Table S1. X-ray data collection and refinement statistics

Data collection	**H7.167 Fab-Sh2/H7 complex**
Beamline	SSRL 12-2
Wavelength (Å)	0.97950
Space group	$I2_13$
Unit cell parameters (Å, º)	a = b = c=207.3, α =β =γ = 90.0
Resolution (Å)	50 – 4.65 (4.73 – 4.65) [a]
Unique reflections	8,097 (393) [a]
R_{merge} (%) [b]	7.6 (97.2) [a]
R_{pim} (%) [b]	1.9 (28.3) [a]
I/sigma	46.7 (2.2) [a]
Completeness (%)	100.0 (100.0) [a]
Redundancy	18.4 (12.5) [a]
Z_a [c]	1
Refinement statistics	
Resolution	46.3 – 4.66
Reflections used in refinement	8,095
R_{cryst} (%) [d]	32.6
R_{free} (%) [e]	35.4
Protein atoms	5,599
Waters	0
Other	0
Average B-value (Å^2)	
Overall	194
Wilson	295
RMSD from ideal geometry	
Bond length (Å)	0.002
Bond angles (°)	0.582
Ramachandran statistics (%) [f]	
Favored	90.1
Outliers	1.2
PDB ID	5F45

[a] Numbers in parenthesis refer to the highest resolution shell.
[b] $R_{merge} = \Sigma_{hkl} \Sigma_i | I_{hkl,i} - \langle I_{hkl} \rangle | / \Sigma_{hkl} \Sigma_i I_{hkl,I}$ and $R_{pim} = \Sigma_{hkl} [1/(n-1)]^{1/2} \Sigma_i | I_{hkl,i} - \langle I_{hkl} \rangle | / \Sigma_{hkl} \Sigma_i I_{hkl,I}$, where $I_{hkl,i}$ is the scaled intensity of the i^{th} measurement of reflection h, k, l, $\langle I_{hkl} \rangle$ is the average intensity for that reflection, and n is the redundancy.
[c] Z_a is the number of HA monomer-Fab complexes per crystallographic asymmetric unit.
[d] $R_{cryst} = \Sigma | F_o - F_c | / \Sigma | F_o | \times 100$, where F_o and F_c are the observed and calculated structure factors, respectively.
[e] R_{free} was calculated as for R_{cryst}, but on a random test set comprising 5% of the data excluded from refinement.
[f] Calculated using MolProbity (43).

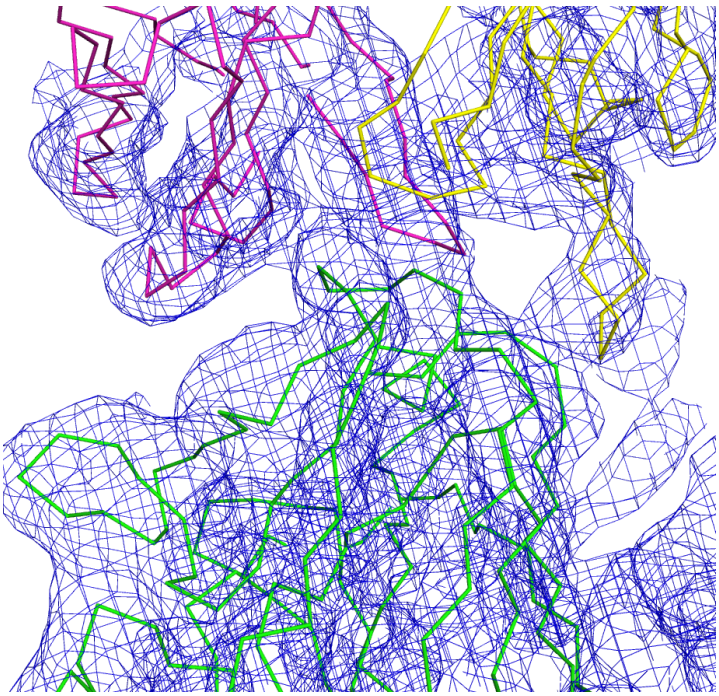

Figure S1. Representative electron density at the H7.167 Fab-Sh2/H7 complex interface. The H7.167 variable heavy and light chains are colored magenta and yellow and the HA1 is colored green. The $2F_o$-F_c electron density map (blue mesh) is contoured at 1σ.

