OFFLU swine influenza virus meeting
27 – 28 March 2017
FAO Headquarters, Rome, Italy

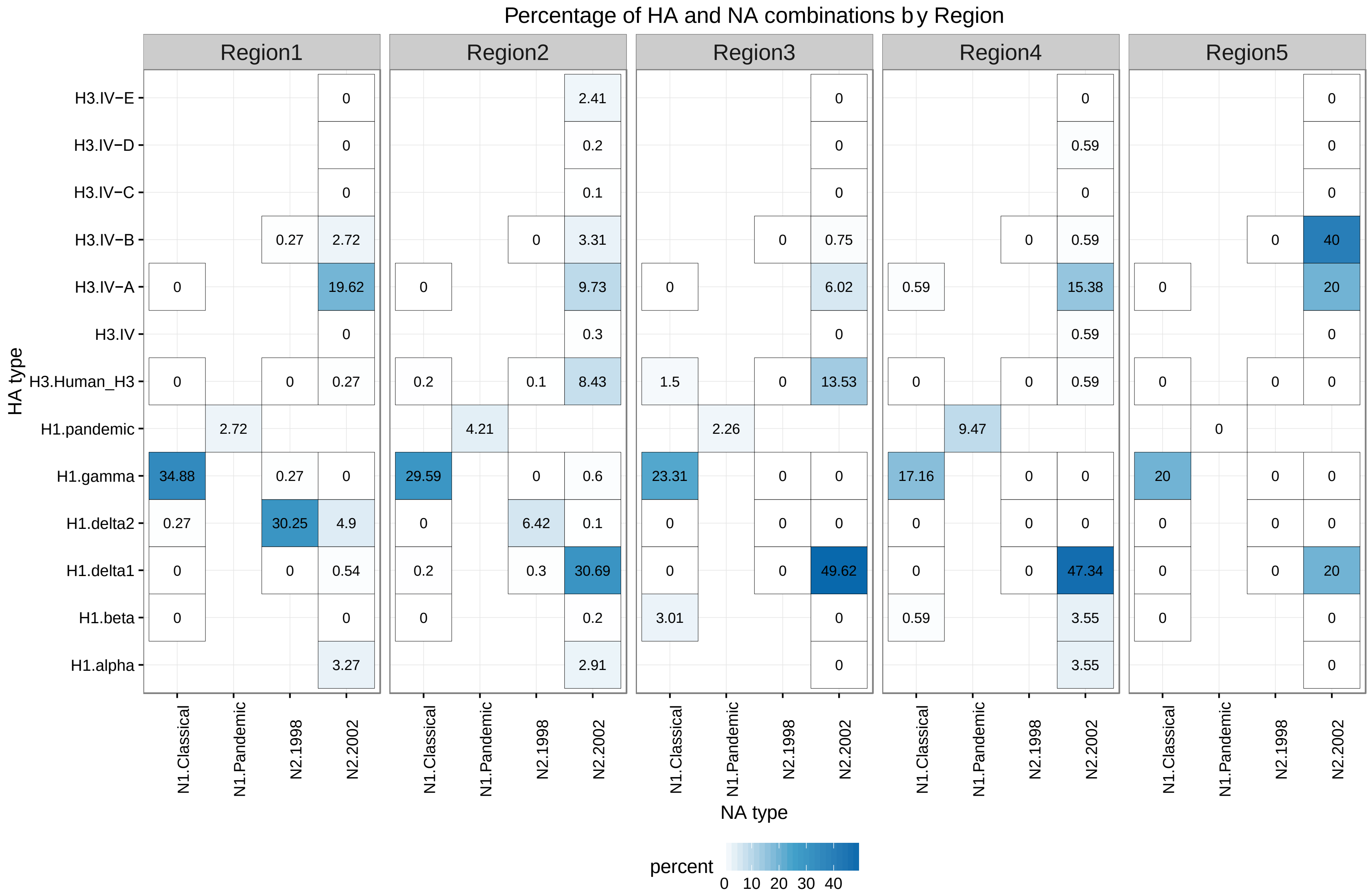
Amy Vincent
USDA-ARS
National Animal Disease Center

USDA IAV-S Surveillance
NADC Quarterly Summary – Q1FY17

- H1
  - Delta-1 and gamma viruses were the predominant H1
  - Continued detection of alpha with 2 aa deletions (n=9)
- H3
  - Human-like H3 was the predominant H3
    - Out of 33 H3s in Q1 FY17, 26 are Human-like H3s
    - Detection of human-like H3 in SD
- NA – N1, N2
  - Classical N1 represents 91% of N1 collections
  - 2002-lineage N2 represents 86% of N2 collections
  - 1998-lineage N2 paired with delta 2 H1

