Update on Zoonotic Infections with Influenza A Viruses in the USA

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Reporting Requirements for Novel Influenza A Infections in Humans

- June 2007, CSTE voted to make novel influenza A infections nationally reportable to the National Notifiable Diseases Surveillance System (NNDSS)
- Novel influenza A viruses = those that are different from currently circulating human H1 and H3 viruses
- Includes those that cannot be subtyped using standard methods and reagents

Summary of Human Cases Variant Influenzas 2005 - 2012

- Since July 2011
  - 12 cases H3N2v
  - 1 case H1N1v
  - 1 case H1N2v

A(H3N2)v UPDATE

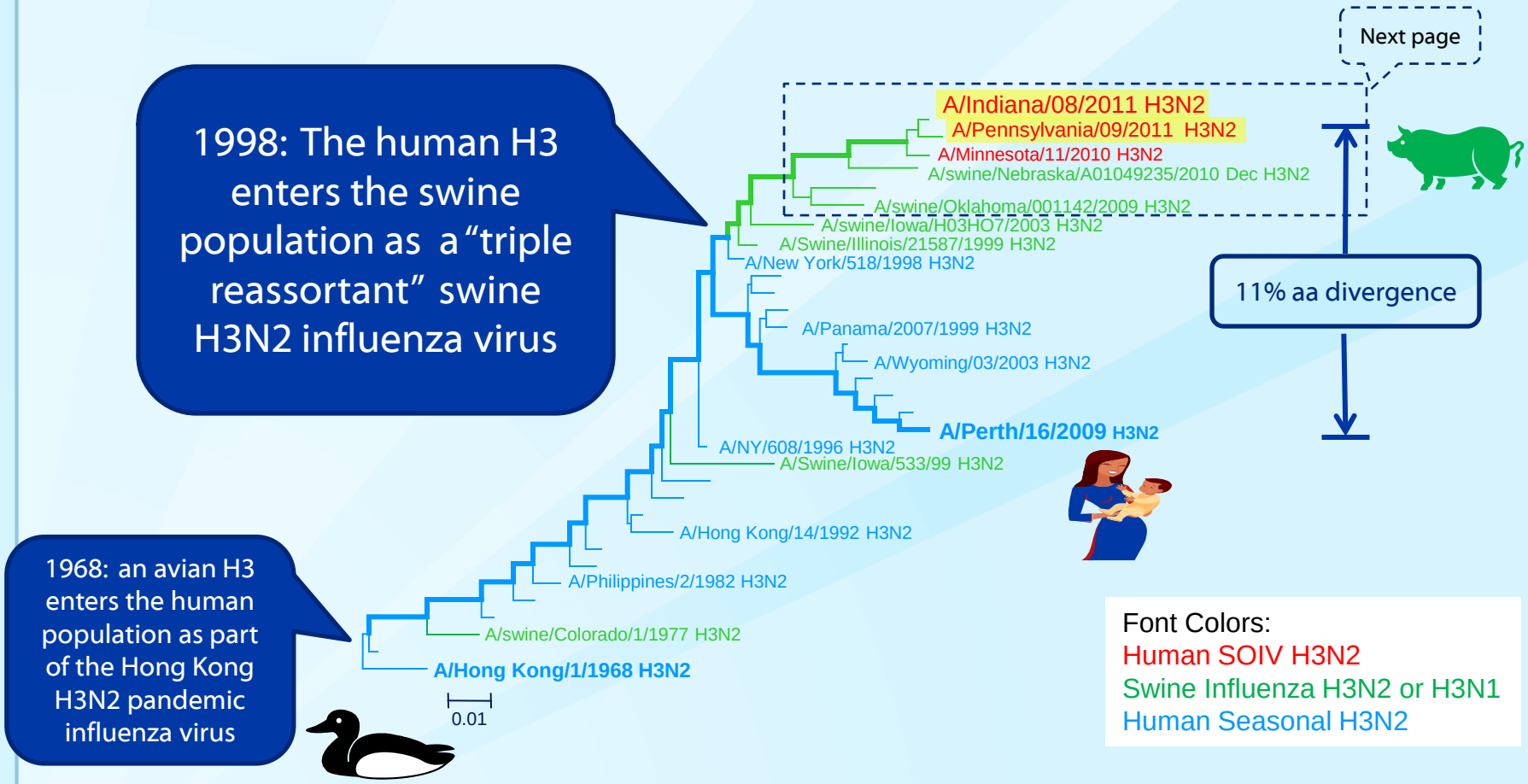
Recent H3N2, H1N2, H1N1 Variant (v) Infections

