Pandemic H1N1 influenza A virus in pigs – Vaccine research

Amy L. Vincent, DVM, PhD
Alessio Lorusso, DVM, PhD
Janice Zanella, DVM, PhD
Eraldo Zanella, DVM, PhD
Kelly A. Lager, DVM, PhD
Kay S. Faaberg, PhD
Marcus E. Kehrli, Jr., DVM, PhD

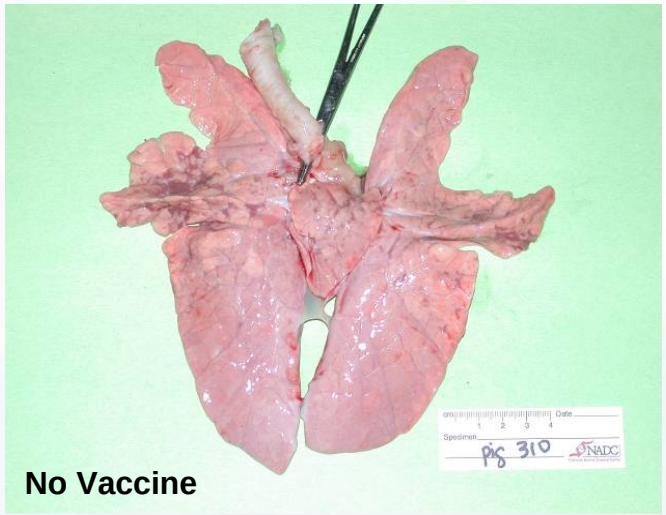
Swine and Prion Diseases Research Unit
National Animal Disease Center
USDA-ARS, Ames, IA

Challenges with Swine Influenza Vaccines

- The circulating viruses under constant evolution or emergence
  - Historically difficult to update veterinary vaccines
- No “one size fits all” vaccine
  - More than 2-3 dominant strains in the US
    - H3N2
    - 4 (or 5) antigenic clusters of H1
  - Commercial vaccines are years behind contemporary viruses
  - Use of autogenous vaccines very common
- Our understanding of heterologous immunity for influenza is incomplete
  - Inactivated versus MLV or vectored vaccines
- Passively acquired antibody interferes with killed vaccines in young piglets

Challenges for vaccines, cont.

- KV enhancement of disease in swine is a real, reproducible phenomenon
  - Implications of mismatch w/ outdated vaccines
- Vaccines perform differently in naïve versus maternal antibody interference model – real world implications



No Vaccine

Mismatched killed vaccine

Challenges for controlling SIV in U.S.

- No centralized data system
  - Sequence database
  - Virus or anti-sera collection
  - Case database

- Needs of the swine industry
  - Rapid identification and notification of emerging viruses
  - Serologic and diagnostic reagent development
  - **Informed vaccine strain selection**

Pilot National SIV Surveillance & Research

- Collaboration between USDA and CDC - 2008
  - APHIS: SIV surveillance system
  - ARS: Research activities
  - CDC: Human surveillance and research
- Develop national surveillance system for SIV
  - Identify emerging SIV
  - Identify antigenic drifts in SIV
  - Identify transmission/reassortment events
  - Identify viruses with human infection potential
- Outcomes
  - Timely changes in vaccine strains for pigs
  - Relevant diagnostic reagents
  - Protect health of swine and human populations
  - *Improved communication and collaboration*

Pandemic H1N1 – Vaccine studies

- Will current U.S. vaccines protect against pandemic H1N1?

- Will natural immunity against U.S. H1N1 or H1N2 SIV protect?

Serologic cross-reactivity – Endemic SIV panel

H1α Phylogenetic cluster (3 viruses)

Antiserum specificity	Sample ID	Homologous HI titer	CA/09 HI titer	Fold-Reduction CA/09	MX/09	Fold-Reduction MX/09
MN/37866/99	532	1280	20	64	160	8
	588	2560	80	32	320	8
MN/02053/08	874	320	<10	320	20	16
	875	320	<10	320	<10	320
MN/02093/08	876	320	<10	320	<10	320
	877	320	<10	320	<10	320

H1β Phylogenetic cluster (5 viruses)

Antiserum	Sample ID	Homologous HI titer	CA/09 HI titer	Fold-Reduction CA/09	MX/09 HI titer	Fold-Reduction MX/09
NC/36883/02	535	640	40	16	160	4
	558	640	20	32	80	8
IA/00239/04	576	1280	20	64	80	16
	577	1280	20	64	40	32
KY/02086/08	873	80	<10	80	<10	80
	874	640	<10	640	20	32
IA/02096/08	870	160	<10	160	<10	160
	871	80	<10	80	<10	80
NE/02013/08	878	640	<10	640	<10	640
	879	160	<10	160	<10	160
NC/03084/08	880	640	<10	640	<10	640
	881	320	<10	320	<10	320

