OFFLU Swine Influenza Virus Regional Meeting

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XXIX Brazilian Virology Congress and XIII Mercosul Virology Meeting
Gramado, RS, Brazil

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USA

Team and collaborators

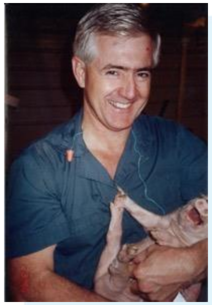
Vincent Lab team

- Carine K. Souza (Antigenic Cartography)
- Brian Kimble (Antigenic Cartography)
- Tavis Anderson (Bioinformatics)
- Jennifer Chang (Bioinformatics)
- Bryan Kaplan (NA Antigenic Cartography)

National Animal Disease Center - USDA

Collaborators

- Nicola Lewis (Royal Veterinary College)
- Divya Venkatesh (University of Cambridge)
- Ignacio Mena, Randy Albrecht and Adolfo García-Sastre (Mount Sinai)
- Gaelle Simon (ANSES, France)
- Susan Detmer (University of Saskatchewan)
- Martha Nelson (NIH)
- Marie Culhane (UMN)
- Daniel Perez and Daniela Rajão (UGA)
- Richard Webby and Scott Krauss (St Jude)



Typical pig flow in a commercial farm in USA

All in, All out by farrowing room – piglets weaned offsite

Multiplier – Gilt Developer
Replacement Gilts/boars

Replacement Gilts

ISOL

Breeding and Gestation

Boar Stud Semen

Farrowing Building

This farm structure represents ~70% of the U.S. industry.

Weaned piglets to Offsite Nursery or Wean-to-Finish, often over large distances

Cull Sows & Boars comingled with others at Abattoir or Buying Stations

Variant IAV

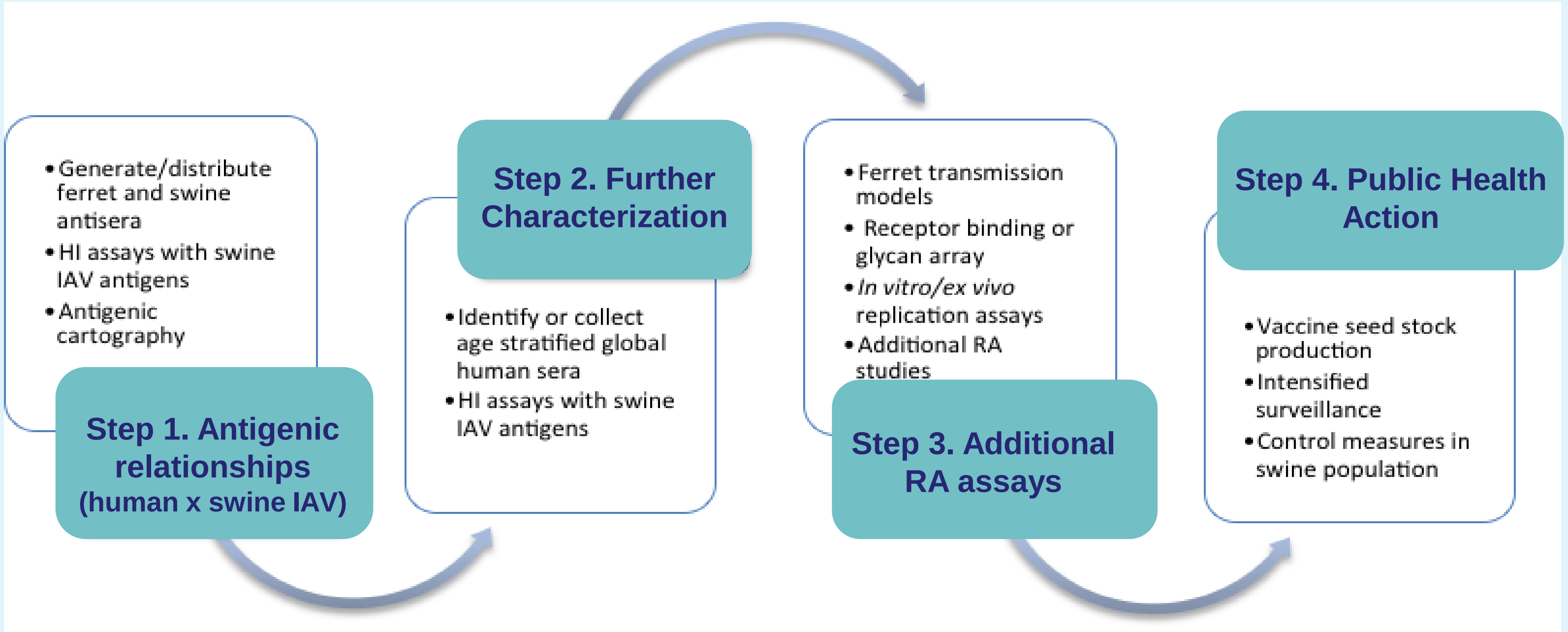
- When a swine-lineage IAV is detected in humans, it is called **“variant”** to distinguish it from human seasonal and avian lineages (e.g. H3N2v).
- Non-seasonal detections became reportable to WHO under the International Health Regulations in **2007**.
- In response, the CDC developed PCR tests implemented in public health labs to differentiate variant IAV from seasonal IAV and created a Zoonotic Virus Team.
  - 485 total variant detections of H3N2, H1N1 and H1N2 subtypes.
  - 309 variants were H3N2v detected in 2012 – swine exhibits identified as a “hot spot.”
- Variants tend to be dead end with limited human to human transmission.
- CDC routinely checks cross-reactivity of variants against ferret anti-sera to seasonal vaccine strains and human population sera.
  - Children born after 2001 had limited immunity to C-IV origin H3N2v.
- The CDC presents this data at the WHO vaccine consultation meetings.
  - ~9 variants from the US selected as pandemic preparedness candidate vaccine viruses (along with Eurasian swine H1N1 and several avian influenza strains).