H3N2 Cases	Age	Sex	Collection Date	Virus Name
#1	<18	M	7/27/2011	A/Indiana/08/2011-MDCK
#2	<18	F	8/20/2011	A/Pennsylvania/09/2011
#3	<18	F	8/26/2011	A/Pennsylvania/10/2011
#4	<18	F	8/25/2011	A/Pennsylvania/11/2011
			9/6/2011	
#5	<18	M	10/10/2011	A/Maine/06/2011
#6	>18	M	10/22/2011	A/Indiana/10/2011
#7	<18	M	10/24/2011	A/Maine/07/2011
#8	<18	F	11/14/2011	A/Iowa/07/2011
#9	<18	M	11/14/2011	A/Iowa/08/2011
#10	<18	M	11/14/2011	A/Iowa/09/2011
#11	<18	F	11/21/2011	A/West Virginia/06/2011
#12	<18	M	12/7/2011	A/West Virginia/07/2011
H1N2	<18	F	11/4/2011	A/Minnesota/19/2011
H1N1	>18	M	12/1/2011	A/Wisconsin/28/2011

Summary of Human Cases of H3N2v Influenza

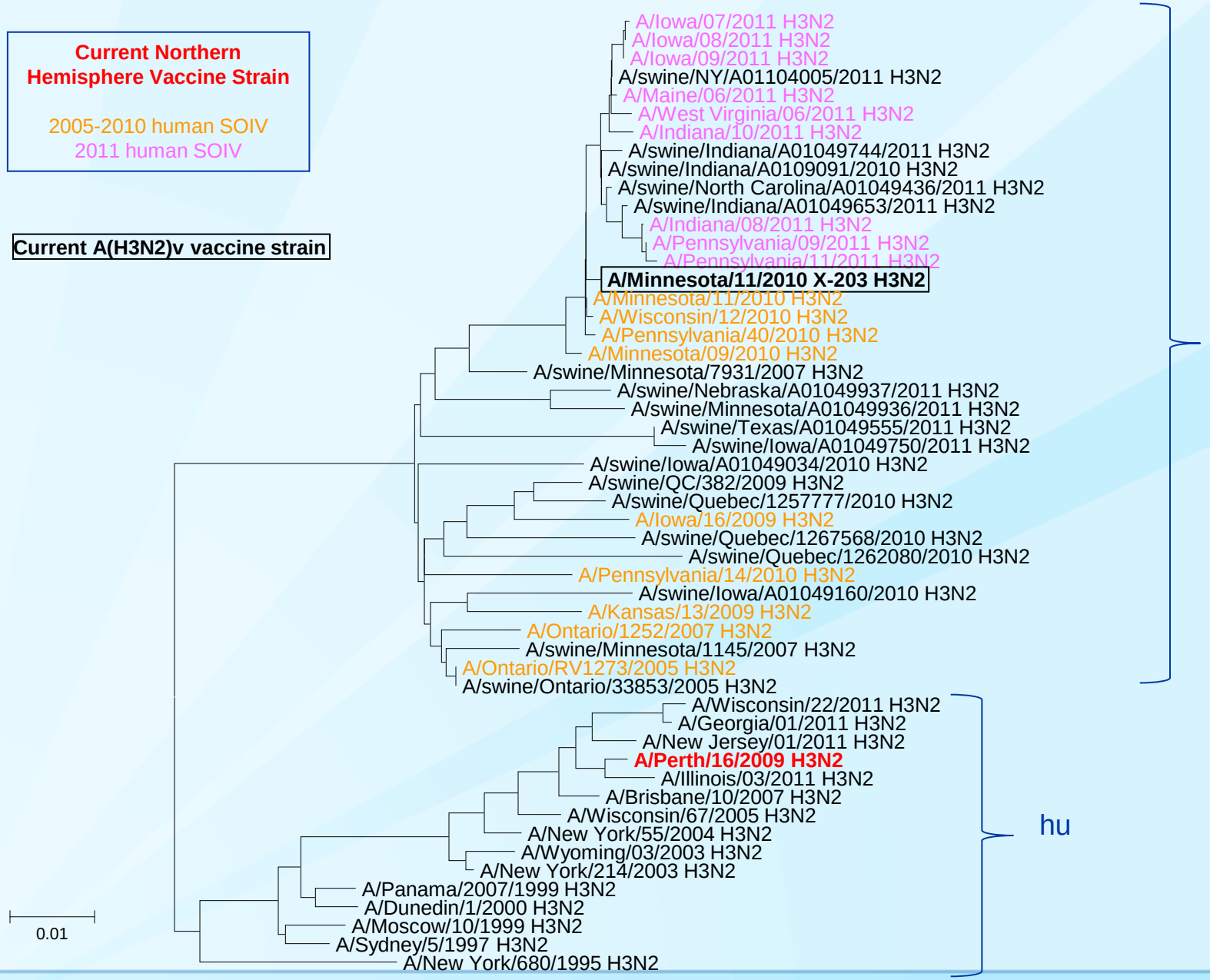
- 12 human cases since August 2011
- 5 states (IA, IN, ME, PA, WV)
- Virus is H3N2v
  - 7 genes are swine triple reassortment
  - 1 gene is from an H1N1 pdm09 virus
- 3 hospitalized; all recovered
- Median age
  - 3 years (range 9 mos - 58 years)
- 6 with swine exposure
- 1 w/indirect swine exposure?
- 5 indication of limited H-2-H transmission

