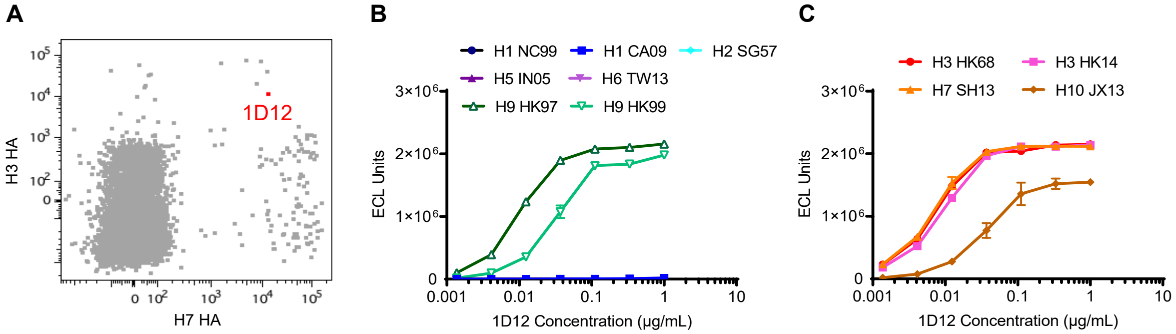


Figure S1. Isolation and HA binding of 315-19-1D12 antibody, related to Figure 1
(A) B cell sorting plot of the PBMCs collected from a human donor two weeks after the vaccine boost. In red is the cell from which the 315-19-1D12 genes were amplified and sequenced that showed binding to both H7 and H3 HAs. (B) Binding measurement of 1D12 antibody to Group 1 HA. (C) Binding measurement of 1D12 antibody to Group 2 HA. Error bars in (B) and (C) represent SD of the antibody tested in duplicate, representative of two independent experiments.

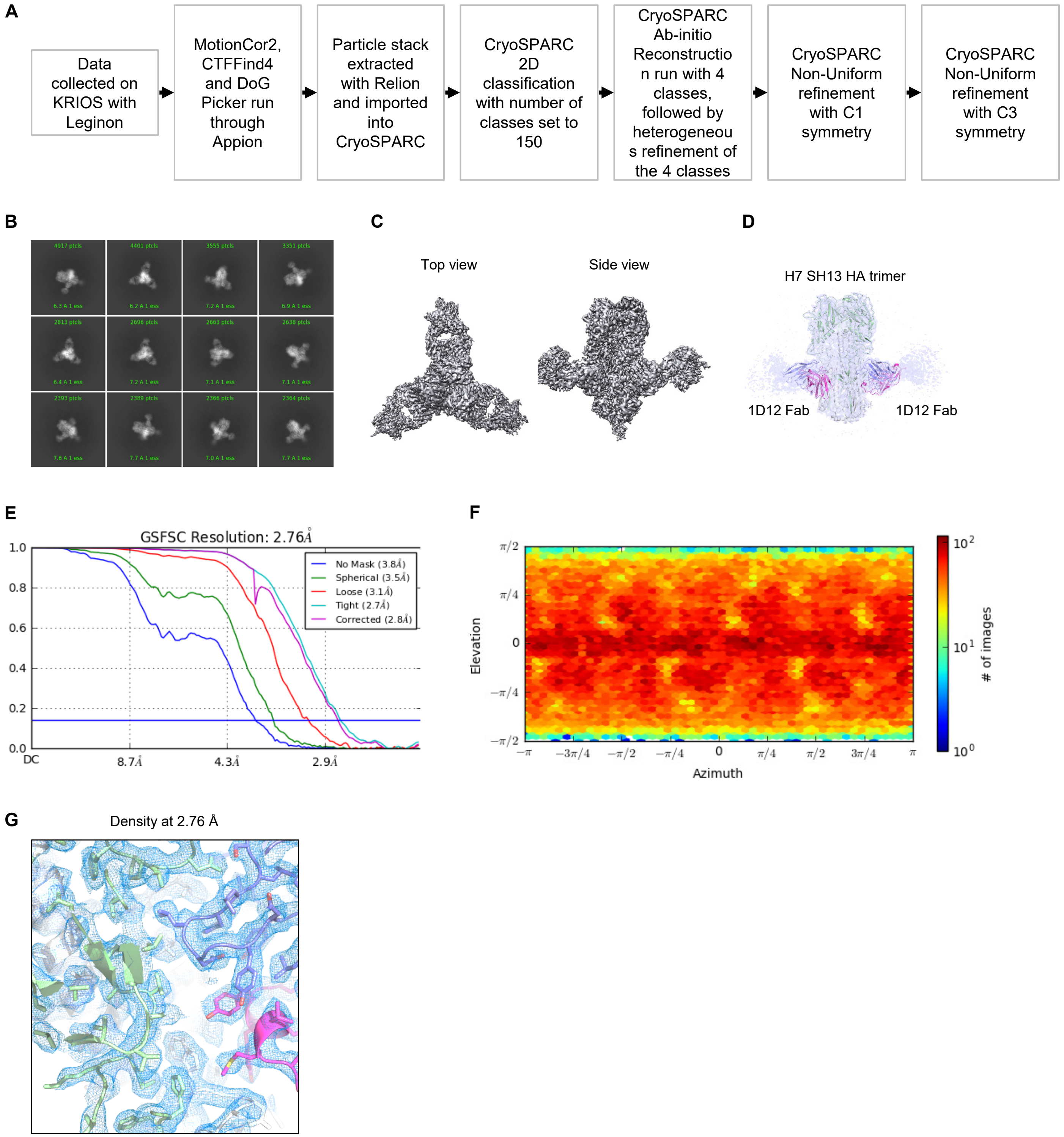


Figure S2. EM supporting data and HA-Fab binding data, related to Figure 1

(A) Workflow of data processing is shown. (B) Representative 2D class averages calculated from selected particles. (C) Three-D reconstruction of electron density map. (D) Superposition of refined coordinates with the cryo-EM reconstructed density map. (E) FSC curves of the 3D reconstructions with horizontal blue line indicating $FSC_{0.143}$. (F) The angular distribution plot is shown indicating no preferred orientation issues. (G) A section of representative electron density at 2.76 Å superimposed on the refined coordinates.