Rasna Walia

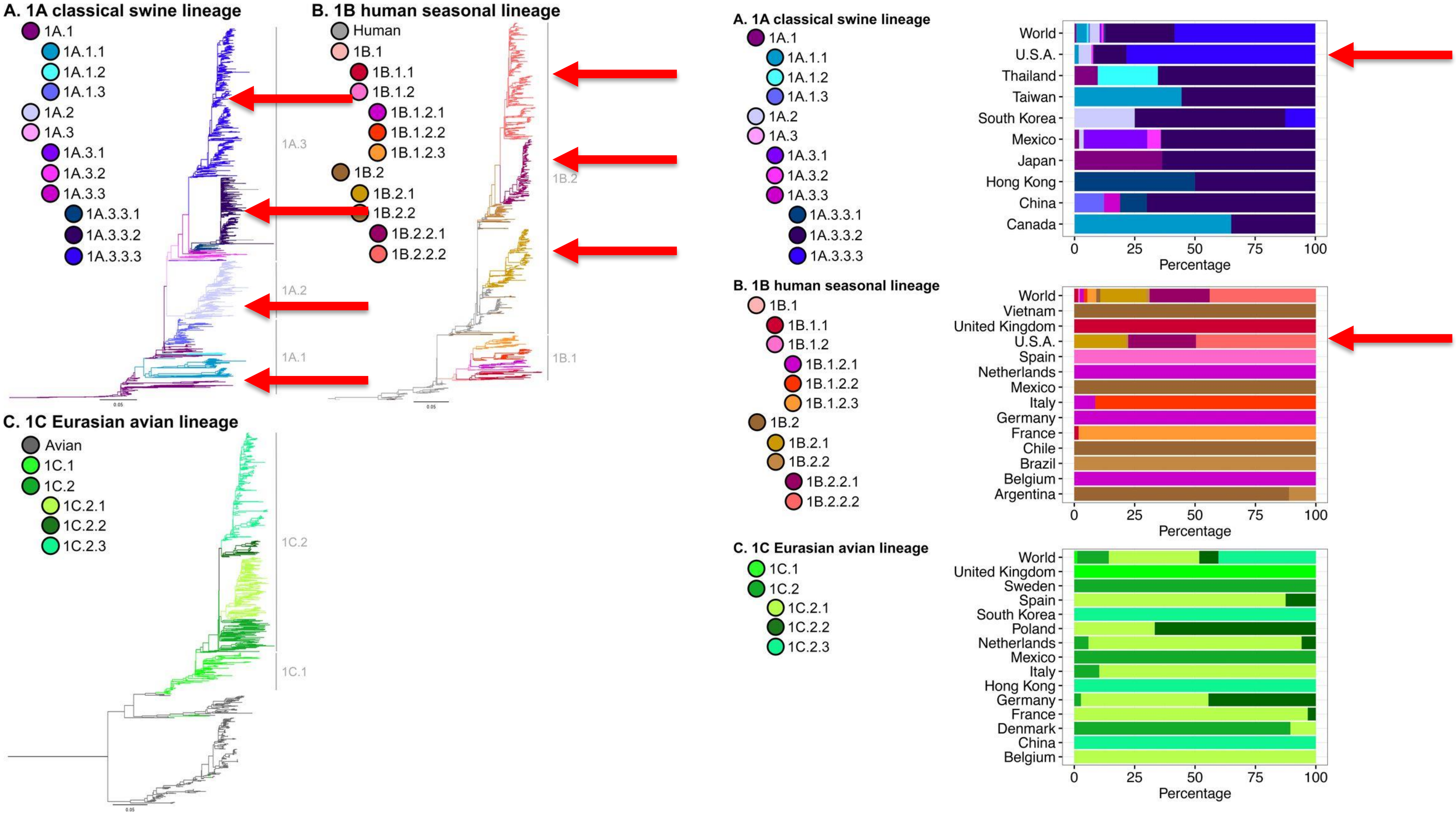
Regional Patterns 2014-16



HA type	Region1				Region2				Region3				Region4				Region5			
	N1.Classical	N1.Pandemic	N2.1998	N2.2002	N1.Classical	N1.Pandemic	N2.1998	N2.2002	N1.Classical	N1.Pandemic	N2.1998	N2.2002	N1.Classical	N1.Pandemic	N2.1998	N2.2002	N1.Classical	N1.Pandemic	N2.1998	N2.2002
H3.IV−E				0				2.41				0				0				0
H3.IV−D				0				0.2				0				0.59				0
H3.IV−C				0				0.1				0				0				0
H3.IV−B			0.27	2.72			0	3.31			0	0.75			0	0.59			0	40
H3.IV−A	0			19.62	0			9.73	0			6.02	0.59			15.38	0			20
H3.IV				0				0.3				0				0.59				0
H3.Human_H3	0		0	0.27	0.2		0.1	8.43	1.5		0	13.53	0		0	0.59	0		0	0
H1.pandemic		2.72				4.21				2.26				9.47				0		
H1.gamma	34.88		0.27	0	29.59		0	0.6	23.31		0	0	17.16		0	0	20		0	0
H1.delta2	0.27		30.25	4.9	0		6.42	0.1	0		0	0	0		0	0	0		0	0
H1.delta1	0		0	0.54	0.2		0.3	30.69	0		0	49.62	0		0	47.34	0		0	20
H1.beta	0			0	0			0.2	3.01			0	0.59			3.55	0			0
H1.alpha				3.27				2.91				0				3.55				0

Rasna Walia

Global distribution of swine H1 influenza A virus hemagglutinin clades from 2010 to present.