Table S2. Conservation of H7.167 epitope residues in H7 HAs and comparison with representative HAs from H1, H2, H3 and H5 (H3 numbering).

Subtype	Isolate	Contacting residues at position in HAs									
		131	157	158A	158B	159	160	161	197	200	248
H7N9	A/Shanghai/02/2013	R	N	D	N	A	A	F	S	K	N
H7N9	A/Shanghai/01/2013	R	N	D	N	A	A	F	S	K	N
H7N7	A/Netherlands/219/2003	R	N	D	N	A	A	F	S	K	N
H7N2	A/New York/107/2003	R	N	D	N	A	A	F	S	K	N
H1N1	A/Texas/36/1991	T	K	*	*	S	S	Y	N	D	T
H2N2	A/Japan/305/1957	T	K	*	*	S	N	Y	N	G	T
H3N2	A/Victoria/361/2011	T	L	*	*	F	K	Y	Q	S	T
H5N1	A/Vietnam/1203/2004	A	K	*	*	S	T	Y	N	T	N

* No residue inserts at this position.

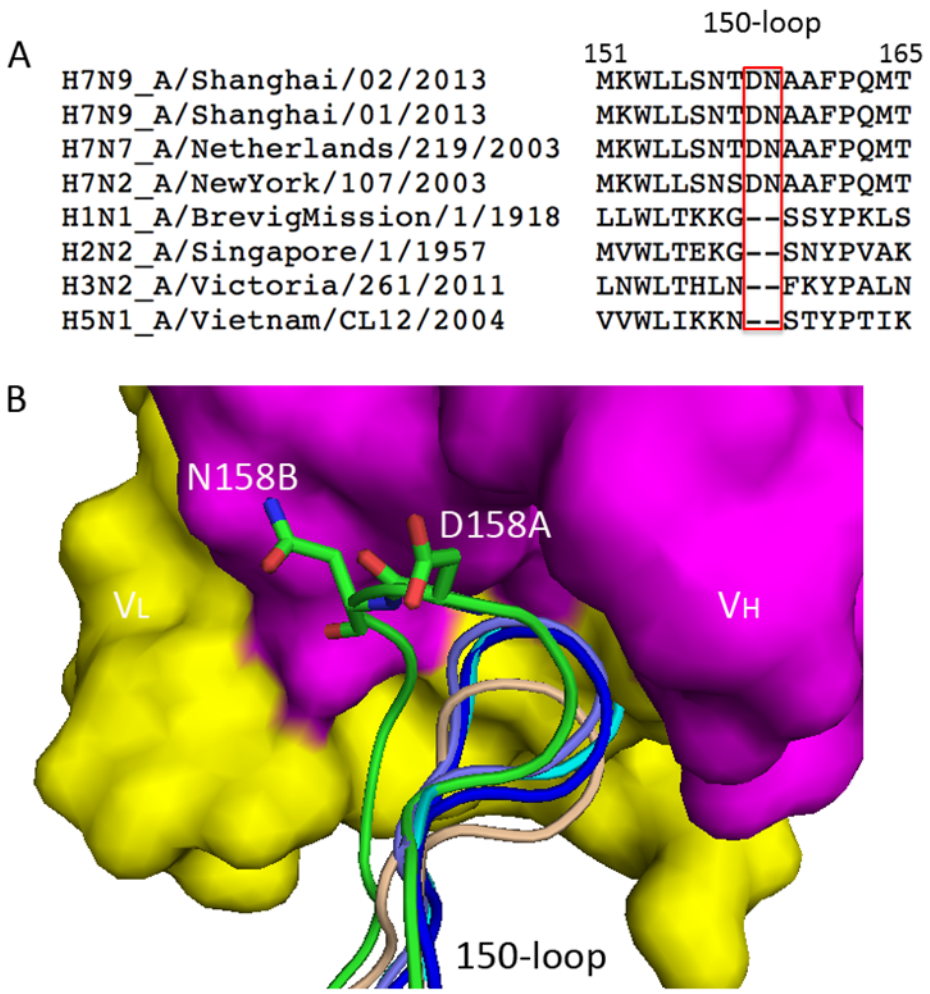

Figure S2. Sequence and structure comparison of the 150-loop from different HA subtypes. (A) Sequence alignment of the 150-loop in H7 HAs with those from H1/H2/H3/H5. The inserted residues 158A and 158B are labeled with red box. (B) Superposition of the 150-loop from H7N9 (A/Shanghai/02/2013) (green, PDB 4N5J), H1N1 (A/BrevigMission/1/1918) (cyan, PDB 3GBN), H2N2 (A/Singapore/1/1957) (wheat, PDB 4HFU), H3N2 (A/Victoria/261/2011) (blue, PDB 4O5N) and H5N1 (A/Vietnam/CL12/2004) (lavender, PDB 4BGX) HAs. The 158A and 158B side chains in H7 HA are shown in green sticks. The unique conformation of the 150-loop of H7 HA and insertion of 158A and 158B in this loop are likely associated with the particular specificity of this H7.167 HA.

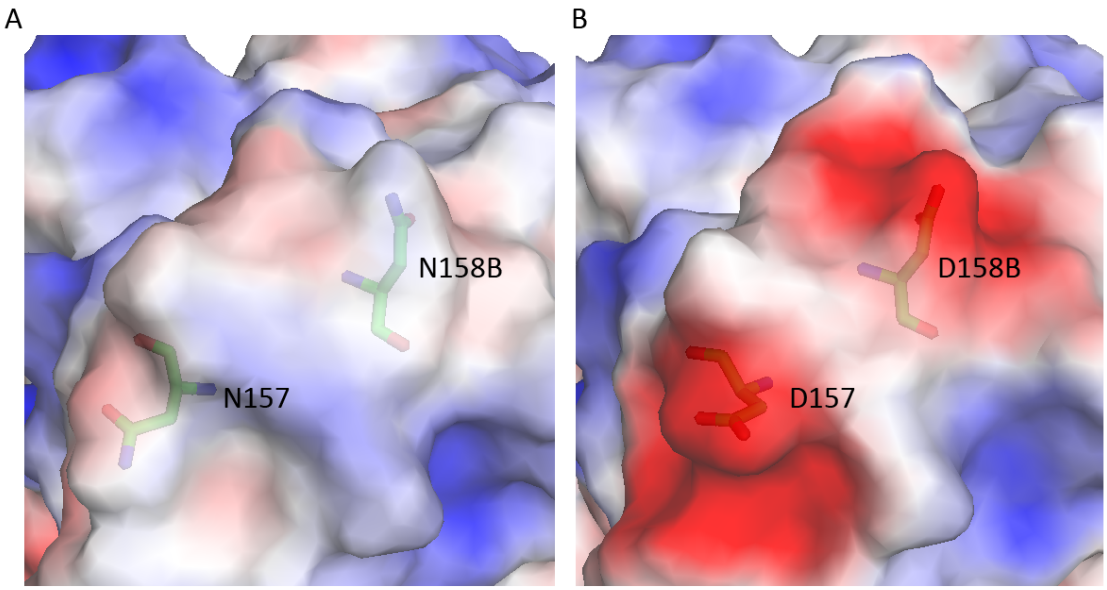

Figure S3. Surface representation analysis of the escape mutants N157D and $N158_BD$ of Sh2/H7 HA to antibody H7.167. (A) Electrostatic potential surfaces (red, negative, -5.4 kT; blue, positive, +5.4 kT; white, neutral) around wild-type Sh2/H7 HA with N157 and $N158_B$ (green sticks). (B) Electrostatic potential surfaces around Sh2/H7 HA mutants model with N157D and $N158_BD$ (green sticks), in the same orientation as A. The N157D and $N158_BD$ mutations alter the electrostatic potential from near neutral (A) to weakly acidic (B) around HA1 position N157 and $N158_B$, rendering it unfavorable for binding to H7.167, which is also weakly acidic around the paratope site of interaction with HA1 N157 and $N158_B$ (B).