A Heavy and light chain sequences of inferred germline and mature 1D12 (Kabat)

```
      <--------------FR1-----------><CDR><-----FR2----><-----CDR2------><------------FR3---------------><------CDR3------><--FR4---->
  iGL QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGRINPNSGGTNYAQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCATKRGAVTAMVYYYYYGMDVWGQGTTVTVSS
Heavy QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYLHWVRQAPGQGLEWMGRINPDTGGTNYAQKFQGRVSMTRDMSISTHYMELSRLTSDDTAVYYCATKRGAVTAMVYYYFYGMDVWGQGTTVTVSS

      <----------FR1---------><----CDR1------><------FR2----><CDR2-><------------FR3---------------><--CDR3---><--FR4--->
  iGL DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQALQTPPGLTFGGGTKVEIK
Light DIVMTQSPLSLSVTPGEPASISCRSSHSLLHLNGYNYLDWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGIYYCMQALRTPPGLTFGGGTKVDIK
```

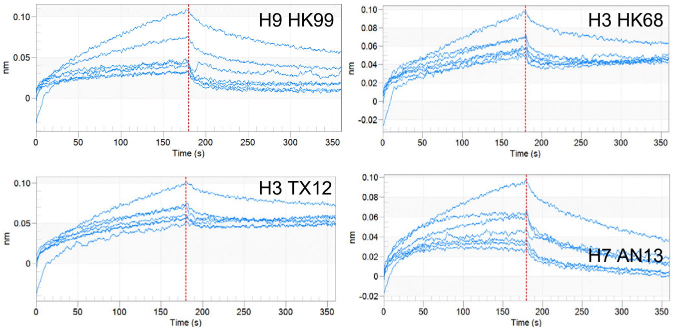
B

Antibody	HV	HD	HJ	HV identity (%)	CDR H3	LV	LJ	LV identity (%)	CDR L3
315-019-1D12	HV1-2	HD2-21	HJ6	96.6	KRGAVTAMVYYYFYGMDV	KV2-28	KJ4	96.6	MQALRTPPGLT

C Summary of germline and mature 1D12 binding K_D

	HA	Germline-reverted	Mature
Group 1	H1 SI06	NB	NB
	H1 CA09	NB	NB
	H2 CAN05	NB	NB
	H5 VN04	NB	NB
	H9 HK99	NB	23.0 nM
Group 2	H3 HK68	NB	14.1 nM
	H3 TX12	NB	32.3 nM
	H7 AN13	NB	34.4 nM

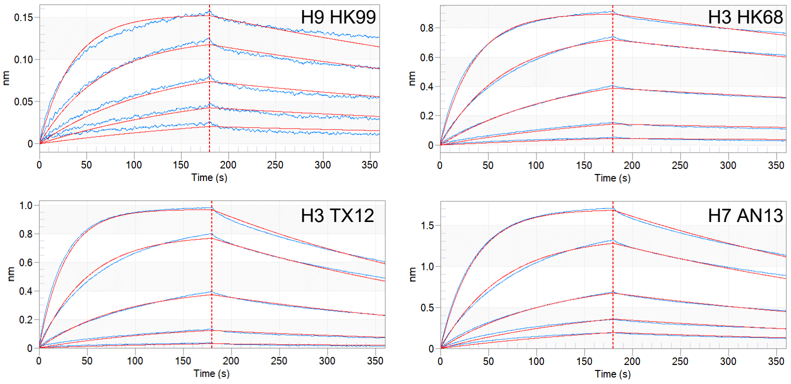
Octet binding curves of germline-reverted 1D12



