

# ¿Podremos conseguir una vacuna frente a todas las cepas de la gripe?

*Adolfo García-Sastre*

Icahn School of Medicine at Mount Sinai, New York



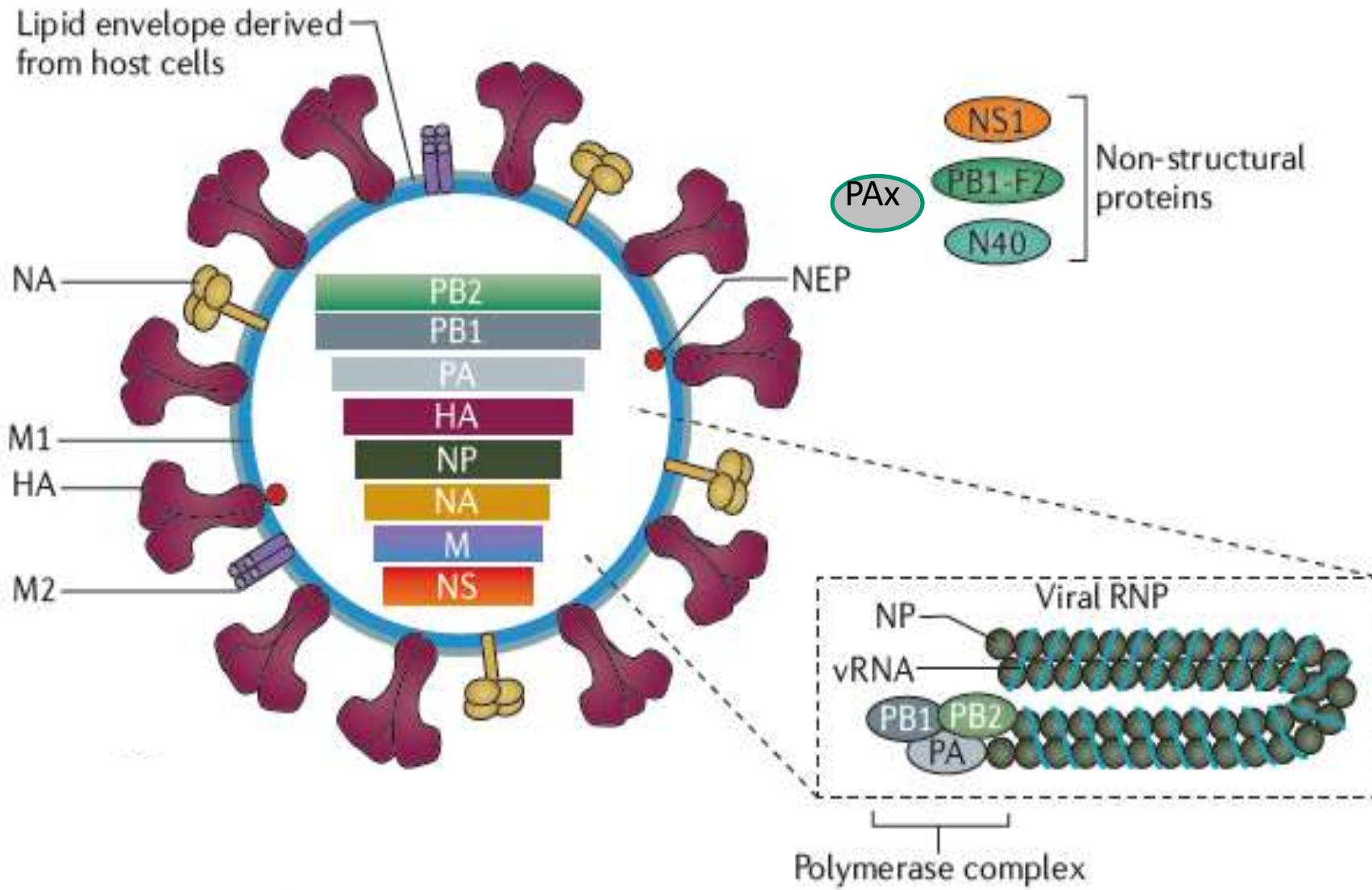
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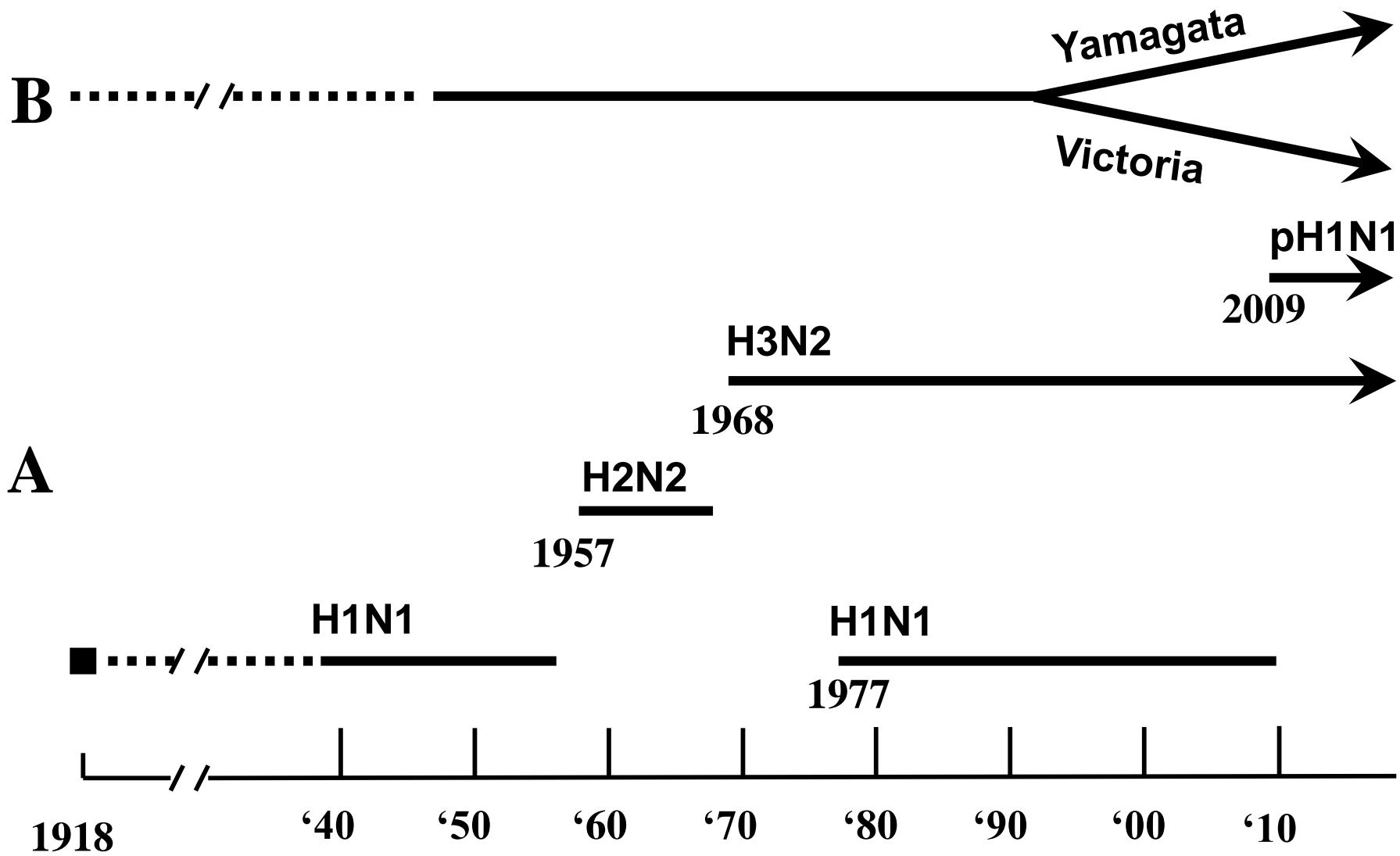
# DISCLOSURES

- My laboratory has received research moneys from Pfizer, Senhwa Biosciences, Kenall Manufacturing, Avimex, Johnson & Johnson, Dynavax, 7Hills Pharma, Pharmamar, ImmunityBio, Accurius, Nanocomposix, Hexamer, N-fold LLC, Model Medicines, Atea Pharma and Merck
- I'm a consultant for Vivaldi Biosciences, Contrafект, 7Hills Pharma, Avimex, Vaxalto, Pagoda, Accurius, Esperovax, Farmak, Applied Biological Laboratories, Pharmamar, Paratus, CureLab Oncology, CureLab Veterinary, Synairgen and Pfizer.
- I'm inventor of patents in the field of influenza virus and COVID-19 vaccines owned by the Icahn School of Medicine at Mount Sinai, New York, some of which have been licensed to Medimmune, Vivaldi and Avimex.