Evolution of the H3 Hemagglutinin: 1968-2011

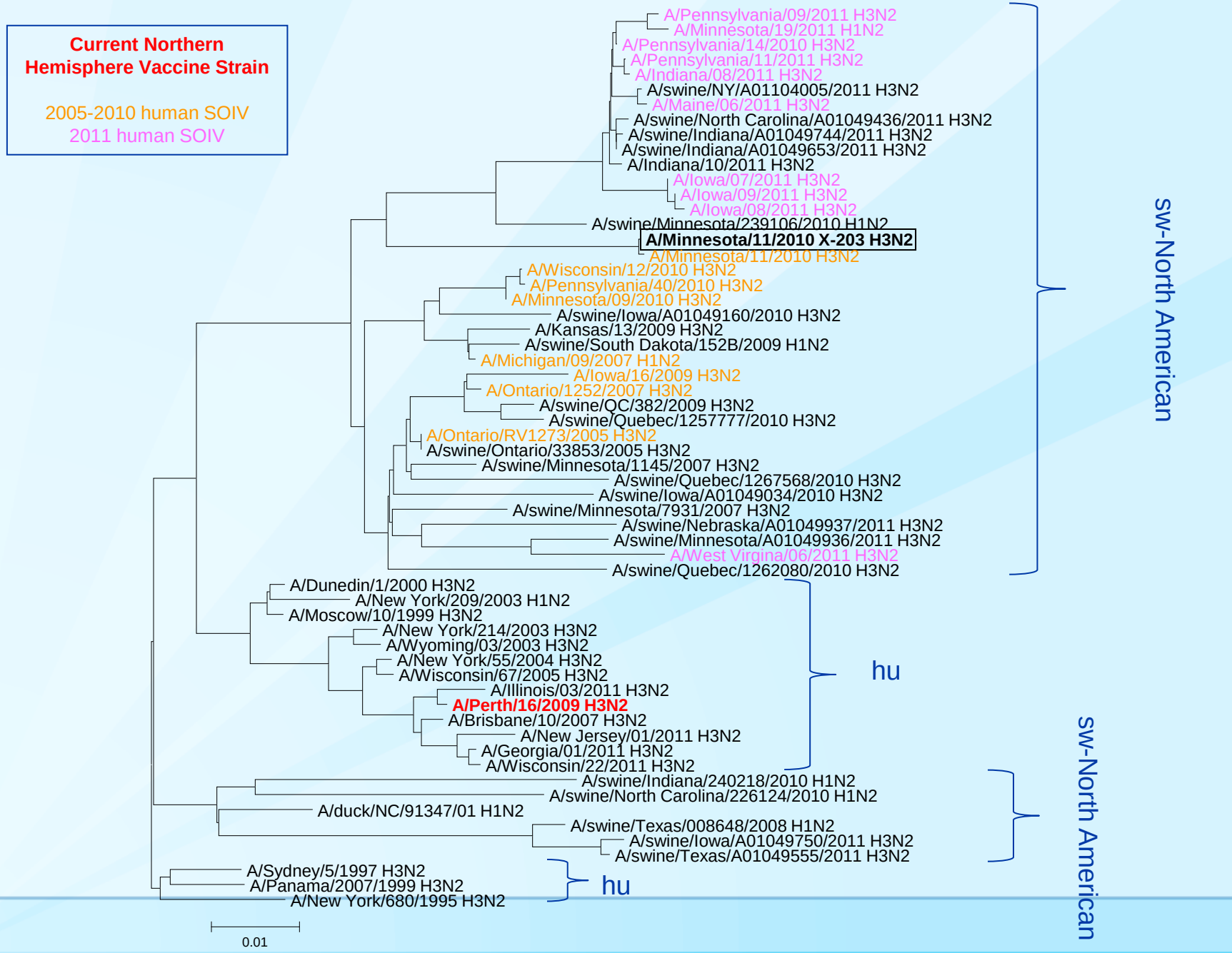


Note: pre-2009 seasonal H1 vs. 2009 