D Classification of influenza antibodies from published papers and this paper

Antibody	Specificity	Classes	VH	CDR H3	VL	CDR L3	Epitope, Structure and Sequence	1D12 Class
MEDI8852	STEM	VH6-1	IGHV6-1	CARSGHITVFGVNVDAFDMW	IGKV1-39	CQQSRTF	MEDI8852 fits VH6-1 sequence signature	-
315-55-1E08	STEM	-	IGHV4-31	CARVPFYYDTRGVFYGNAEGGFEIW	IGKV1-17	CLQHNSYQWTF	1E08 uses different VH and VL pair	-
315-55-1E11	STEM	-	IGHV4-4	CAAGRLDYSDTTGYYKPPPLDYW	IGKV2-30	CMQGTHWPLTF	1E11 uses different VH and VL pair	-
3E1	STEM	-	IGHV4-4	CAREEHITFGGVIVRYW	IGKV1-5	CQQYNSYPWTF	3E1 uses different VH and VL pair	-
FI6v3	STEM	-	IGHV3-30	CAKDSQLRSLLYFEWLSQGYFDYW	IGKV4-1	CQQHYRTPPTF	FI6v3 uses different VH and VL pair	-
Mab3.1	STEM	-	IGHV3-30	CARDLGGYFIRGIMDVW	IGKV1-12	CQQANSFPLTF	Mab3.1 uses different VH and VL pair	-
315-23-1C09	STEM	-	IGHV3-30	CAKDPAFIEMAFHW	IGLV1-47	CAAWDNSLSAHYVF	1C09 uses different VH and VL pair	-
315-53-1A07	STEM	-	IGHV3-30	CTRAIGTTDAFDIW	IGLV1-51	CGTWDRSLSAMVF	1A07 uses different VH and VL pair	-
CR9114	STEM	VH1-69	IGHV1-69	CARHGNYYYYSGMDVW	IGLV1-44	CAAWDDSLKGAVF	CR9114 fits IGHV1-69 sequence signature	-
CR6261	STEM	VH1-69	IGHV1-69	CAKHMGYQVRETMDVW	IGLV1-51	CATWDRRPTAYVVF	CR6261 fits IGHV1-69 sequence signature	-
310-33-1F04	HEAD	-	IGHV3-23	CAKGPASTWQLDPSHHYNGMDVW	IGKV1-17	CLQHISYPLTF	1F04 binds HA head region	-
5J8	HEAD	-	IGHV4-38-2	CARHVRSGYPDTAYYFDKW	IGLV3-21	CQVWDISTDQAVF	5J8 binds HA head region	-
C05	HEAD	-	IGHV3-23	CHMSMQQVVSAGWERADLVGW	IGKV1-33	CQQYDGLPFTF	C05 binds HA head region	-
F005-126	HEAD	-	IGHV1-18	CARVEGVRGVMGFHYYPMDVW	IGLV1-40	CQSYDSSLSGSVF	F005-126 binds HA head region	-
F045-092	HEAD	-	IGHV1-69	CAGPSITESHYCLDCAAKDYYYGLDVW	IGLV1-44	CASWDDSLNGVVF	F045-092 binds HA head region	-
315-09-1B12	STEM	VH1-18 +QxxV	IGHV1-18	CARGLLQGAVILDSYHYALDFW	IGKV3-20	CQQYDTSPRWTF	315-09-1B12 fits VH1-18+QxxV sequence signature	-
CR8020	STEM	CR8020	IGHV1-18	CAREPPLFYSSWSLDNW	IGKV3-20	CQQYGTSPRTF	CR8020 uses different VH and VL pair	-
CR8043	STEM	CR8043	IGHV1-3	CARGASWDARGWSGYW	IGKV4-1	CHQYYTAPWTF	CR8043 uses different VH and VL pair	-
315-53-1A09	STEM	-	IGHV3-11	CARTRLGDIVQAPGVIGYYYGMDVW	IGKV1-39	CQQSHETPLTF	1A09 uses different VH and VL pair	-
CT149	STEM	VH1-18 +QxxV	IGHV1-18	CARDKVQGRVEVGSGGRHDYW	IGKV3-20	CQQFSVSPWTF	CT149 fits VH1-18+QxxV sequence signature	-

Octet binding curves of mature 1D12



Mature 1D12 Fab binding kinetics		
HA	k_{on}(1/s)	k_{off}(M/s)
H9 HK99	6.77E+04	1.56E-03
H3 HK68	7.02E+04	9.89E-04
H3 TX12	8.55E+04	2.76E-03
H7 AN13	6.64E+04	2.28E-03

Figure S3. Inferred germline-reverted 1D12 antibody does not bind influenza HA, related to Figure 3
(A) Sequence alignments of germline and mature 1D12 heavy and light chains. (B) Summary of antibody 1D12 sequence characteristics. (C) Binding affinity and kinetics of 1D12 to various HAs measured by Octet. Hemagglutinin analyte concentrations used 2-fold dilutions starting at 100 nM and ending with 6.25 nM.

