U.S. Update on SIV Surveillance and Research

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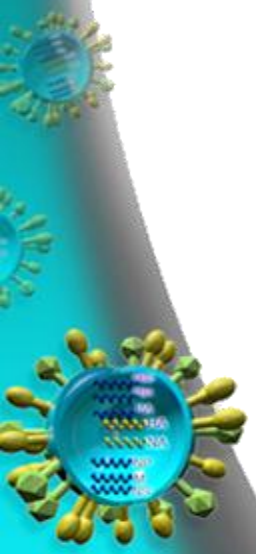
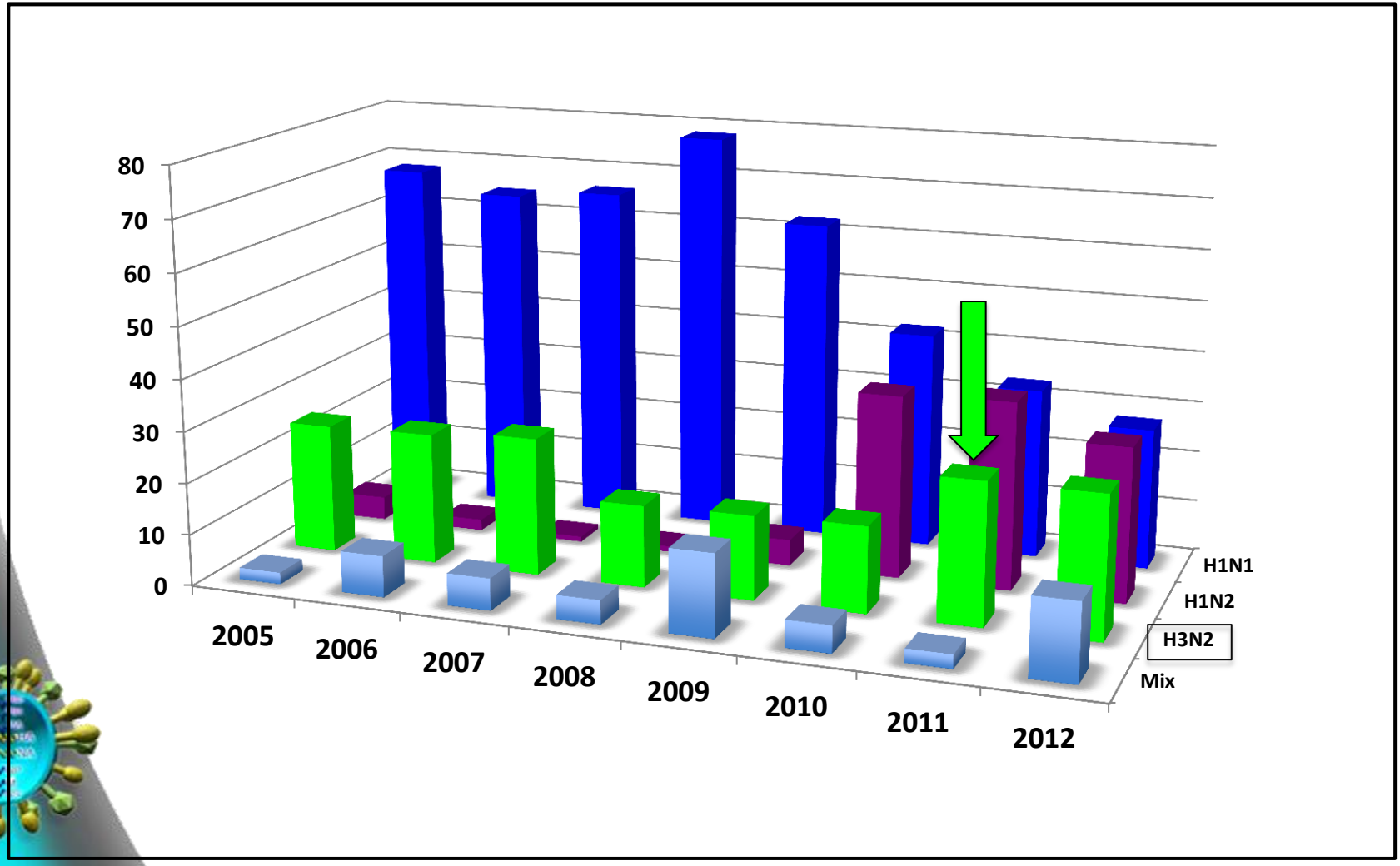
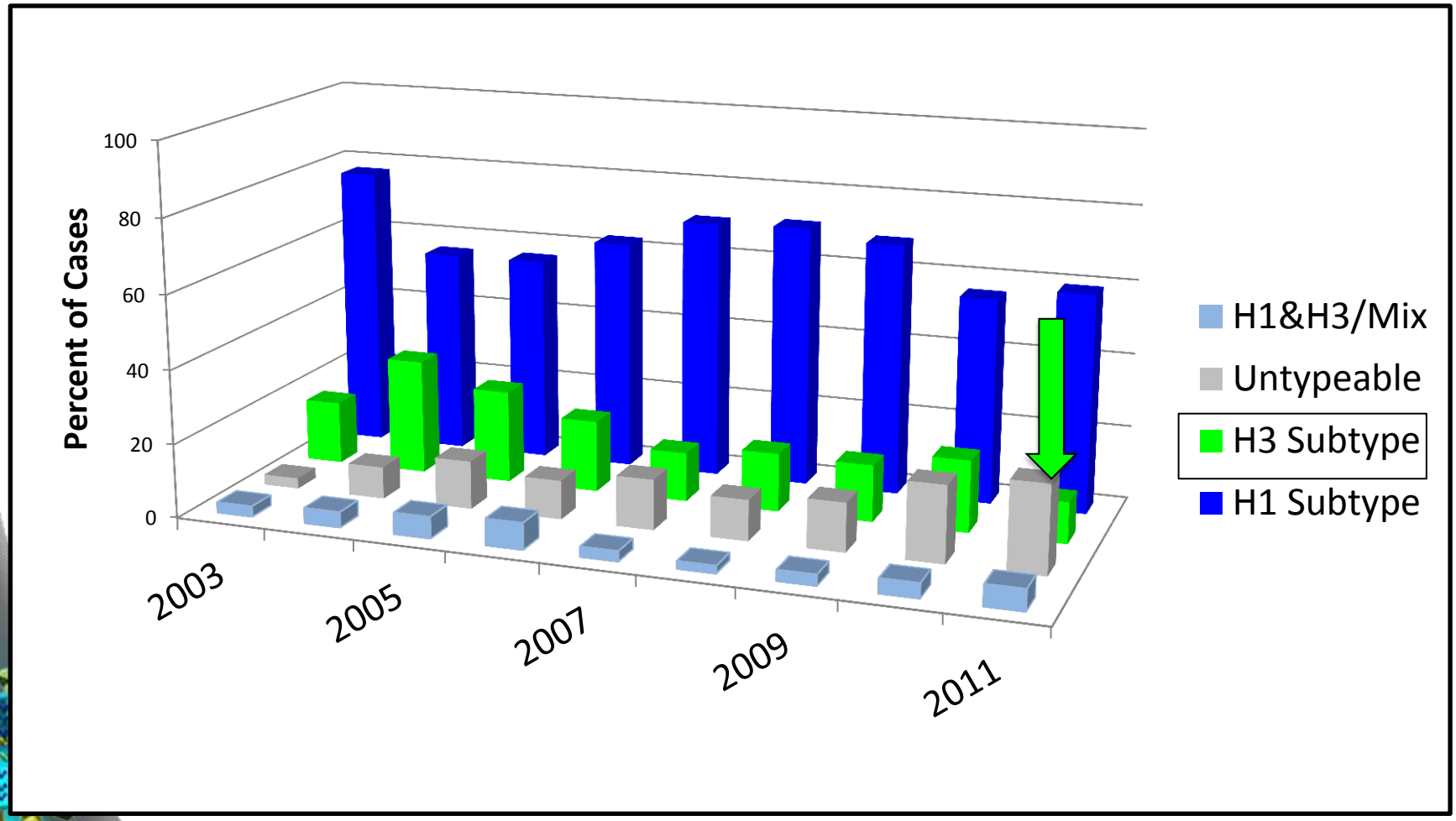
What information will we gain from the USDA SIV surveillance data?