pdm H1 showed 22% divergence

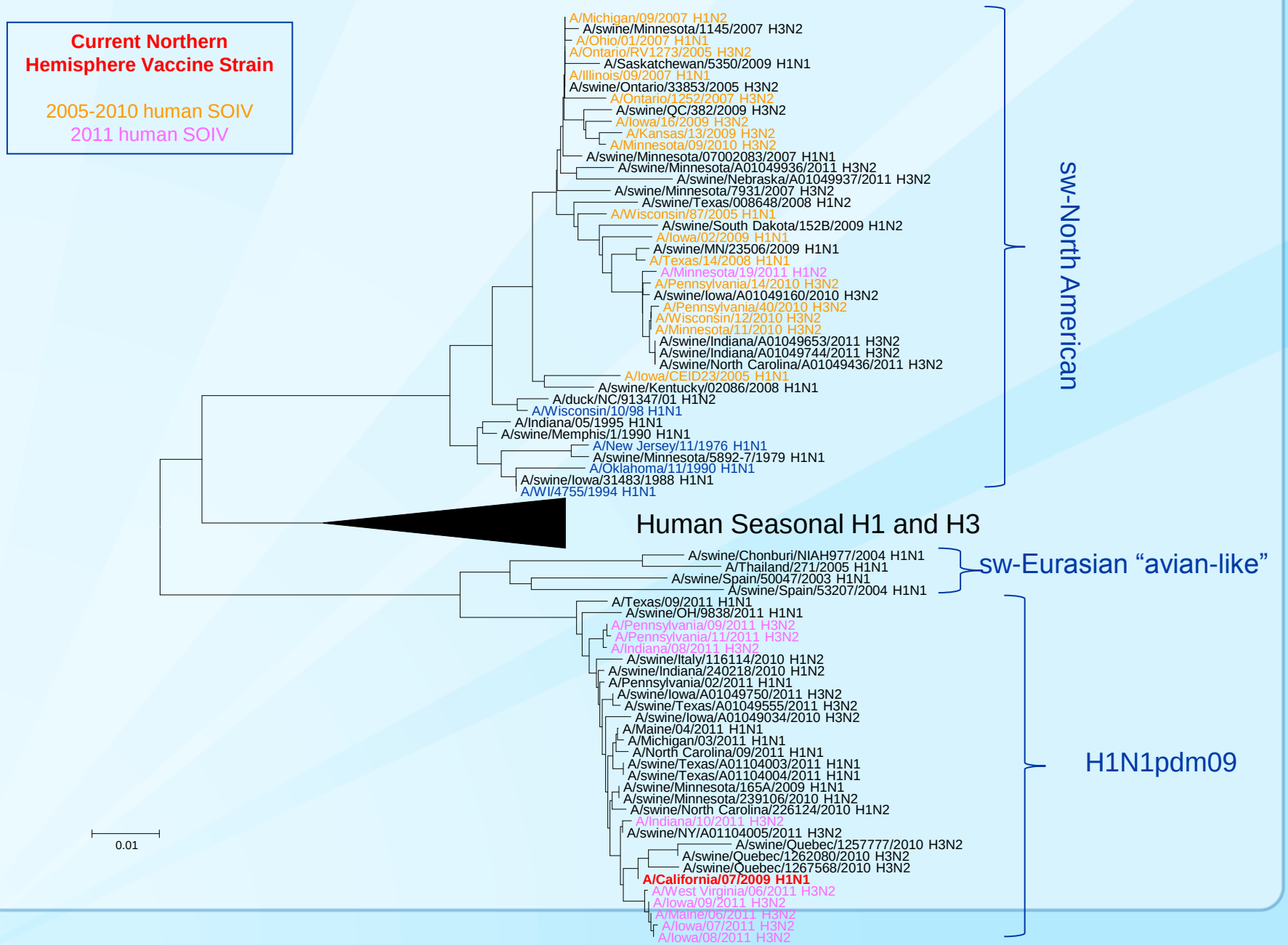
Evolution of Influenza A (H3) Hemagglutinin (HA) Genes



