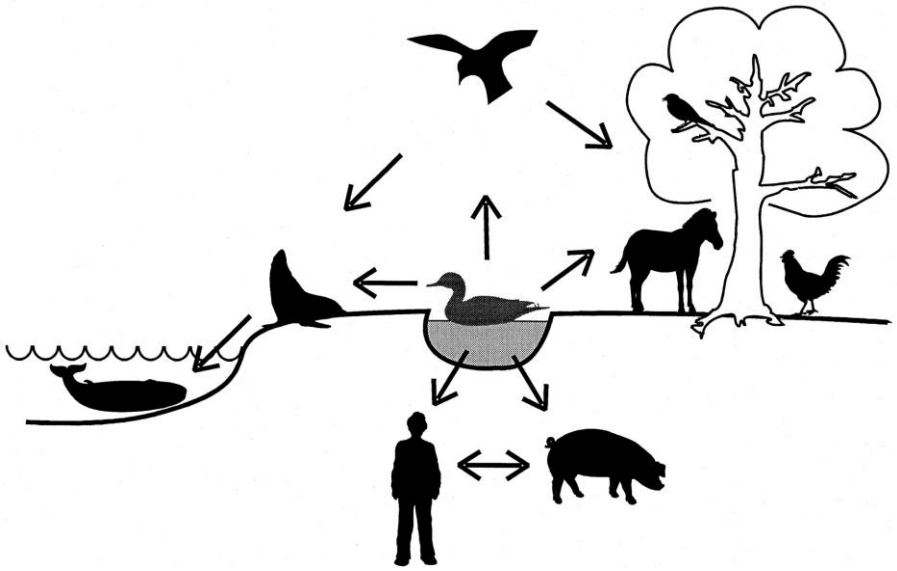
Swine influenza A viruses: a more global picture

Dr Nicola S. Lewis BSc BVetMed PhD MRCVS

Centre for Pathogen Evolution and WHO Collaborating Centre
for Modeling and Control of Emerging Infectious Diseases

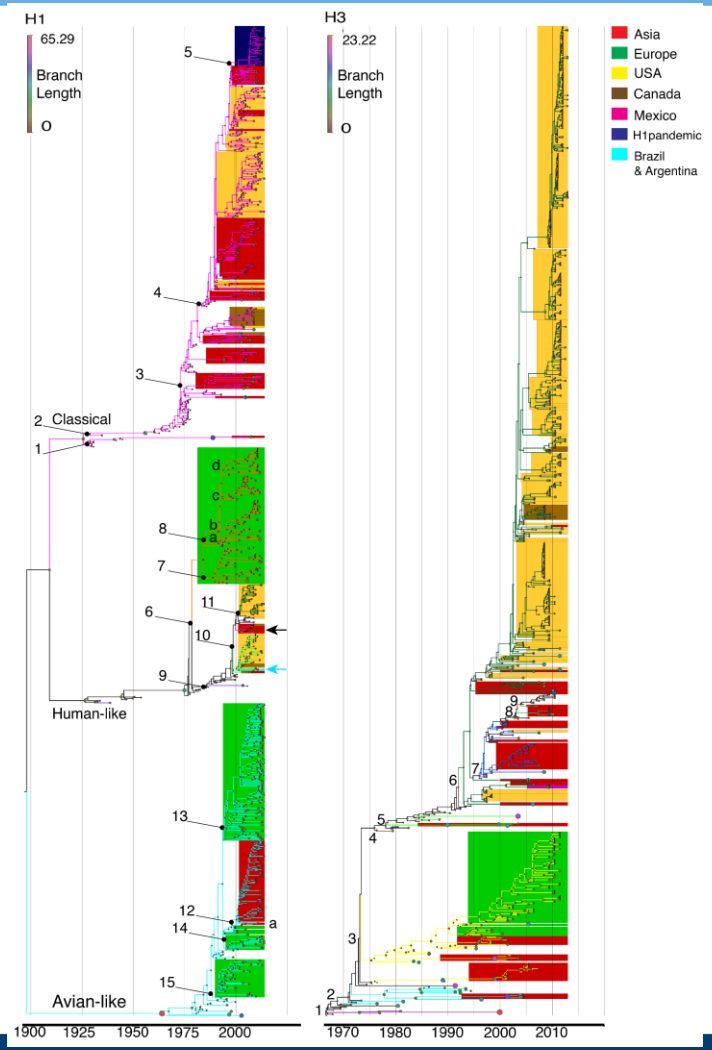
Department of Zoology
University of Cambridge