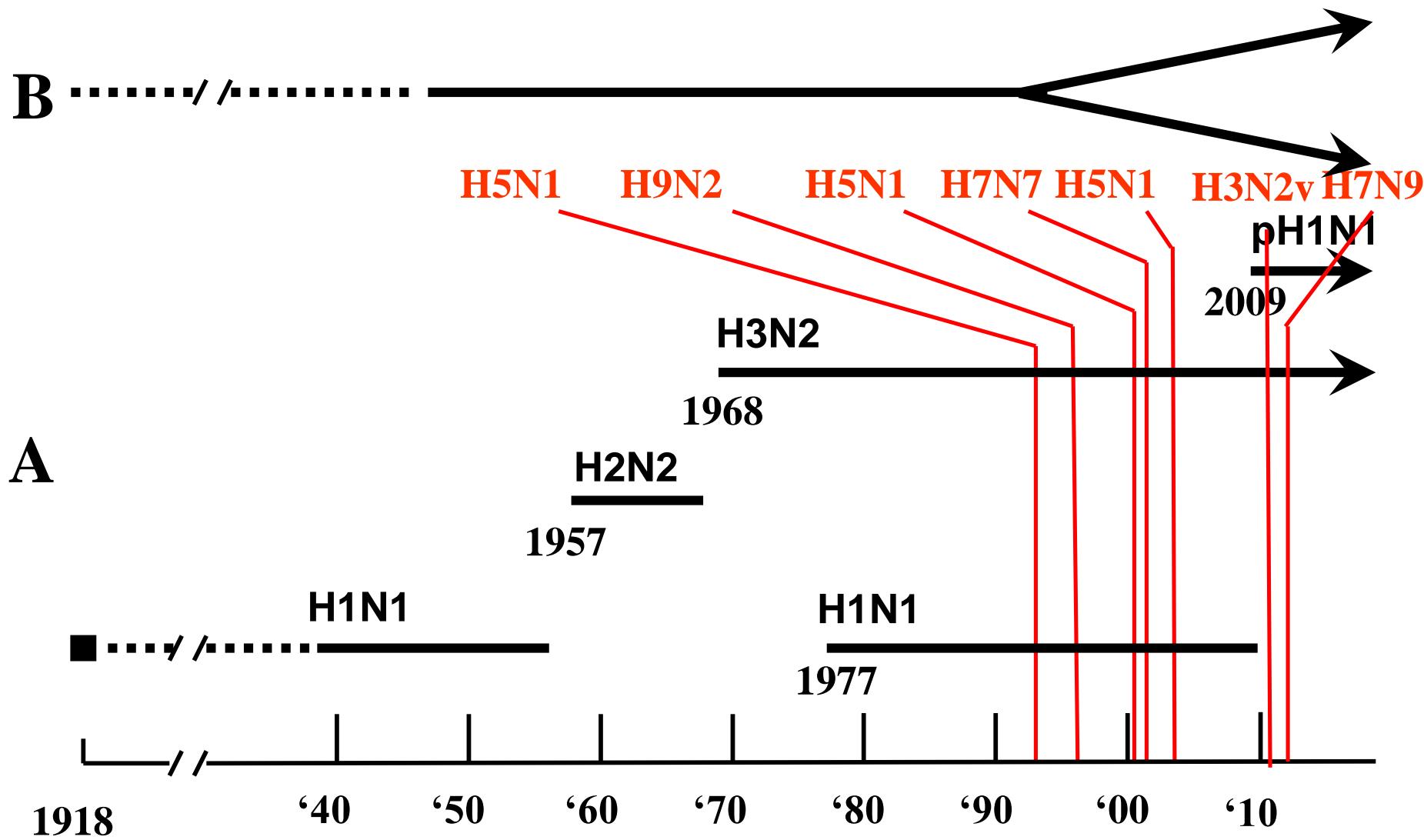
# INFLUENZA VIRUSES



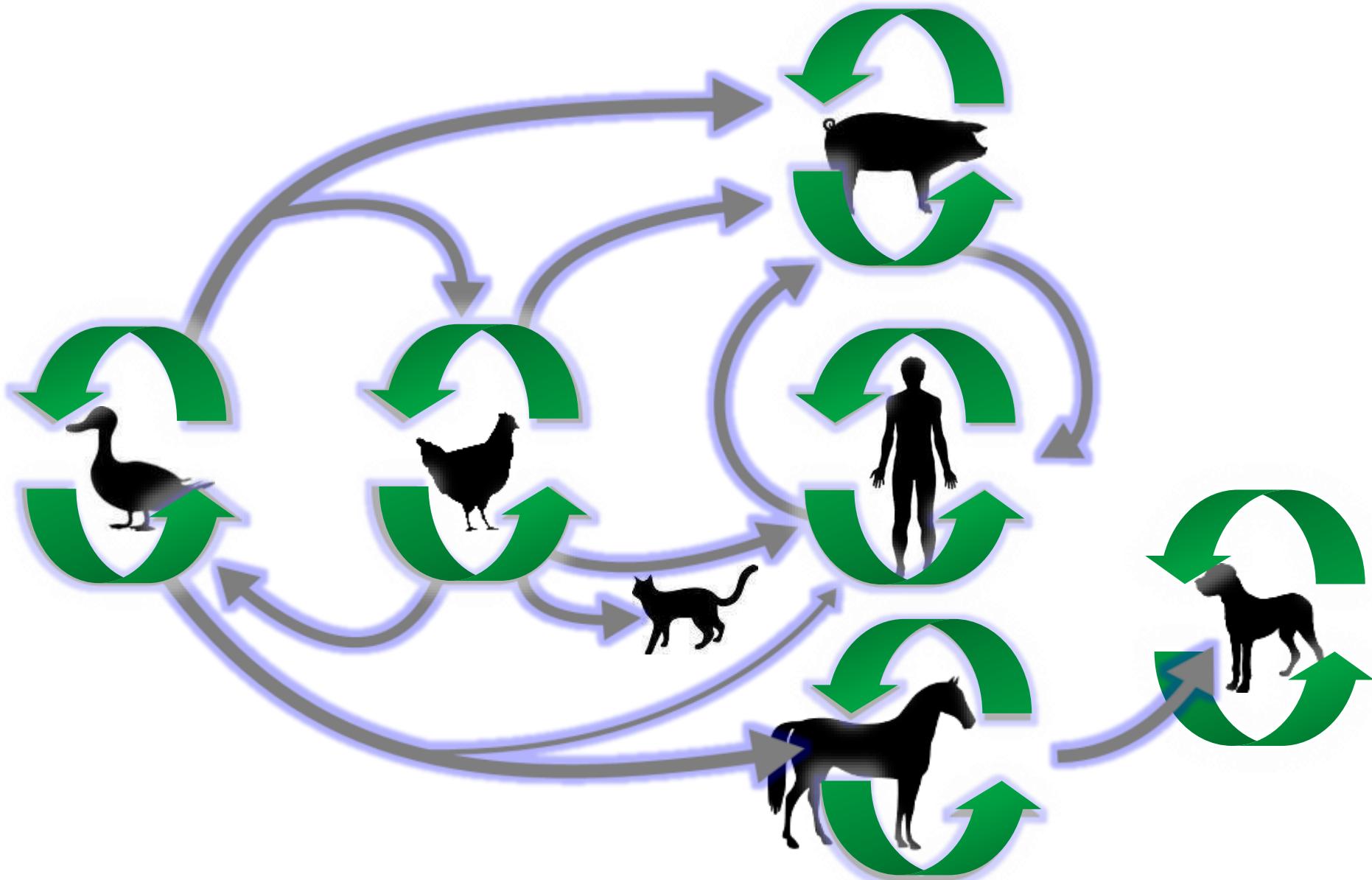
# EPIDEMIOLOGY OF HUMAN INFLUENZA VIRUSES

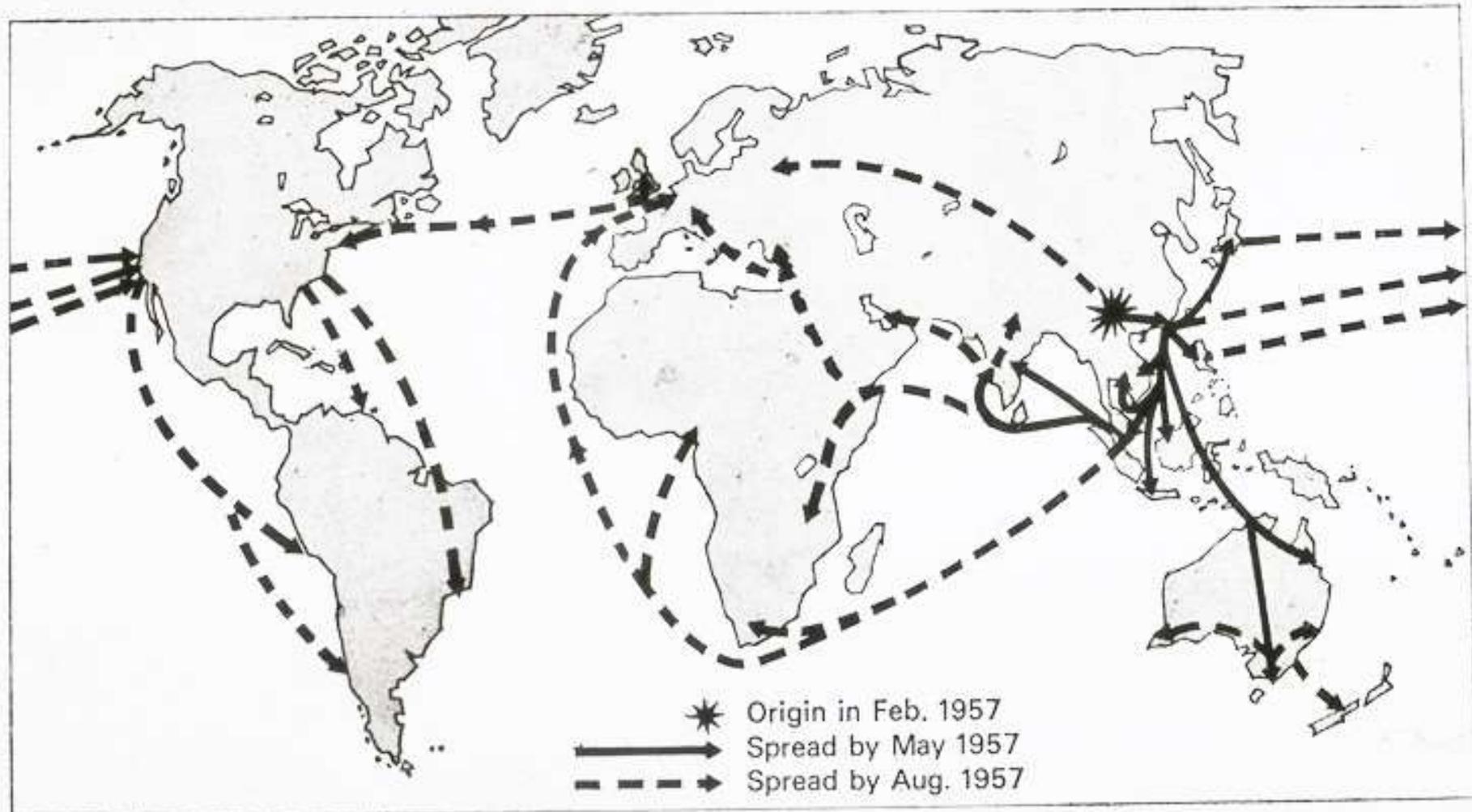


# INFECTIONS IN HUMANS WITH AVIAN AND SWINE INFLUENZA A VIRUSES



# Evolution and spread of flu viruses

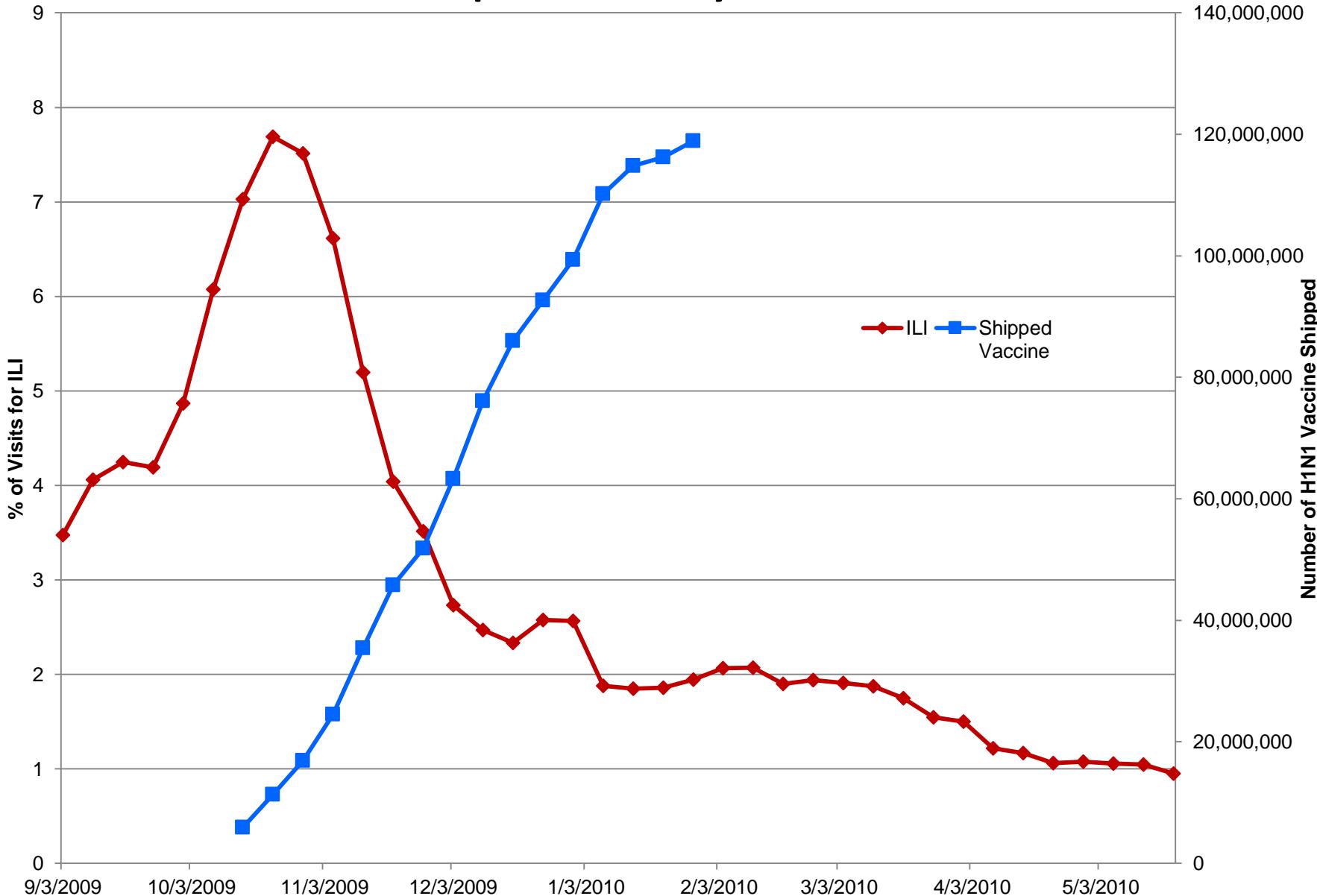




*The spread of Asian influenza around the world. It started in China in February 1957 and reached Hong Kong in April. The solid black lines indicate the spread up until May, the broken lines the spread up until August. (Data from Chronicle of World Health Organization, Sept. 1957.)*