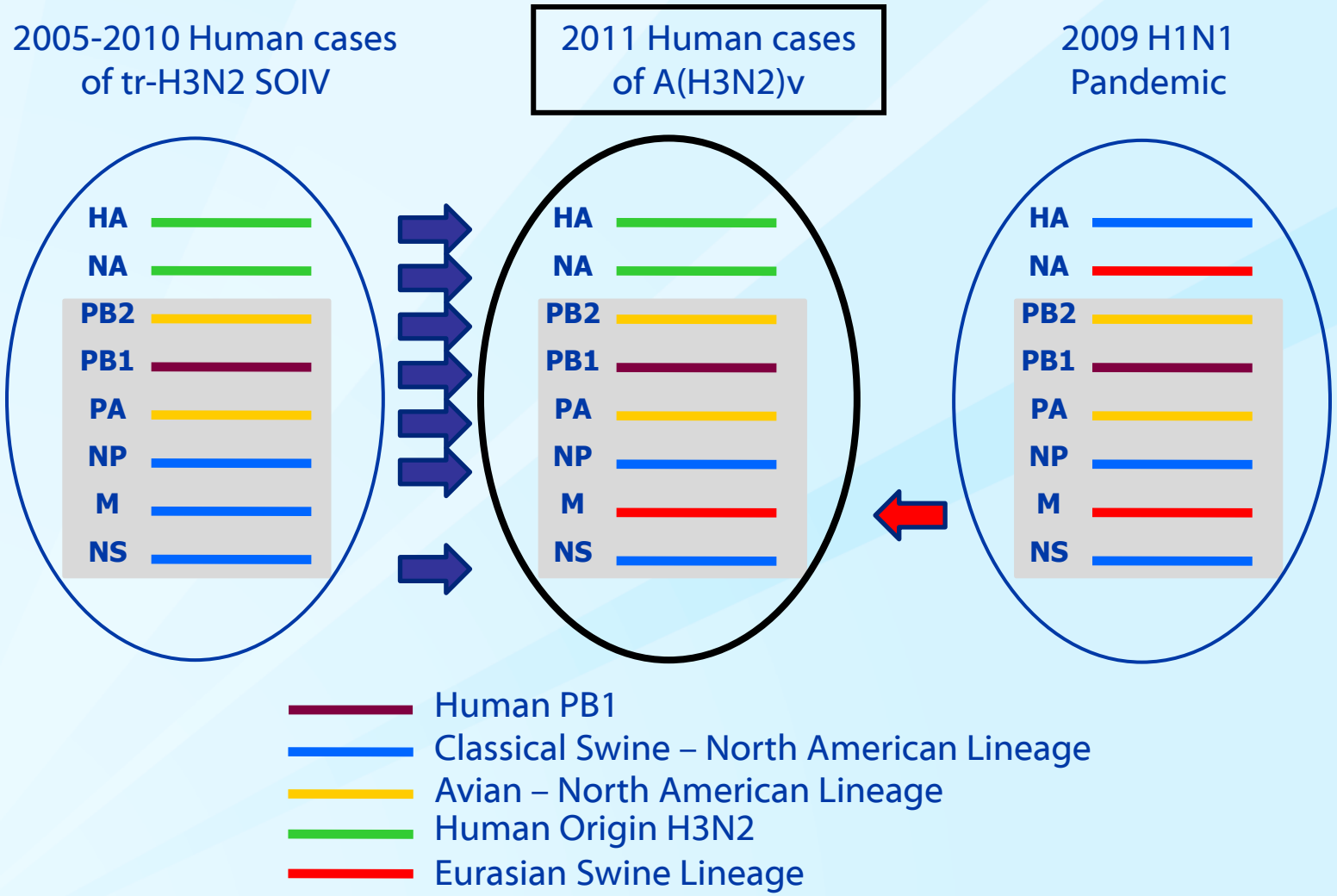
Evolution of Influenza A (N2) Neuraminidase (NA) Genes



Evolution of Influenza A Matrix (M) Genes



Genotype of (H3N2)v, 2011



Candidate Vaccine Virus

HEMAGGLUTINATION INHIBITION REACTIONS--SWINE (12/08/11)

		REFERENCE FERRET ANTISERA									Date	
REFERENCE ANTIGENS		PER/16	KS/13	PA/14	IN/08	IN/10	IN/10	WI/12	MN/11	X-203	collected	Passage
	RECENT H3											
1	A/PERTH/16/2009	640	5	5	5	5	10	10	5	40	4/7/2009	E3/E2
	H3-SOIV											
2	A/KANSAS/13/2009	5	1280	320	80	80	40	160	40	80	7/29/2009	C2
3	A/PENNSYLVANIA/14/2010	5	160	640	640	640	640	640	320	320	10/26/2010	E2
4	A/INDIANA/08/2011	5	10	640	2560	1280	1280	2560	1280	640	7/24/2011	C2
5	A/INDIANA/10/2011-MDCK	5	20	640	1280	1280	640	2560	1280	640	10/22/2011	X1/C2
6	A/INDIANA/10/2011-EGG	5	10	320	1280	1280	640	1280	640	320	10/22/2011	E2
7	A/WISCONSIN/12/2010	5	20	320	640	1280	640	2560	640	320	9/10/2010	M1/C1
8	A/MINNESOTA/11/2010	5	10	160	320	160	160	320	1280	1280	11/26/2010	E2
9	A/MINNESOTA/11/10 X-203	5	5	40	160	40	160	80	320	1280	REASS	EX/E1
TEST ANTIGENS												
10	A/WEST VIRGINIA/06/2011	5	40	640	1280	1280	640	2560	1280	640	11/21/2011	C1
11	A/IOWA/07/2011	5	40	640	1280	1280	1280	2560	1280	640	11/14/2011	C1
12	A/IOWA/08/2011	5	20	640	1280	1280	640	2560	1280	640	11/14/2011	C1
13	A/IOWA/09/2011	5	20	640	1280	1280	640	2560	1280	640	11/14/2011	C1