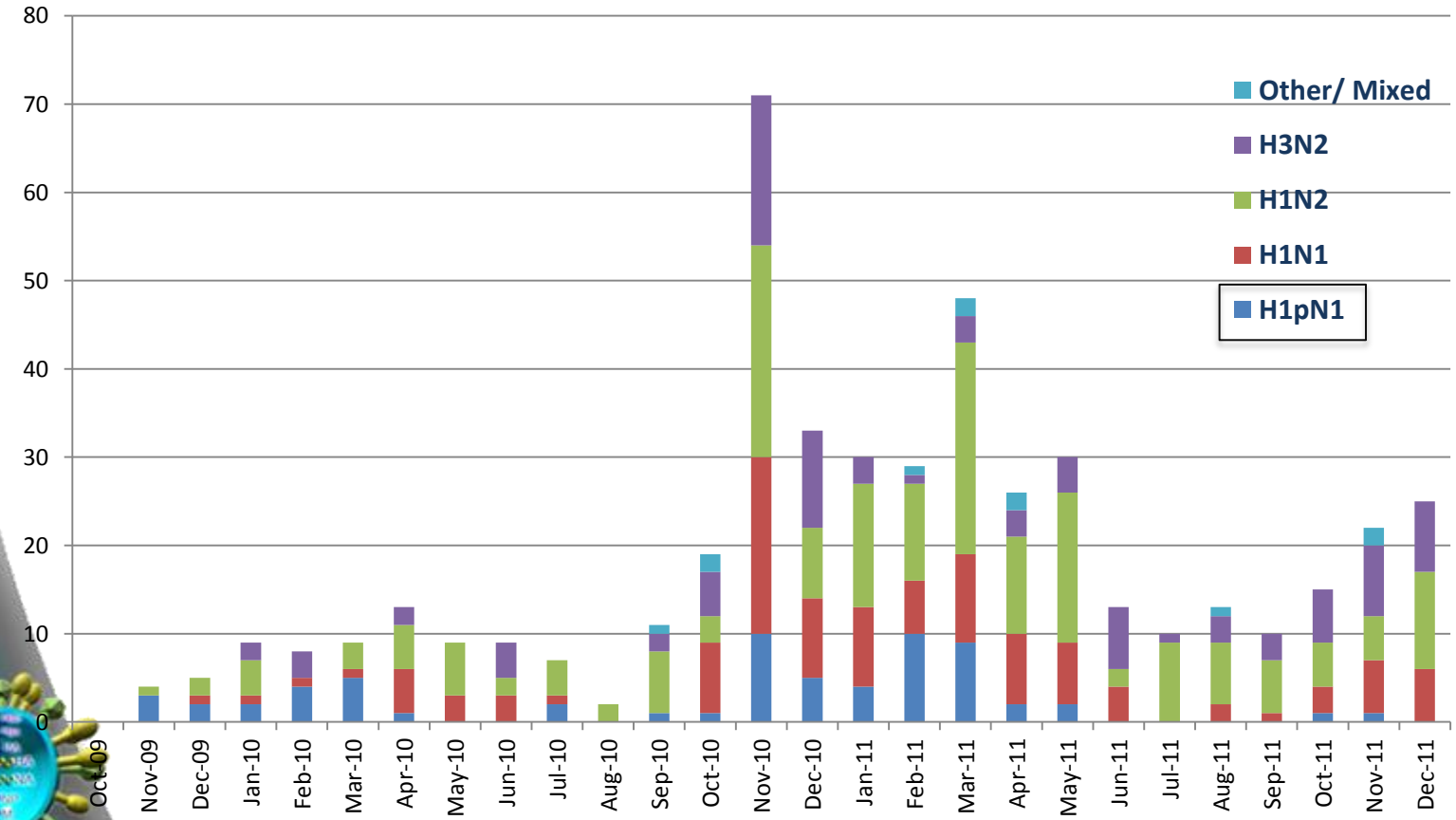
UM-VDL Subtype