# Pandemic H1N1 cases and vaccinations in US

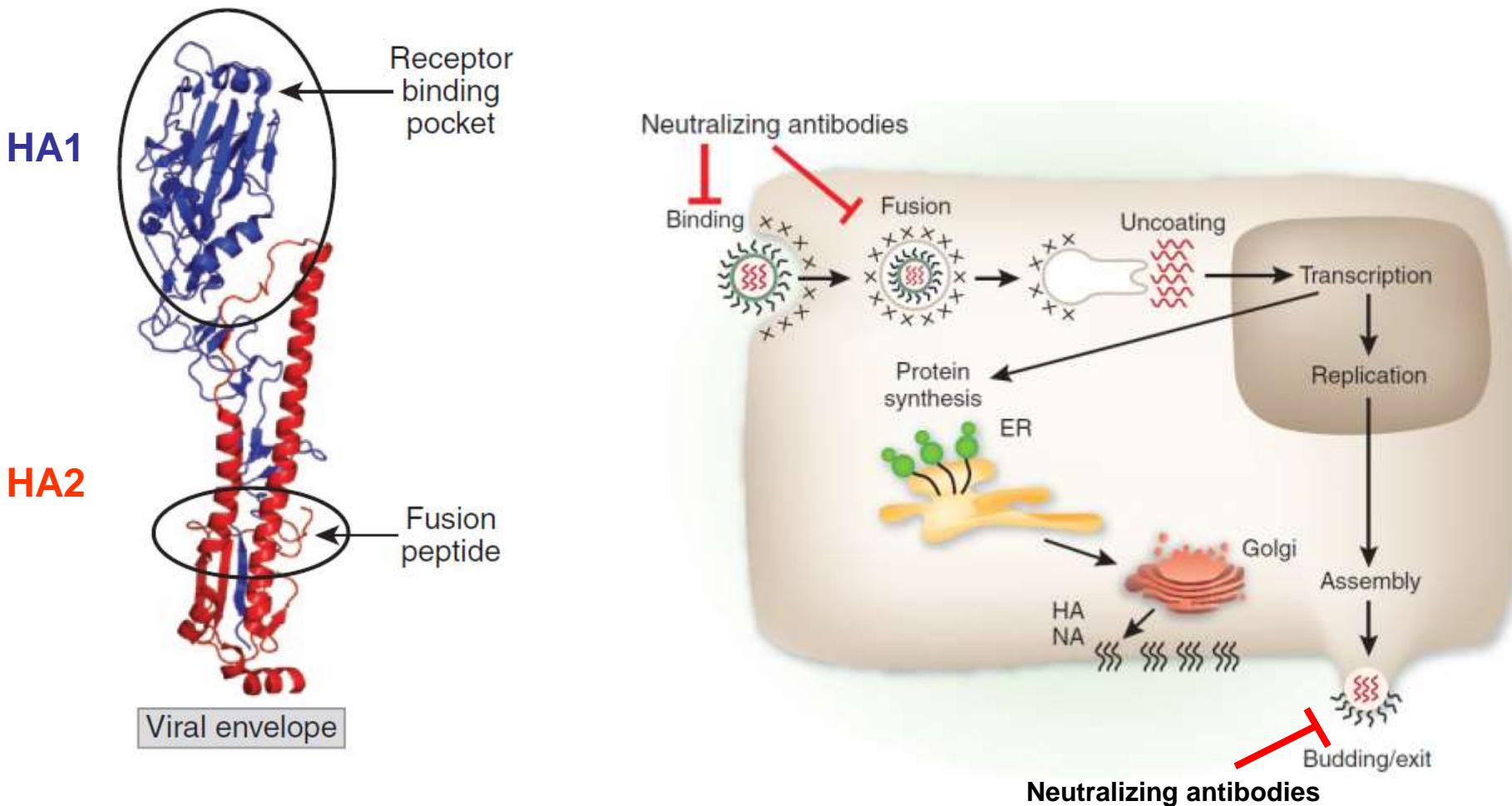
## Sept 2009 – May 2010



# Universal flu vaccines?

*In collaboration with Peter Palese and Florian Krammer*

# Neutralization of influenza viruses



# **UNIVERSAL FLU VACCINES?**

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**Repeated vaccination with influenza virus chimeric HA vaccines induce protective antibodies against multiple subtypes of influenza virus.**

**Irina Margine**

**Florian Krammer**

**Rong Hai**

**Gene Tan**

**Peter Palese**

**Weina Sun**

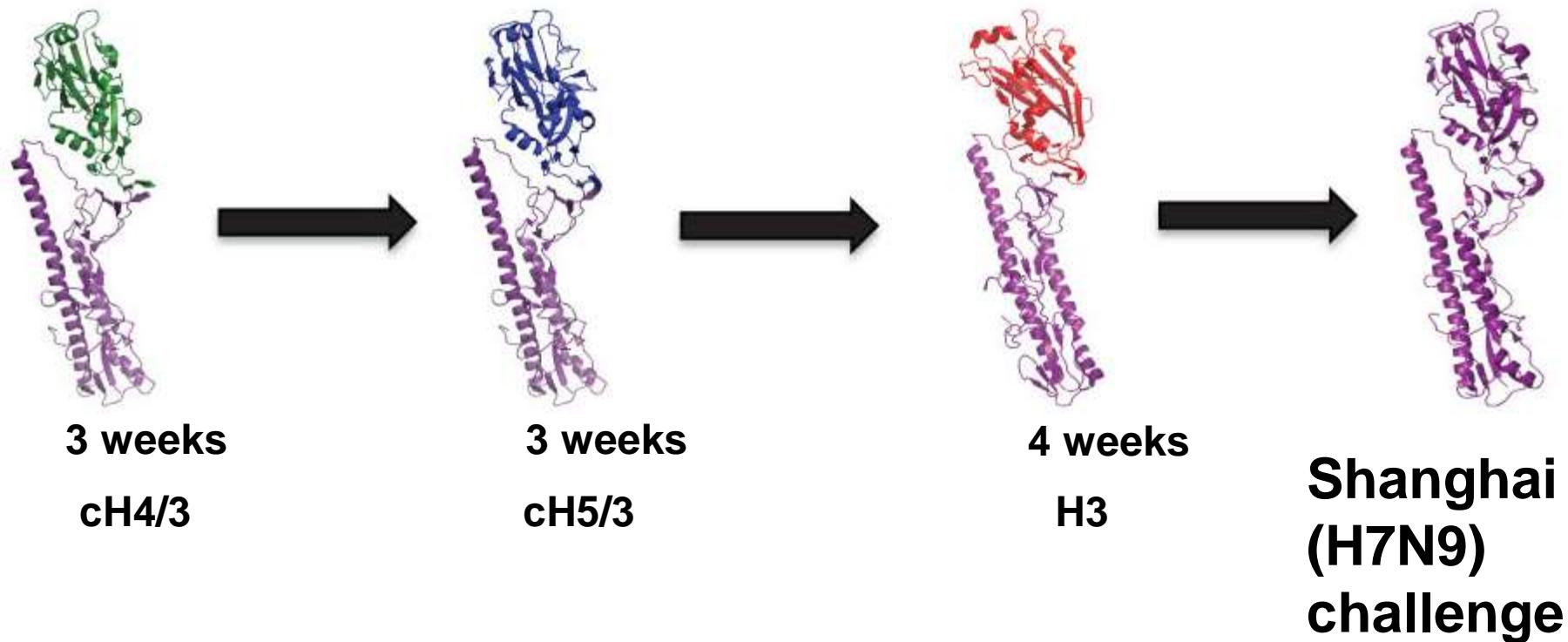
**Randy Albrecht**

**Patrick Wilson**

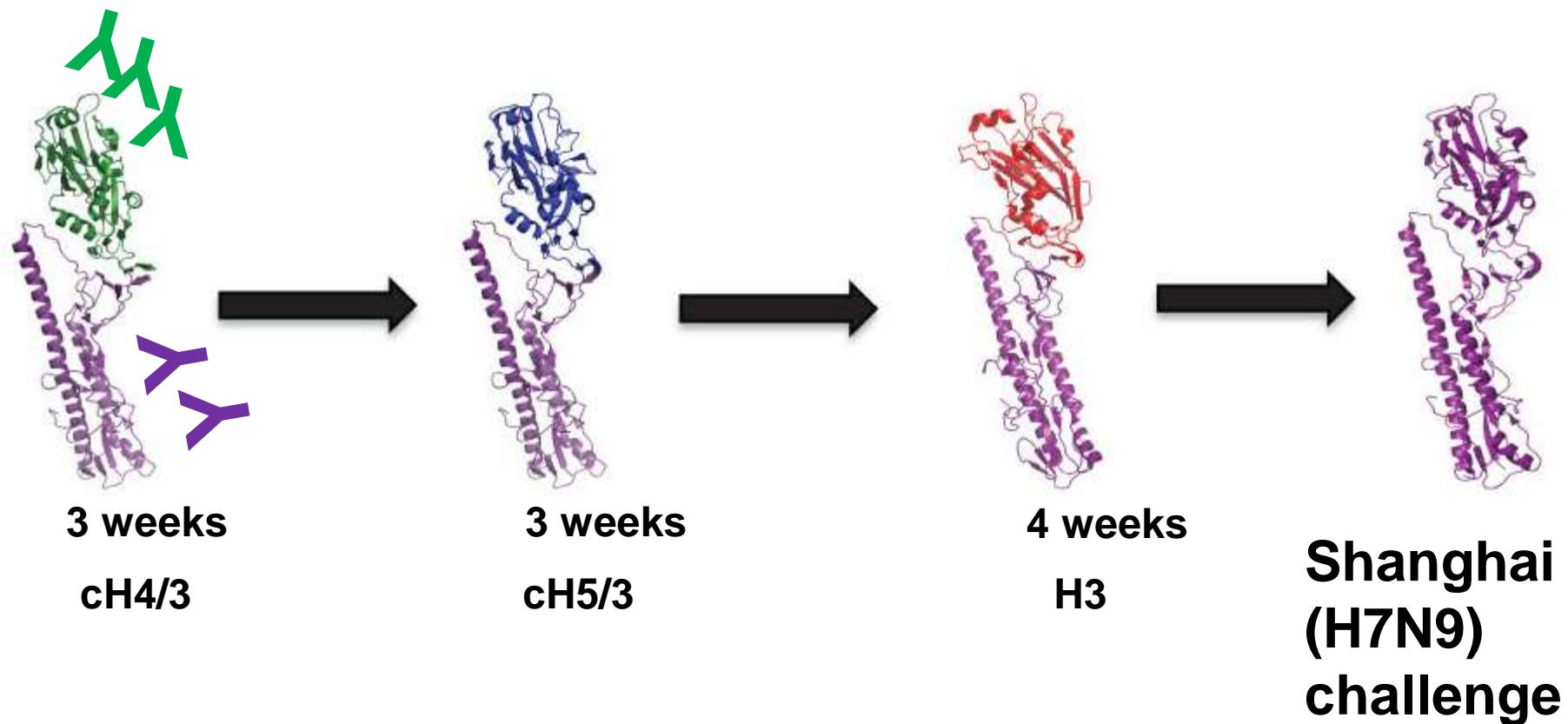
**S.A. Andrews**

**Jon Runstadler**

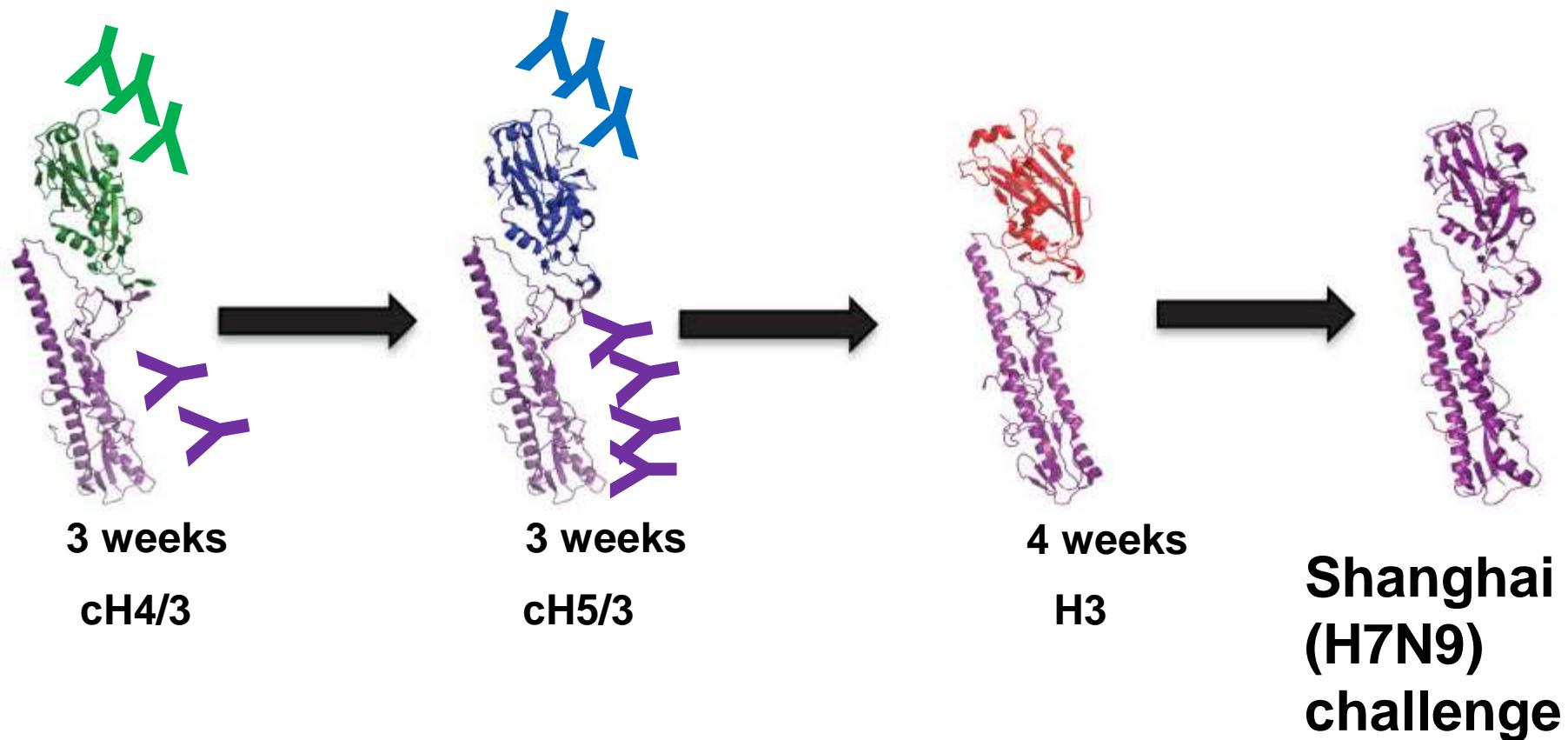
# Induction of protective levels of stalk-reactive antibodies using chimeric HA constructs in mice