Antigenic and genetic diversity



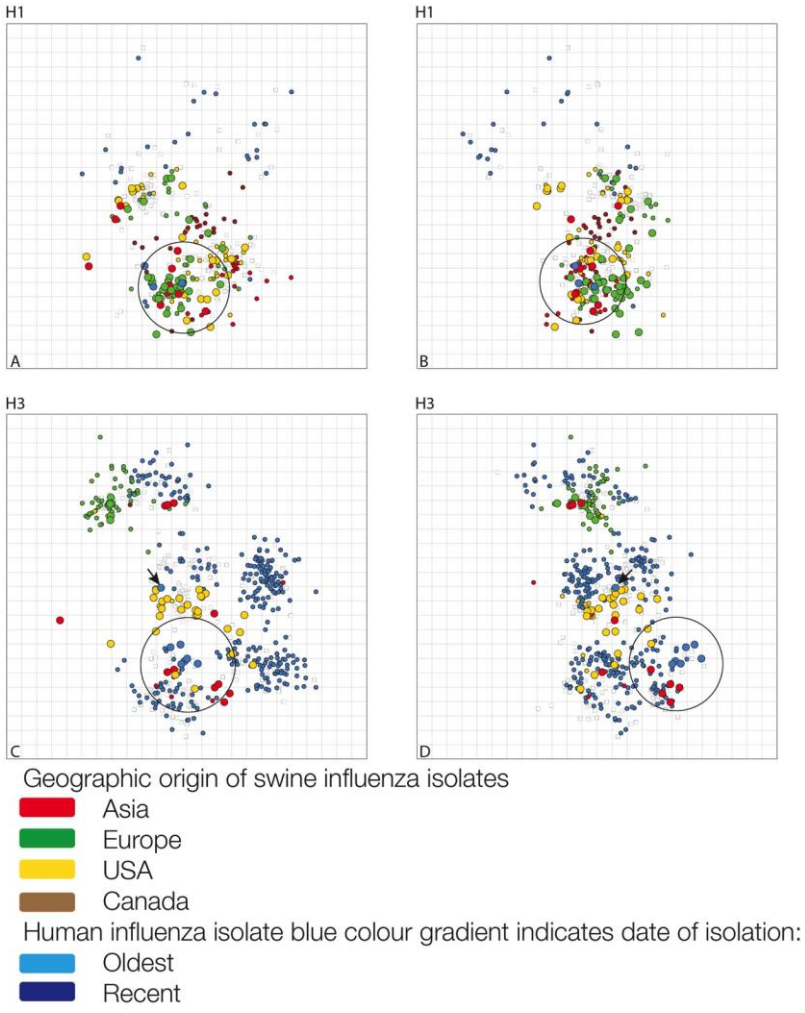
Reservoirs of infection
Drivers of emergence
Transmission and disease

Estimated dates of introduction



Lewis et al., submitted

Phenotype analyses



Comparative analyses of factors involved ecology and evolution of swine IAV
Herd-level and structure, age, immune status/vaccination, between and among countries/regions