Tavis K. Anderson et al. mSphere 2016;1:e00275-16

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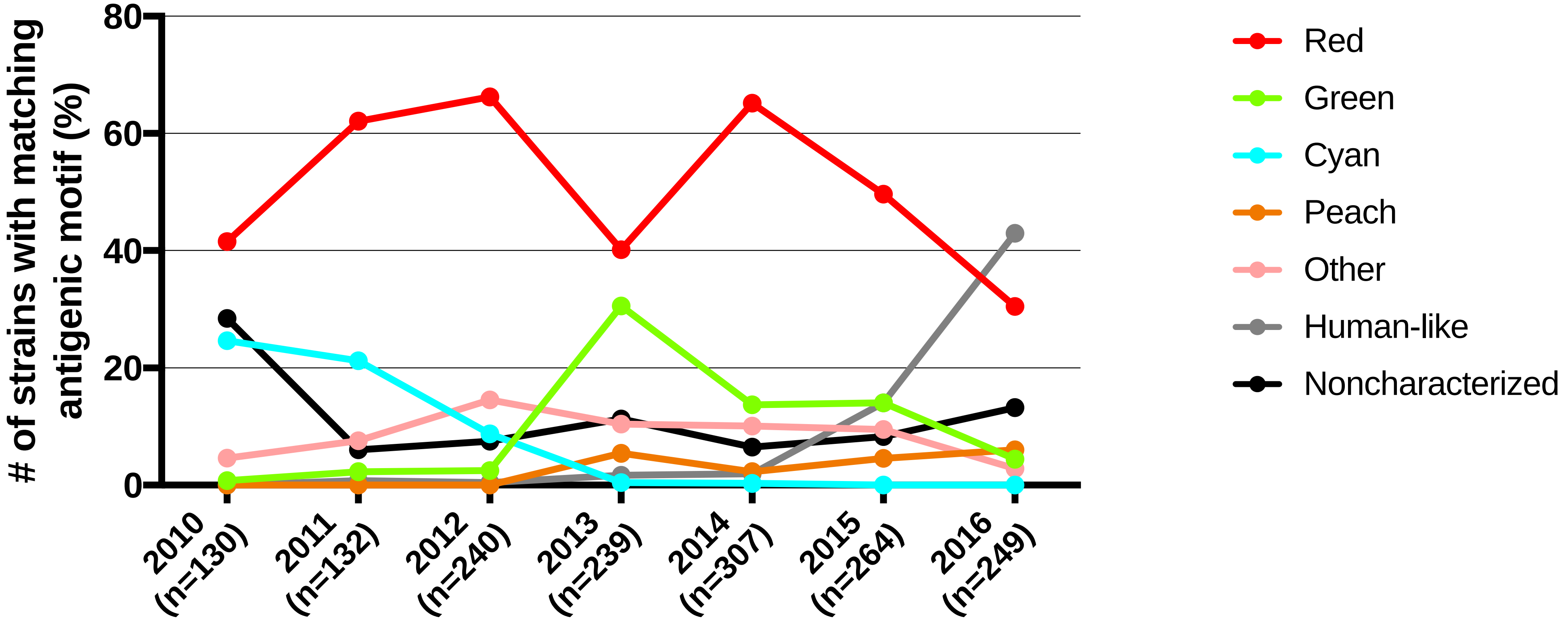
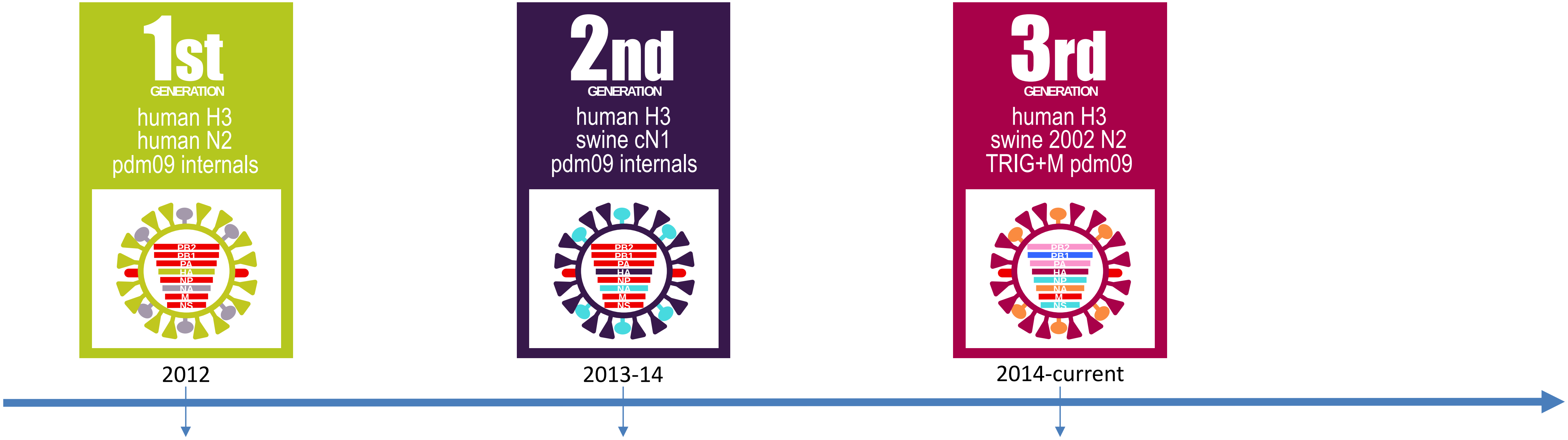
Temporal Dynamics of H3 Antigenic Motifs



- H3 IAV-S continue to evolve antigenically.
- Previously predominant red antigenic viruses are not as frequently detected.
- Human-like H3 IAV-S are emerging as the most frequently detected H3.
- Novel antigenically distinct viruses have emerged (KYHNNK/KHHNNK)

Marcus Bolton & Eugenio Abente

Reassortant H3N2 and H3N1 from human seasonal H3N2 introduction into swine



1st GENERATION
human H3
human N2
pdm09 internals

2012

2nd GENERATION
human H3
swine cN1
pdm09 internals

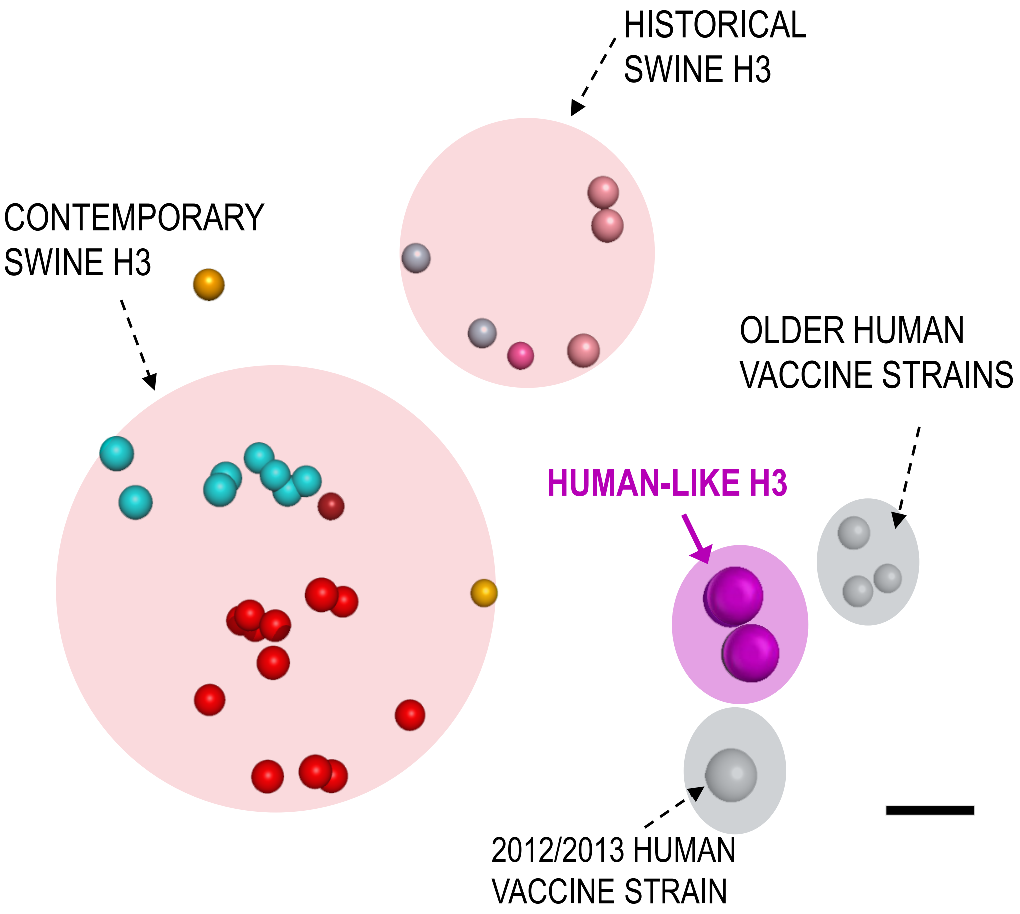
2013-14

3rd GENERATION
human H3
swine 2002 N2
TRIG+M pdm09

2014-current

There were over 100 detections of the 3rd genotype of human-like H3N2 in the USDA swine surveillance system since 2014. **This genotype also infected 16 humans in close contact with swine at fair exhibits in the summer of 2016.**

