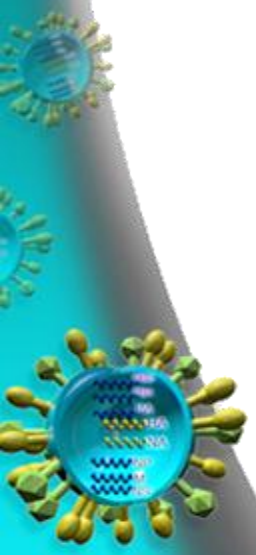
Viruses used in NADC pig studies

Are the genetic clusters impacting antigenic diversity?

H3 antibodies had inconsistent cross-reactivity among sub-clusters and with vaccines

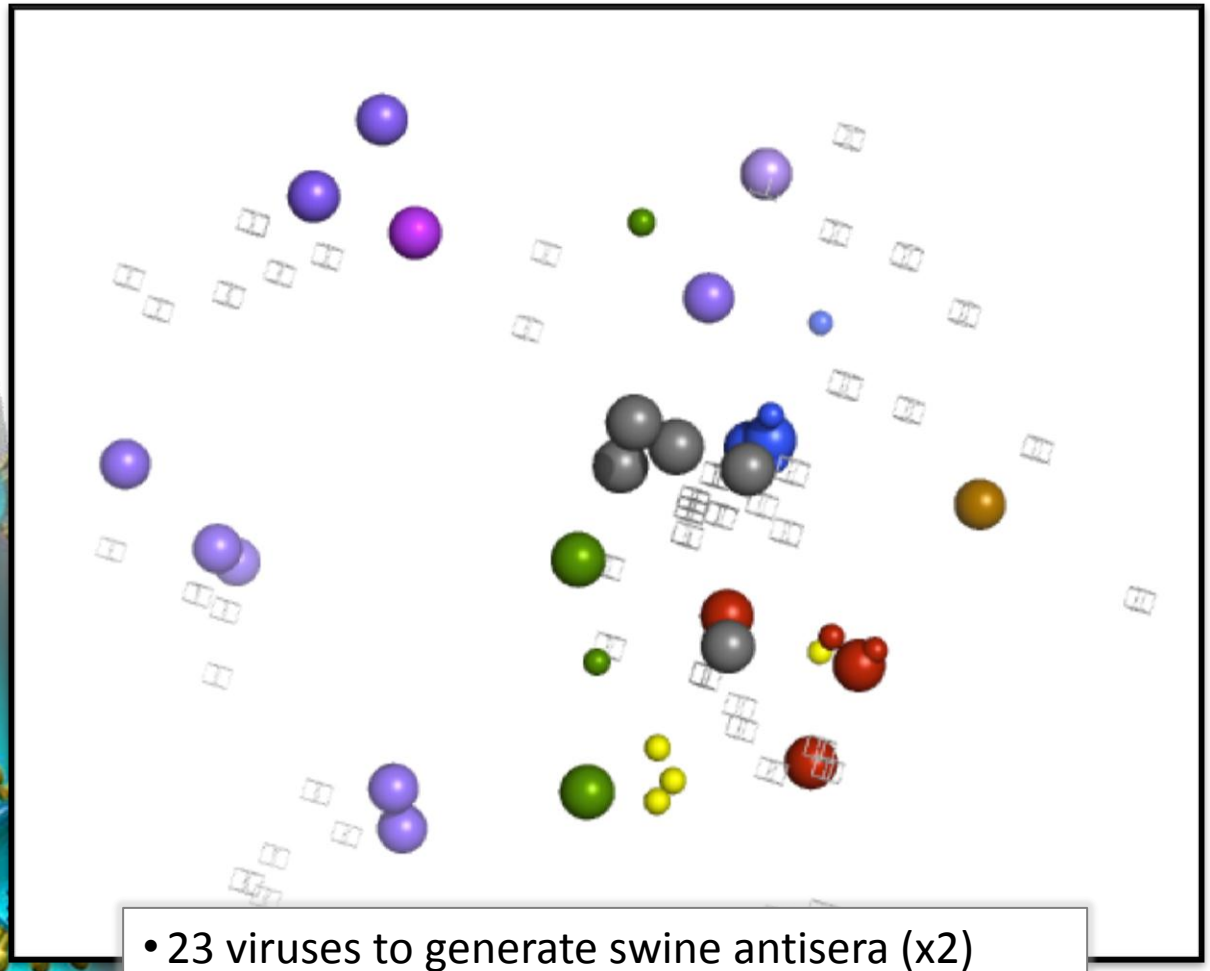
- Homologous
- < 4-fold reduction
- = 4-8-fold reduction
- > 8-fold reduction

Virus (cluster) \ Sera	I	IV					A			C	D		F		IV	I&IV	I
	TX/1998	MN/2006	IA/2007	MN/2009	IL/2009	PA/2010	IN/2011	NY/2011	IN/2012	IN/2011	IL/2011	IA/2011	IA/2011	TX/2011	Vaccine1	Vaccine2	Vaccine3
TX/1998 (I)																	
MN/2006 (IV)																	
IA/2007 (IV)																	
MN/2009 (IV)																	
IL/2009 (IV)																	
PA/2010 (IV)																	
IN/2011 (A)																	
NY/2011 (A)																	
IN/2012 (A)																	
IL/2012 (A)																	
MI/2012 (A)																	
MN/2012 (B)																	
MN/2012 (B)																	
MN/2012 (B)																	
IA/2012 (B)																	
IN/2011 (C)																	
IL/2011 (D)																	
IA/2011 (D)																	
IA/2011 (D)																	
IA/2012 (D)																	
IA/2011 (F)																	
TX/2011 (F)																	
IL/2012 (F)																	
IA/2012 (F)																	
NE/2012 (F)																	