Relative human-swine contact rates in different production systems

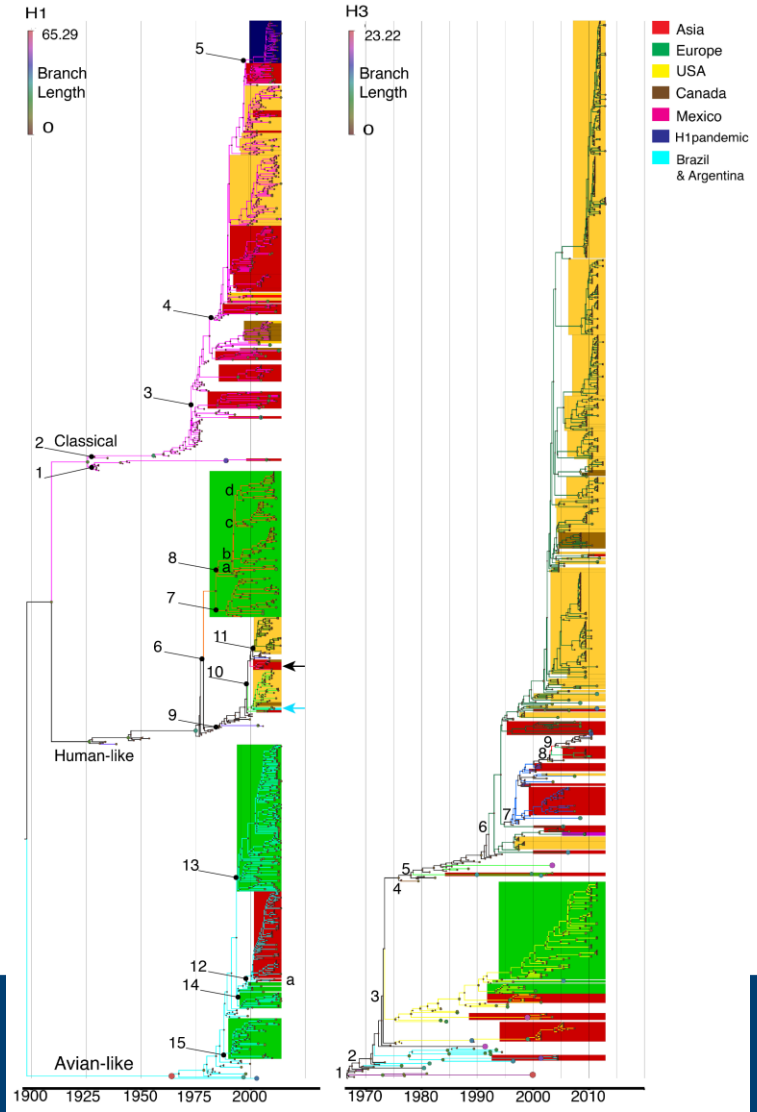
Vaccine efficacy (formulation and use), strain selection

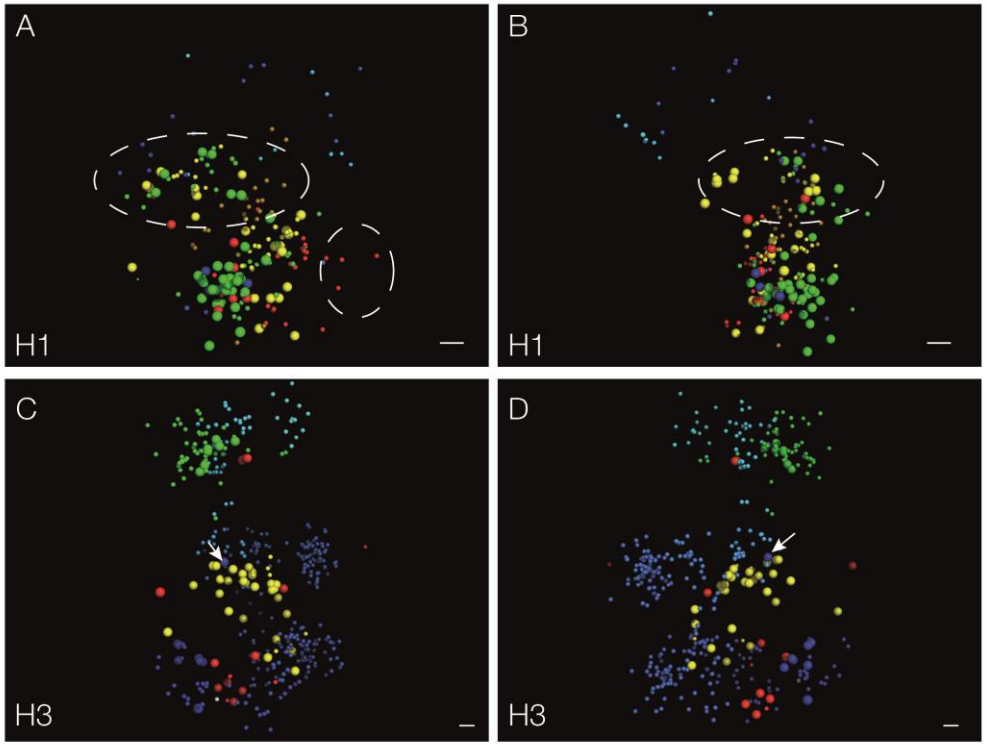
Competition among subtypes/ within-subtype variants