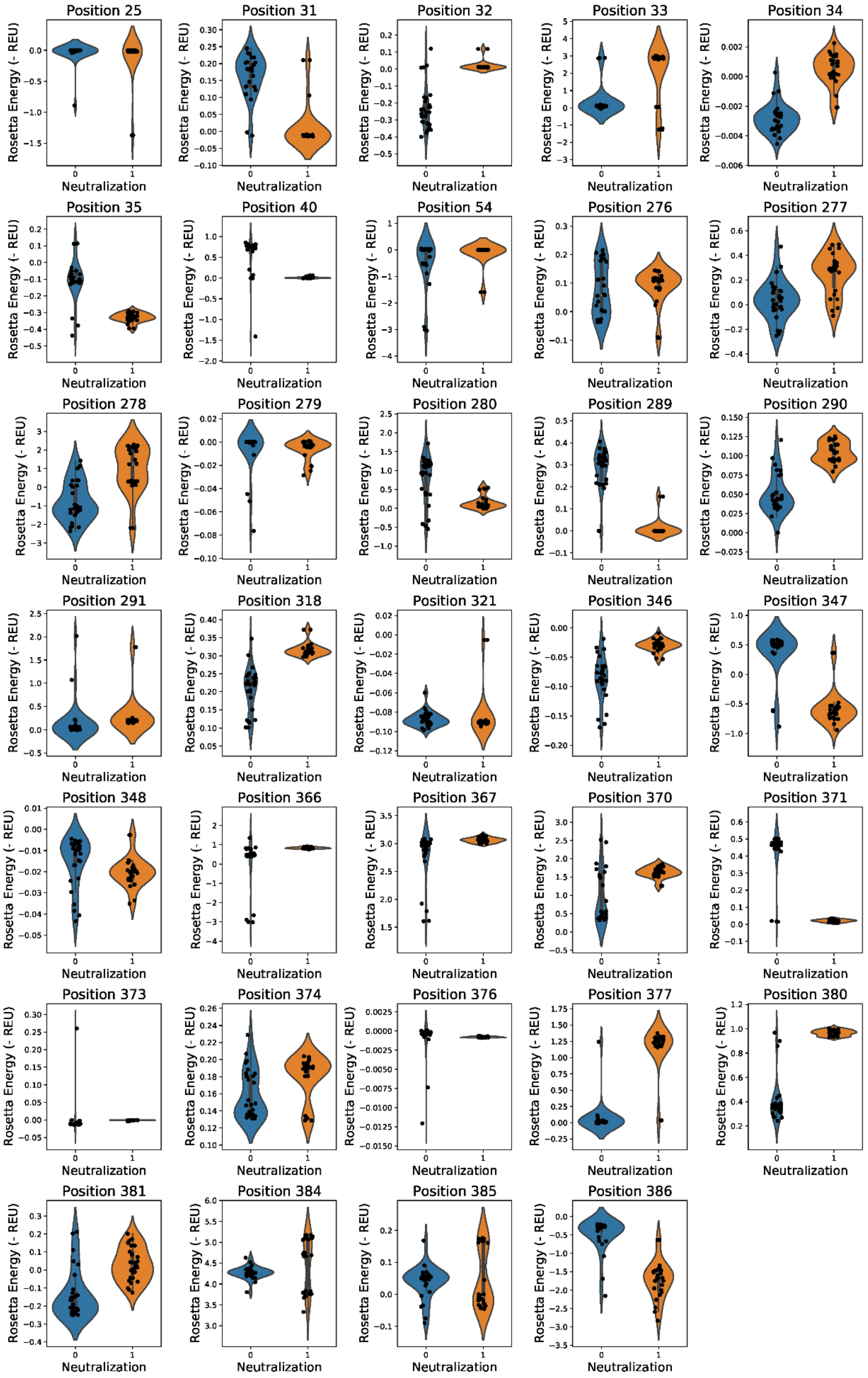
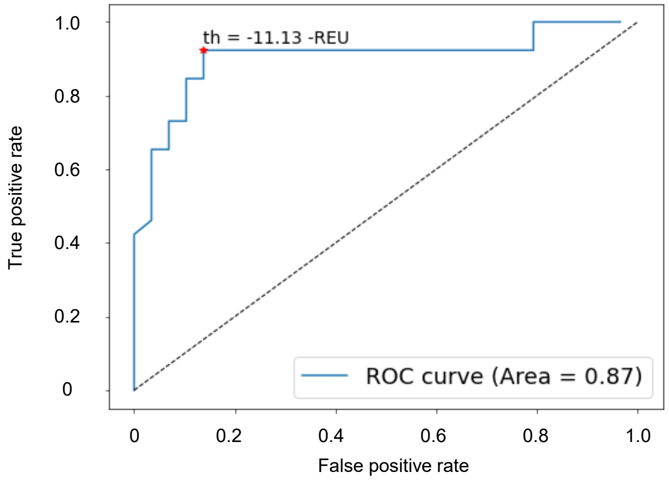
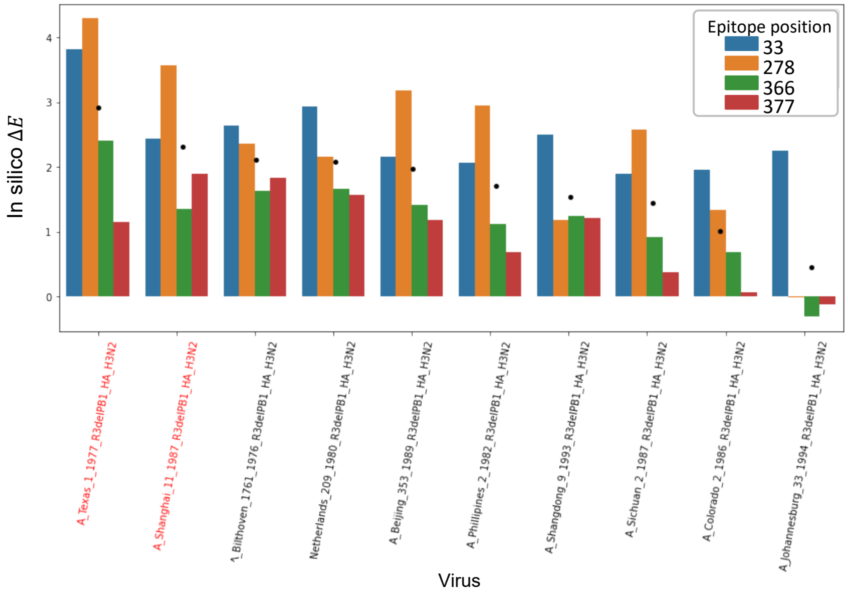


Figure S4. Rosetta energies per position, related to Figure 5
Rosetta energies for sensitive and resistant sets for specific subset of the extended epitope positions. Only 34 out of the 46 extended epitope positions are shown, with the remaining 10 positions having no detectable in-silico energy contributions.