Pravina Kitikoon, unpublished

USA H3 Cartography



Virus Key

- H3-c1
- H3-c3
- H3-c4
- H3-c4A
- H3-c4B
- H3-c4C
- H3-c4D
- H3-c4F
- Human H3

- 23 viruses to generate swine antisera (x2)
  - 8 human seasonal strains
  - 15 USA swine strains
- 34 viruses tested against antisera panel

Pravina Kitikoon & Nicola Lewis, unpublished

Vaccines Tested in rH3N2 Studies

- Pfizer – FluSureXP (2 doses)
  - Cluster IV H3N2
- Novartis – PneumoStar SIV (1 dose)
  - Cluster I H3N2
- Intervet/Schering-Plough – MaxiVac Excell 5.0 (2 doses)
  - Cluster I and IV H3N2
- LAIV-1 – ΔNS1 (truncated NS1, no longer inhibits IFN-α)
  - Cluster I – TX98 with 1998 N2
- LAIV-1 – temperature-sensitive (polymerase mutations)
  - Cluster IV – OH04 with **2002 N2**

- **Challenge with A/Sw/NY/A01104005/2011 or A/swine/Indiana/A00968373/2012**
  - **Genotype 1, H3 cluster A, N2 Cluster 2002**

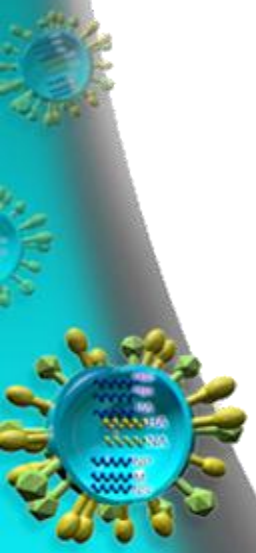
rH3N2p Vaccine studies

- Study 1: Vaccine study with commercial vaccine with and without maternal antibody
  - **A/Sw/NY/A01104005/2011 rH3N2p-G1: mild challenge virus**
  - Commercial vaccine partially protective: reduced febrile response and replication, but did not prevent shedding
  - MDA interfered entirely with partial protection of vaccine
  - LAIV gave complete protection
  - WIV partial protection
- Study 2: 3 commercial WIV compared to 1998 LAIV and 2004 LAIV
  - **A/swine/Indiana/A00968373/2012: mild challenge virus**
  - 1 commercial Vx = "best" partial protection
    - Contained only 1 H3N2 virus (IV)
      - HI titer > 40 to IN/12 Ch virus
    - Still transmitted to naïve indirect contacts
  - 1 commercial vaccine = partial protection
    - Contained 2 H3N2 viruses (I & IV)
      - HI titer > 40 to IN/12 Ch virus
  - 1 commercial vaccine = minimal/no protection
    - Contained 1 H3N2 virus (I)
      - HI titer < 40 to IN/12 Ch virus
  - 1 LAIV = COMPLETE protection
    - IN delivery, 2004 H3N2 virus (IV)
      - HI titer < 40 to IN/12 Ch virus
    - No transmission to naïve contacts
  - 1 LAIV = partial protection
    - IN delivery, 1998 H3N2 virus (I)
      - HI titer < 40 to IN/12 Ch virus
      - Decreased lung viral burden
      - Decreased NS titers

NADC Team efforts

Summary of latest VAERD studies

- Cross-reacting IgG from WIV targets HA2 domain
- Mismatched HA subunit vaccine➔**VAERD**
- NA matters too!
  - NA lineage mismatch, 1998 (A) vs. 2002 (B), with HA mismatch (N2≠N2) ➔ **VAERD**
  - NA subtype mismatch with HA mismatch (N2≠N1) ➔ **VAERD**
  - NA match with HA mismatch (N2=N2) ➔ No VAERD
  - NA mismatch with HA match ➔ No VAERD



Acknowledgments

NADC

- **Michelle Harland**
- **Gwen Nordholm**
- **Pravina Kitikoon**
- **Tavis Anderson**
- **Daniela Rajao**
- **Matt Sandbulte**
- **Katie Gibson**

- **Kelly Lager**
- **Crystal Loving**
- **Mark Kehrli**
- **Jason Huegel**
- **Jason Crabtree**
- **Darrell Bayles**

- **Phil Gauger**
- **Jamie Henningson**
- **Alessio Lorusso**
- **Doug Braucher**
- **Janice Zanella**
- **Eraldo Zanella**
- Sabrina Swenson
- John Korslund
- Marie Gramer
- Nicola Lewis
- Daniel Perez
- Martha Nelson
- Richard Webby
- James Roth
- Ruben Donis
- Sasha Klimov
- Hana Golding
- Surender Khurana

- U.S. Producers and Swine Vets

- Funding:
  USDA-ARS
  USDA-APHIS
  National Pork Board
  CDC

Many thanks to
USDA NCAH Visual Services