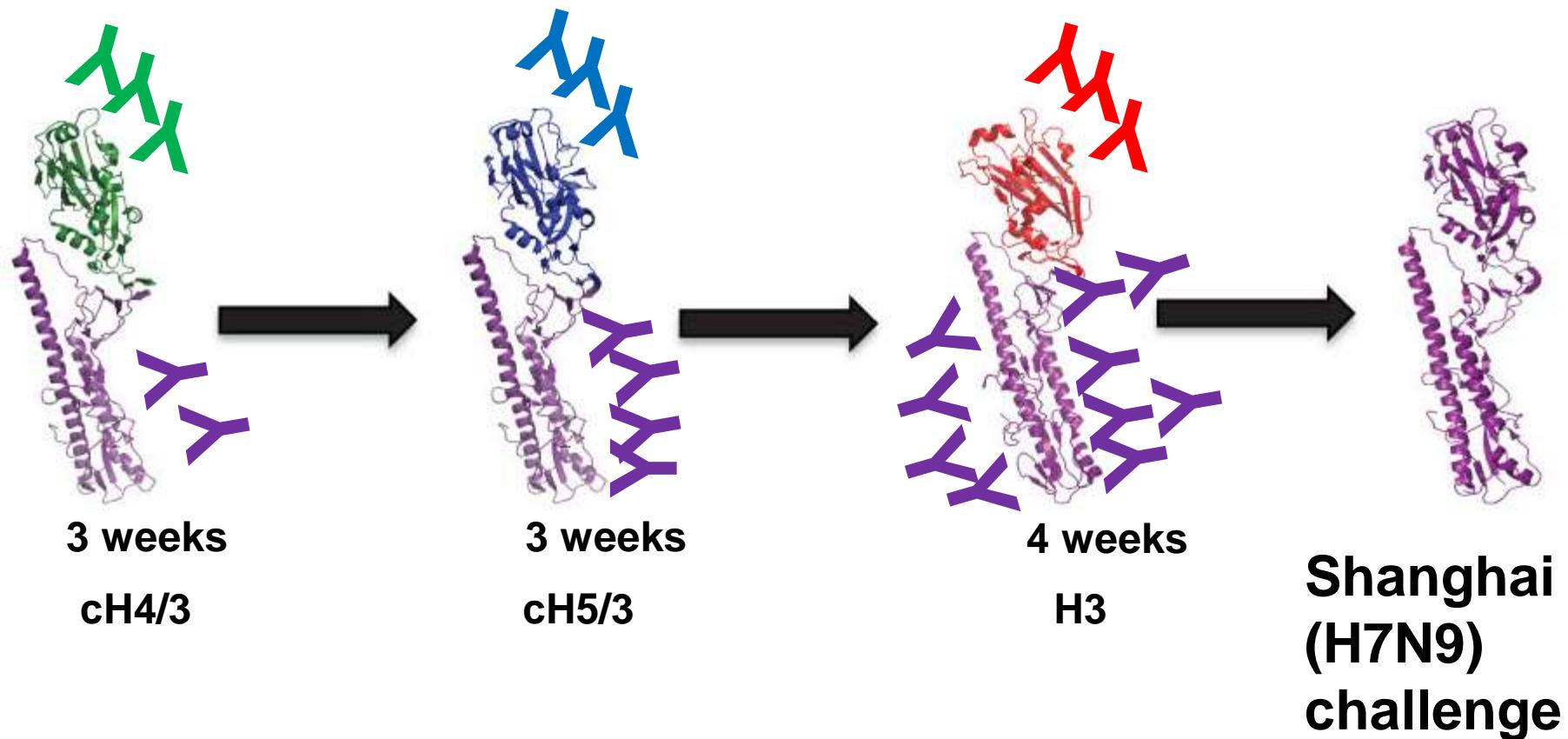
# Induction of protective levels of stalk-reactive antibodies using chimeric HA constructs in mice



# Induction of protective levels of stalk-reactive antibodies using chimeric HA constructs in mice

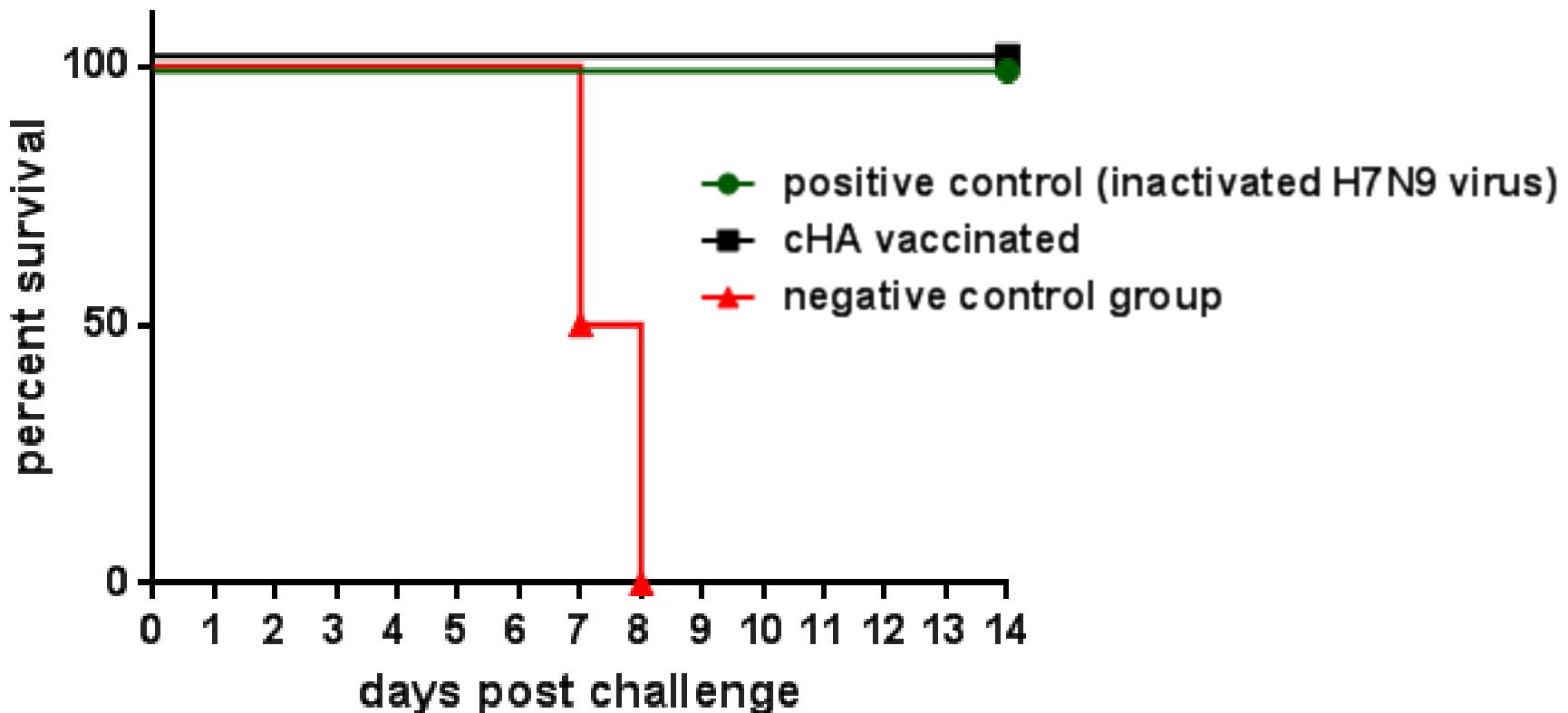


# Induction of protective levels of stalk-reactive antibodies using chimeric HA constructs in mice



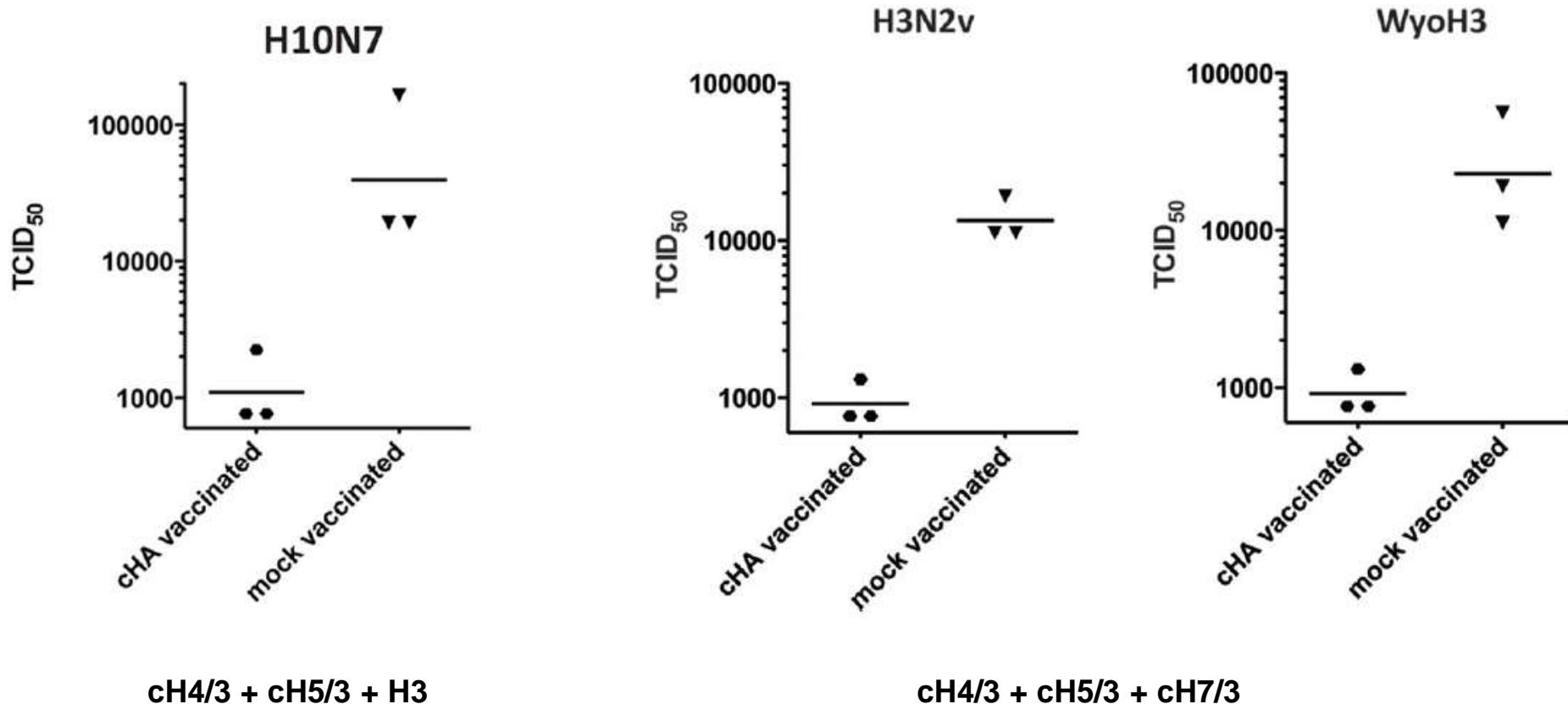
# cHA vaccine protects against challenge with novel H7N9 virus