A *In silico* classification ROC



B Sensitive strains ΔE for 4 key epitope positions



C *In silico* ΔE correlated to experimental binding

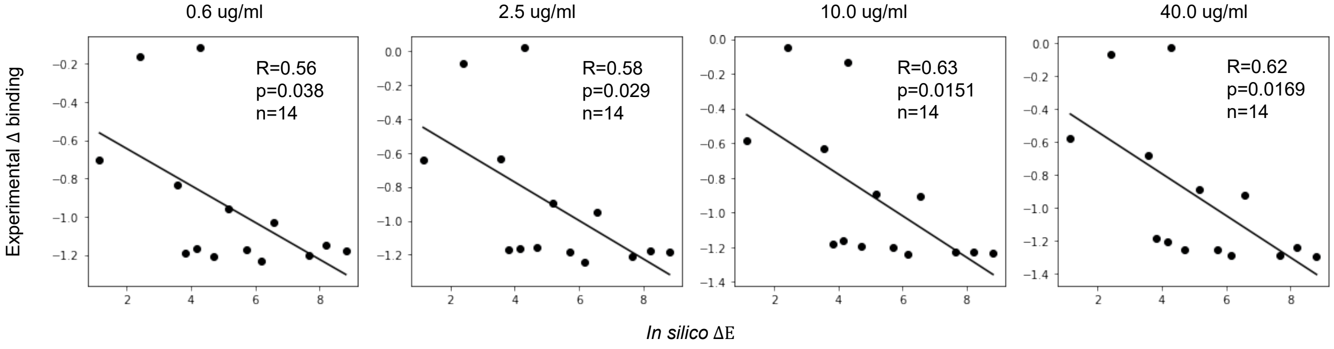


Figure S5. Experimental assessment of *in silico* predictions shows high accuracy and correlates with experimental binding data, related to Figure 5
(A) HA neutralization was predicted with *in silico* energies. The classification performance was assessed by the ROC AUC and achieves 89% accuracy at the best energy threshold. (B) Two sensitive strains containing the most frequent residues at the key epitope positions from the sensitive set were selected based on the highest average *in silico* ΔE energy for further experimental validation. Black dots represent the average ΔE across the 4 positions. (C) *In silico* ΔE correlated to experimental ΔBinding at multiple 1D12 antibody concentrations.

Table S1. Cryo-EM data collection and refinement statistics, related to Figure 1

	H7 SH13 HA Trimer in complex with 1D12 Fab
EMDB ID	**21961**
PDB ID	**6WXL**
Data Collection	
Microscope	FEI Titan Krios
Voltage (kV)	300
Electron dose ($e^-/Å^2$)	49.90
Detector	Gatan K3
Pixel Size (Å)	1.083
Defocus Range (µm)	-0.1 to -3.3
Magnification	81000
Images	1878
Reconstruction	
Software	cryoSparcV2.12
Particles	142,628
Symmetry	C3
Box size (pix)	400
Resolution Å ($FSC_{0.143}$)	2.76
Refinement (Phenix)	
Protein residues	2175
CC (mask)	0.78
CC (box)	0.64
CC (peak)	0.58
CC (volume)	0.77
Chimera CC	0.89
d $FSC_{0.143}$ Model Resolution (Å)	2.5
EMRinger Score	3.72
R.m.s. deviations	
Bond lengths (Å)	0.005
Bond angles (°)	0.697
Validation	
Molprobity score	1.28
Clash score	2.9
Rotamer outliers (%)	0.16
Ramachandran	
Favored regions (%)	96.79
Disallowed regions (%)	0.0

Table S2. Interactions between 1D12 Fab and influenza A virus HA, related to Figure 1

The data were output from PISA (https://www.ebi.ac.uk/pdbe/pisa) analysis of the cryo-EM structure of the 1D12-SH13 HA complex. (Table continued on next page)

(A) Epitope and paratope areas

	HA	Light chain
Interface (Å²)	591.6	600.1
	HA	Heavy chain
Interface (Å²)	480.6	544.1

(B) Hydrogen bonds between 315-19-1D12 and SH13 HA

	1D12 atom	Bond distance [Å]	SH13 HA atom
1	H:LYS 95[NZ]	3.31	B:GLN 42[OE1]
2	H:TYR 100E[OH]	3.12	B:ASP 19[O]
3	H:TYR 100H[OH]	3.19	B:THR 49[OG1]
4	H:TYR 100H[OH]	2.78	B:ASP 46[OD1]
5	H:TYR 100E[O]	3.04	B:GLN 42[NE2]
6	L:ARG 24[NH2]	2.89	A:ASP 276A[O]
7	L:ARG 93[NH2]	3.03	A:ASN 291[OD1]
8	L:SER 27A[O]	2.99	A:ASN 291[ND2]
9	L:LEU 27C[O]	2.75	A:ASN 291[ND2]
10	L:LEU 27E[O]	3.01	A:THR 40[OG1]
11	L:HIS 27D[NE2]	2.78	B:ASN 53[OD1]
12	L:ARG 93[NH2]	2.83	B:ILE 56[O]
13	L:ARG 93[NE]	3.05	B:ILE 56[O]

Table S2 (continued from prior page). Interactions between 1D12 Fab and influenza A virus HA, related to Figure 1

H: hydrogen bond; ASA: accessible surface area, Å²; BSA: buried surface area, Å²; ΔiG: solvation energy effect, kcal/mol; ||||: buried area percentage, one bar per 10%. (Table continued on next page)

