OFFLU avian influenza virus characterisation meeting
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Focus on H9N2

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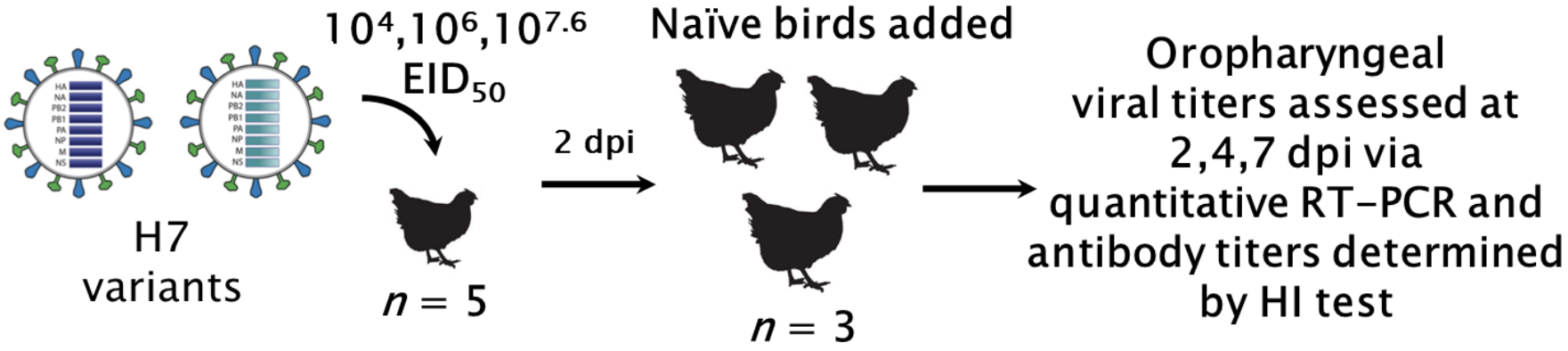
H9N2

- H9N2 avian influenza is widely endemic in Asia, the Middle East and North Africa
- 3 major poultry lineages
  - Commonly referred to G1, Y280, and Y439
  - Other lineages in wild birds and an additional lineage in Germany
- Poultry adapted lineages cause important clinical disease
- Several reported cases of zoonotic infection with only mild respiratory disease

H9 Phylogenetic tree

Poultry transmission studies



Transmission of infected and contact chickens with H7N9 viruses and H9N2 viruses

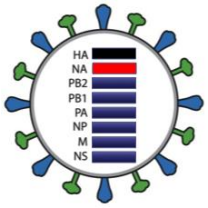
Number of seroconverted Chickens

Poultry/Dose (EID_{50}/Bird)	Challenged	Contacts	
A/Hong Kong/5942/13 10^4	1/5	0/3	H7N9
10^6	5/5	0/3	
A/Hong Kong/734/14 10^4	5/5	0/3	
10^6	5/5	2/3	
A/Hong Kong/2212982/14 10^4	2/5	0/3	
10^6	5/5	1/3	
A/Hong Kong/308/2015 10^4	5/5	3/3	H9N2
10^6	5/5	3/3	

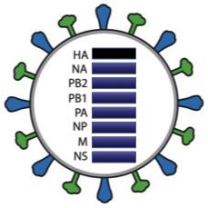
Modified: Spackman, Erica. et al. Virol. 2015;477:72-81

Can other HA and NA genes mediate efficient viral transmission with the A/Anhui/1/2013 and A/CK/Wenzhou/678/2013 internal gene cassette?