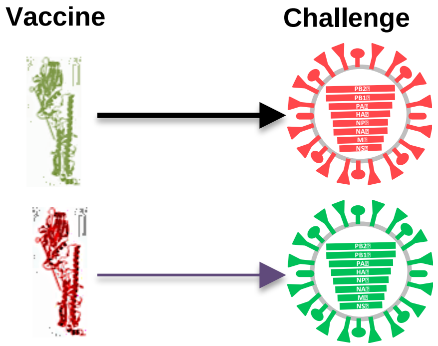
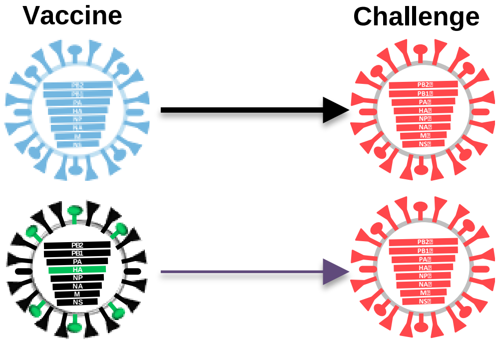
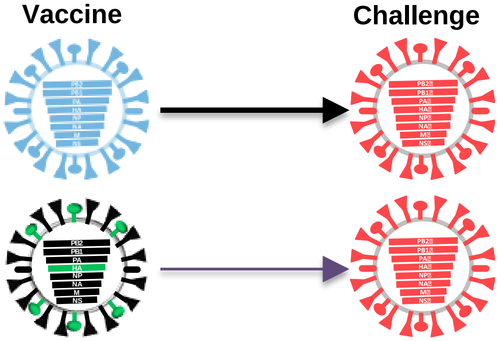
Antigenic distance of swine hu-like H3N2



16 H3N2v swine exhibit cases in 2016

Rajao et al. J. Virol. 2015

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)	-Not licensed in the USA -Possibility of reversion
			
	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	Sterilizing protection observed against challenge with an antigenically distinct virus

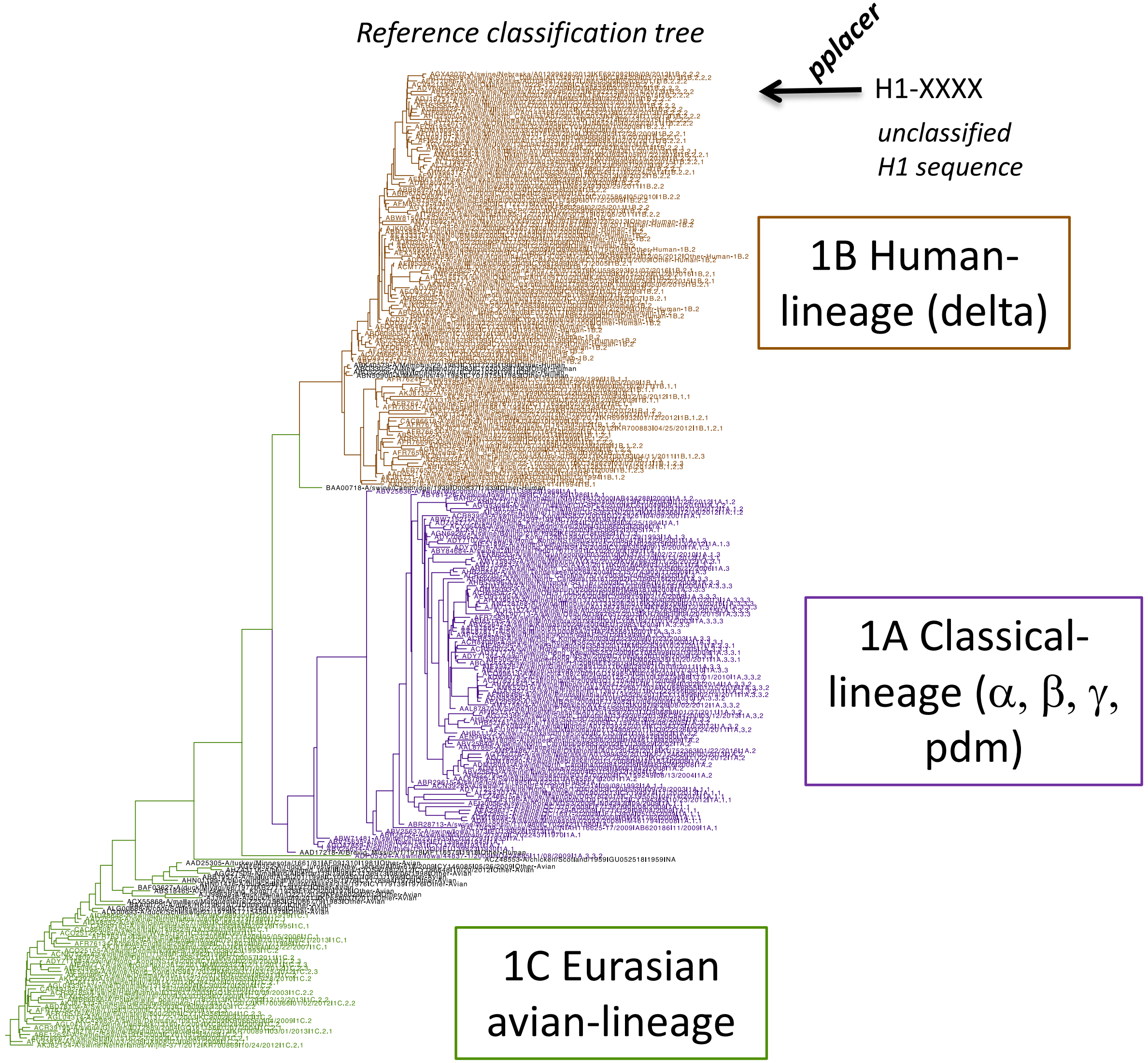
Eugenio Abente

Swine H1 clade classification (more from Tavis)