(C) HA Residues that interact with heavy chain

<table>
<tr><th></th><th>HA atoms</th><th>ASA</th><th>BSA</th><th>ΔiG</th></tr>
<tr><td>HA1</td><td>A:HIS 18</td><td>106.81</td><td>18.78</td><td>0.05</td></tr>
<tr><td></td><td>[CB] [CG] [CD2] [CE1] [NE2]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>A:THR 318</td><td>87.28</td><td>2.70</td><td>-0.03</td></tr>
<tr><td></td><td>[O]</td><td></td><td>|</td><td></td></tr>
<tr><td>HA2</td><td>B:LEU 17</td><td>29.50</td><td>0.86</td><td>-0.01</td></tr>
<tr><td></td><td>[O]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>B:ILE 18</td><td>159.65</td><td>23.12</td><td>-0.18</td></tr>
<tr><td></td><td>[CA] [C] [O]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>B:ASP 19</td><td>99.80</td><td>60.07</td><td>0.25</td></tr>
<tr><td></td><td>[CA] [C] [O]^H [CB] [OD1]</td><td></td><td>|||||||</td><td></td></tr>
<tr><td></td><td>B:GLY 20</td><td>13.29</td><td>8.45</td><td>0.02</td></tr>
<tr><td></td><td>[N] [CA] [C] [O]</td><td></td><td>|||||||</td><td></td></tr>
<tr><td></td><td>B:TRP 21</td><td>116.72</td><td>27.42</td><td>0.13</td></tr>
<tr><td></td><td>[CD1] [NE1] [CZ2]</td><td></td><td>|||</td><td></td></tr>
<tr><td></td><td>B:ASP 37</td><td>12.99</td><td>0.24</td><td>-0.00</td></tr>
<tr><td></td><td>[O]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>B:TYR 38</td><td>159.49</td><td>55.23</td><td>0.52</td></tr>
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<tr><td></td><td>B:LYS 39</td><td>174.57</td><td>52.48</td><td>0.26</td></tr>
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<tr><td></td><td>[N] [CA] [CB] [CG] [CD] [OE1]^H [NE2]^H</td><td></td><td>||||||||||</td><td></td></tr>
<tr><td></td><td>B:SER 43</td><td>42.27</td><td>1.61</td><td>0.01</td></tr>
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<tr><td></td><td>[CB] [OG1]^H [CG2]</td><td></td><td>||||||</td><td></td></tr>
</table>

(D) Heavy chain residues that interact with HA

<table>
<tr><th></th><th>Heavy chain atoms</th><th>ASA</th><th>BSA</th><th>ΔiG</th></tr>
<tr><td>HA1</td><td>H:MET 100B</td><td>148.11</td><td>20.92</td><td>0.33</td></tr>
<tr><td></td><td>[CE]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>H:TYR 100F</td><td>164.94</td><td>2.45</td><td>-0.03</td></tr>
<tr><td></td><td>[OH]</td><td></td><td>|</td><td></td></tr>
<tr><td>HA2</td><td>H:THR 28</td><td>141.86</td><td>15.75</td><td>-0.16</td></tr>
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<tr><td></td><td>[CA] [O] [CD1] [CE1] [CE2] [CZ]</td><td></td><td>|||||||</td><td></td></tr>
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<tr><td></td><td>[CE] [NZ]^H</td><td></td><td>||||||</td><td></td></tr>
<tr><td></td><td>H:ALA 98</td><td>113.26</td><td>5.53</td><td>0.09</td></tr>
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<tr><td></td><td>[C] [O]</td><td></td><td>||</td><td></td></tr>
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Table S2 (continued from prior page). Interactions between 1D12 Fab and influenza A virus HA, related to Figure 1

H: hydrogen bond; ASA: accessible surface area, Å²; BSA: buried surface area, Å²; ΔiG: solvation energy effect, kcal/mol; ||||: buried area percentage, one bar per 10%.

(E) HA residues that interact with light chain

<table>
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<tr><td></td><td>[CA] [C] [O]^{H}
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<tr><td></td><td>[N] [O] [CB] [CG]
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<tr><td></td><td>A:ASP 280</td><td>68.25</td><td>2.69</td><td>0.04</td></tr>
<tr><td></td><td>[CB]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>A:ILE 289</td><td>82.77</td><td>31.70</td><td>0.48</td></tr>
<tr><td></td><td>[O] [CG2]</td><td></td><td>||||</td><td></td></tr>
<tr><td></td><td>A:SER 290</td><td>41.78</td><td>7.22</td><td>0.12</td></tr>
<tr><td></td><td>[CA] [C]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>A:ASN 291</td><td>157.68</td><td>110.42</td><td>-0.82</td></tr>
<tr><td></td><td>[N] [CA] [C] [O]
[CB] [CG] [OD1]^{H}
[ND2]^{H}</td><td></td><td>||||||||</td><td></td></tr>
<tr><td></td><td>A:LEU 292</td><td>53.07</td><td>16.12</td><td>0.26</td></tr>
<tr><td></td><td>[CA] [CD2]</td><td></td><td>||||</td><td></td></tr>
<tr><td></td><td>A:PRO 293</td><td>68.16</td><td>12.82</td><td>0.21</td></tr>
<tr><td></td><td>[CG] [CD]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>A:LEU 316</td><td>108.08</td><td>14.82</td><td>0.24</td></tr>
<tr><td></td><td>[CD2]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>A:THR 318</td><td>87.28</td><td>18.06</td><td>0.29</td></tr>
<tr><td></td><td>[CB] [CG2]</td><td></td><td>|||</td><td></td></tr>
<tr><td>HA2</td><td>B:THR 49</td><td>63.75</td><td>28.94</td><td>0.45</td></tr>
<tr><td></td><td>[O] [CB] [CG2]</td><td></td><td>|||||</td><td></td></tr>
<tr><td></td><td>B:LEU 52</td><td>97.87</td><td>53.99</td><td>0.85</td></tr>
<tr><td></td><td>[C] [O] [CB] [CG]
[CD1] [CD2]</td><td></td><td>||||||</td><td></td></tr>
<tr><td></td><td>B:ASN 53</td><td>86.58</td><td>26.44</td><td>-0.37</td></tr>
<tr><td></td><td>[CG] [OD1]^{H} [ND2]</td><td></td><td>||||</td><td></td></tr>
<tr><td></td><td>B:LEU 55</td><td>92.32</td><td>14.26</td><td>0.22</td></tr>
<tr><td></td><td>[O] [CB] [CD2]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>B:ILE 56</td><td>137.78</td><td>97.68</td><td>1.04</td></tr>
<tr><td></td><td>[C] [O]^{H} [CB]
[CG1] [CG2] [CD1]</td><td></td><td>||||||||</td><td></td></tr>
<tr><td></td><td>B:GLU 57</td><td>126.34</td><td>8.37</td><td>0.13</td></tr>
<tr><td></td><td>[CA] [CB]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>B:LYS 58</td><td>173.96</td><td>5.37</td><td>0.06</td></tr>
<tr><td></td><td>[N] [CB]</td><td></td><td>|</td><td></td></tr>
</table>