Table S3. Primer sets used for RT-PCR amplification of antibody gene cDNAs

Name	Primer Sequence (5′ →3′)
Heavy-chain primers	
Forward primers	
IgExp-A_5′L-VH1	GTTTTAAAAGGTGTCCTGTGTCARRTNCAGCTGGTRCAGTC
IgExp-A_5′L-VH2	GTTTTAAAAGGTGTCCTGTGTCAGRTCACCTTGARGGAGTC
IgExp-A_5′L-VH3	GTTTTAAAAGGTGTCCTGTGTSARGTGCAGCTGGTGGAGTC
IgExp-A_5′L-VH4	GTTTTAAAAGGTGTCCTGTGTCAGSTGCAGCTRSAGGAGTC
IgExp-A_5'L-VH5	GTTTTAAAAGGTGTCCTGTGTGARGTGCAGCTGGTGCAGTC
IgExp-A_5′L-VH6	GTTTTAAAAGGTGTCCTGTGTCAGGTACAGCTGCAGCAGTC
IgExp-A_5′L-VH7	GTTTTAAAAGGTGTCCTGTGTCAGGTGCAGCTGGTGCAGTC
Reverse primer	
IgExp-B_3′CH1	GATGGGCCCTTGAAGCTTGCTGAGGAGACGGTGACCAGGGT
Light-chain primers	
Forward κ-chain primers	
IgExp-A_5′L-VK1	GAATCCCAGGCATGAGATCTGMCATCCRGWTGACCCAG
IgExp-A_5′L-VK2	GAATCCCAGGCATGAGATCTGAKRTTGTGATGACYCAG
IgExp-A_5′L-VK3	GAATCCCAGGCATGAGATCTGAAATWGTRWTGACRCAG
IgExp-A_5′L-VK4	GAATCCCAGGCATGAGATCTGACATCGTGATGACCCAG
IgExp-A_5′L-VK5	GAATCCCAGGCATGAGATCTGAAACGACACTCACGCAG
IgExp-A_5′L-VK6	GAATCCCAGGCATGAGATCTGAWRTTGTGMTGACWCAG
Reverse κ-chain primer	
IgExp-B_3′CK1	GATGGCGGGAAGATGAAGACAGATGGTGCGGCCGCAGT
Forward λ-chain primers	
IgExp-A_5′L-VL1	GAATCCCAGGCATGAGATCTCAGTCTGTSBTGACKCAG
IgExp-A_5′L-VL2	GAATCCCAGGCATGAGATCTCARTCTGCCCTGACTCAG
IgExp-A_5′L-VL3	GAATCCCAGGCATGAGATCTTCCTMTGDGCYRAYWCAG
IgExp-A_5′L-VL4	GAATCCCAGGCATGAGATCTCWGCYTGTGCTGACTCAA
IgExp-A_5′L-VL5	GAATCCCAGGCATGAGATCTCAGSCTGTGCTGACTCAG
IgExp-A_5′L-VL6	GAATCCCAGGCATGAGATCTAATTTTATGCTGACTCAG
IgExp-A_5′L-VL7	GAATCCCAGGCATGAGATCTCAGRCTGTGGTGACTCAG
IgExp-A_5′L-VL8	GAATCCCAGGCATGAGATCTCAGWCTGTGGTGACCCAG
IgExp-A_5′L-VL9	GAATCCCAGGCATGAGATCTCAGCCTGTGCTGACTCAG
IgExp-A_5′L-VL10	GAATCCCAGGCATGAGATCTCAGGCAGGGCTGACTCAG
IgExp-A_5′L-VL11	GAATCCCAGGCATGAGATCTCGGCCCGTGCTGACTCAG
Reverse λ-chain primer	
IgExp-B_3′CL1	AGGGGGGAACAGAGTGACASTTGGAGCGGCCTTAGGCTG