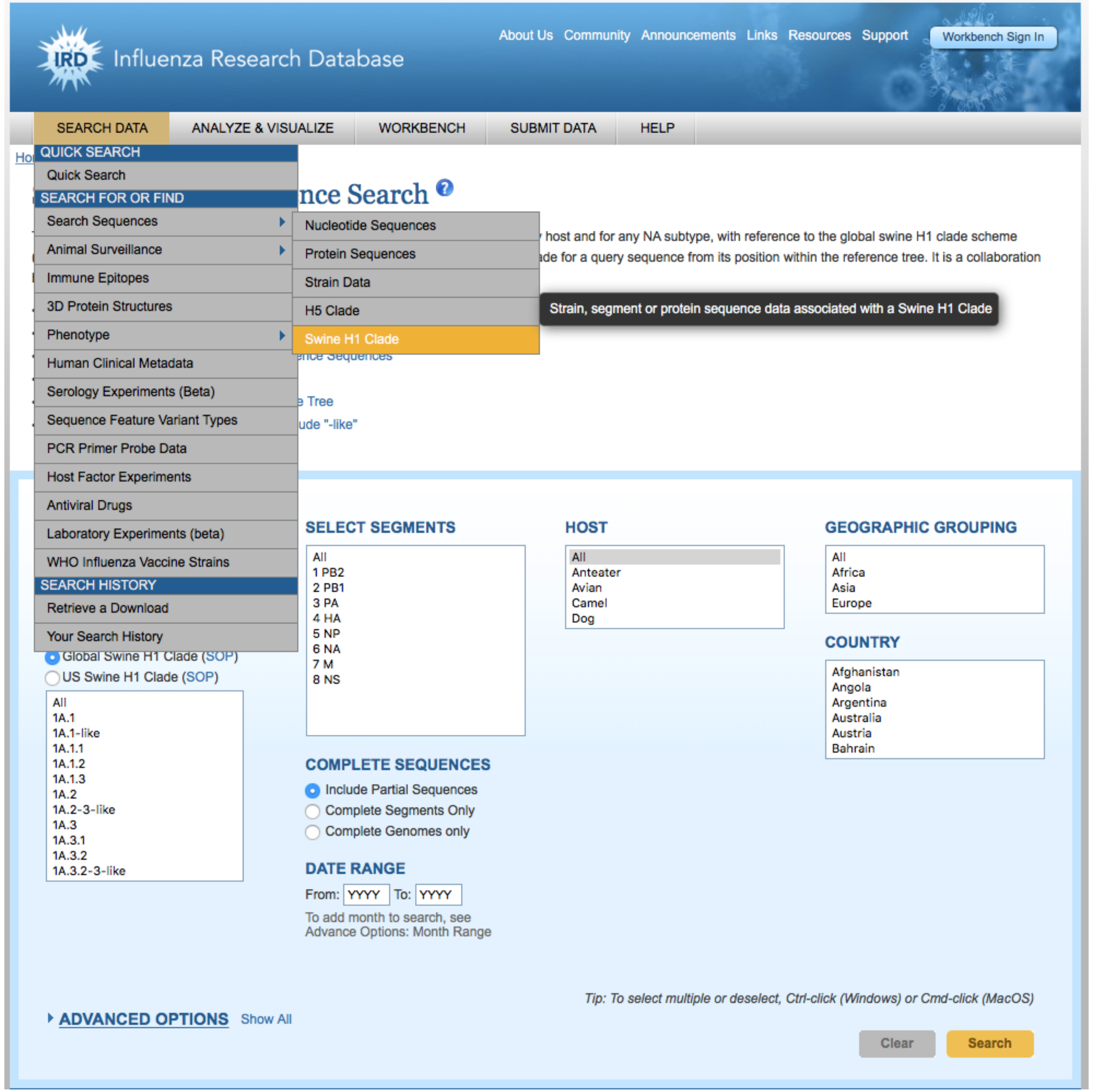
www.fludb.org

T. Anderson (USDA), C. Macken, Y. Zhang, R. Scheuermann

Reference classification tree



Anderson et al. MSphere, 2016; Zhang et al 2016



host and for any NA subtype, with reference to the global swine H1 clade scheme
ade for a query sequence from its position within the reference tree. It is a collaboration

Strain, segment or protein sequence data associated with a Swine H1 Clade

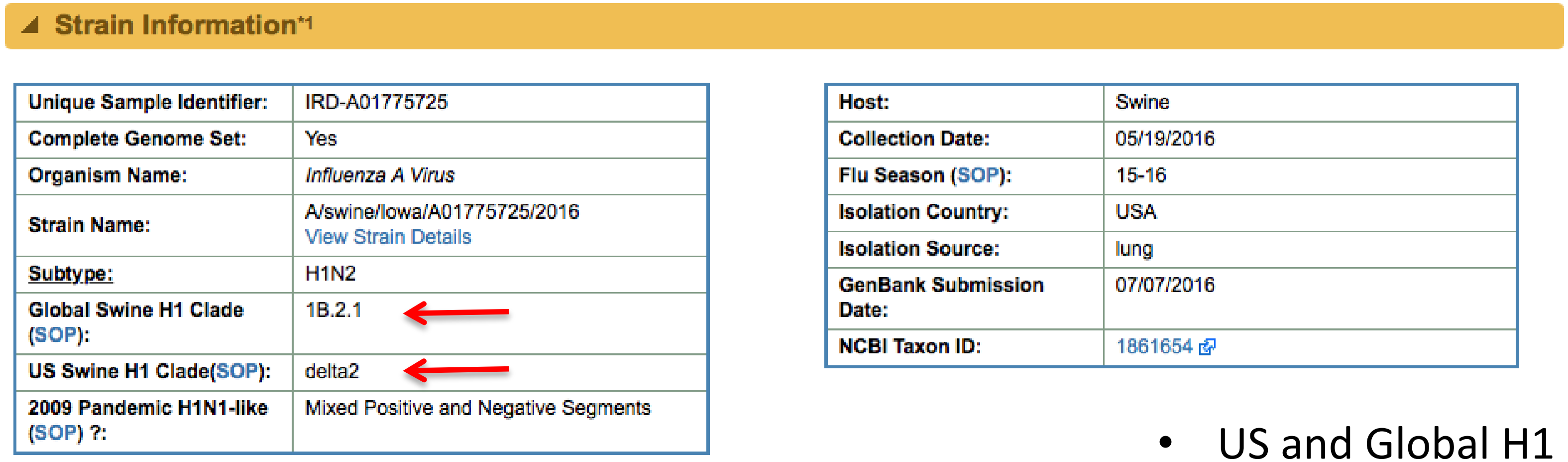
To add month to search, see Advance Options: Month Range