(F) Light chain residues that interact with HA

<table>
<tr><th></th><th>Light chain atoms</th><th>ASA</th><th>BSA</th><th>ΔiG</th></tr>
<tr><td>HA1</td><td>L:ARG 24</td><td>152.45</td><td>55.68</td><td>-0.81</td></tr>
<tr><td></td><td>[CD] [NE] [CZ] [NH1]
[NH2]^{H}</td><td></td><td>||||</td><td></td></tr>
<tr><td></td><td>L:SER 26</td><td>60.84</td><td>43.82</td><td>-0.36</td></tr>
<tr><td></td><td>[CA] [O] [CB] [OG]</td><td></td><td>||||||||</td><td></td></tr>
<tr><td></td><td>L:HIS 27</td><td>86.20</td><td>21.26</td><td>0.28</td></tr>
<tr><td></td><td>[CA] [CB] [ND1] [CE1]</td><td></td><td>|||</td><td></td></tr>
<tr><td></td><td>L:SER 27A</td><td>58.16</td><td>43.32</td><td>0.44</td></tr>
<tr><td></td><td>[N] [O]^{H} [CB] [OG]</td><td></td><td>||||||||</td><td></td></tr>
<tr><td></td><td>L:LEU 27C</td><td>86.28</td><td>18.95</td><td>-0.22</td></tr>
<tr><td></td><td>[O]^{H}</td><td></td><td>|||</td><td></td></tr>
<tr><td></td><td>L:HIS 27D</td><td>74.58</td><td>2.69</td><td>0.04</td></tr>
<tr><td></td><td>[CA] [C] [O]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>L:LEU 27E</td><td>180.99</td><td>109.00</td><td>1.13</td></tr>
<tr><td></td><td>[N] [CA] [C] [O]^{H} [CB]
[CG] [CD1] [CD2]</td><td></td><td>|||||||</td><td></td></tr>
<tr><td></td><td>L:ASN 28</td><td>84.53</td><td>16.21</td><td>0.26</td></tr>
<tr><td></td><td>[CA] [C] [CB]</td><td></td><td>||</td><td></td></tr>
<tr><td></td><td>L:THR 69</td><td>47.30</td><td>9.54</td><td>0.15</td></tr>
<tr><td></td><td>[CG2]</td><td></td><td>|||</td><td></td></tr>
<tr><td></td><td>L:LEU 92</td><td>22.34</td><td>4.85</td><td>0.08</td></tr>
<tr><td></td><td>[CD1] [CD2]</td><td></td><td>|||</td><td></td></tr>
<tr><td></td><td>L:ARG 93</td><td>124.57</td><td>20.53</td><td>-0.76</td></tr>
<tr><td></td><td>[NH2]^{H}</td><td></td><td>||</td><td></td></tr>
<tr><td>HA2</td><td>L:LEU 27C</td><td>85.59</td><td>1.59</td><td>-0.02</td></tr>
<tr><td></td><td>[O]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>L:HIS 27D</td><td>75.39</td><td>63.22</td><td>-0.20</td></tr>
<tr><td></td><td>[CA] [C] [CG] [ND1]
[CD2] [CE1] [NE2]^{H}</td><td></td><td>|||||||||</td><td></td></tr>
<tr><td></td><td>L:LEU 27E</td><td>181.66</td><td>72.00</td><td>1.07</td></tr>
<tr><td></td><td>[N] [C] [O] [CB] [CG]
[CD1]</td><td></td><td>||||</td><td></td></tr>
<tr><td></td><td>L:ASN 28</td><td>84.78</td><td>35.68</td><td>-0.03</td></tr>
<tr><td></td><td>[N] [CA] [CB] [ND2]</td><td></td><td>|||||</td><td></td></tr>
<tr><td></td><td>L:TYR 32</td><td>57.84</td><td>5.16</td><td>-0.06</td></tr>
<tr><td></td><td>[OH]</td><td></td><td>|</td><td></td></tr>
<tr><td></td><td>L:LEU 92</td><td>22.50</td><td>11.09</td><td>0.03</td></tr>
<tr><td></td><td>[O] [CG] [CD1] [CD2]</td><td></td><td>|||||</td><td></td></tr>
<tr><td></td><td>L:ARG 93</td><td>124.20</td><td>58.58</td><td>-0.86</td></tr>
<tr><td></td><td>[CA] [CG] [CD] [NE]^{H}
[CZ] [NH2]^{H}</td><td></td><td>|||||</td><td></td></tr>
<tr><td></td><td>L:THR 94</td><td>106.72</td><td>4.85</td><td>0.08</td></tr>
<tr><td></td><td>[CG2]</td><td></td><td>|</td><td></td></tr>
</table>

Table S3. The HA residues that compose the 1D12 epitope, related to Figure 5

Residues that differ from the H7N9 SH13 (reference sequence) are in gray shade. Glycans present at positions 33 and 280 in group 1 HA1 are highlighted in red.