I.N. + I.M. with polyI:C

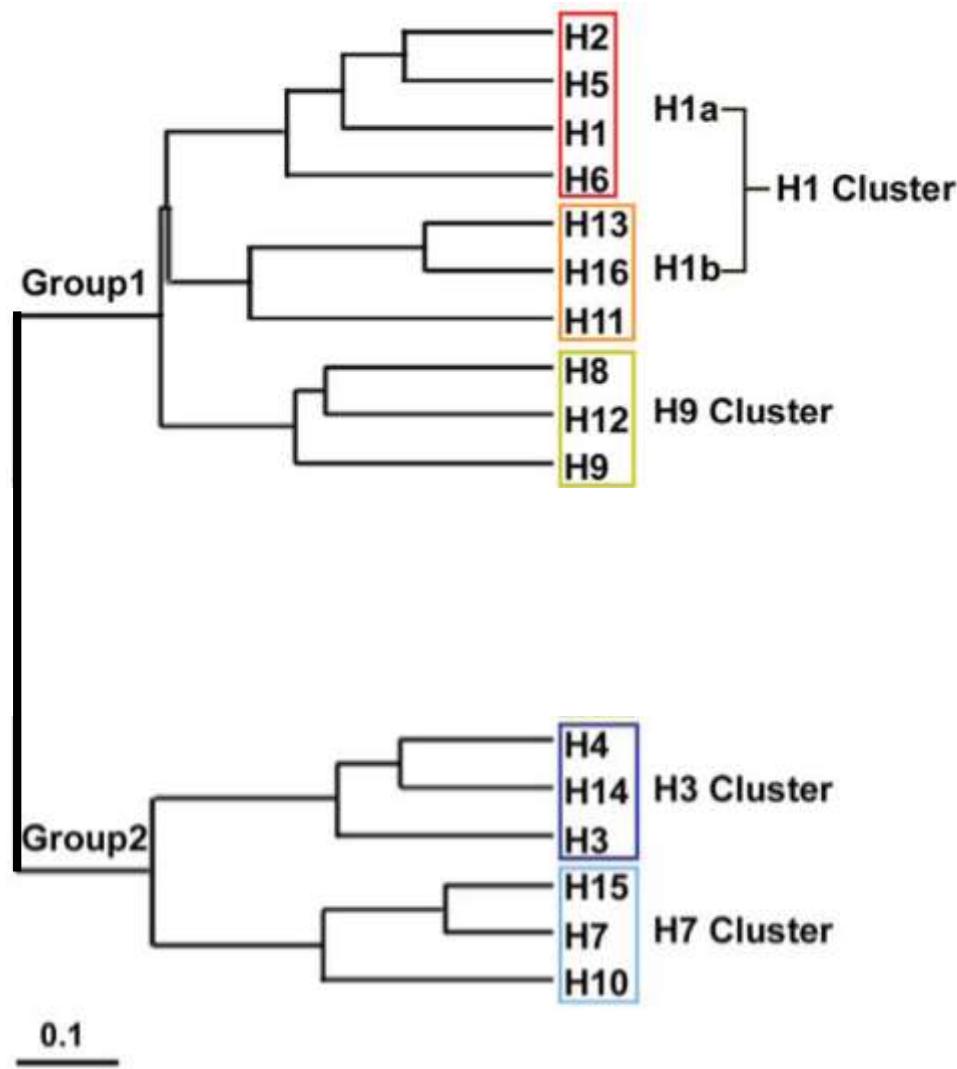


# cHA vaccine protects against challenge with H10 and H3 viruses

Titers in mouse lungs, day 3 postinfection



# Hemagglutinin subtypes

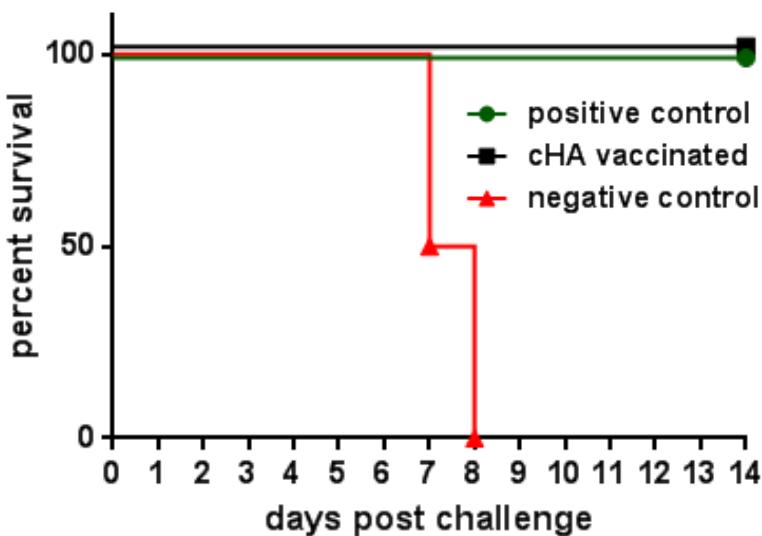


# cHA vaccine protects against challenge with group 1 and group 2 viruses in mice

## Influenza A group 2 immunization

cH4/3 → cH5/3 → H3

H7N9 challenge

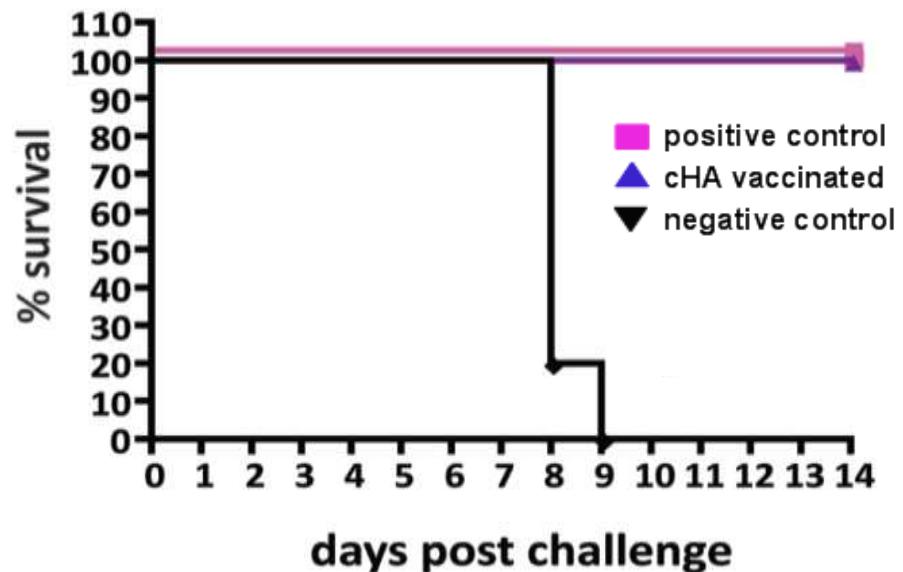


Also protected against other group 2 viruses

## Influenza A group 1 immunization

cH9/1 → cH6/1 → H5/1

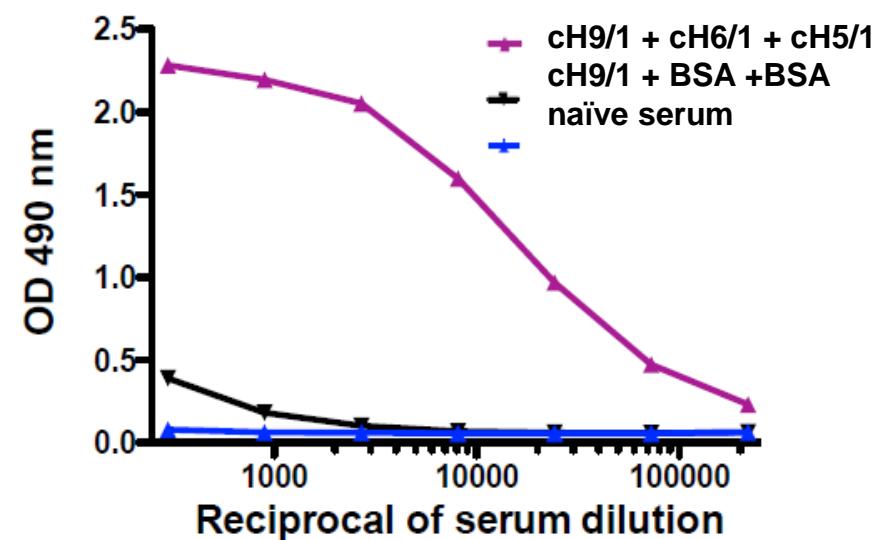
H1N1 challenge



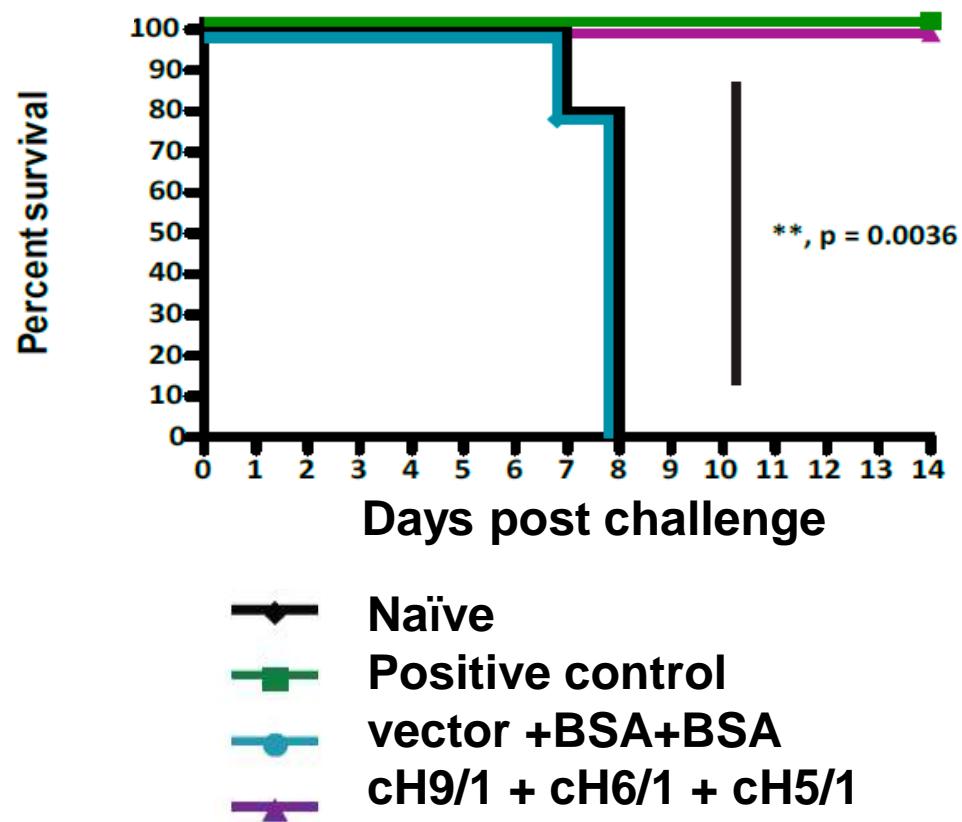
Also protected against other group 1 viruses

# Protection is antibody mediated

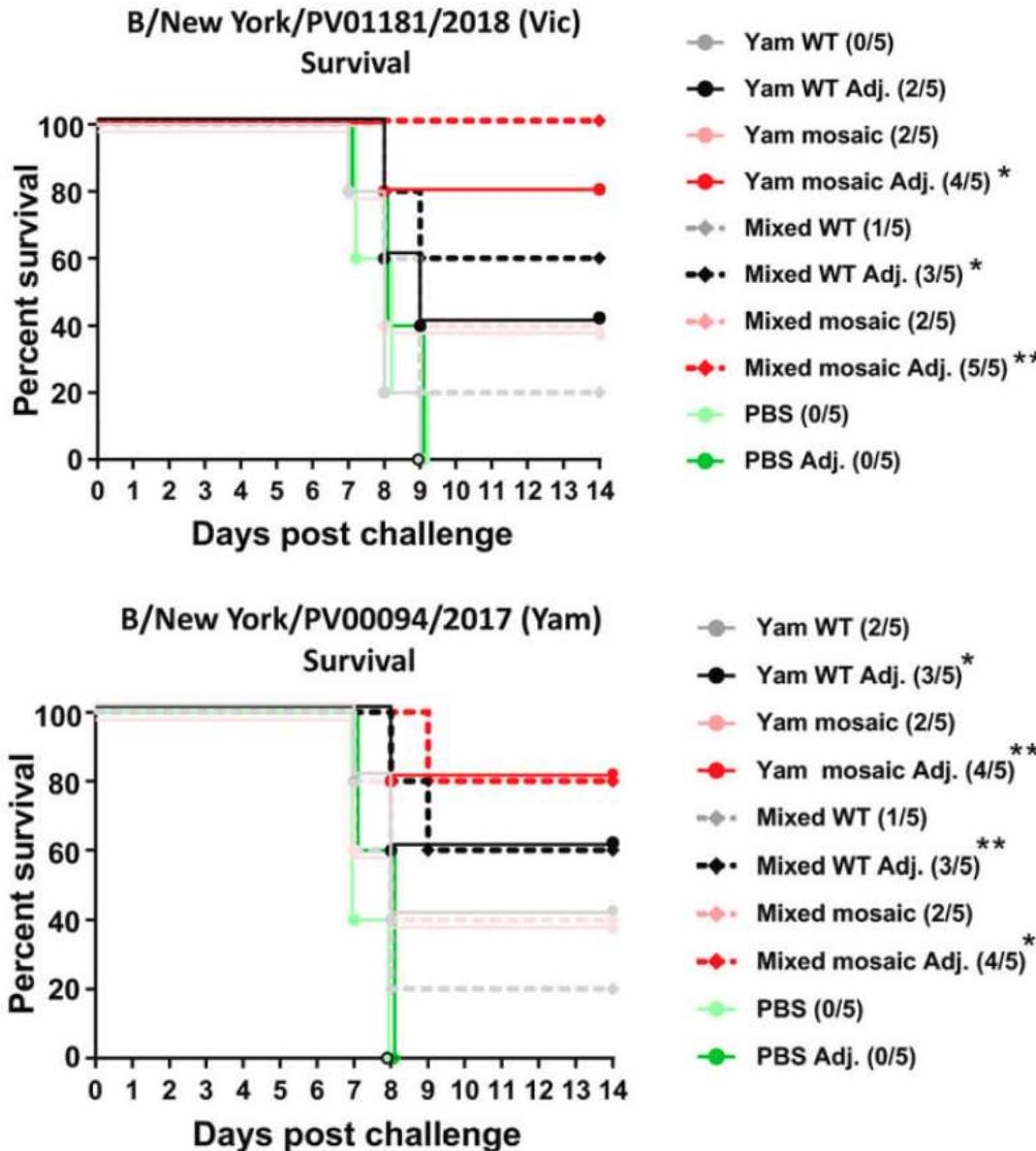
## ELISA reactivity to Cal09 (pH1N1) protein