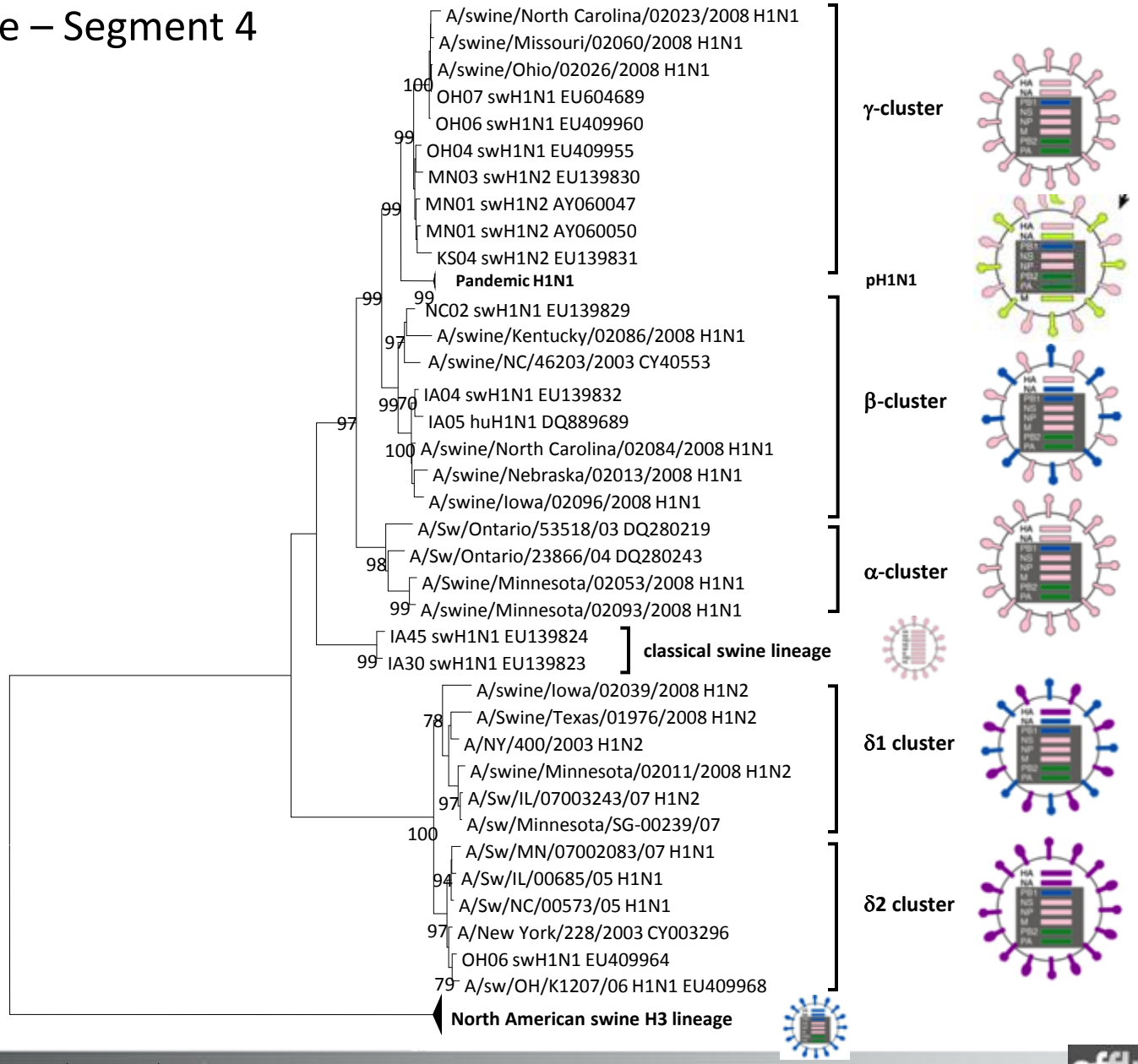
ISU-VDL: HA Subtype



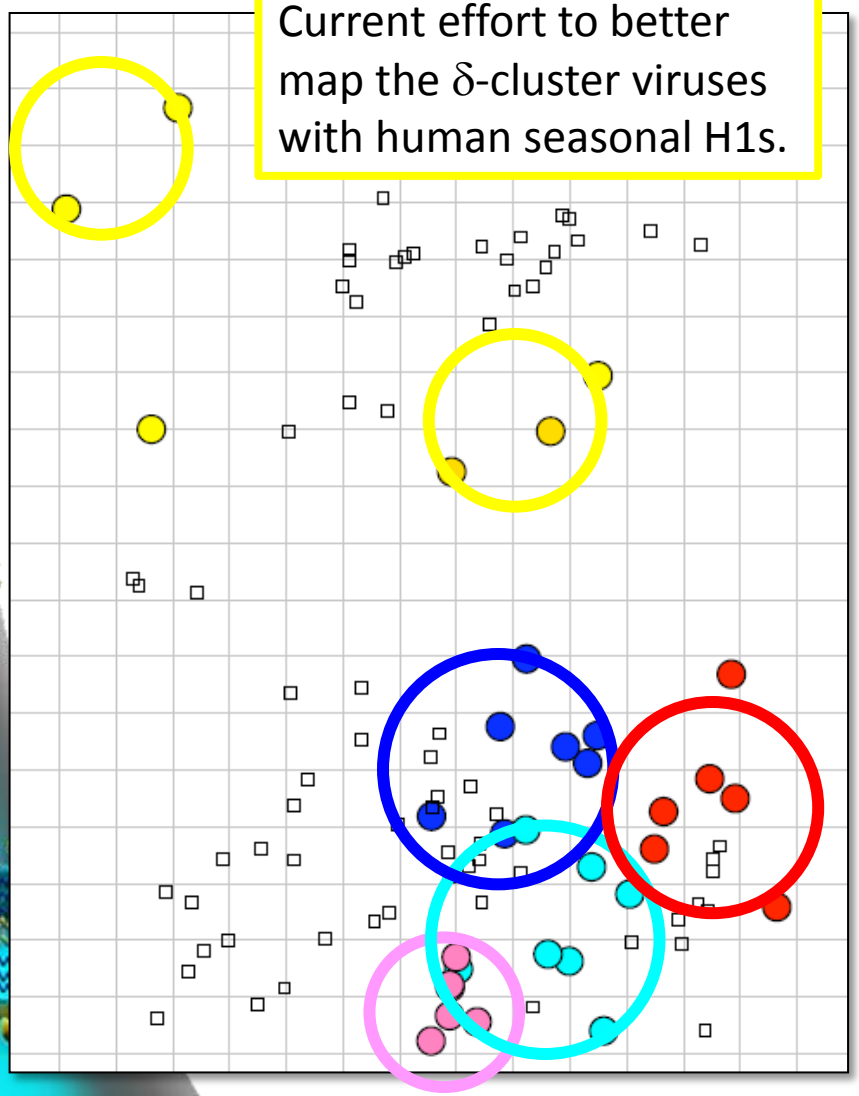
USDA SIV Surveillance by Subtype 10/1/2009-1/31/2012



