



**Figure S3. Influenza H1 HA binding competition, negative stain electron microscopy, autoreactivity analyses, stem-directed epitope, and antibody heavy and light chain recognition, related to Figures 1-6.** (A) Antibodies isolated from vaccinated subjects were tested for binding to H1 HA (either from A/California/04/2009 (H1N1) or A/New Caledonia/20/1999 (H1N1)) starting at 10 µg/ml with three-fold dilutions. HA proteins were pre-incubated with CR9114 prior to antibody incubation to assess whether antibody binding was affected by a HA-stem antibody in a binding-competition assay. (B) Analysis of antibody Fab-HA complexes by negative stain electron microscopy. Aligned particle averages are shown with each image 28 nm x 28 nm in size. HA control and known HA-stem binding antibodies in complex (CR8020 and Fl6v3) are shown for reference. Fab concentration was varied to allow one Fab to one HA complex formation for visualization of the side-view of the complexes. The HA head and stem domains are indicated in the top left panel and stem-binding HAs are indicated in all other images. (C) Hep-2 cell staining at 50 µg/ml antibody concentration is shown for representative antibodies from each convergent class and also for a set of HA stem-reactive antibodies and control antibodies. (D) Anti-cardiolipin ELISA (GPL units) results are shown for antibodies at a concentration of 33 µg/ml. (E) Epitopes for group 1 and 2-neutralizing HA-stem directed antibodies colored by the average HA-buried surface area of the antibodies. One HA protomer is depicted in ribbon representation with larger ribbon diameter and yellow or red coloring indicating increased buried surface. Antibodies that neutralize both group 1 and 2 influenza A viruses bind primarily to an epitope which includes the HA2 helix A and fusion peptide, but avoids the group 2-conserved N-linked glycan at Asn 38<sub>HA2</sub>. (F) Heavy and light chain orientation of human antibodies capable of neutralizing group 1 and 2 influenza A.