## Passive transfer of serum protects from viral challenge



# mHA influenza B vaccine protects against challenge with influenza B viruses from both lineages



# Prime–Boost cHA vaccines based in LAIV and IIV platforms

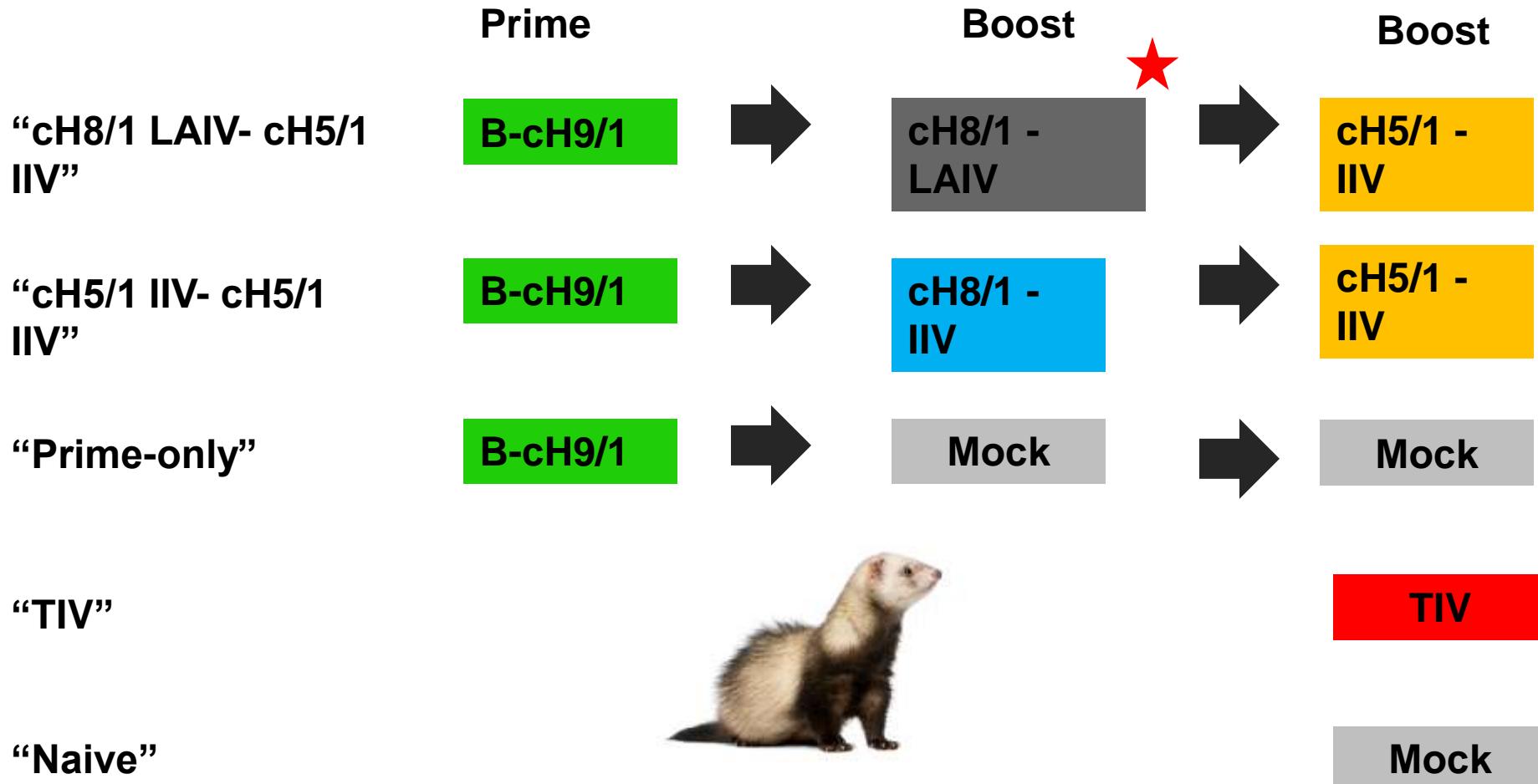
Florian Krammer, Raffael Nachbagauer,  
Adolfo García-Sastre, Peter Palese and Randy A. Albrecht



Mount  
Sinai

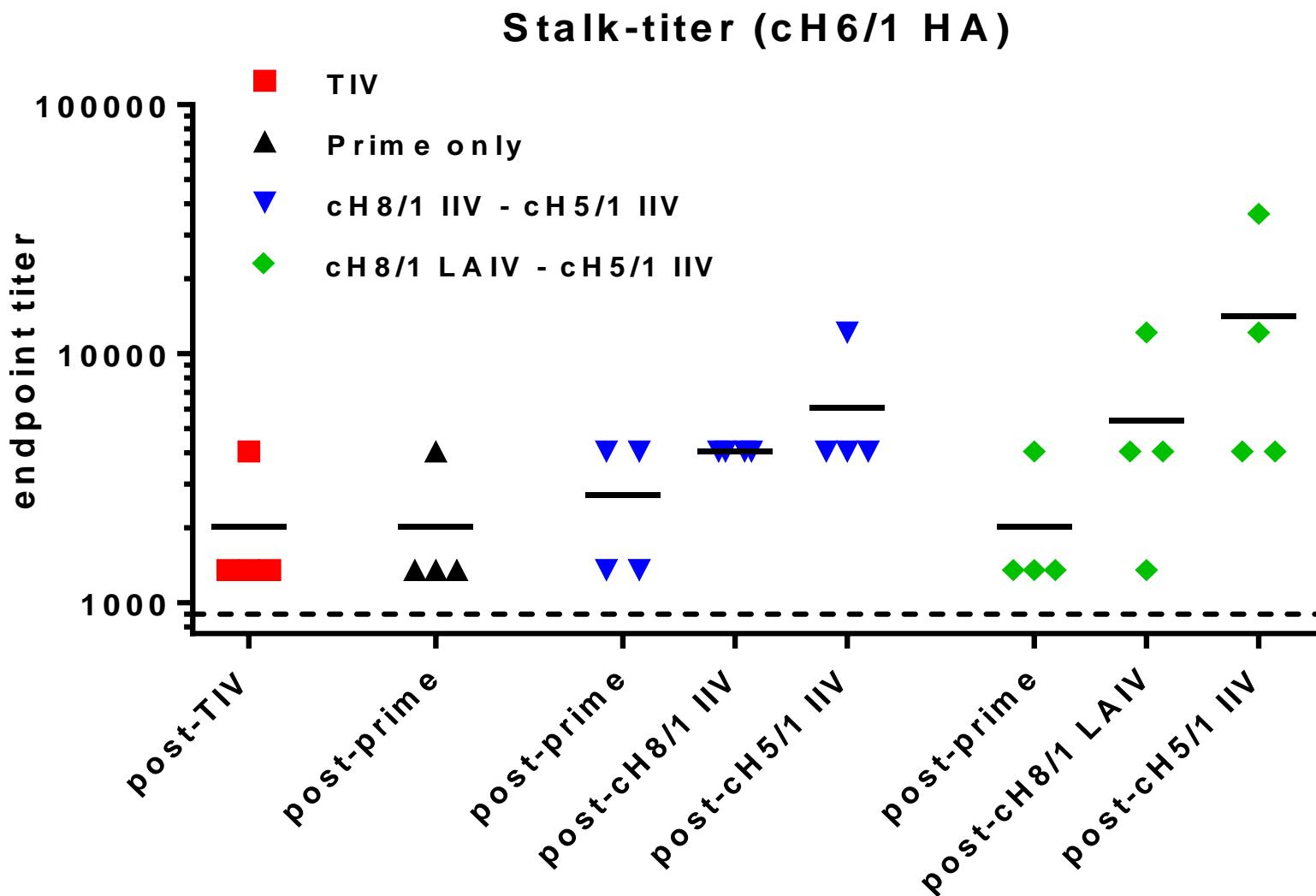


# Prime-Boost cHA vaccines based in LAIV and IIV platforms



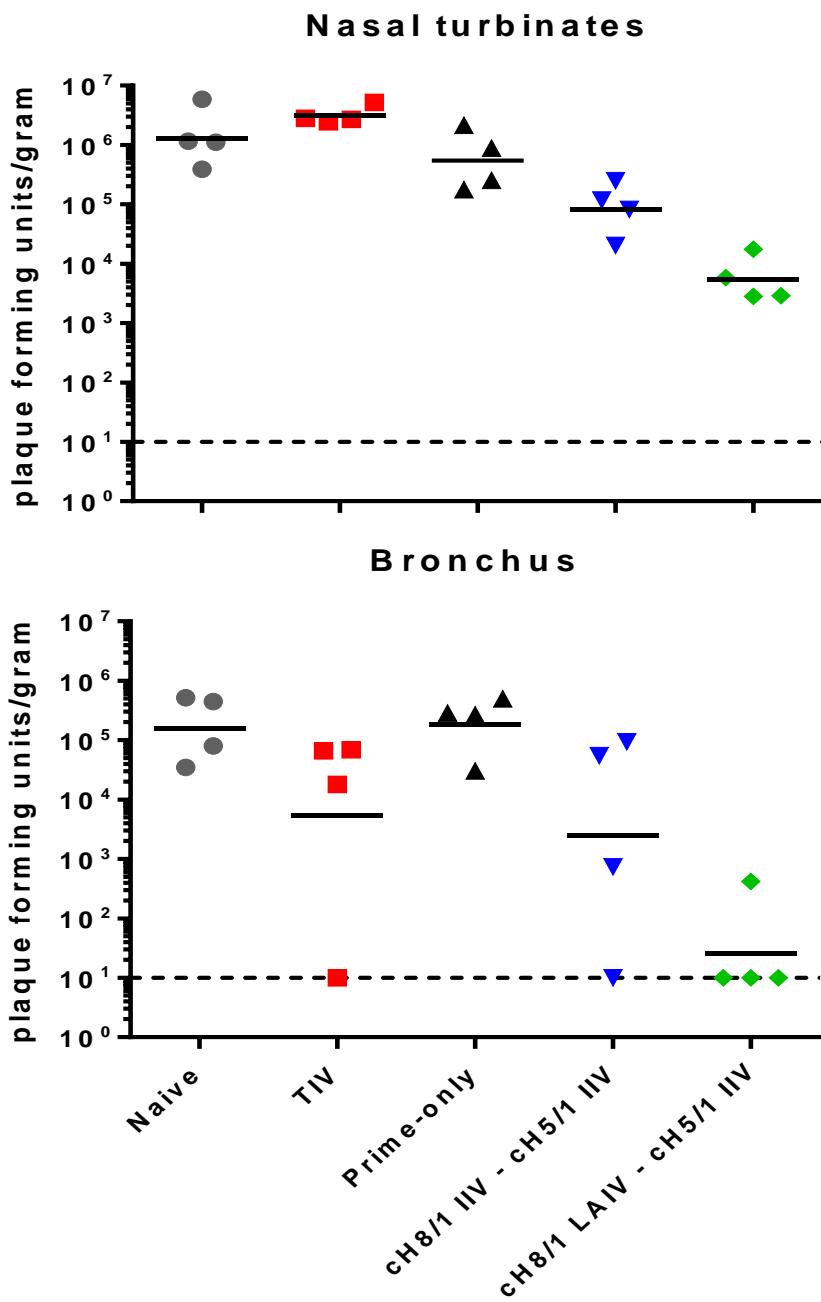
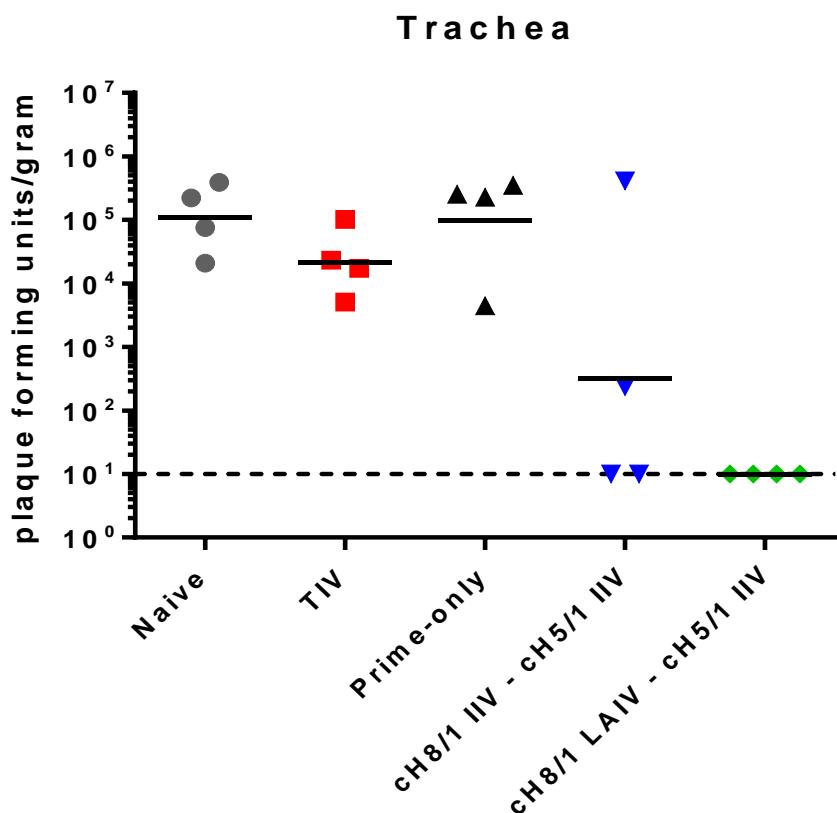
★ LAIV is based on the Ann Arbor backbone