Hemagglutinin Gene – Segment 4

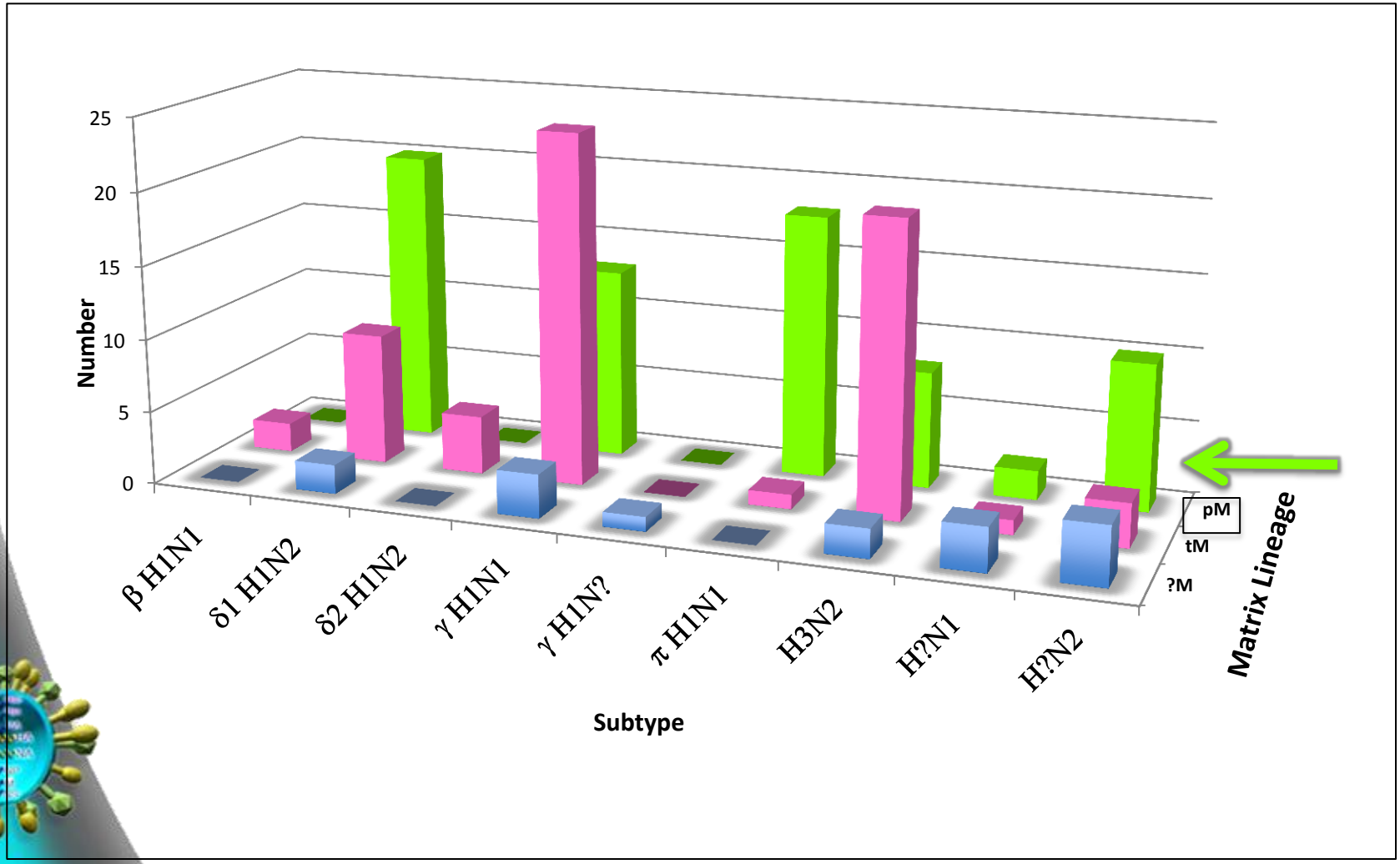


Antigenic Cartography – swine H1



- Cross-HI assays
  - α = classic-like
  - β = rH1-like swH1
  - γ = IN/00 or H1N2-like
  - δ = human-like
  - 2009 pH1N1
- Important for virus evolution, vaccine strain selection, HI antigen selection, etc.
- H1 serum panel shared among OFFLU SIV group members
- Plan to do H3 viruses this year
- Nicola Lewis

Reassortants with H1N1pdm09 M gene
USDA SIV Surveillance 2010-11



H3N2 + H1N1pdm09 Reassortants

H3N2 SIV 8 gene constellations 2009-2011

North American H3 and N2 human lineage
pandemic H1N1 origin
TRIG[a] avian lineage
TRIG swine lineage