			HA1																		HA2																				
Group	Subtype	Strain	31	32	33	40	41	42	54	276A	277	278	280	289	290	291	292	293	316	318	17	18	19	20	21	37	38	39	40	41	42	43	45	46	49	52	53	54	55	56	57
2	**H7N9**	**A/Shanghai/1/2013**	**E**	**R**	**G**	**T**	**E**	**T**	**K**	**A**	**C**	**E**	**D**	**I**	**S**	**N**	**L**	**P**	**L**	**T**	**L**	**I**	**D**	**G**	**W**	**D**	**Y**	**K**	**S**	**T**	**Q**	**S**	**I**	**D**	**T**	**L**	**N**	**L**	**I**	**E**	**K**
	H7N9	A/Netherlands/219/2003	E	R	G	T	E	T	K	A	C	E	D	I	S	N	L	P	L	T	L	I	D	G	W	D	Y	K	S	T	Q	S	I	D	T	L	N	L	I	E	K
	H7N9	A/Anhui/1/2013	E	R	G	T	E	T	K	A	C	E	D	I	S	N	L	P	L	T	L	I	D	G	W	D	Y	K	S	T	Q	S	I	D	T	L	N	L	I	E	K
	H3N2	A/Hong Kong/1/1968	D	D	Q	T	E	L	N	/	C	I	E	P	N	D	K	P	L	T	M	I	D	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	V	I	E	K
	H3N2	A/Bangkok/1/1979	N	D	Q	T	E	L	S	/	C	S	E	P	N	D	K	P	L	T	M	I	D	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	V	I	E	K
	H3N2	A/Phillipines/2/1982	N	D	Q	T	E	L	S	/	C	S	E	P	N	D	K	P	L	T	M	I	D	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	V	I	E	K
	H3N2	A/Beijing/353/1989	N	D	Q	T	E	L	S	/	C	S	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	V	I	E	K
	H3N2	A/Moscow/10/1999	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	N	N	L	N	V	I	E	K
	H3N2	A/Wyoming/3/2003	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	N	N	L	N	L	I	G	K
	H3N2	A/Wisconsin/67/2005	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	N	N	L	N	L	I	G	K
	H3N2	A/Brisbane/10/2007	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Perth/16/2009	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Victoria/361/2011	N	D	Q	T	E	L	S	/	C	N	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Texas/06/2012	N	D	Q	T	E	L	S	/	C	N	A	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Texas/50/2012	N	D	R	T	E	L	S	/	C	K	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Switzerland/9715293/2013	N	D	R	T	E	L	S	/	C	K	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H3N2	A/Alaska/29/2014	N	D	R	T	E	L	S	/	C	K	E	P	N	D	K	P	L	T	M	I	N	G	W	D	L	K	S	T	Q	A	I	D	N	L	N	L	I	G	K
	H10N8	A/Jiangxi/IPB13/2013	N	E	Q	T	E	T	K	N	C	E	K	N	T	R	L	P	L	T	M	V	D	G	W	D	Y	K	S	T	Q	A	I	D	T	L	N	L	V	E	K
1	H1N1	A/South Carolina/1/1918	E	K	@	V	N	L	K	/	C	N	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	D	T	V	N	V	I	E	K
	H1N1	A/Puerto Rico/8/1934	E	K	@	V	N	L	K	/	C	N	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/New Jersey/1976	E	K	@	V	N	L	G	/	C	N	K	@	T	S	L	P	M	T	M	I	D	G	W	D	Q	R	S	T	Q	N	I	D	T	V	N	V	I	E	K
	H1N1	A/Singapore/6/1986	E	K	@	V	N	L	K	/	C	D	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/Beijing/262/1995	E	K	@	V	N	L	K	/	C	D	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/New Caledonia/20/1999	E	K	@	V	N	L	K	/	C	D	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/Solomon Island/3/2006	E	K	@	V	N	L	K	/	C	D	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/Brisbane/59/2007	E	K	@	V	N	L	K	/	C	D	K	@	S	S	L	P	M	T	M	I	D	G	W	D	Q	K	S	T	Q	N	I	N	T	V	N	V	I	E	K
	H1N1	A/California/04/2009	E	K	@	V	N	L	K	/	C	@	T	@	T	S	L	P	M	T	M	I	D	G	W	D	L	K	S	T	Q	N	I	D	T	V	N	V	I	E	K
	H2N2	A/Singapore/1/1957	E	R	@	K	D	I	N	/	C	E	K	@	T	T	L	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	F	D	T	V	N	V	I	E	K
	H2N2	A/Canada/720/2005	E	R	@	K	D	I	N	/	C	E	K	@	T	T	L	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	F	D	T	V	N	V	I	E	K
	H5N1	A/Hong Kong/483/1997	E	K	@	Q	D	I	N	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	Q	E	S	T	Q	K	I	D	T	V	N	I	I	N	K
	H5N1	A/Vietnam/1203/2004	E	K	@	Q	D	I	D	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H5N1	A/Thailand/1(Kan-1)/2004	E	K	@	Q	D	I	D	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H5N1	A/Indonesia/05/2005	E	K	@	Q	D	I	D	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H5N1	A/Turkey/Turkey/1/2005	E	K	@	Q	D	I	D	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H5N1	A/Anhui/1/2005	E	K	@	Q	D	I	D	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H5N1	A/Egypt/0636-NAMRU3/2007	E	K	@	Q	D	I	N	/	C	N	K	@	S	S	M	P	M	T	M	I	D	G	W	D	K	E	S	T	Q	K	I	D	T	V	N	I	I	D	K
	H9N2	A/Hong Kong/1074/1999	E	T	N	K	E	L	S	/	C	V	Q	@	S	T	L	P	L	V	L	V	A	G	W	D	R	D	S	T	Q	K	I	D	T	V	N	I	V	D	K