Tip: To select multiple or deselect, Ctrl-click (Windows) or Cmd-click (MacOS)

IRD H1 Clade Tool Interfaces

Strain Detail Page

Pre-computed annotations for ***all H1 viruses in all hosts***



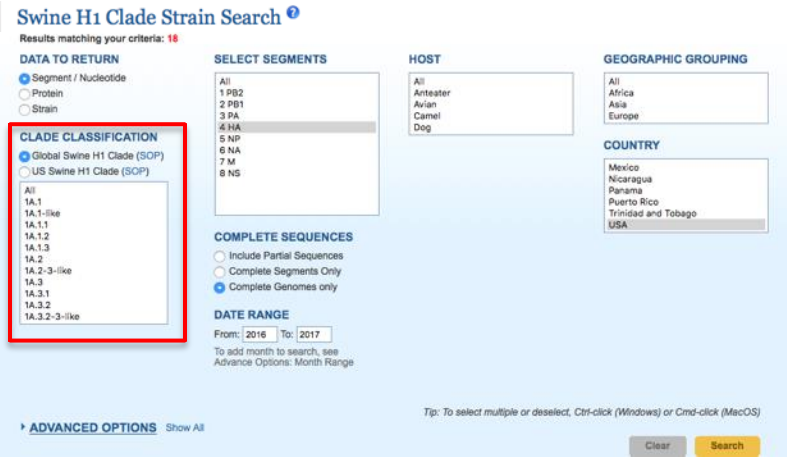
Strain Information*1

Unique Sample Identifier:	IRD-A01775725
Complete Genome Set:	Yes
Organism Name:	*Influenza A Virus*
Strain Name:	A/swine/Iowa/A01775725/2016 View Strain Details
Subtype:	H1N2
Global Swine H1 Clade (SOP):	1B.2.1
US Swine H1 Clade(SOP):	delta2
2009 Pandemic H1N1-like (SOP) ?:	Mixed Positive and Negative Segments

Host:	Swine
Collection Date:	05/19/2016
Flu Season (SOP):	15-16
Isolation Country:	USA
Isolation Source:	lung
GenBank Submission Date:	07/07/2016
NCBI Taxon ID:	1861654

Search Data Menu

Clade-specific strain/segment /protein search



Swine H1 Clade Strain Search

Results matching your criteria: 18

DATA TO RETURN: ● Segment / Nucleotide ○ Protein ○ Strain

CLADE CLASSIFICATION: ● Global Swine H1 Clade (SOP) ○ US Swine H1 Clade (SOP)

SELECT SEGMENTS: 4 HA

COUNTRY: USA

COMPLETE SEQUENCES: ○ Include Partial Sequences ○ Complete Segments Only ● Complete Genomes only

DATE RANGE: From: 2016 To: 2017

To add month to search, see Advance Options: Month Range

Tip: To select multiple or deselect, Ctrl-click (Windows) or Cmd-click (MacOS)

Analyze Tool Menu

Clade assignment of user sequences

Swine H1 Clade Classification Tool

ANALYSIS NAME

INPUT SEQUENCES

○ Upload a file containing my sequences in FASTA format.

○ Paste sequences in FASTA format.

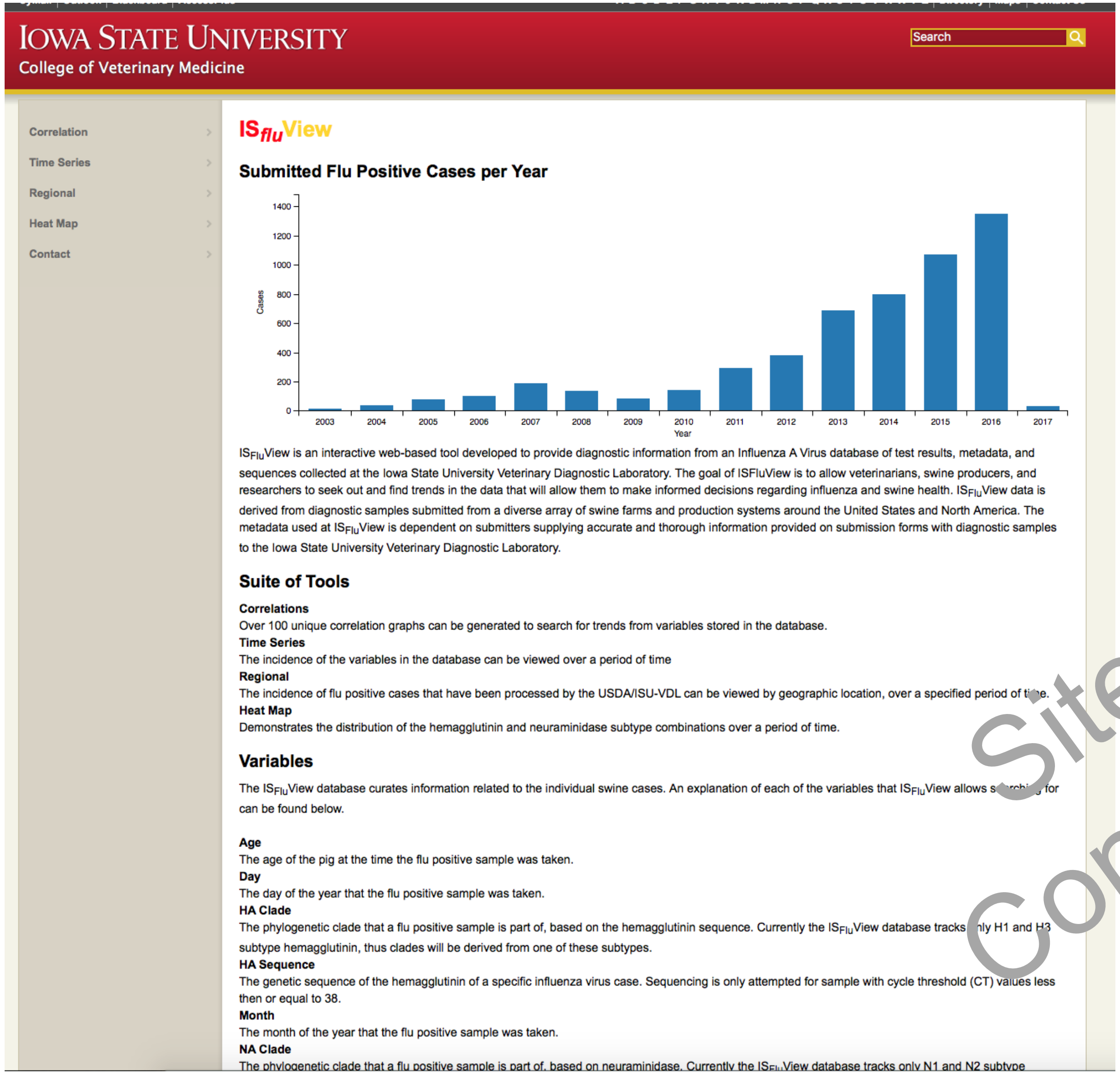
○ Analyze my custom sequences and associated metadata with IRD/ViPR sequences.