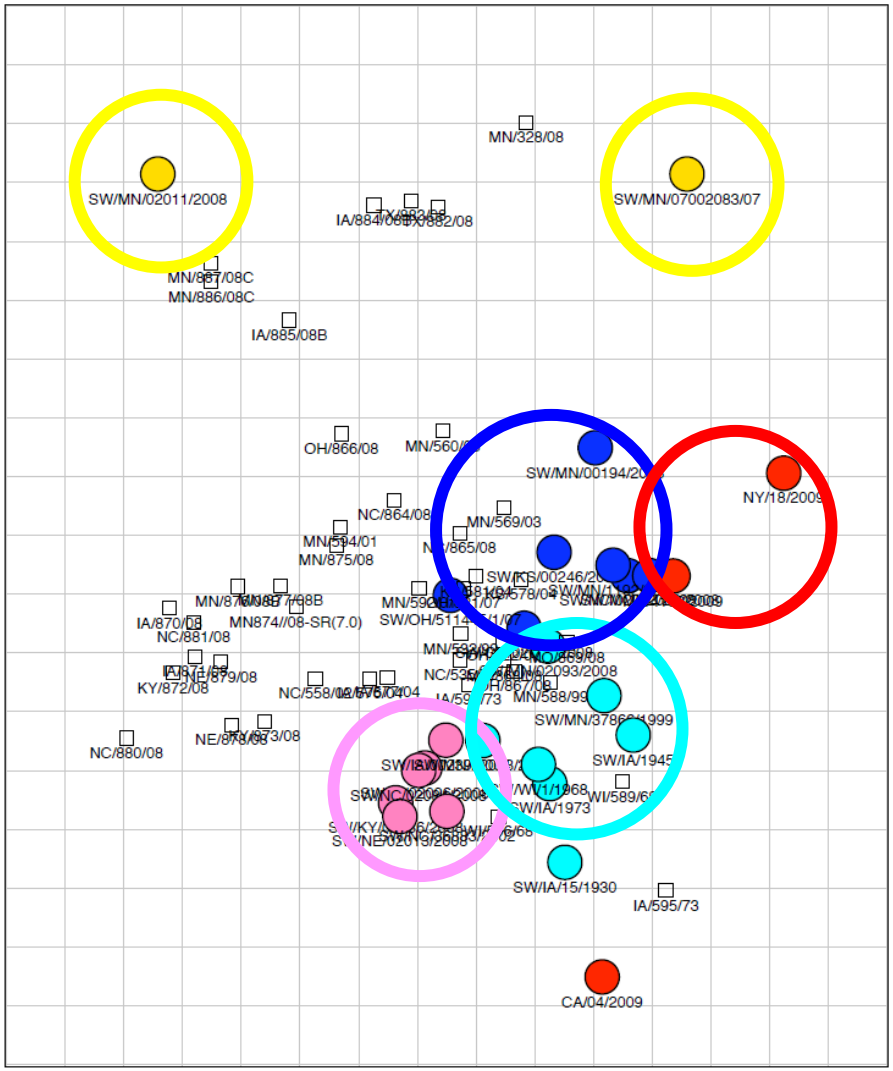
H1γ Phylogenetic cluster (8 viruses)

Antiserum	Sample ID	Homologous HI titer	CA/09 HI titer	Fold-Reduction CA/09	MX/09 HI titer	Fold-Reduction MX/09
OH/511445/07	821	640	20	32	160	4
	882	2560	80	32	640	4
MO/02060/08	868	1280	40	32	160	8
	869	640	80	8	320	2
OH/02026/08	867	640	40	8	80	8
	866	160	<10	160	10	16
NC/02023/08	864	320	<10	320	40	8
	865	320	<10	320	80	4
KS/00246/04	578	1280	<10	1280	160	8
	581	1280	<10	1280	160	8
MN/00194/03	560	1280	<10	1280	160	8
	569	320	<10	320	320	1
MN/1192/01	592	320	<10	320	160	2
	594	80	<10	80	20	4

H1δ phylogenetic cluster (3 viruses)

Antiserum	Sample ID	Homologous HI titer	CA/09 HI titer	Fold-Reduction CA/09	MX/09 HI titer	Fold-Reduction MX/09
TX/01976/08	882	320	<10	320	<10	320
	883	160	<10	160	<10	160
IA/02039/08	884	320	<10	320	<10	320
	885	160	<10	160	<10	160
MN/02011/08	886	2560	<10	2560	<10	2560
	887	640	<10	640	<10	640

Antigenic Cartography – pandemic H1N1



- Adding the pandemic H1 against swine sera
- Cambridge University – Nicola Lewis

Serologic cross-reactivity - Vaccines

Commercial vaccine strains

Antiserum	Sample ID	Homologous HI titer	CA/09 HI titer	Fold-Reduction CA/09	MX/09 HI titer	Fold-Reduction MX/09
Vaccine A	1	1280	10	128	20	64
	2	1280	<10	1280	<10	1280
	3	640	<10	640	<10	640
	4	640	<10	640	<10	640
Vaccine B	1	320	<10	320	40	8
	2	640	<10	640	<10	640
	3	640	40	16	40	16
Vaccine C	1	-	<10	-	<10	-
	2	-	10	-	10	-
Vaccine D	1	1280	20	64	40	32
	2	1280	40	32	80	16
	3	1280	20	64	40	32
Vaccine E	1	-	<10	-	<10	-
	2	-	<10	-	<10	-

NADC Vaccine Studies

- Inactivated vaccine study
  - 2 Commercial vaccines
  - Homologous vaccine
- MLV study
  - RG attenuated H1N1/SIV (D. Perez)
- Natural exposure

USDA Center for Veterinary Biologics

- CVB providing virus isolates to Biologic Firms
  - A/California/04/2009
  - A/Mexico/4108/2009
  - X-179A: RG derived H1N1/PR-8
- Extraneous agent tested completed at CVB and seeds available to firms
- Conditional licensing of monovalent H1N1 encouraged
  - Driven by biologic and swine industries
- Autogenous vaccine would likely be allowed if U.S. case identified