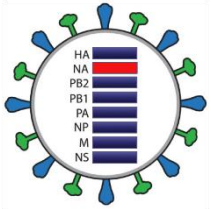
rgH9N2$_{Anhui}$



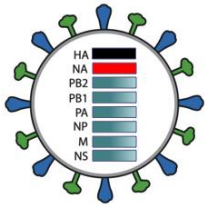
rgH9N9$_{Anhui}$



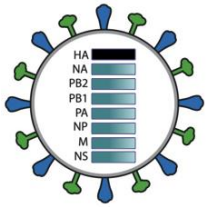
rgH7N2$_{Anhui}$



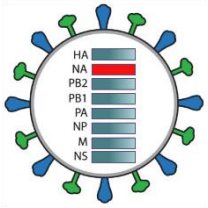
rgH9N2$_{Wenzhou}$



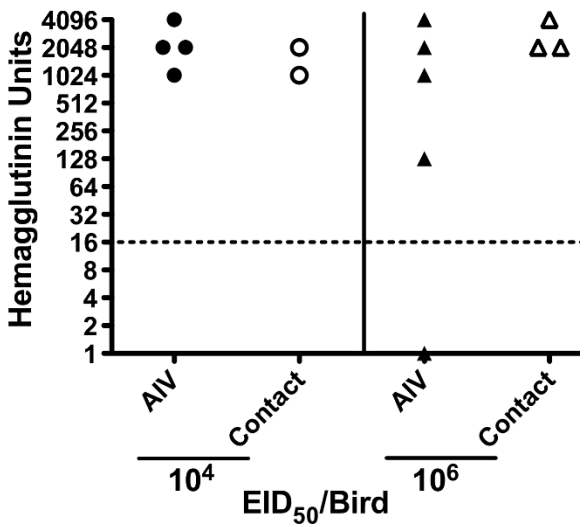
rgH9N7$_{Wenzhou}$

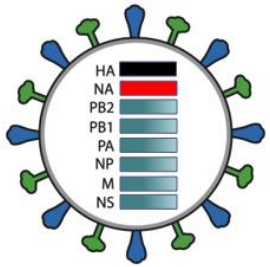


rgH7N2$_{Wenzhou}$

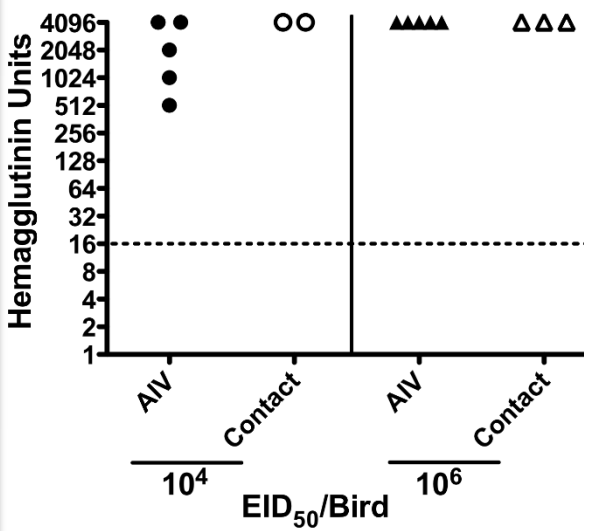


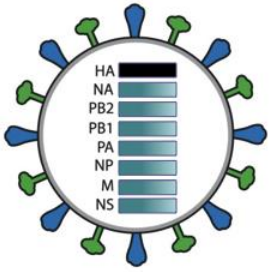
$rgH9N2_{Wenzhou}$ and $rgH9N7_{Wenzhou}$ efficiently transmits in poultry