Hemagglutination-Inhibition Antibody Responses in Populations Receiving 2010-2011 Influenza Trivalent Inactivated Vaccine

Population	N	Antigen	Pre-Vaccine GMT** (CI)	Post-Vaccine GMT (CI)	% with HI > 40***	
					Pre-Vaccine	Post- Vaccine
Pediatric* (6-35 months)	20	Seasonal H3N2	5.50	21.44 ~4 fold increase	0	40
	20	Swine H3N2	5.00 (-)	5.00 no increase	0	0
Adult (18-49 years)	30	Seasonal H3N2	16.70	84.73 ~4.4 fold increase	30	80
	30	Swine H3N2	17.80	31.57 ~2-fold increase	33	50
Elderly (≥ 65 years)	30	Seasonal H3N2	12.88	62.41 ~5-fold increase	27	67
	30	Swine H3N2	13.10	21.54 ~<2 fold increase	17	40

* This age group received two doses of vaccine.
**Geometric Mean Titer
***An HI titer of ≥ 40 is a surrogate marker of influenza immunity in populations.

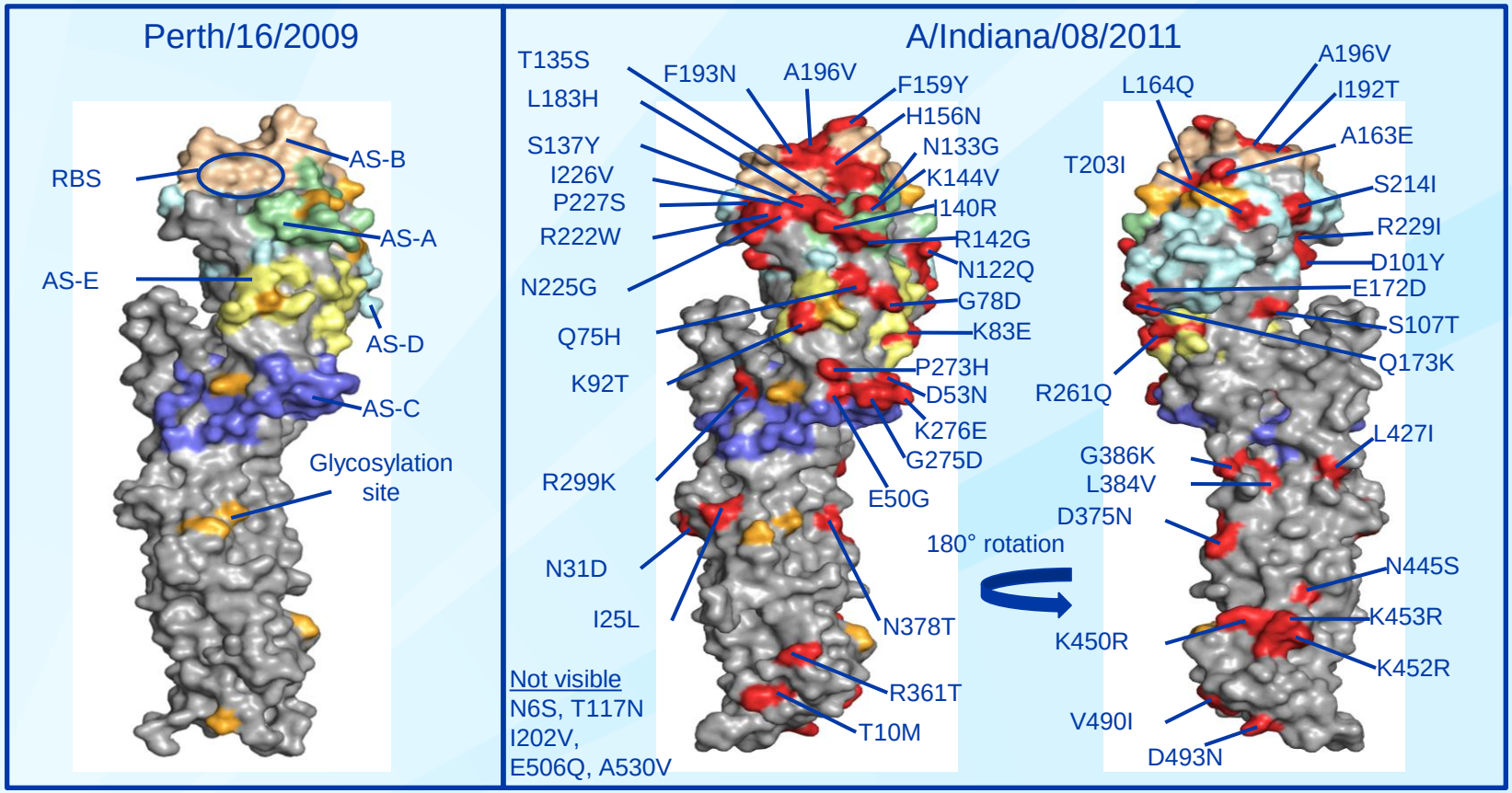
Summary of Human Serology by HI

- **Does seasonal H3N2 vaccine increase HI titers to SOIV H3N2?**
  - Pediatric vaccinee population