Upload your sequence file to the workbench.

- US and Global H1 clade tools are both available.
- Strain information annotated with both US and Global H1 designation for all H1.
- Can be used to search for viruses in certain clades:
  - Do US and Mexico share similar H1?
- Can be used to annotate your own unknown sequence:
  - What clade is my diagnostic HA sequence?

Anderson et al. MSphere, 2016

ISU Influenza Cases: http://influenza.cvm.iastate.edu



Submitted Flu Positive Cases per Year

IS$_{Flu}$View is an interactive web-based tool developed to provide diagnostic information from an Influenza A Virus database of test results, metadata, and sequences collected at the Iowa State University Veterinary Diagnostic Laboratory. The goal of ISFluView is to allow veterinarians, swine producers, and researchers to seek out and find trends in the data that will allow them to make informed decisions regarding influenza and swine health. IS$_{Flu}$View data is derived from diagnostic samples submitted from a diverse array of swine farms and production systems around the United States and North America. The metadata used at IS$_{Flu}$View is dependent on submitters supplying accurate and thorough information provided on submission forms with diagnostic samples to the Iowa State University Veterinary Diagnostic Laboratory.

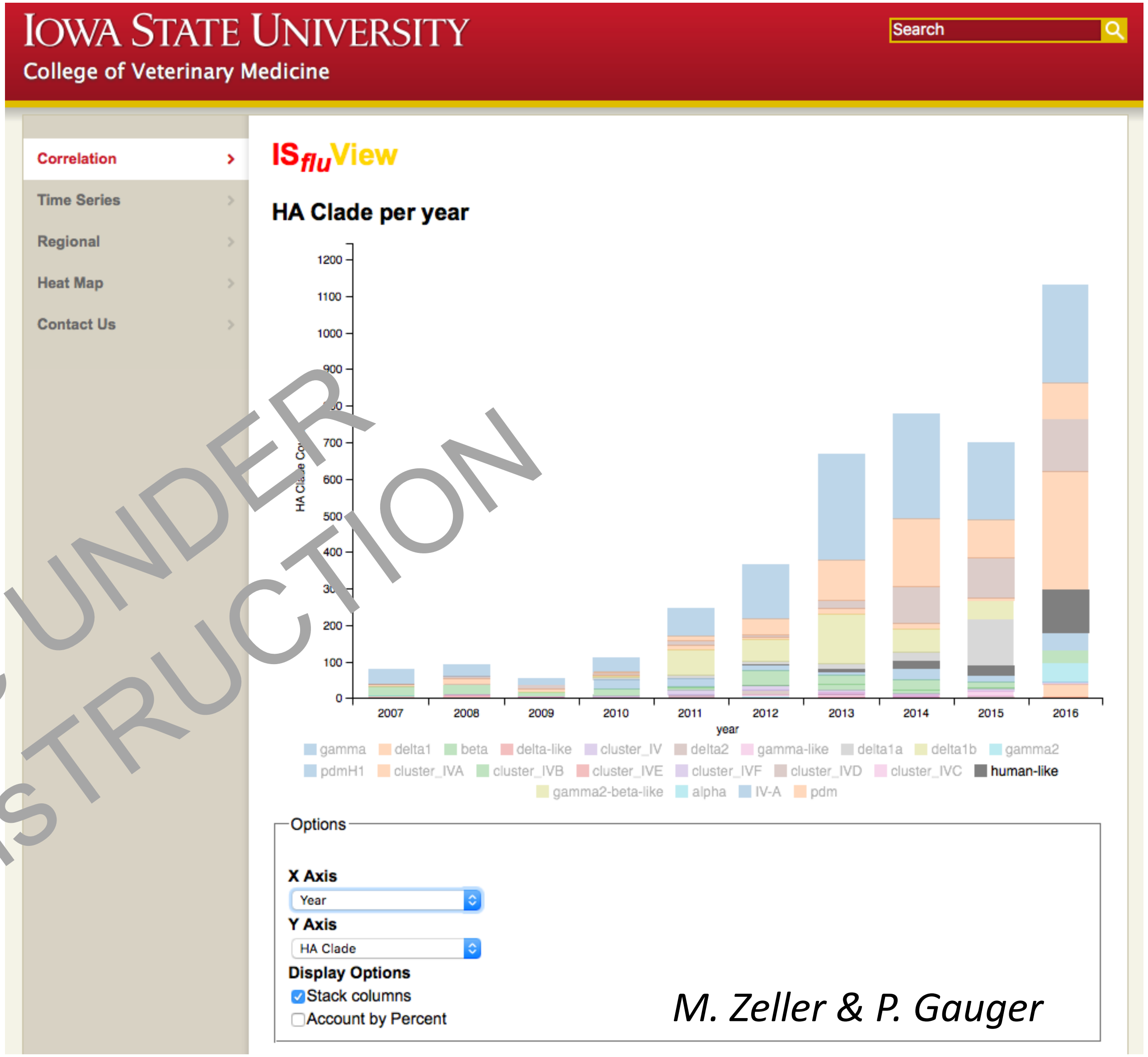
Suite of Tools

Correlations
Over 100 unique correlation graphs can be generated to search for trends from variables stored in the database.
Time Series
The incidence of the variables in the database can be viewed over a period of time
Regional
The incidence of flu positive cases that have been processed by the USDA/ISU-VDL can be viewed by geographic location, over a specified period of time.
Heat Map
Demonstrates the distribution of the hemagglutinin and neuraminidase subtype combinations over a period of time.