Relative risk of introduction to other pig pu populations and to humans

Swine Influenza- Pandemic Threats Concept

Dr Amy Vincent (USDA)
Dr Nicola Lewis (University of Cambridge)
Adolfo Garcia-Sastre (Mt. Sinai)





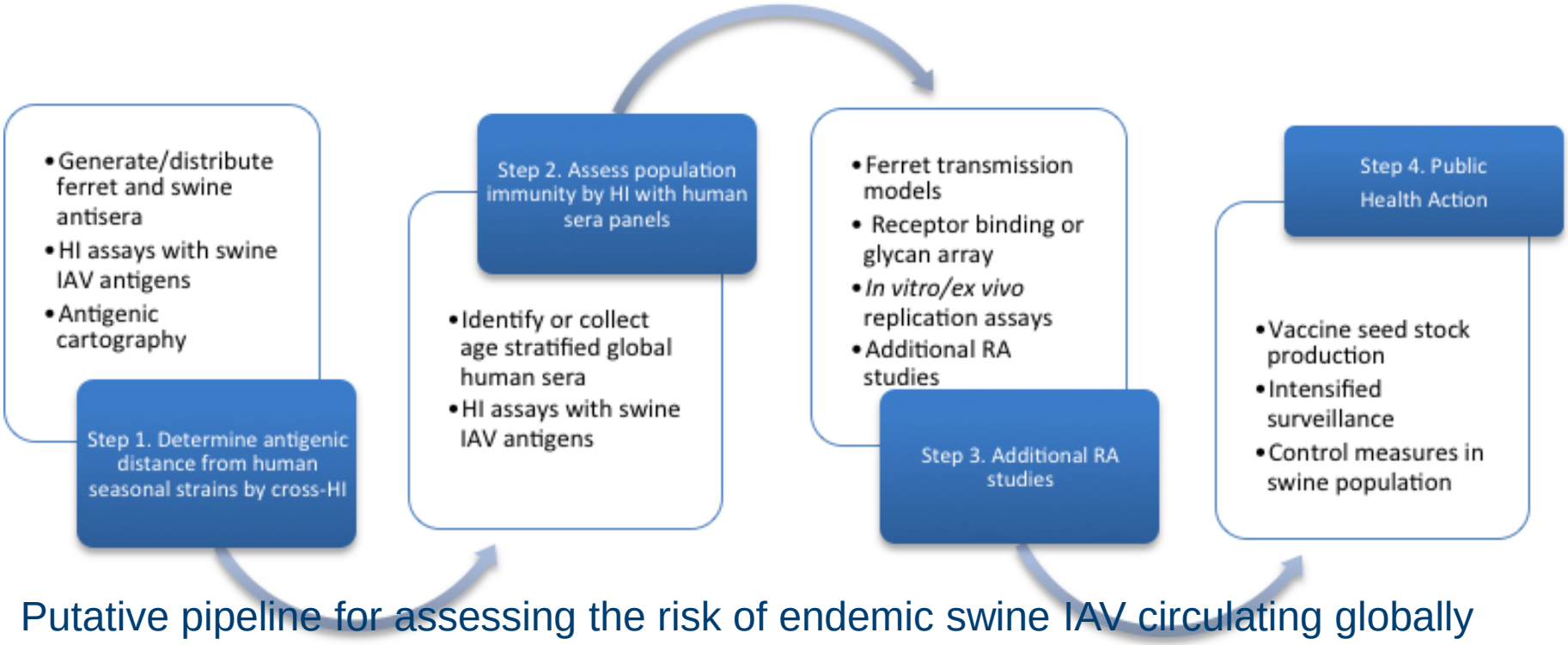
Geographic origin of swine influenza isolates

- Asia
- Europe
- USA
- Canada

Human influenza isolate blue colour gradient indicates date of isolation:

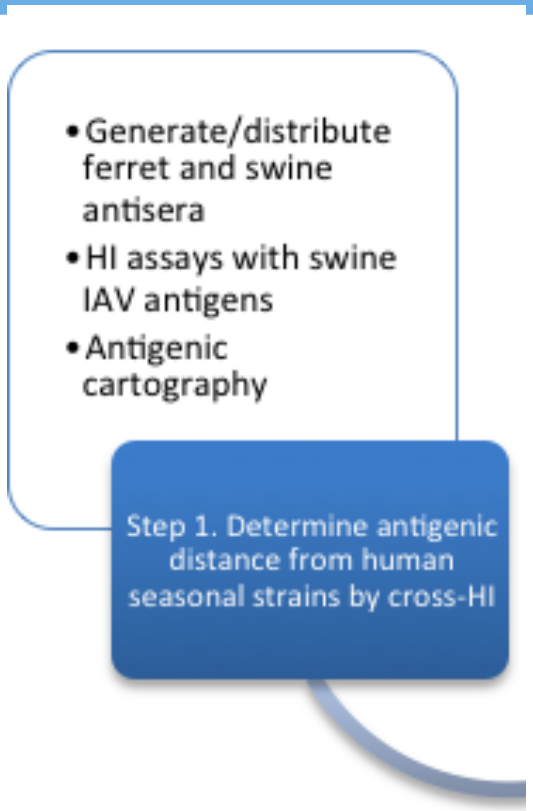
- Oldest
- Recent

Proposed swine RA pipeline



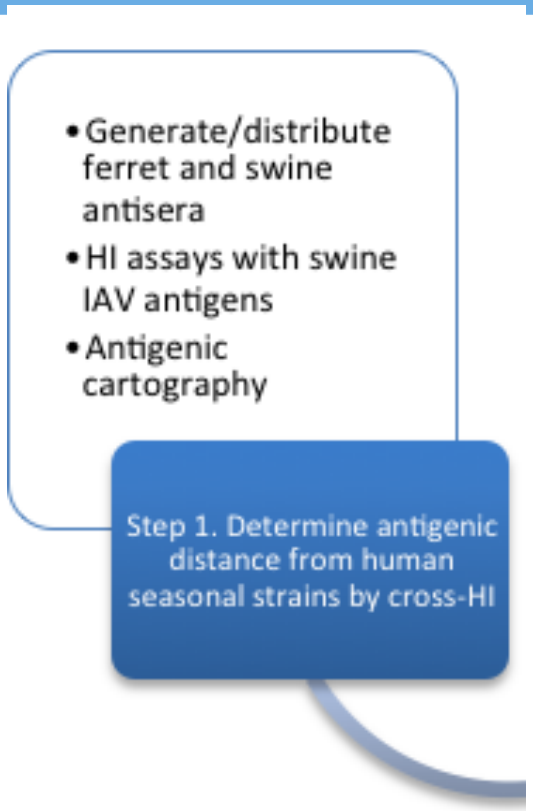
Putative pipeline for assessing the risk of endemic swine IAV circulating globally to the human population. Swine isolates identified through surveillance and sequencing efforts will be selected to enter the pipeline. The cycle will be repeated annually or as needed as newly characterized swine IAV with antigenic distance from human seasonal viruses are identified.

Step 1
Swine-human antigenic distance



- **CRIP: Amy Vincent NADC**
  - USDA swine surveillance sequence and antigenic analyses and CDC variant viruses.
  - Raise swine sera to selected swine and human seasonal influenza viruses.
  - Provide swine reference antisera and antigens to other Centres and participants -> St Jude's, Emory, Mt. Sinai.
  - HI with swine strains using swine & ferret antisera.
- **CRIP: Nicola Lewis University of Cambridge**
  - Antigenic cartography and phylogenetic analyses of swine viruses.
  - Selection of reference panels in consultation with AV.
  - Define and identify 'highly' divergent swine strains in consultation with AV.
- **CRIP: Adolfo Garcia-Sastre/Randy Albrecht**
  - HI with swine isolates obtained through CRIP with swine & ferret antisera.
  - Raise ferret antisera to selected swine and human seasonal strains in consultation with NADC/Cambridge.

Step 1 continued
Swine-human antigenic distance



- **St Jude's: Richard Webby and Stacey Shultz Cherry**
  - HI with swine isolates obtained through SJCEIRS with panel of swine & ferret antisera.
  - Raise ferret antisera to selected swine and human seasonal strains in consultation with NADC/Cambridge. Share ferret antisera panel with other CEIRS.
  - Contribute highly divergent strains to the pipeline.
- **Emory: Ralph Tripp/Mark Tompkins**
  - HI with swine isolates obtained through Emory CEIRS with panel of swine & ferret antisera.
  - Contribute highly divergent strains to the pipeline.
- **Non-CEIRS**
  - AHPA/ANSES: HI with swine isolates circulating in Europe against selected NADC swine antiserum and/or ferret antisera Contribute highly divergent strains to the pipeline.
  - Share ferret antisera panel with other CEIRS.
- .