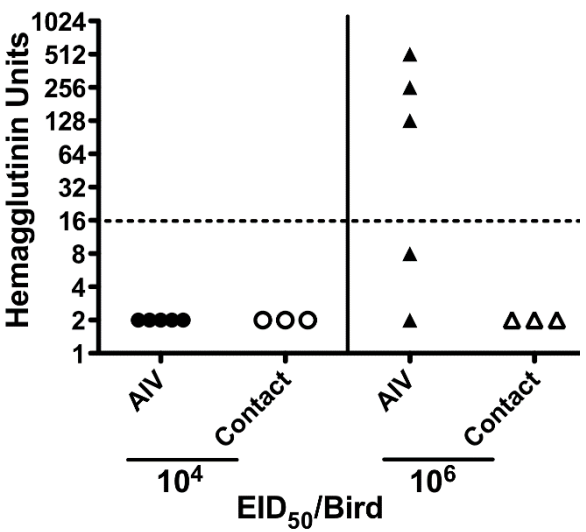


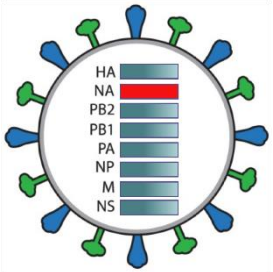
$rgH9N2_{Wenzhou}$





$rgH9N7_{Wenzhou}$

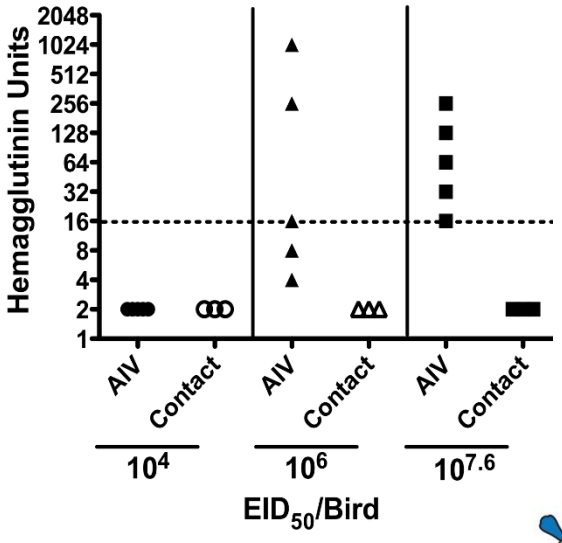




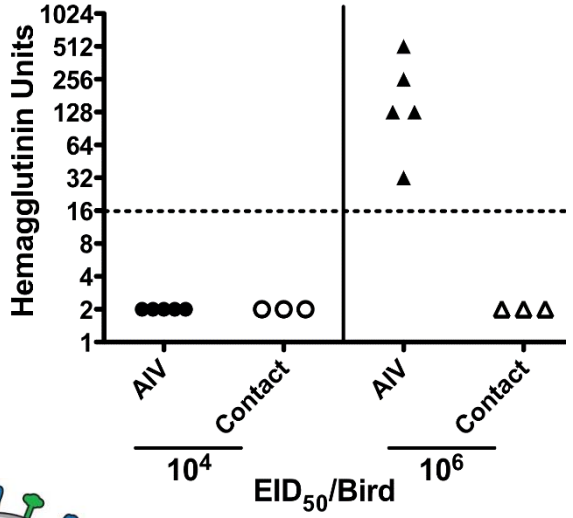
$rgH7N2_{Wenzhou}$

Various HPAIV H5Nx genes do not efficient transmit in chickens when expressed with H7N9 internal genes