CEIRS
Centers of Excellence for Influenza Research and Surveillance

Pipeline

Swine Influenza Risk Assessment

- Except for variant viruses, antigenic relationships between swine and human seasonal IAV are not systematically evaluated to inform potential risk to public health.



Step 1. Antigenic relationships (human x swine IAV)

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

Step 2. Further Characterization

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

Step 3. Additional RA assays

- 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

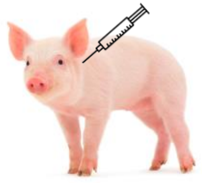
Objectives

- Quantify antigenic distance between contemporary swine IAV strains and human seasonal vaccine strains using a panel of monovalent anti-sera raised in pigs.

- Identify swine viruses against which the human population would lack cross-reactive HI antibodies for further characterization.

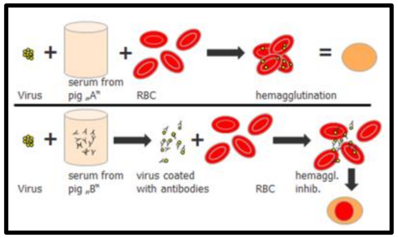
Methods for Pipeline

Anti-sera production



- WIV immunization
- Blood collection: minimum reciprocal HI titer required ≥ 160

HI assays

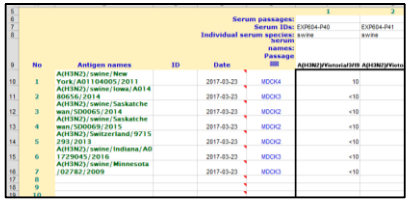


- Selection of strains and anti-sera

HI results in AC tables

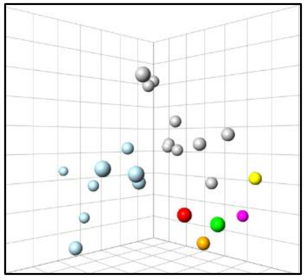
anti-sera

antigens



				Serum passages:		
				Serum IDs:	EXP604-P40	EXP604-P41
				Individual serum species:	swine	swine
				Serum names:		
No	Antigen names	ID	Date	Passage	A(H3N2)/Victoria/3/	A(H3N2)/Victo
1	A(H3N2)/swine/New York/A01104005/2011		2017-03-23	MDCK4	10	
2	A(H3N2)/swine/Iowa/A01480656/2014		2017-03-23	MDCK3	<10	
3	A(H3N2)/swine/Saskatchewan/SD0065/2014		2017-03-23	MDCK2	<10	
4	A(H3N2)/swine/Saskatchewan/SD0069/2015		2017-03-23	MDCK2	<10	
5	A(H3N2)/Switzerland/9715293/2013		2017-03-23	MDCK2	<10	
6	A(H3N2)/swine/Indiana/A01729045/2016		2017-03-23	MDCK3	<10	
7	A(H3N2)/swine/Minnesota/02782/2009		2017-03-23	MDCK3	<10	
8						
9						
10						

HI data
3-D visualization



acmacs-web.antigenic-cartography.org

- 1AU = 2-fold loss in HI cross-reactivity
- 3AU = significant antigenic drift or distance

Panel of anti-sera raised in pigs against human seasonal IAV vaccine strains by decade

	70s	80s	90s	2000s	2010s
H1	A/USSR/unkown/77 A/Brazil/11/78	A/Chile/1/83 A/Singapore/unkown/86 A/Taiwan/1/86	A/Texas/36/91 A/Beijing/262/95 A/New Caledonia/20/99	A/Michigan/02/03 A/Solomon Islands/3/06 A/Brisbane/59/07 A/California/04/09	A/Michigan/45/15
H3	A/Port Chalmers/1/73 A/Victoria/3/75 A/Texas/1/77 A/Bangkok/01/79	A/Philippines/2/82 A/Leningrad/360/86 A/Shanghai/11/87 A/Sichuan/02/87 A/Beijing/353/89	A/Beijing/32/92 A/Wuhan/359/95 A/Sydney/5/97	A/Moscow/10/99 A/Fujian/411/02 A/Wisconsin/67/05 A/Brisbane/10/07 A/Perth/16/09	A/Victoria/361/11 A/Switzerland/9715293/13 A/Hong Kong/4801/14