Strain name	Host	PB2	PB1	PA	HA	NP	NA	M	NS
A/IN/08/2011[b]	human								
A/Sw/IL/A010201606/2011[b,c]	swine								
A/Sw/NY/A01104005/2011	swine								
A/Sw/IA/A01049750/2011	swine								
A/Sw/TX/A01049914/2011	swine								
A/Sw/TX/A01049915/2011	swine								
A/Sw/TX/A01049555/2011	swine								
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A/Sw/KS/11-101926/2011	swine								
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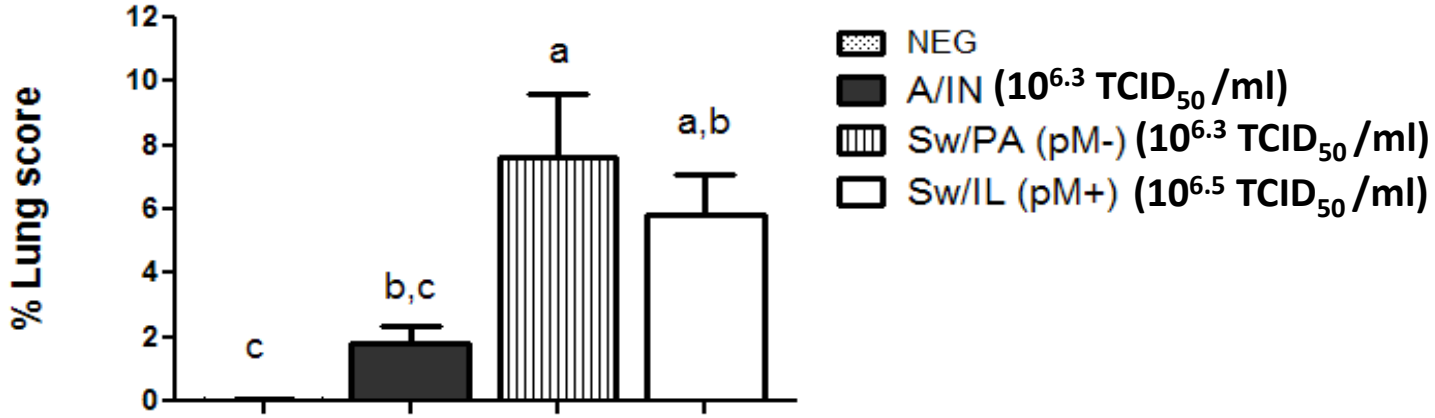
A/Sw/KS/11-107824/2011	swine								
A/Sw/KS/11-109700/2011	swine								
A/Sw/KS/11-110529/2011	swine								
A/Sw/KS/10-91088/2010	swine								
A/Sw/IA/A01049034/2010	swine								
A/Sw/IA/A01049035/2010	swine								
A/Sw/MN/239105/2009	swine								
A/Sw/PA/62170-1/2010[b]	swine								
A/Sw/IN/A01076191/2010	swine	*	*	*					
A/Sw/MN/A01076196/2010	swine								
A/Sw/NC/A01076199/2010	swine	*							
A/Sw/NC/A01076204/2010	swine								
A/Sw/NC/A01076212/2010	swine								
A/Sw/MN/A01076218/2010	swine	*							
A/Sw/NC/A01076178/2009	swine			*					

Select novel viruses for *in vivo* study



A/IN

Sw/PA

Sw/IL

H3N2 with TRIG was most virulent and efficient in transmission kinetics. H3N2v was least, but all 3 were pathogenic in swine. Unclear if there is a selective advantage for pM in swine.

VAERD

Vaccine-Associated Enhanced Respiratory Disease

- δ1-H1N2 vaccine with H1N1pdm09 H1N1 challenge
- Whole Virus Inactivated + Oil-in-Water Emulsion Adjuvant (KV)
- Naïve pigs, ~4 weeks of age
- 2 doses, 3 weeks apart
  - Intramuscular route
- Challenge 3 or 6 weeks post boost
  - Intratracheal route
  - Intranasal route
  - 10^3 or 10^5 $TCID_{50}$ challenge dose
- Monovalent or bivalent vaccines
  - Vaccines induces cross-reacting whole-virus antibodies that ***do not cross-react by HI or SN***

VAERD Vaccine Summary

	Monovalent KV	KV mismatch H1/H3	KV match-mismatch H1/H1	AdVV (IN or IM)	MLV
Cross-HI or SN Ab					
Cross-reacting IgG					
Cross-rxt mucosal IgA				IN	
Cross-reacting CMI					
Macroscopic pneumonia					
Microscopic pneumonia					
Tracheitis					
Nasal shedding					
Clinical Disease					

- Mechanism may be initiated by cross-reacting but non-neutralizing IgG antibody, but role of CMI not to be excluded.
  - Quality versus Quantity of immune response?
    - Ratio of HA2 to HA1 antibodies may be important
- Has real implications for the swine population with multiple subtype variants and vaccine practices.
  - Implications in humans?

Non-Protective/Enhanced	
Neutral	
Protective	
Unknown	

VAERD Model

Possible Mechanisms

- Dysregulated pro-inflammatory & antiviral response
- Neutrophil influx
- Complement activation
- Opsonized uptake of virus
- Cell Mediated Immunity (CTL)

Cause or Effect?