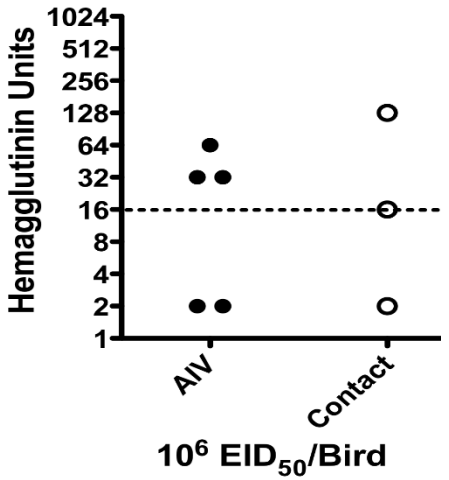
H5N6
A/DK/Guangdong/01/2014

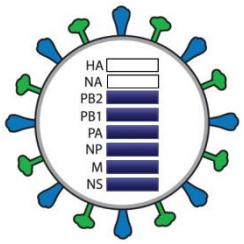


H5N8
A/Gyrfalcon/WA/40188-6/2014

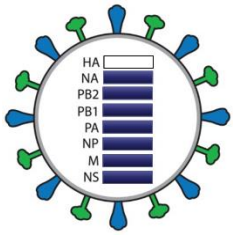


H5N2
A/CK/Taiwan/1997/2012





$rgH5Nx_{Anhui}$



$rgH5N9_{Anhui}$

Conclusions:

- Recent H9N2 have a low chicken infectious dose 50 and easily transmit to contact controls
- H7N9, H5Nx 2.3.4.4 viruses, and many other viruses poorly transmit in poultry
- Reverse genetics studies confirm the H9 hemagglutinin gene is the primary determinant of transmission in chickens

H9N2

- Poultry adapted H9N2 viruses are highly diverse with multiple different lineages
- Vaccination can be effective at reducing clinical disease
- Antigenic drift requiring vaccine update is necessary
- Low infectious dose and highly transmissible
- Zoonotic infection, although currently of low virulence

H9N2 Nomenclature

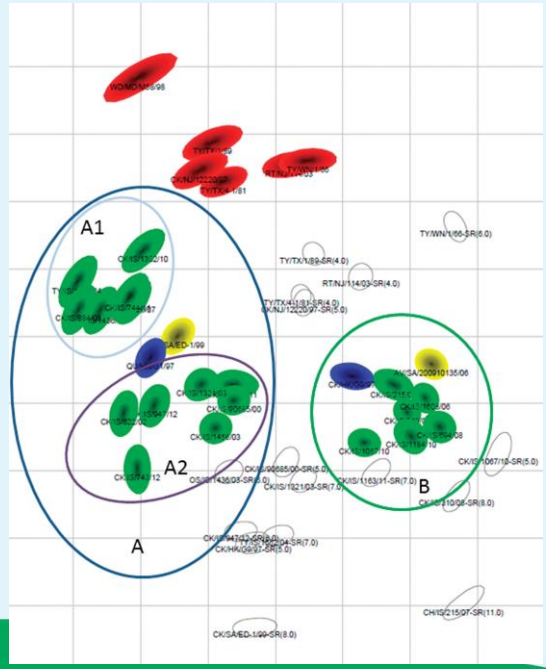
- Establish a nomenclature system to provide standardization (clade system?)
- Provide more informative naming of lineages
- 3 poultry adapted lineages with likely different precursor
- Acceptance of system by reference laboratories is critical
- Establish on online source, like the Influenza Research Database, to predict lineage for easy analysis (currently available for H5 and swine viruses)

H9N2-Diagnostics

- Provide validated H9 real-time RT-PCR tests to identify H9 influenza viruses
  - Existing tests may be adequate
  - Provide comparison testing
- Provide serologic reagents to assure accurate HI testing
  - Traditional reagents
  - Adenovirus serotype 5 vector from commercial source

H9N2-Antigenic Cartography

- Using standardized reagents do cross HI studies of representative H9N2 viruses
  - Provide support for identifying phylogenetic clades
  - Provide understanding of cross reactivity between different sublineages



H9N2-Vaccines

- Multiple examples of antigenic drift requiring vaccines to be updated
- Fortunately vaccines are LPAI and can be more easily updated
- Provide science based research using sequence, antigenic cartography, and challenge studies to provide guidance on when vaccines should be updated

Conclusions

- H9N2 viruses remain a threat to poultry world wide
- No known wild bird spread
- Providing standardization of nomenclature and diagnostic reagents will allow clearer understand of risks
- Control of virus in endemic or outbreak countries will reduce the risk of spread to everyone
- Antigenic cartography and vaccine studies will support countries that vaccinate