    - No increase HI titers (in contrast to 4-fold rise to seasonal)
  - Adult vaccinees
    - ~2-fold increase (in contrast to ~ 4.5 fold rise to seasonal)
  - Elderly vaccinees
    - ~ 2-fold increase (in contrast to ~5-fold rise to seasonal)
- **HI titers correlated with H3N2v protection after seasonal vaccine: 0% in pediatric, 40% in elderly and 50% in adults**
- **Small sample suggest that 0%, 33% and 17% of pediatric, adult and older adults respectively have pre-existing (pre-vaccination) HI titers of ≥40**

Summary of Human Serology by MN

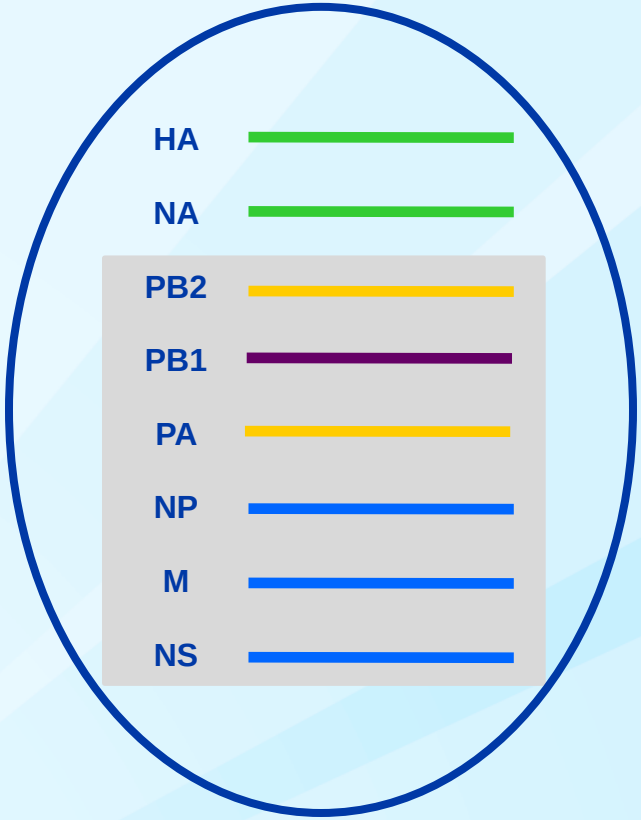
- MN titers that correlate with HI seroprotective titers (HI of ≥40) after seasonal vaccine: 0% in pediatric, 30% in elderly and 63% in adults
- MN data support the findings of HI serology
- Conclusion: seasonal influenza vaccine antigen composition is suboptimal to immunize against H3N2v, especially in infants