# Induction of HA stalk-specific antibodies (ELISA)

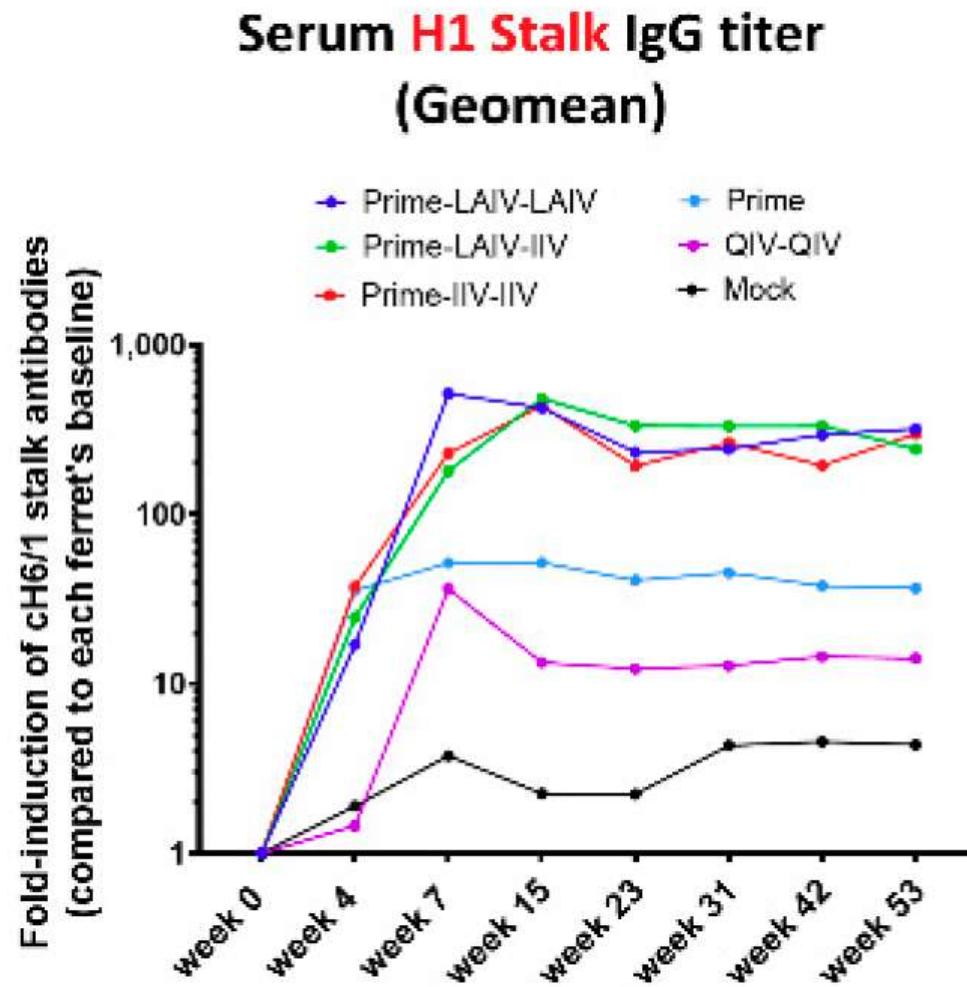


\*No detectable HI titers following vaccination

# Viral titers in tissues following H1N1 challenge infection, day 4



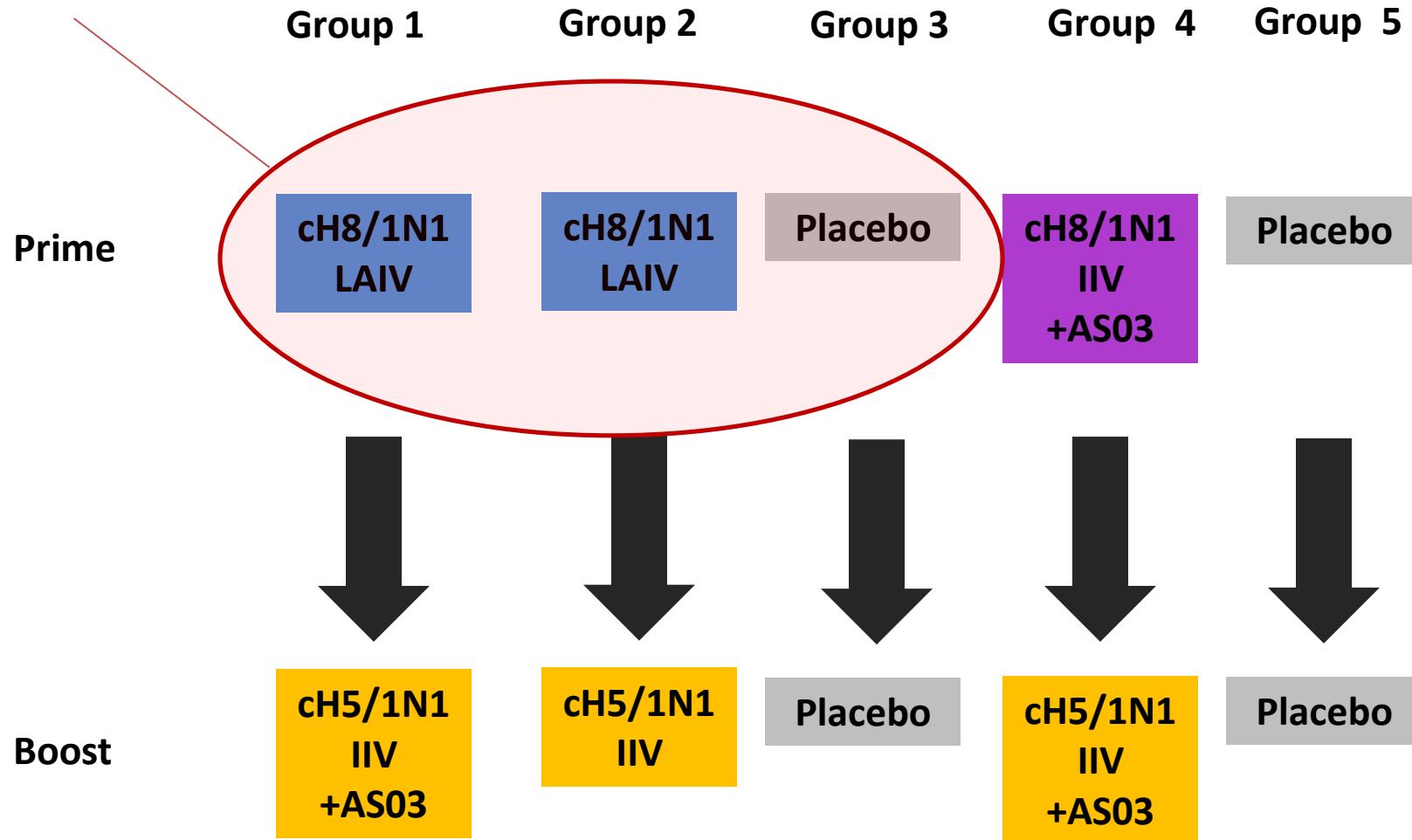
# HA stalk-specific antibodies are long-lived in ferrets



# Initial clinical trial outline for phase I trial (CVIA 057)

Study start date: December 2017

in isolation unit



LAI: Live-attenuated influenza virus vaccine (Leningrad backbone)

IIV: Inactivated influenza virus vaccine → split vaccine

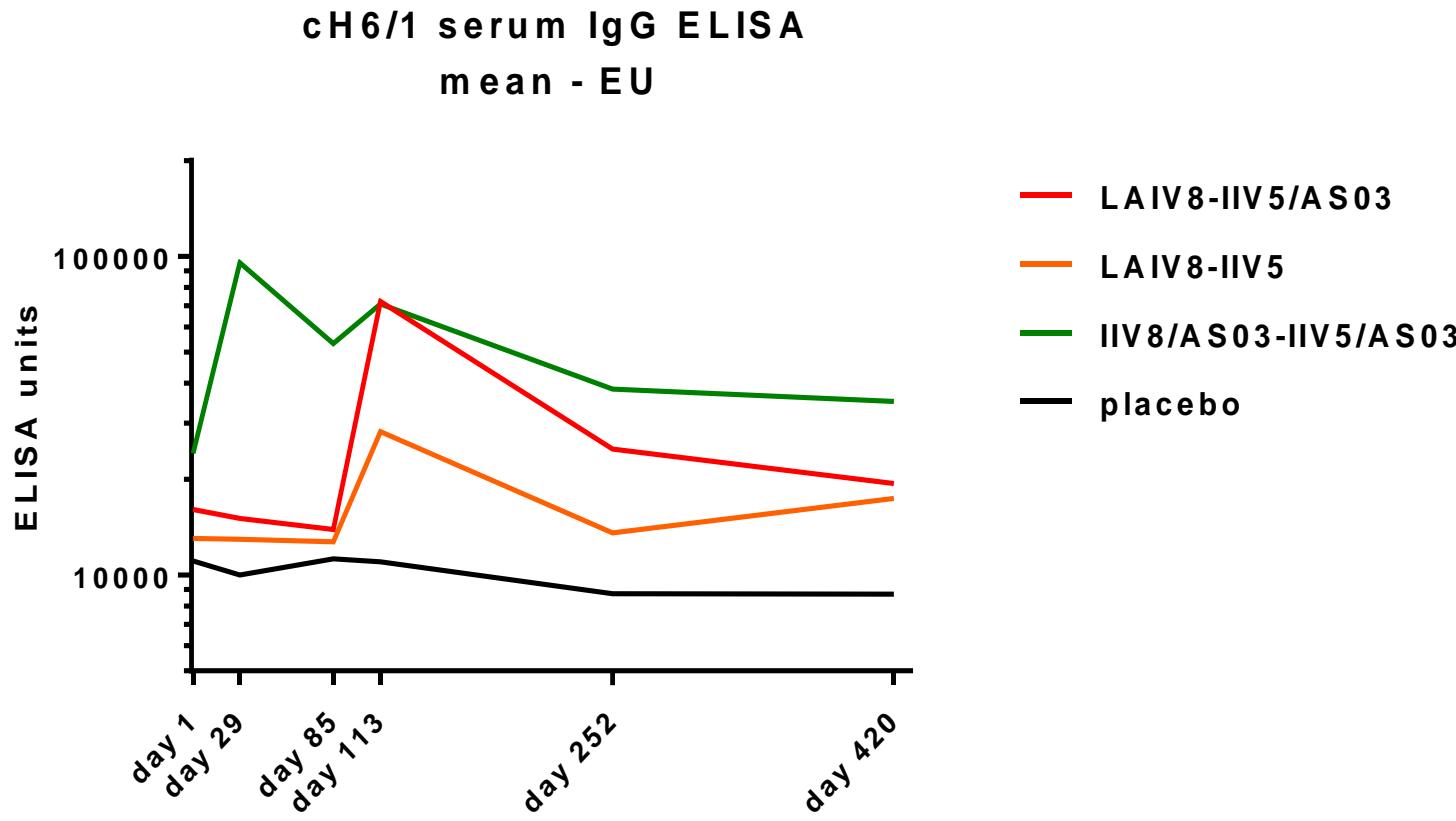
AS03: Adjuvant

# Trial design overview

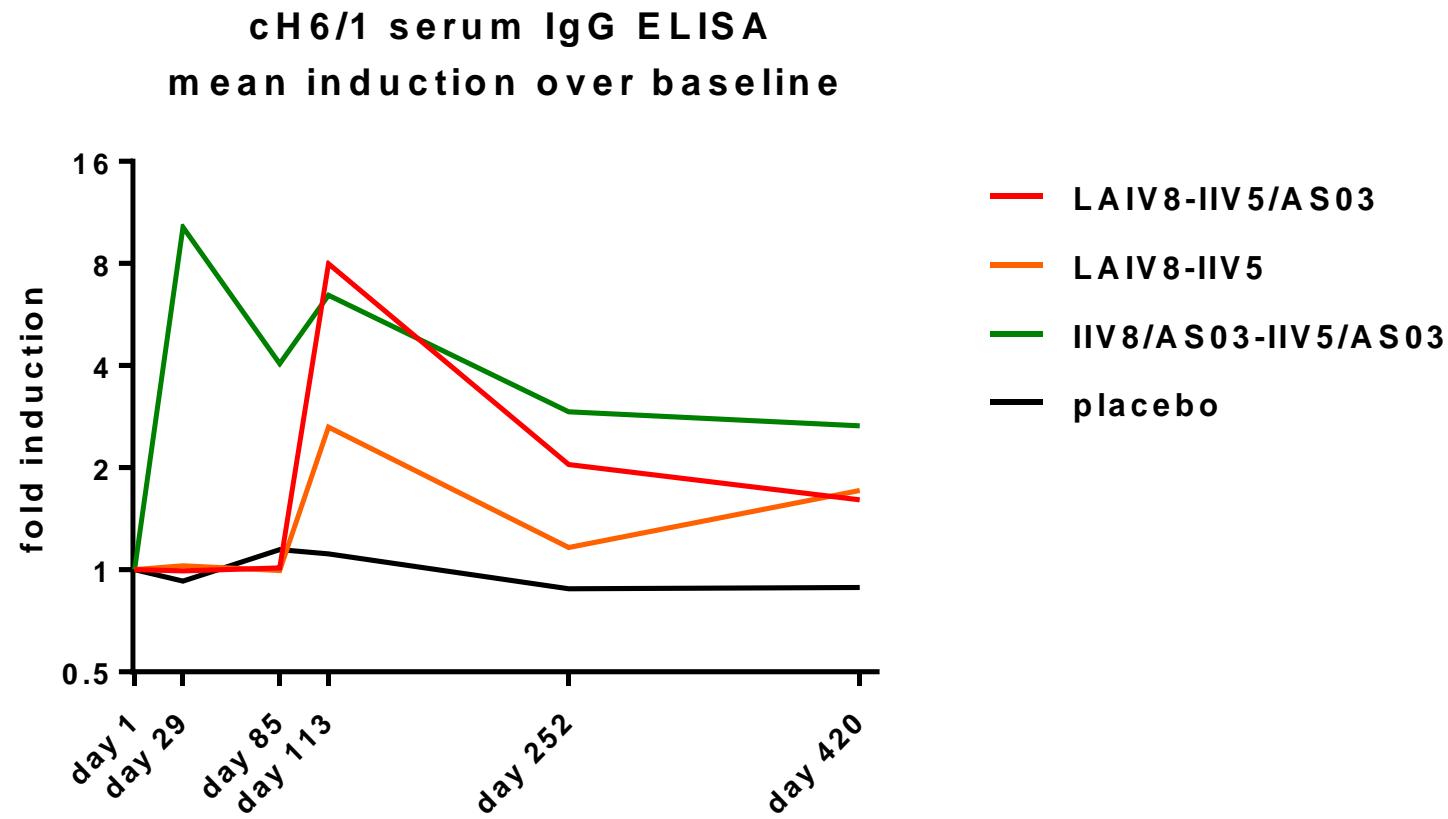
- Prospective, randomized, controlled, observer-blind, phase 1 trial
- Healthy male and female adults 18 through 39 years of age
- 65 subjects (39 Duke, 26 CCHMC) randomized to one of five groups
- Median age 29 years; 40 female, 25 male