Main results

- North American 1A.1 α and 1B δ strains lineage had substantial distance from recent human vaccine strains (8-13 AU).
- H1 1A.3.3 γ and pdm strains (2010-13) were antigenically related to the current human vaccine strains, while later strains (2014-16), including a human variant (A/Ohio/9/2015), were 4-5 AU away.

- Swine H3.1990 strains are antigenically distinct from recent human vaccine strains, while H3.2010 lineages demonstrated closer antigenic relationships to recent human vaccine strains from late 2000 and early 2010 decades.

Ongoing and Future projects

- Continual addition of contemporary swine strains.
- Comparison between swine and ferret sera in HI assays and antigenic maps.
- Selection of strains for antigenic characterization using age stratified human sera.
  - These data may indicate loss in cross-reactivity to human vaccine strains and reduced human population immunity stratified by age demographics and can be used to identify swine IAV for further risk analysis.

USDA-ARS NADC Contributions to the Latin American Group

- USDA conducts the most comprehensive national surveillance of IAV in swine with standardized lab methods and data sharing processes.
- Sequence analysis (Anderson & Chang):
  - Incorporation of surveillance data from new regions for N. and S. America comprehensive analyses
  - Global H1 and H3 nomenclature
  - Selection of representative strains for antigenic characterization
- Panel of swine antisera for antigenic characterization:
  - Use of consistent anti-sera and reference antigens allows new data to be merged with previous data for regional/global maps and to monitor antigenic evolution over time.
  - Comparison of swine antigens among and between regions, as well as quantitative measure of antigenic distance between swine strains and human vaccine strains.
- Antigenic data analysis and data synthesis in collaboration with Nicola Lewis at Royal Veterinary College in the UK.

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- Keiko Sampson
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Collaborators

- Nicola Lewis
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- Daniel Perez
- Daniela Rajão
- Ignacio Mena
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- Randy Albrecht
- Richard Webby
- Scott Krauss

NAHLN Labs

U.S. Producers and Swine Vets

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CEIRS

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