Human Vaccine Strains for Swine Anti-sera

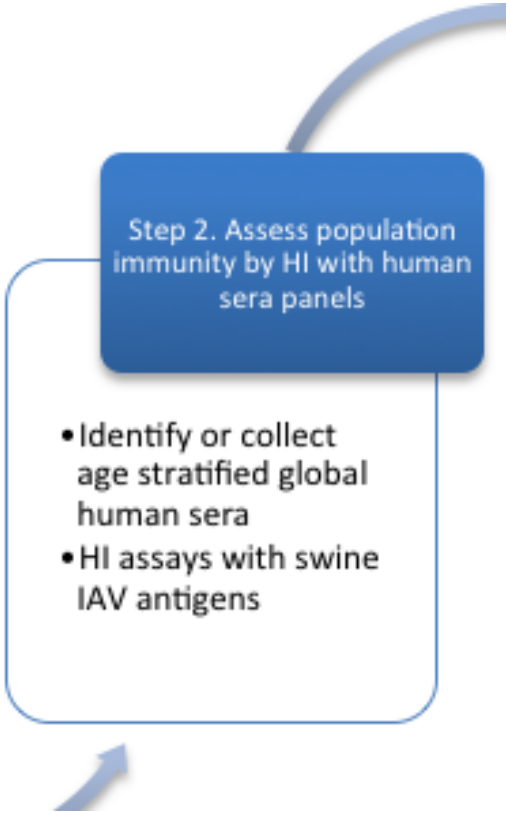
Vaccine Strain	Year	Subtype	Vaccine Season	NADC Sera
A/California/04/09	2009	H1N1	2010-15	Yes
A/Brisbane/59/07	2007	H1N1	2007-10	Yes
A/Solomon Island/3/06	2006	H1N1	2007-08	Yes
A/ Michigan/02/2003	2003	H1N2	N/A	Yes
A/New Caledonia/20/1999	1999	H1N1	2000-07	Yes
A/Victoria/361/2011	2011	H3N2	2012-14	Yes
A/Perth/16/2009	2009	H3N2	2010-12	Yes
A/Brisbane/10/2007	2007	H3N2	2008-10	Yes
A/Wisconsin/67/2005	2005	H3N2	2006-08	Yes
A/Fujian/411/2002	2002	H3N2	2004-05	Yes
A/Moscow/10/99	1999	H3N2	2000-04	Yes
A/Sydney/5/97	1997	H3N2	1998-2000	Yes
A/Wuhan/359/95	1995	H3N2	1996-98	Yes

Vaccine Strain	Year	Subtype	Vaccine Season	NADC Sera	Received from St. Jude
A/Singapore/86	1986	H1N1	1987-97	No	✔
A/Brazil/11/78	1978	H1N1	1980-84	No	✔
A/Beijing/262/95	1995	H1N1	1999-2000	No	✔
A/Texas/36/91	1991	H1N1	1995-97	No	✔
A/Taiwan/1/86	1986	H1N1	1987-97	No	✔
A/Chile/1/83	1983	H1N1	1984-86	No	✔
A/USSR/77	1977	H1N1	1978-79	No	✔
A/Switzerland/9715293/13	2013	H3N2	2015-16	No	
A/Beijing/32/92	1992	H3N2	1993-94	No	✔
A/Beijing/353/89	1989	H3N2	1991-93	No	✔
A/Sichuan/02/87	1987	H3N2	1988-89	No	✔
A/Shanghai/11/87	1987	H3N2	1989-90	No	✔
A/Leningrad/360/1986	1986	H3N2	1987-88	No	✔
A/Philippines/2/82	1982	H3N2	1983-86	No	✔
A/Bangkok/01/1979	1979	H3N2	1981-83	No	✔
A/Texas/1/77	1977	H3N2	1978-79	No	✔
A/Victoria/3/75	1975	H3N2	1976-78	No	✔
A/Port Chalmers/1/1973	1973	H3N2	1974-76	No	✔