A/Indiana/08/2011 H3N2v HA Compared to A/Perth/16/2009



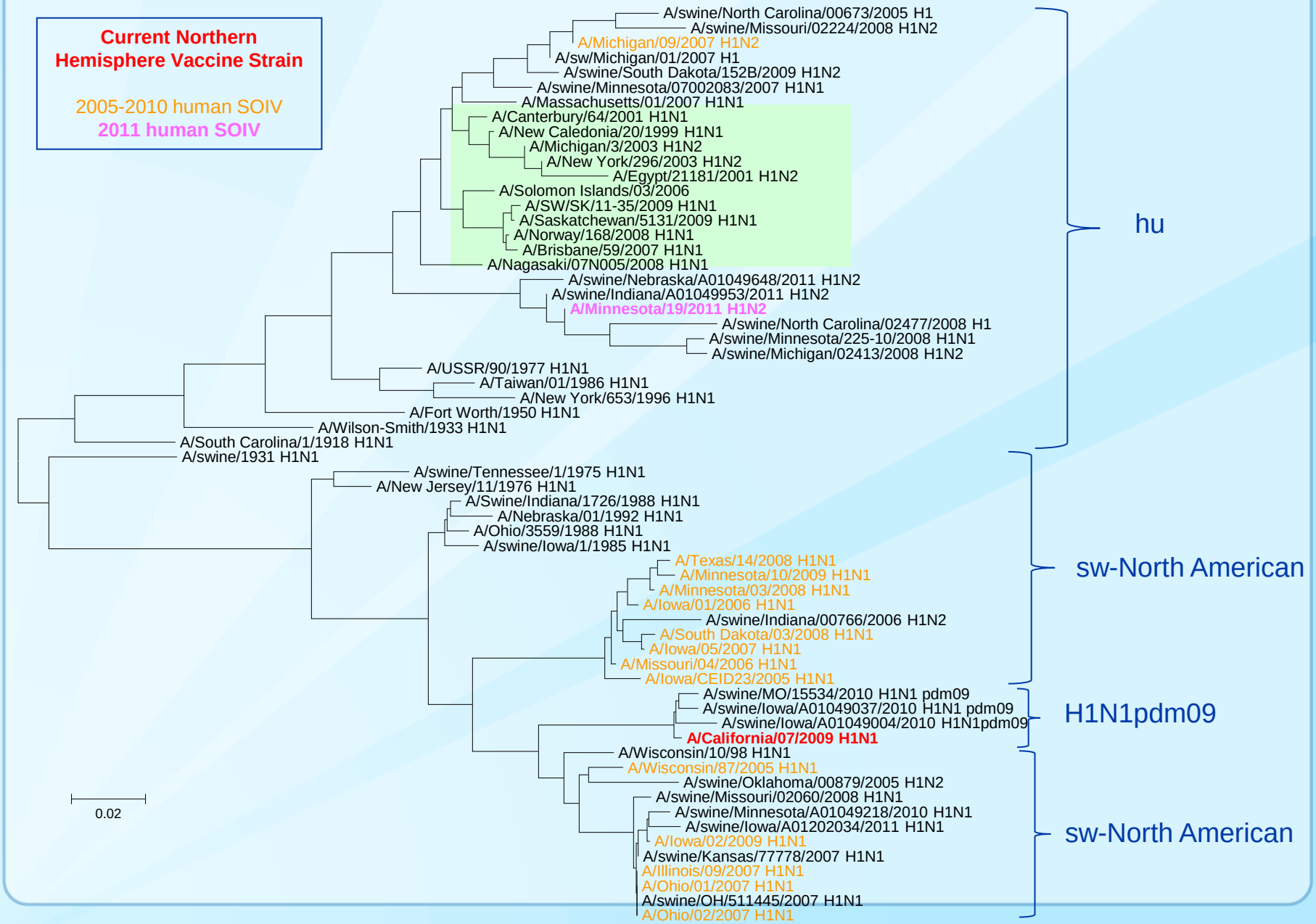
A(H1N1)v UPDATE

Zoonotic Infection with (H1N2)v, 2011



Human PB1
Classical Swine – North American Lineage
Avian – North American Lineage
Human Origin H1N2

Evolutionary Relationships Among Influenza A (H1) Hemagglutinin (HA) Genes



HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA SWINE H1 VIRUSES (12/09/11)

		FERERENCE FERRET ANTISERA							
	STRAIN DESIGNATION	BJ/262	N.CAL/20	SI/03	BRIS/59	IOWA/02	SW/MI	CAL/07	Passage
	SEASONAL H1's								
1	A/BEIJING/262/1995	640	320	20	20	5	160	5	E3/E2
2	A/NEW CALEDONIA/20/1999	160	640	80	80	5	320	5	E4/E1
3	A/SOLOMON ISLANDS/03/2006	40	40	320	160	5	10	5	E2/E2
4	A/BRISBANE/59/2007	20	20	320	320	5	5	5	E2/E1
	SOIV H1								
5	A/IOWA/2/2009	5	5	5	5	2560	5	2560	E3
	SWINE H1								
6	A/SWINE/MICHIGAN/01/2007	80	160	40	20	5	320	5	E2
	H1N1 pdm 09								
7	A/CALIFORNIA/07/2009	5	5	5	5	1280	5	2560	E3
	TEST ANTIGENS								
8	A/MINNESOTA/19/2011 (H1N2)	5	10	40	80	5	5	5	M1M2/C1
9	A1047604 PIG'S HEAD/2010	5	10	40	80	5	5	5	C1/C1
10	A/SWINE/S. DAKOTA/152B/2009	640	640	40	80	5	1280	5	C1/C1

Summary

- Human infections with SOIV rarely detected and cause usually mild disease

- 2011 tr-H3N2v
  - 7 gene segments from tr-H3N2 North American swine viruses and the M gene from a human H1N1pdm09 virus
  - H3N2v are antigenically similar to A/Minnesota/11/2010 vaccine candidate (NYMC X-203 reassortant)
  - Minimal to no protection from seasonal vaccine
  - Resistant to adamantanes; sensitive to oseltamivir

- 2011 tr-H1N2v
  - Genetically close to North American swine influenza viruses of the H1N2 subtype
  - Antigenically close to A/Brisbane/59/2007-like viruses
  - Sensitive to amantadine, rimantadine, oseltamivir and zanamivir

Acknowledgments

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