Variables

The IS$_{Flu}$View database curates information related to the individual swine cases. An explanation of each of the variables that IS$_{Flu}$View allows searching for can be found below.

Age
The age of the pig at the time the flu positive sample was taken.
Day
The day of the year that the flu positive sample was taken.
HA Clade
The phylogenetic clade that a flu positive sample is part of, based on the hemagglutinin sequence. Currently the IS$_{Flu}$View database tracks only H1 and H3 subtype hemagglutinin, thus clades will be derived from one of these subtypes.
HA Sequence
The genetic sequence of the hemagglutinin of a specific influenza virus case. Sequencing is only attempted for sample with cycle threshold (CT) values less then or equal to 38.
Month
The month of the year that the flu positive sample was taken.
NA Clade
The phylogenetic clade that a flu positive sample is part of, based on neuraminidase. Currently the IS$_{Flu}$View database tracks only N1 and N2 subtype



HA Clade per year

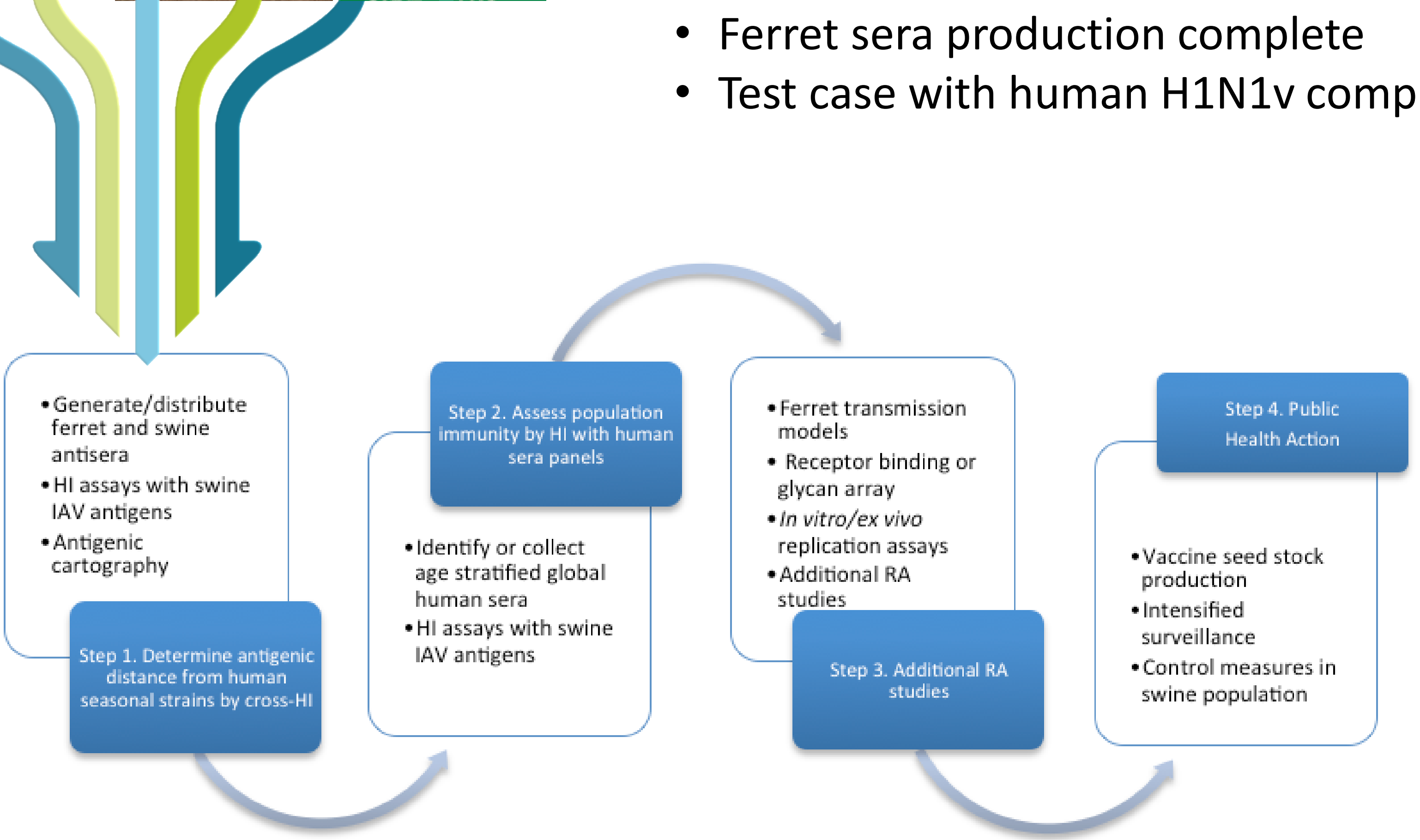
Options

X Axis
Year
Y Axis
HA Clade
Display Options
☑ Stack columns
☐ Account by Percent

M. Zeller & P. Gauger

Swine Risk Assessment Pipeline

- **2016 Accomplishments: Generation of swine and ferret antisera**
  - Swine sera generated, HI in progress
  - H3 HI completed with swine sera
  - Ferret sera production complete
  - Test case with human H1N1v completed with swine sera



Step 1. Determine antigenic distance from human seasonal strains by cross-HI

- Generate/distribute ferret and swine antisera
- HI assays with swine IAV antigens
- Antigenic cartography

Step 2. Assess population immunity by HI with human sera panels

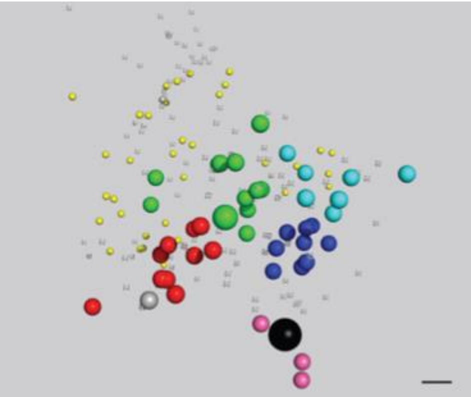
- Identify or collect age stratified global human sera
- HI assays with swine IAV antigens

Step 3. Additional RA studies

- Ferret transmission models
- Receptor binding or glycan array
- *In vitro/ex vivo* replication assays
- Additional RA studies

Step 4. Public Health Action

- Vaccine seed stock production
- Intensified surveillance
- Control measures in swine population



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