**Supplementary materials.**

**Experimental procedures**

HI assays

A modified HI assay using horse erythrocytes was performed as previously described *(1)*. Sera were first heat inactivated, tested for nonspecific agglutinins, and adsorbed with packed horse erythrocytes as needed. To eliminate potential nonspecific inhibitors introduced from hemadsorption, sera were then treated with receptor destroying enzyme (RDE) at 37oC for 18–20 hours, followed by heat inactivation before HI assays.

For HI assays, sera were first pre-diluted at a 1:10 ratio, then serially two-fold diluted and incubated with 4 HA units/25µl of virus for 30 minutes. Horse erythrocytes were then added to the wells and incubated for 60 minutes before reading. HI titers were defined as the reciprocal of the last dilution of serum that completely inhibited hemagglutination. Antibody titers <10 were reported as 5 for calculation purposes.

MN assays

MN assays were performed as previously described *(2).* Human sera were heat inactivated at 56°C for 30 minutes and pre-diluted at a 1:10 ratio. Two-fold serially diluted sera were incubated with one-hundred 50% tissue culture infection dose (TCID50) of influenza viruses and incubated at 37°C 5% CO2 for 1 hour. The virus serum mixture was used to infect 1.5 × 104/well Madin-Darby canine kidney cells, and incubated for 18–20 hours at 37°C with 5% CO2. After cold acetone fixation, the presence of viral protein was quantified by ELISA using monoclonal antibodies specific to the nucleoproteins of the influenza A viruses. MN titers were defined as the reciprocal of the highest dilution of serum that gave 50% neutralization. Antibody titers <10 were reported as 5 for calculation purposes.

*rH7, rH3 specific ELISA*

HisGrab™ Nickel coated plates (Thermo Fisher Scientific, Illinois, USA) were coated with 200 ng/well of purified, trimeric, recombinant HAs from A/feline/New York/108/2016 (H7N2) or A/Maryland/26/2014 (A/Hong Kong/4801/2015-like H3N2)(kindly provided by Dr James Stevens, Influenza Division, CDC) by the C-terminus 6X-histidine tag. Trimeric HAs were expressed and purified from the supernatant of recombinant baculovirus infected Sf9 cells using methods as described by Stevens et al. *(3).* Plates were incubated at 4°C overnight. All sera were two-fold serial diluted starting from a 1:100 ratio and added to rHA coated plates. The plates were incubated at room temperature for 1 hour. After washing, horseradish peroxidase-labeled goat anti human IgM or anti human IgG conjugate was added to the plates followed by TMB Microwell Peroxidase Substrate and stop solution, before reading at 450 nm using a plate spectrophotometer. The anti-HA IgM and IgG titers were determined by the reciprocal of the highest serum dilution at which OD450 nm was higher than 0.2 and more than two-fold higher than no serum control well.

*Antibody adsorption*

One hundred microliters of serum sample was incubated with 300l 105 HAU of purified whole virus A(H7N2) (A/New York/108/2016), A(H3N2) (A/Hong Kong/4801/2014), A(H1N1)pdm09 (A/Michigan/45/2015), or PBS control for 2.5 hours at 4oC followed by ultracentrifugation at 110,000 x g for 45 min to remove virus-antibody complexes. To remove residue virus, sera were incubated with packed turkey red blood cells at 4oC for 30 min, then centrifuged at 400 x g at 4oC for 5 minutes. Adsorbed sera were treated with RDE and heat inactivated at 56oC for 1 hour before MN and ELISA assays.

**References**

1. Levine MZ, Holiday C, Liu F, Jefferson S, Gillis E, Bellamy AR, et al. Cross-reactive antibody responses to novel H5Nx influenza viruses following homologous and heterologous prime-boost vaccination with a prepandemic stockpiled A(H5N1) vaccine in humans. J Infect Dis. 2017;216(suppl\_4):S555-S9.

2. WHO Global Influenza Surveillance Network. Manual for the laboratory diagnosis and virological surveillance of influenza. Geneva, Switzerland: WHO Press; 2011.

3. Stevens J, Corper AL, Basler CF, Taubenberg JK, Palese P, Wilson IA. Structure of the uncleaved human H1 hemagglutinin from the extinct 1918 influenza virus. Science. 2004;303(5665):1866-1870.