Study Groups	Number of Subjects	Dose 1		Dose 2	
		Treatment	Route	Treatment	Route
1	20	cH8/1N1 LAIV	Intranasal	cH5/1N1 IIV + AS03 <sub>A</sub>	Intramuscular
2	15	cH8/1N1 LAIV	Intranasal	cH5/1N1 IIV	Intramuscular
3	5	Normal Saline	Intranasal	PBS	Intramuscular
4	15	cH8/1N1 IIV + AS03 <sub>A</sub>	Intramuscular	cH5/1N1 IIV + AS03 <sub>A</sub>	Intramuscular
5	10	PBS	Intramuscular	PBS	Intramuscular

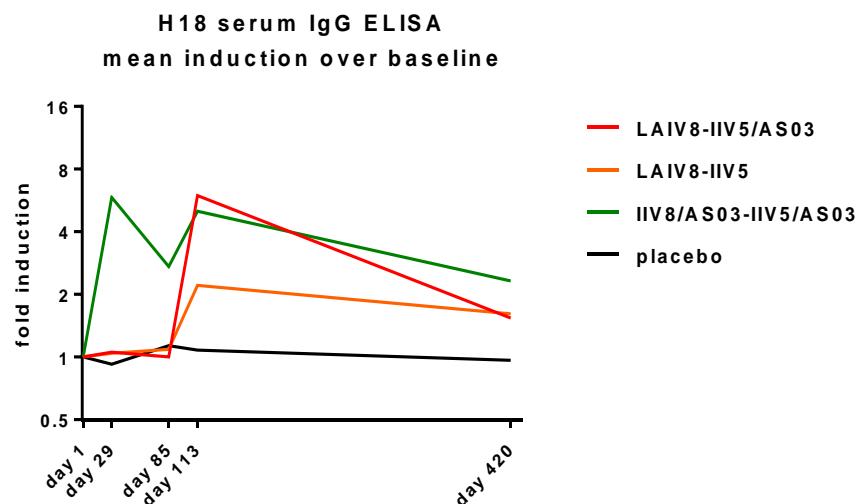
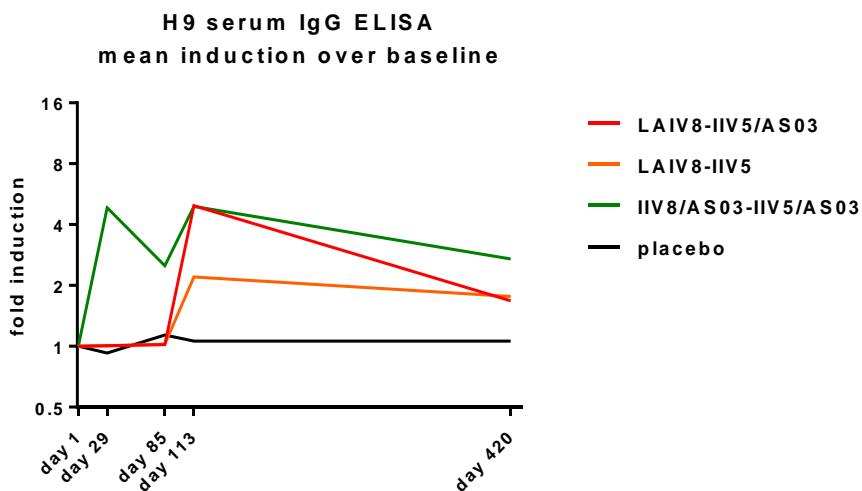
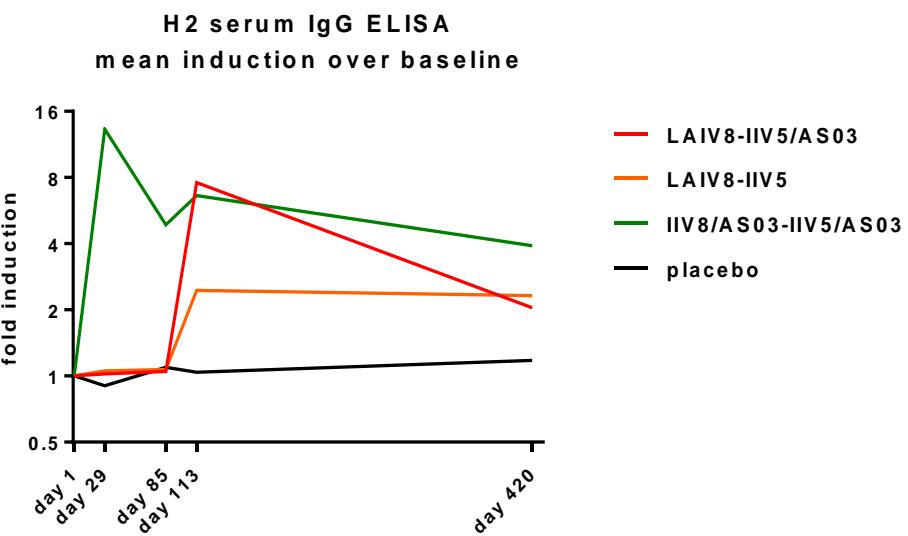
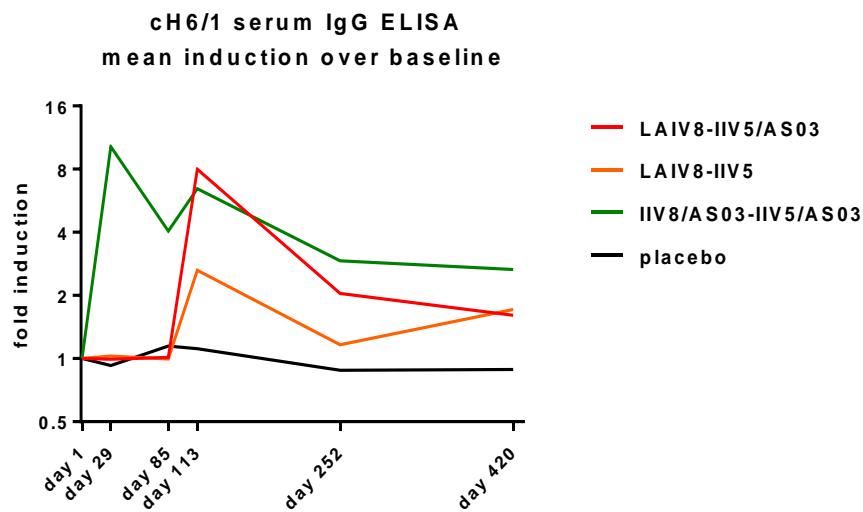
# Serum IgG stalk responses



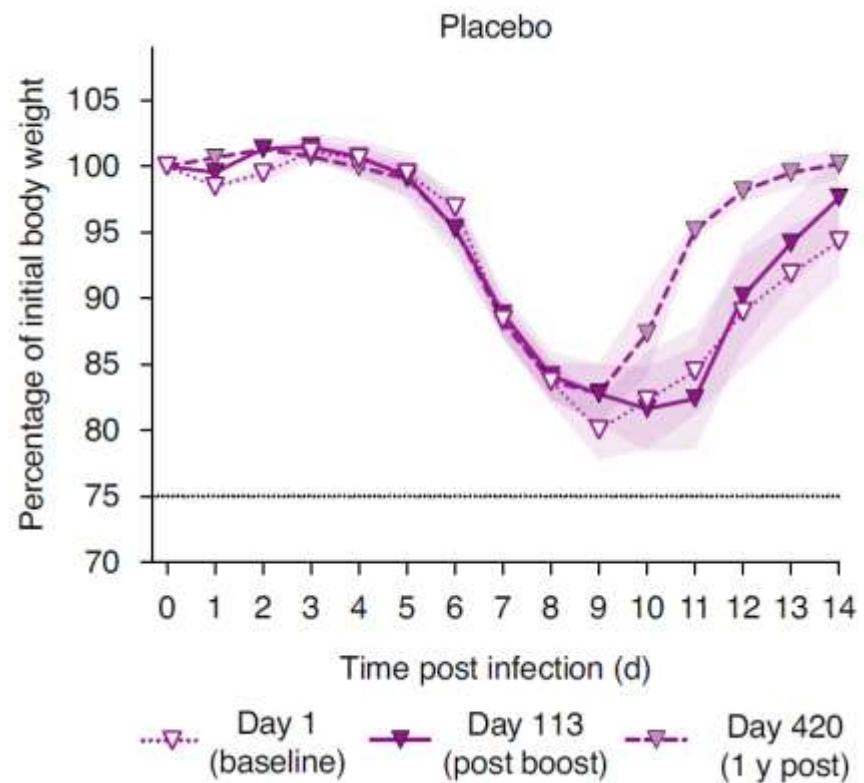
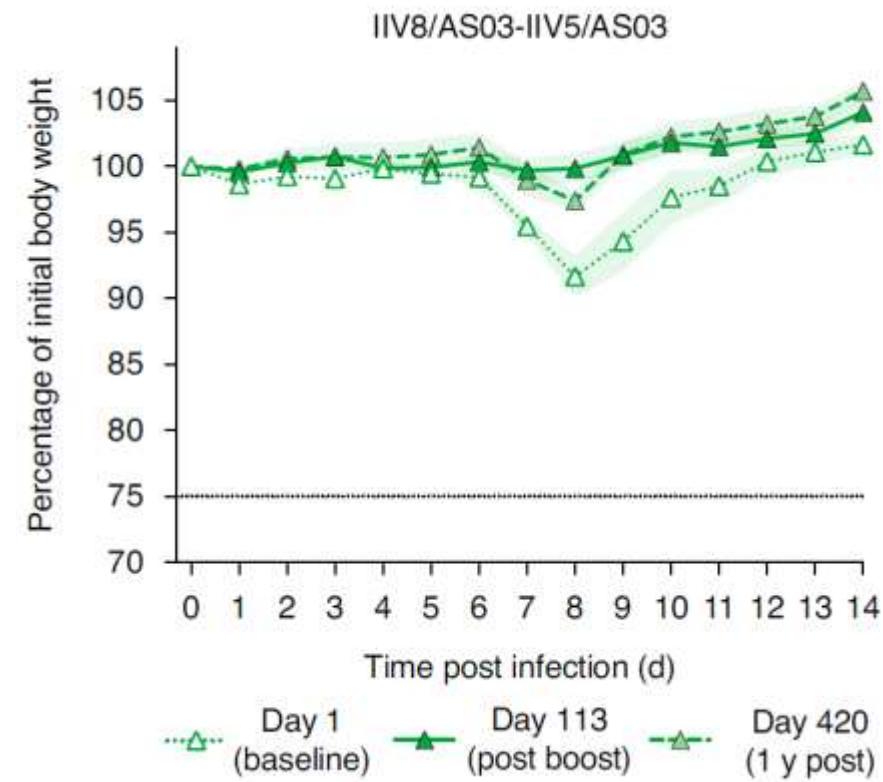
# Serum IgG stalk responses – fold induction



# Binding breadth - induction



# Passive transfer of serum from cHA vaccinated individuals protects mice against heterosubtypic influenza virus challenge



cH6/1N5 virus challenge

# CONCLUSIONS

VACUNACION SECUENCIAL CON VACUNAS DE  
GRIPE BASADAS EN PROTEINAS HA QUIMERICAS  
INDUCEN ANTICUERPOS CONTRA EL TALLO DE LA  
HA CAPACES DE PROTEGER CONTRA GRIPE  
SEVERA CON HOMOLOGOS Y HETEROLOGOS  
VIRUS DE LA GRIPE

T  
H  
A  
N  
K  
S



...and  
let's get  
vaccinated