Comparison of influenza virus phenotype
characterised using ferret and swine antisera

Step two

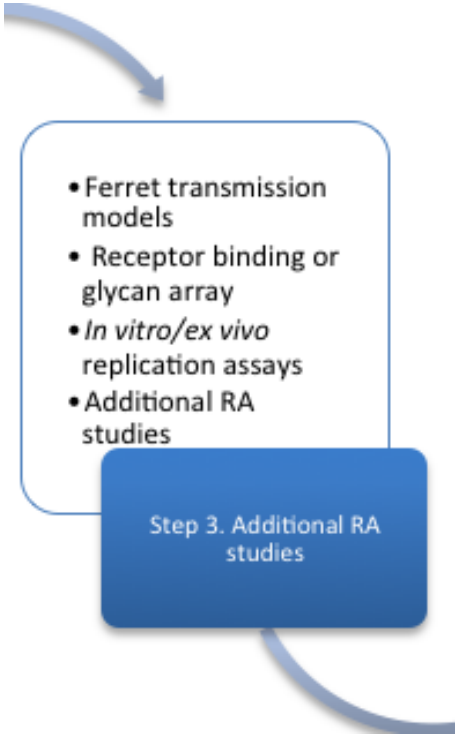
Step 2
Population immunity to swine strains



- JHCEIRS: Andy Pekosz
  - Collect a stratified by age human serum panel from community-based sampling in NY.
  - Contribute a Taiwanese human serum panel.
  - Characterise selected swine strains against the human serum panel and submit results for antibody landscaping.
- St Jude's: Richard Webby and Stacey Shultz-Cherry
  - Contribute a South American human serum panel.
  - Characterise selected swine strains against the human serum panel and submit results for antibody landscaping.
- CRIP: Nicola Lewis
  - Produce antibody landscapes of human sera relative to selected 'highly' divergent swine influenza viruses.

Step three

Step 3
Laboratory testing “high risk” swine



- SJCEIRS:
  - Pathogenesis (mouse model and ferret) and pre-pandemic vaccine work
- CRIP:
  - Pathogenesis in ferrets and other (Mt. Sinai)
  - Receptor binding studies
  - Vaccine efficacy studies (NADC)
- Emory:
  - Receptor binding studies
- JHCEIRS: Andy Pekosz
  - Infectivity studies in human primary respiratory epithelial cells
- Other Centers?

Step four

Step 4
Inform Public Health

- CRIP, SJCEIRS, Emory, JHCEIRS:
  - Disseminate results through presentations, reports, & publications to key stakeholders.
    - NIH-CEIRS
    - CDC
    - WHO
    - USDA-APHIS
    - Swine industry
    - Veterinary biologics companies
- St. Jude: Richard Webby
  - Share data at WHO Composition of Vaccine Meetings.
- Public Health: Candidate pandemic preparedness vaccine seed strains selected and developed as needed.
  - Pilot lot vaccine production

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Colin Russell and Kathryn Berger Department of Veterinary Medicine, University of Cambridge

David Burke, Judy Fonville and Eugene Skepner Department of Zoology, University of Cambridge

Ian Brown and Sharon Brookes and the ESNIP3 consortium Animal Health and Plant Agency, UK

T. Saito and Nobuhiro Takemae National Institute of Animal Health, Ibaraki, Japan

G. Simon Anses, Ploufragan-Plouzané Laboratory, Swine Virology Immunology Unit, France

R. Webby St. Jude Children's Research Hospital, Memphis, TN, USA

K. Van Reeth Ghent University, Ghent, Belgium

L. Larsen Denmark Technical University, Copenhagen, Denmark

A. L. Vincent and Tavis Anderson Virus and Prion Research Unit, National Animal Disease Center, USDA-ARS, Ames, USA

Ron Fouchier and Bjorn Koel* Erasmus MC - Department of Viroscience, Rotterdam, The Netherlands (*now at Department of Medical Microbiology, University of Amsterdam, The Netherlands)

Paul Kellam and Simon Watson Wellcome Trust Sanger Institute, Hinxton, UK

T. Nguyen Department of Animal Health, National Centre for Veterinary Diagnostics, Hanoi, Vietnam

B. Nuansrichy National Institute of Animal Health, Bangkok, Thailand

M. Peiris Hong Kong University, Hong Kong City, Hong Kong

CEIRS

USDA